15th Annual
Science Symposium
Volume I
May 14, 2009
Paradise Valley College
Foreword

The 15th Annual Science Symposium was held on May 14, 2009. Students enrolled in Organic Chemistry from Paradise Valley Community College (PVCC) participated in the event. Each contributor was responsible for selecting and researching their topic and preparing a paper. A few orally presented their project to their peers. This booklet contains each of those papers.

As an instructor and faculty advisor for this symposium, I want to thank and congratulate each participant for their effort, courage and dedication. By participating, these individuals perpetuate this event annually. I am both proud and honored to present the work of these individuals.

William L. “Hank” Mancini, PhD
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Asmanex Twisthaler

Asal Abdulahad

April, 20 2009
Abstract

Asmanex Twisthaler is a corticosteroid medication, used to prevent certain cells in the lungs breathing passages from releasing substances that cause inflammation of the airways. Mometasone furoate (MF) is the active component of Asmanex Twisthaler. Asmanex Twisthaler is used to prevent or reduce the frequency and seriousness of bronchial asthma attack. (1) When patient use Mometasone furoate regularly it helps to reduce the wheezing and shortness of breath that can occurs with asthma. Asmanex Twisthaler was approved for maintenance treatment of asthma in patients 12 years and older on March, 30 2005. (2) In this paper, the description, pharmacology, clinical trials, dosage, side effects, proper use for the inhaler will be discussed.

Description

The active component of Asmanex Twisthaler is Mometasone furoate which is a corticosteroid with the chemical name 9,21-dichloro-11(betta),17-dihydroxy-16(alpha)-methylpregna-1,4-diene-3,20-dione 17-(2-furoate) and the following chemical structure

![Chemical Structure](image)

Mometasone furoate is a white powder with an empirical formula of C_{27}H_{36}Cl_{2}O_{6}, and molecular weight of 521.44 Daltons. (2) Asmanex Twisthaler 110 mcg or 220 mcg inhaler provides a measured dose of 0.75 or 1.5 mg Mometasone furoate inhalation powder each one contains 110 or 220 mcg of Mometasone furoate respectively. Based on the flow rates of 30 L/min and 60 L/min, the product will delivers 100 mcg or 200 mcg of Mometasone furoate from the mouthpiece. The amount of the medication delivered to the lung will depends on the patient factors such as inspiratory flow and peak inspiratory flow through the device.

Pharmacology

Mechanism of Action

How the Mometasone furoate works is unknown but the corticosteroids have been shown to inhibit multiple cell types and processes involved in inflammation. Corticosteroids do
not have an immediate effect on asthma. In order to achieve improvement in asthma symptoms, treatment with Mometasone furoate for 1 to 2 weeks or longer may be needed.

**Metabolism and Excretion**

By the liver the Mometasone furoate is primarily metabolized. The half-life is said to be about 5 hours. Mometasone furoate is excreted in the feces and also in urine.

**Pharmacodynamics**

The effect of Mometasone furoate on the hypothalamic pituitary-adrenal was estimated in clinical studies and indicated that the difference between Asmanex Twinhale 880 mcg twice daily (twice the maximum recommended dose) and the placebo was significant.

**Drug-Drug Interaction**

The occurring administration of Asmanex Twinhale inhaler and other medications used in the treatment of asthma was not associated with any adverse events. Caution should be exercised when co-administering Mometasone furoate with Ketoconazole, a medication used to treat fungal infections. Plasma concentration of Mometasone furoate increased in patients given both medications.

**Clinical Trials**

The efficacy of various doses of Asmanex Twinhale has been studied in several double-blind, placebo controlled, 12 week clinical trials. In pediatric patients the inhaled corticosteroid may cause a reduction in growth. In studies, the mean reduction in growth velocity for patients was approximately 1 cm per year and appears to depend upon dose and duration of exposure. The most common adverse events with Asmanex Twinhale (vs. placebo) reported with ≥2 % incident in a clinical trial involving patients 4 to 11 previously on bronchodilator and / or inhaled corticosteroid were: fever 7% (vs. 5%), allergic rhinitis 4% (vs. 3%), abdominal pain 6% (vs. 2%), vomiting 3% (vs. 2%), urinary tract infection 2% (vs. 1%), and bruise 2% (vs. 0%). The most adverse events with Asmanex Twinhale (vs. placebo) reported in clinical trials involving patients 12 and older previously maintained on inhaled corticosteroid and / or bronchodilator were: headache, 17% to 22% (vs. 20%), allergic rhinitis, 11% to 15% (vs. 13%), pharyngitis, 8% to 13% (vs. 7%), and upper respiratory infection, 8% to 15% (vs. 7%). The most common adverse events versus placebo for patients 12 and older previously maintained on oral corticosteroids were: (Asmanex vs. placebo) muscle relaxation pain (22% vs. 14%), oral candidiasis (22% vs. 9%), allergic rhinitis (20% vs. 5%), arthralgia (13% vs. 7%), fatigue (13% vs. 2%), depression (11% vs. 0%), and sinus congestion (9% vs. 0%).
### Adverse Reaction

Adverse Reactions with \( \geq 3\% \) Incidence in 10 Controlled Clinical Trials with ASMANEX TWISTHALER in Patients 12 Years of Age and Older Previously on Bronchodilators and/or Inhaled Corticosteroids.\(^{(2)}\)

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Asmanex Twisthaler (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>220 mcg BID</td>
<td>440 mcg QD</td>
</tr>
<tr>
<td>Headache</td>
<td>22</td>
<td>17</td>
</tr>
<tr>
<td>Allergic Rhinitis</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Upper Respiratory Infection</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Candiiasis, oral</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Dysmenorrheal</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Musculoskeletal Pain</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Back Pain</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Average Duration of Exposure (Days)</td>
<td>81</td>
<td>70</td>
</tr>
</tbody>
</table>

### Recommended Dosage for Asmanex Twisthaler Treatment

<table>
<thead>
<tr>
<th>Previous therapy</th>
<th>Recommended starting dosage</th>
<th>Highest recommended daily dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients ≥ 12 years who received bronchodilators alone</td>
<td>220 mcg once daily in the evening*</td>
<td>440 mcg**</td>
</tr>
<tr>
<td>Patients ≥ 12 years who received inhaled corticosteroids</td>
<td>220 mcg once daily in the evening*</td>
<td>440 mcg**</td>
</tr>
<tr>
<td>Patients &gt; 12 years who received oral corticosteroids†</td>
<td>440 mcg twice daily</td>
<td>880 mcg</td>
</tr>
<tr>
<td>Children 4-11 years of age‡</td>
<td>110 mcg once daily in the evening*</td>
<td>110 mcg*</td>
</tr>
</tbody>
</table>
* When administered once daily, ASMANEX TWISTHALER should be taken only in the evening.\(^{(2)}\)
** The 440 mcg daily dose may be administered in divided doses of 220 mcg twice daily or as 440 mcg once daily.\(^{(2)}\)

Asmanex Twisthaler is not indicated for the relief of acute bronchospasm and can not be used for children less than 4 years old. Bronchospasm may occur with an immediate increase in wheezing after dosing. If bronchospasm occurs following dosing with Asmanex Twisthaler inhaler, it should be treated immediately with a fast-acting inhaled bronchodilator.

**Indications and Usage**

Asmanex Twisthaler is the first once-a-day inhaled corticosteroid to receive FDA approval for children age 4 and older.\(^{(5)}\) Using Asmanex Twisthaler for children 4 to 11 reduces daytime and nighttime symptoms and emergency medical visits. The dosage for children 4 to 11 is 110 mcg, which is half the adult dose. Asmanex Twisthaler is used by the orally inhaled route only. Patient should inhale rapidly and deeply, and the mouth should be rinsed after the inhalation.

**How Supplies**

Asmanex Twisthaler 220 mcg, which delivers 200 mcg Mometasone furoate is available in several units:

- 14 inhalation (institutional use only)
- 30 inhalation units (for the 220 mcg daily dose)
- 60 inhalation units (for the 440 mcg daily dose)
- 120 inhalation units (for the 880 mcg daily dose)

Discard the inhaler 45 days after opening the foil pouch in which it is supplied or when dose counter reads “00”, whichever comes first.

**Information for Patients**

All the patients treated with asmanex Twisthaler should be aware for the following information for their safety and the effective use of the inhaler. Asmanex twisthaler is not a bronchodilator and should not be used to relief acute asthma symptoms. Acute asthma symptoms treated with an inhaled, short-acting beta\(_2\) - agonist such as albuterol. Asmanex Twisthaler should be used at regular intervals. Maximum benefit many not be achieved for 1 to 2 weeks or longer after starting treatment. Asmanex Twisthaler can not be used for patients who have hypersensitivity to mometasone or any of the ingredients in asmanex. patients who is treating with asmnaex should avoid exposure to chickenpox or measles.
Pregnancy

Mometasone furoate is a pregnancy category C drug. Administration of Mometasone furoate in mice, rats, and rabbits caused increased fetal malformation. Asmanex Twisthaler like other corticosteroid should be used during pregnancy only if the potential benefits justify the potential risks to the fetus. Because there is a natural increase in corticosteroid production during pregnancy, most women will require a lower corticosteroid dose and many will not need corticosteroid treatment during pregnancy.

Nursing Mother

Till the moment it is not known if mometasone furoate is excreted in human milk. Because other corticosteroids are excreted in human milk, caution should be used when asmanex twisthaler is administered to nursing women.

Side Effects

Asmanex twisthaler may cause side effects, patient should tell the doctor if any of these symptoms are severe and do not go away:
- headache
- bone, muscle, joint, or back pain
- heartburn
- loss of appetite
- stomach pain
- vomiting
- nose irritation or nosebleed
- dry throat
- difficult, frequent, or painful urination
- painful menstrual periods

Mometasone inhalation may cause slow growth in children, and may cause a decrease in bone mineral density (bone strength and thickness).

Proper Use of The Twisthaler

Asmanex Twisthaler have mometasone furoate, which is a synthetic corticosteroid, used as treatment that helps to prevent and control asthma symptoms. Asmanex Twishaler can not be used to stop sudden symptoms of shortness of breath. This medication is a very fine powder that the patient should not taste, smell, or feel, and if the patient was not be able to sense the delivery of the dose, the patient should not take an extra dosage unless under the instructed of the health care provider. The inhaler should be used regularly and at the same time each day.
Asmanex 110 mcg for children 4 to 11 is different

1. No need for a spacer of nebulizer when using Asmanex Twinthaler.
2. No pumping is required, just take the cap off and it is ready to deliver the dose.
3. The inhaler is breath activate. The child should be ask to close their lips around the mouthpiece and take a fast deep breath.
4. A built in dosage counter is provided in the inhaler to help the patient know when it is time to get a refill.

Asmanex twinthaler is maintenance inhaler your child use just once daily to help them breath easier, in addition to using a rescue inhaler for sudden symptoms.\(^{(8)}\)

**Transition From Oral Corticosteroids to Asmanex**

Particular care is needed for the patients who are transferred from systemically active corticosteroids to the asmanex twinthaler inhaler because deaths due to adrenal insufficiency have occurred in asthmatic patients during and after from systemic corticosteroids to less systemic available inhaled corticosteroids.\(^{(9)}\) Patients who used to take prednisone 20 mg per day may be the most susceptible especially when their systemic corticosteroids have been almost completely withdrawn. Although the asmanex twinthaler is showed to improve and control asthma symptoms during these episodes, in recommended doses it supplies less than normal physiological amounts of glucocorticoid systemically and does not provide the mineralocorticoid activity necessary for coping with these emergencies.

**Conclusion**

Asmanex twinthaler, manufactured and distributed by Schering-Plough Corporation, is a daily asthma inhaler designed to be used for the patients who seek for maintenance inhaler to control asthma rather than the using of the fast acting inhaler but it can not replace a fast acting inhaler for sudden asthma symptoms. Asmanex is a corticosteroid drug that works directly in the lungs to reduce the swelling of the airways and to make breathing easier. Asmanex can not be used to relief acute bronchospasm. Asmanex is the first and only once-daily inhaled corticosteroid inhaler approved for kids as young as age 4.\(^{(4)}\) Some side effects can occur when using Asmanex Twinthaler like dry or irritated throat, hoarseness or coughing as the body adjusts to this drug. A serious allergic reaction to this drug is unlikely to happen. Inhaled Mometasone furoate (Asmanex) is a synthetic corticosteroid indicated for the first-line maintenance prophylactic therapy of persistent asthma in adults and adolescents.\(^{(10)}\) Asmanex is designed to deliver the medication in a dry powder inhaler form. It is an anti-inflammatory agent and work as effective as other inhaled corticosteroids. It is used in two divided dosage or as once daily inhaler.
Bibliography

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Valtrex (Valacyclovir)

Megan Adamowicz

Dr. Hank Mancini

Organic Chemistry 236

April 24, 2009
Abstract

The drug valtrex or valacyclovir was originally developed to help patients with the herpes virus. Valtrex was approved in 1995 to treat herpes zoster or known as shingles.\textsuperscript{1} Throughout the next few years the FDA approved this medication for other herpes viruses.\textsuperscript{9} Valtrex helps prevent three different types of herpes, cold sores (herpes labialis), genital herpes (herpes simplex virus), and shingles (herpes zoster). Below will explain the correct dosage that should be taken for different age groups who may be infected with herpes. As well as understanding the mechanism of valtrex and the pharmacokinetics. Furthermore know the side effects along with interactions and the adverse reactions this drug may have on a patient. Plus know more about the three kinds of herpes valtrex can treat that were stated above.

Valtrex (Valacyclovir)

Valtrex is an antiviral drug that is used to treat or contain the disease of herpes. It may be used for the treatment of cold sores and other conditions. All through this drug does not cure herpes but just helps heal sores and prevents new ones from forming. This medication can also be used for those patients that have HIV but the dosage will have to be adjusted for the patient. If taken every day it will help reoccurrence of an outbreak and with safer sex practices it will help prevent the spread. But even with it it’s not 100% guaranteed to prevent the spread of herpes.\textsuperscript{10} Valtrex is either 500 milligrams tablets or 1 gram (1000 mg) tablets. L-valine, 2-[(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]ethyl ester, monohydrochloride is the chemical name and below is the complete structure for valacyclovir (valtrex).\textsuperscript{7}

\begin{center}
\includegraphics[width=0.5\textwidth]{valtrex-chem-struct.png}
\end{center}

Dosage

For each age group and different herpes virus there is a different dosage. If the patient has a disease or any other conditions that also will vary the dosage they receive. The doctor or pharmacist should be aware of any other medications that the patient may be taking as it may cause an interaction of the drugs taking or may affect the way others work. Although many other drugs need to be taken with food because of the cause of an upset stomach valtrex does not need to be take with food.\textsuperscript{10} Depending on the patient and if they have any kind of disease the dosage of valtrex will be decreased whether or not the doctor believes it will benefit the patient. An example dosage of a patient with shingle would be prescribed to take two tablets of the 500 mg three times a day or take the 1 gram tablet and would only have to take one three times a day. A shingles dosage usually will last about seven days.\textsuperscript{11} Each patient may vary depending on the doctor and how bad the outbreaks are. For cold sores it’s a one day treatment taking four tablets (2 grams) twice a day and spacing each dose twelve hours apart.\textsuperscript{11} When taking valtrex for a cold
The best way to help prevent it from getting worse is to take it right at the onset of the cold sore. When taking this medication finishing it is the key. Not finishing the dose could cause it to not fully heal and may come back again sooner than later. Patients with renal impairment would want to follow the chart below and a lower dosage is recommended.\(^\text{10}\)

<table>
<thead>
<tr>
<th>Indications</th>
<th>Normal Dosage Regimen (Creatinine Clearance ≥50)</th>
<th>Creatinine Clearance (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30-49</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1 gm q 8 h</td>
<td>1 gm q 12 h</td>
</tr>
<tr>
<td>Genital herpes Initial treatment</td>
<td>1 gm q 12 h</td>
<td>no reduction</td>
</tr>
<tr>
<td>Genital herpes Recurrent episodes</td>
<td>500 mg q 12 h</td>
<td>no reduction</td>
</tr>
<tr>
<td>Genital herpes Suppressive therapy</td>
<td>1 gm q 24 h</td>
<td>no reduction</td>
</tr>
<tr>
<td>Genital herpes Suppressive therapy in HIV-infected patients</td>
<td>500 mg q 24 h</td>
<td>no reduction</td>
</tr>
<tr>
<td>Herpes labialis (cold sores) Do not exceed 1 day of treatment.</td>
<td>Two 2-gm doses taken about 12 h apart</td>
<td>Two 1-gram doses taken about 12 h apart</td>
</tr>
</tbody>
</table>

q = every h = hours


For the treatment of genital herpes along with cold sores medication works best within the first forty-eight hours of onset of an outbreak. Primary outbreak dosage is 1 gram twice daily for ten days. Research have shown no effectiveness of taking the medication after seventy-two hours of symptoms. For a reoccurring dosage patient needs to take 500 mg twice daily for three days. Just like the first outbreak taking valtrex within the first twenty-four hours of signs and symptoms is suggested to get the best results.\(^\text{10}\) Just like every other drug there is a maximum dosage each age group can have and what to do if taken more than directed by the doctor. The elderly, adults, and adolescents should take a maximum of 3 grams a day, while children greater than or equal to the age of two years old should have a maximum of 60mg/kg/day while not exceeding 3 grams a day.\(^\text{1}\) When taking took much of the medication, the best thing a patient can do is either call poison control or call 911.

**Interactions/Side effects**

There are four interaction levels with this drug. Level 1 is severe, level 2 is major, level 3 is moderate and level 4 is minor.\(^\text{1}\) Let the pharmacist or doctor know about all medications taking including over the counter products such as vitamins, minerals, and drugs from another doctor. Doing so will lower the chance of an interaction with other medications taking. Valacyclovir can be harmful to the kidneys as well as many other drugs. But taking this medication can increase
the risk of harming the kidneys if it's taking along with others that are also harmful to the kidneys. Like all drugs there are many different side effects when taking a medication. Usually the pharmacist will go over the most common side effects that occur and will tell the patient if you get a certain one to stop taking the medication and contact the doctor immediately. Along with the pharmacist going over it, all the information will be given to the patient in the leaflets that comes with the prescription. The most common effects people see while taking valtrex are headaches, nausea/vomiting, dizziness, and abdominal pain. Below is a list of other effects a patient might have due to the medication.

- Agitation
- Anaphylactoid reactions
- Aplastic anemia
- Arthraglia
- Coma
- Confusion
- Depression
- Diarrhea
- Pruritus
- Hallucinations
- Photosensitivity
- Rash
- Renal failure
- Tremor
- Fever
- Delirium

While taking the medication and one or more of the side effects listed above occur contact the doctor or pharmacist before continuing to take this medication. People often mistake a side effect for an allergic reaction. The reaction could be mild or severe; if any of the following occur it could be an allergic reaction to valtrex and want to discontinue the use of the medication until further notice.

- Wheezing
- Swelling of the lips/mouth
- Hay fever
- Lumpy rash (hives)
- Fainting
- Difficulty in breathing

**Mechanism**

When valacyclovir is rapidly converted into acyclovir it then hinders DNA synthesis. It has confirmed the antiviral activity against herpes simples virus 1 and 2. The enzyme thymidine kinase (TK) that's encoded with the herpes simplex virus (HSV) or varicella zoster virus (VZV) has a similarity the inhibitory activity of acyclovir so it makes it highly selective. It is then converted into acyclovir monophosphate by this viral enzyme. Acyclovir monophosphate is known as a nucleotide analogue that then transfers it into diphosphate. It uses cellular kinase that converts it into triphosphate by cellular enzymes. The viral DNA replication is then stopped by this and has three ways it is done. The first way is competitive inhibition of viral DNA polymerase that is done by acyclovir triphosphate. The second is incorporation and termination of the growing viral DNA chain, finally the third is inactivation of the viral DNA polymerase. The cells in our body only take up a small amount of acyclovir and it concentration is 40 to 100 times higher to the cells that are infected with HSV then those that are not infected. Acyclovir does not remove the dormant herpes virus but will work effectively against the replicating viruses.

**Pharmacokinetics**

Valtrex is taken orally and will be rapidly absorbed by the body. Absorption is not unaffected if it is taken with food. The bioactivity of valacyclovir in a healthy volunteer was compared to
acyclovir and 3.3 to 5 time greater. When acyclovir is administered its absorption was only 15 to 30% while valacyclovir bioavailability was 54%. Researchers have suggested that valacyclovir will soak through the walls of the gastrointestinal tract. Taking more to get a higher dose so the outbreak heals faster does not reduce acyclovir concentrations. The bioavailability of valacyclovir was improved so is requires less dosage than acyclovir does. It will bind to the plasma protein and convert to acyclovir and L-valine. It will do this by first-pass intestinal and/or hepatic metabolism. Acyclovir will go through some metabolism by aldehyde oxidase, alcohol dehydrogenase, and aldehyde dehydrogenase. Then it will go on to produce inactive metabolites.1 The kidneys primarily eliminate the drug acyclovir. And the half life in patients with a normal renal function is between 2.5 and 3.3 hours.10 People with renal disease their half life will increase to about 14 hours. While its half life is only 4 hours in hemodialysis patients.

Herpes Labialis

Herpes labialis also known as cold sores is caused by the herpes simplex virus. This leads to sores and blisters on or around the mouth, gums, and lips.5 This is probably the most common of the herpes viruses. In the United States most people have been infected with herpes labialis by the age twenty.12 Many things can trigger a cold sore to appear such as stress or even a weak immune system when sick. This virus has no symptoms at first and it remains in the nerve tissue. It will reoccur and will be in or around the same spot as the first outbreak. This virus is very contagious it can be spread through towels, dishes and other objects that might have been shared. It also can be spread from oral to genitals and vice versa, so if infected avoiding sex or oral sex is the best way to stop it from spreading to someone else. Once they become in contact with it, it only takes one to two weeks for the first symptom to appear and the latest up to three weeks. The outbreak can last seven to ten days and before it begins to go away.12 Two days prior to the cold sore appearing it’s not unusually to experience itching, burning, and/or a tingling sensation. After that skin lesions and/or a rash will appear around the mouth, gum and lips. Without medication the lesions will go away in about one to two weeks otherwise valtrex can be taken to treat these. The best way to treat cold sores from coming back again and again is to take the antiviral medication as soon as the feeling of a cold sore appears. Because they can become painful putting ice or warmth on the area will help reduce the pain and the use of soap will lessen the risk of spreading.5

altayr.tripod.com/feverblisters.html

Herpes Simplex

Herpes simplex virus is also known to cause genital herpes. More than 500,000 new cases take place each year. And it is known to affect twenty-three percent of American adults. There are two kinds of herpes simplex virus 1 and 2. Usually herpes simplex virus 2 (HSV 2) is the main cause of genital herpes but it can cause sores in the mouth.2 Just like herpes labialis the virus remains in the nerve cells and can reoccur anytime. Contracting genital herpes through sexual contact is the main spread of this disease. Even if the person shows no signs or symptoms of it, it can still be passed on to someone else. These sores can appear in the genital areas, the buttocks and the thigh area. The sores may appear on different parts of the body if not taken care of and
kept the original sores clean. Majority of people do not know that they are infected with the herpes simplex virus. Each symptom varies from person to person one person could be prone to getting many outbreaks where another rarely gets them. Below are a few early symptoms one might experience:

- Itching or burning sensation.
- Pain in buttocks, or genital area.
- Vaginal discharge.
- Feeling of pressure in the abdominal region.

After a few days have passed red bumps or sores will appear that will eventually heal without scaring. Along with the symptoms above that you will get prior to, there are others that go along with the outbreaks and are listed below:

- Fever.
- Headache.
- Muscle aches.
- Painful or difficult urination.
- Swollen glands in the groin area.

Herpes simplex virus cannot be cured it is treated with valtrex and just gets rid of the symptoms but not the virus. It will only decrease the number of outbreaks a person gets and reduce the chance of spreading it to others. By wearing cotton underwear and avoiding tight clothing will help heal the sores. The tight clothes could cut off the air circulation and can slow the healing process. A woman that has HSV and is pregnant has to be careful and not acquire an outbreak because she could pass that on to her child and it could end up being fatal do to the infection the newborn could contract.

Herpes Zoster

Herpes zoster or varicella zoster is commonly known as shingles. This usually occurs on one side of the body normally in a strip, or starting at the spine that comes around to chest or belly area. Just like the others explained above it is also painful rash with blisters. Herpes zoster is caused by chicken pox that has gone dormant after it has resolved. Because chicken pox stays dormant in the body it can go on to form shingles in the elderly. It is very rarely seen in children but there are some cases of it. Varicella zoster becomes dormant in the nerve cell bodies that often do not cause any symptoms. When the virus finally breaks out it will travel down the nerve axons that will cause the skin irritation or rash of the area of the nerves. The first symptom that may occur is tingling or burning on one side. Here are a few others that may follow:

- Abdominal pain
- Chills
- Drooping eyelid (ptosis)
- Fever
- Genital lesions
- Headache
- Hearing loss
- Joint pain
- Loss of eye motion (ophthalmoplegia)
- Swollen glands (lymph nodes)
- Taste problems
- Vision problems
Herpes will generally heal in two to three weeks and can be treated with an antiviral drug such as valtrex. Since the blisters can be painful a lotion that contain calamine may be used to soothe the pain otherwise if the pain is too severe pain medication may be prescribed to the patient. Even a warm compress can be used to help reduce the pain. The image below show the progression of herpes zoster. The first section number one shows a small cluster of bumps. The second one shows that it eventually turns into blisters. Number three is where the blisters will break open and finally number four they will crust over and disappear. If the nerve area is damage it can sometimes lead to postherpetic neuralgia which is number five.

![A_Course_of_Shingles_diagram.png](image)

Conclusion

Valtrex is probably one of the most common drugs people get with a herpes virus whether you get cold sores, have an STD or anything else. Once I started in the pharmacy I couldn’t believe how many people are prescribed this medication. I believe that three out of five people you meet are on valtrex or have taken it. Plus knowing that three people that I work with take valtrex for cold sores is just proof of how common it is to meet someone that is on the medication. I think that valtrex is truly a good and helpful drug. Knowing that it could help with future outbreaks if taken every day is excellent. Or that it can help children or anyone that gets shingles and reduce the outbreak of the virus. No matter what valtrex will always be around to help people and prevent outbreaks and other herpes viruses out there. Although right now it only comes in brand name which is valtrex soon the generic (valacyclovir) will be out and more people will be getting it prescribed or filled on a regular basis.
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A Berry a Day Keeps the Doctor Away

Laura Armijo

April 23, 2009
Recently, the acai berry has become a growing trend throughout the marketing world doted upon for its nutritional, as well as medicinal value. It has been boasted as an antioxidant packed, health food that also contains weight loss properties. This Paper will break down the chemistry of the acai berry and examine why it is portrayed as a “miracle food.”

Native to Central and South America the acai palm is a member of the genus Euterpe which contains eight other species within the genus itself. These types of palms grow mainly in swamps and floodplains where the land is very fertile as well as rich with moisture. The Euterpe palms themselves can be anywhere from 15-30 meters in length or roughly 49-98 feet long. The leaves of the palms are feather like or pinnate.\(^1\) The fruit itself is a small round drupe that is about 25mm or one inch in diameter, a little larger that a blueberry and similar in appearance. The fruit has a single large seed in the middle and the skin of ripe fruits is a deep purple color, but depending on the kind of acai berry and its maturity level, it could also be green. The flesh is pulpy and thin, with a consistent thickness of 1 mm or less. The species Euterpe oleracea pertains to only the acai palm, which means “fruit that cries/or waters” in the South American language of Tupi.\(^1\) In fact, native South Americans have their own story as to the origins of the acai berry and where its name came into existence. According to ancient legend, it is said that a tribal chief’s daughter had a baby girl who was later killed by tribesman due to food shortage caused by overpopulation that was plaguing the tribe. The tribal chief’s daughter was grief stricken and sunk into a depression as she mourned the death of her daughter. It is said that one day after her child’s death she could hear the crying of an infant off into the distance. She desperately fled searching for the source of the familiar sound, hoping that somehow it was her child crying for her return home. While searching for the mysterious cry, she noticed a tree spinning off of the ground. She decided to rest beneath the tree, and died. Her body was later discovered and it is said that the tribe’s people found that the berries of the tree she died under, cured their hunger pains once consumed. The decree of killing infants was then lifted and the tree was named after the tribal chief’s daughter, Acai. Although the validity of this story may never be known, it is true that native people of the Amazon have been using this berry for medicinal purposes for quite some time, and it is now being mainstreamed into the lives of modern society. Although unknown to the native people why the berry’s properties are so beneficial, scientific research has unlocked a key that uncovers where the value comes from. This little berry may very well be one of the most nutritious and powerful foods yet to be discovered. Perhaps this statement can be validated with science and the phytochemicals found within the chemical makeup of acai.

Phytochemicals come from plants and are non-nutritive plant chemicals that have disease preventative or protective properties within them. Phytochemicals have existed as long as plants have, but the world of science has only known about them for a hundred years or so.\(^2\) It is said that these bioactive compounds work with nutrients in nuts, vegetables, and fruits to prevent against diseases such as cancer, heart disease, stroke, high blood pressure, and many other ailments. More than a thousand phytochemicals have been discovered and are known to
scientists. It is believed that plants produce these chemicals in order to help protect themselves. However, recent research has shown that it can also help protect humans as well. Some of the more commonly known phytochemicals are lycopene in tomatoes, isoflavones in soy and flavonoids in fruits. These chemicals are not necessary in order for survival but still hold value within the body. The following picture shows examples of phytochemicals that have been drawn in ring form:

As stated previously, there are many different types of phytochemicals, and each one works differently and can take action through the stimulation of enzymes, hormonal action, physical action, interference with DNA replication, anti-bacterial effect, and perhaps the most publicized when it comes to the açaí berry, antioxidants. An antioxidant is a molecule that is able to slow down or prevent the oxidation of another molecule. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent. Oxidation reactions often time produce something called free radicals. Free radicals start chain reactions that damage cells. The following is an example of what occurs when free radicals are formed through oxidation.

Antioxidants eliminate these chain reactions from occurring by removing free radical intermediates, and inhibit other oxidation reactions by being oxidized themselves. Free radicals can be introduced into the body through a number of different sources, from the things that people eat such as preservatives and hormones, to what people breathe in, such as pollution and cigarette smoke, as well as how an individual’s life is lived. Free Radicals travel through the blood stream and are absorbed by tissues, causing damage to cell walls, cell structures, and genetic material within cells. The harm of having free radicals in the body is that they can severely damage DNA, causing our cells to reproduce improperly and leading to a number of diseases. The worst case scenario that could come out of this is that over a long period of time, the damage done by free radicals can potentially become irreversible and lead to serious
diseases like that of cancer.\textsuperscript{[3]} As a polyphenol the açaí berry has a very high ability to act as an antioxidant and destroy unwanted free radicals. “The Journal of Allergy and Clinical Immunology recently published a study, which found that certain chemicals in antioxidants can switch on a set of antioxidant genes able to combat the effects of free radicals while strengthening the immune system, these antioxidants are prevalently found in açaí berries.” Açaí berries give consumers the highest level of anti-oxidants on the market, with studies showing up to 33 times the anti-oxidant level as in red wine grapes. They are also packed with natural antioxidants, including vitamin C, vitamin E and special phytonutrients called anthocyanins. \textsuperscript{[1]} The polyphenolic anthocyanins in the açaí berry have these double bonds which are available to help soak up the dangerous free radicals which hunt for the nearest electron to satisfy their need for stability. \textsuperscript{[3]} They are particularly rich in cyanidin, with experiments showing an increasingly high level of this chemicals presence.

**Cyanidin (Flavan-3-ol)**

MW: 286/Formula: C_{15}H_{16}O_{6}

Cyanidin is a natural and organic compound that that is a specific type of anthocyanidin. The highest concentration of cyanidin is found in the skin of the açaí berry. Cyanidin along with its glycosides may have pharmacological properties. These phytochemicals are responsible for the deep color of many plants as well as fruits (mostly red, orange, and blue). This is evident in fruits such as: bilberry, blackberry, blueberry, cherry, cranberry, elderberry, hawthorn, loganberry and raspberry, along with açaí and many others. \textsuperscript{[4]} They have many health promoting properties including anticarcinogenic activity, vasoprotective, anti-inflammatory, anti-obesity and anti-diabetes effects. Although, anti-obesity along with diabetes are still in the theoretical stages and have not yet been proven without a doubt. All of these benefits assist in the foundation for the açaí berry being doted as a “super fruit.” Similar to other anthocyanins, cyanidin has antioxidant and radical-scavenging actions. Not allowing the negative chain of reactions to take place causing free radicals.\textsuperscript{[4]} This characteristic of cyanidin helps to protect cells against oxidative damage and reduce the risk of cancer and heart disease. Cyanidin glycosides are also easily absorbed into the plasma, which makes it easier for them to enter the body. \textsuperscript{[4]} Another substance that is prevalent in the pulp of the açaí berry are flavanols, particularly Proanthocyanidin. The following is the chemical structure of a Proanthocyanidin.
Proanthocyanidins (Pycnogenol, OPC, Oligomeric Procyanidins)

MW: 592.5/Formula: C_{31}H_{28}O_{12}

![Chemical Structure]

Many plants produce proanthocyanidin within their fruits, leaves and barks as a defense mechanism. Proanthocyanidins are known to be very strong antioxidants. They are basically long chains of flavanoids. The ones prevalent in the acai berry fall under the category of oligomeric flavanoids which are mainly found in grapes. These in particular have shown in recent studies to help combat cardiovascular disease by fighting the causes of high blood pressure and cholesterol. Scientists have found that proanthocyanidins in general act as anti-cancer and anti-allergic agents, and they improve heart health (as stated above). Being antioxidants, they help to take a role in the stabilizing of collagen as well as the maintaining of elastin which are two crucial proteins when it comes to supporting organs, joints, blood vessels, as well as muscle. They also help improve circulation in the capillary walls which is critical for people suffering from diabetes, arthritis, or those who have suffered from a stroke. Proanthocyanidins also help combat against oxidative damage and can minimize the amount of damage that can be caused by tobacco smoke, pollution and free radical formation that occurs in the body during metabolism. They also work as a protector of the inside of the skin, guarding it from the potential damage of the sun. The acai berry is not just limited to phytochemicals but also is rich in omega fatty acids. The following is the chemical structure for Oleic Acid, the most dominant fatty acid in the acai berry.

Oleic Acid

MW: 282.4614/ Formula: C_{18}H_{34}O_{2}
Essential fatty acids are fatty acids that cannot be produced within the body but rather have to be ingested. The açai berry contains the fatty acids 3, 6, and 9. The body itself cannot produce Omega 3 and Omega 6 fatty acids. Omega-3 fatty acid or Alpha-Linolenic Acid plays a vital role when it comes to brain function. It is believed to aid in the prevention of cardiovascular disease. Omega-3 fatty may be useful in supporting people dealing with arthritis, osteoporosis, some cancer, diabetes, high blood and cholesterol levels, as well as others. Omega-6 fatty acid or Linoleic Acid when combined with Omega-3 helps to better aid in the benefits that it causes listed above. The fatty acid content in açai resembles that of olive oil, and is rich in monounsaturated oleic acid. Omega-9 or Monosaturated Oleic Acid is non essential and can be produced in the body. However, it is also found in food and is prevalent in the açai berry as well. It helps to play a role in preventing heart disease by lowering cholesterol levels. Oleic acid is important for a number of reasons. It helps omega-3 fish oils penetrate the cell membrane. Together they help make cell membranes more supple. By keeping the cell membrane supple, all hormones, neurotransmitter and insulin receptors function more efficiently. All three of these fatty acids found in the açai berry work in conjunction to help the body run smoother. These fats make up 30%-50% of the açai berry’s total weight. Along with fatty acids, the açai berry also contains phytosterols or plant sterols. The following is the chemical structure of a phytosterol molecule in particular the one found in açai berry, beta-sitosterol.

**β-Sitosterol**

MW: 414.71/ Formula: C_{29}H_{50}O

Phytosterols are naturally occurring compounds found in the cells and membranes of plants. They are white powders with a semi-distinctive smell, and soluble in alcohol. Sterols block the absorption of cholesterol and reduce blood cholesterol levels. Specifically in the açai berry, beta-sitosterol is found. When alone or acting with similar sterols, beta-sterol aids in the reduction of blood levels of cholesterol. It is also used in the treatment of hypercholesterolemia, which is when there are high levels of cholesterol detected in the body. It is also said that sterols in the açai berry help to strengthen the digestive tract. They also help reduce cholesterol absorption in the intestines. All of the molecules discussed are examples of ways in which the açai berry helps to aid in the benefit of one’s health.
Throughout this paper, the chemical structure of some of the main components of the açaí berry were taken apart and looked at from a simple beneficial standpoint. Through this research I was able to see exactly what it was that gave the açaí berry all of the qualities that manufacturers are talking about, and whether or not it had any validity. Many açaí products such as “Mona Vie” boast to cure people of any ailments or pain that they are suffering from. By taking a look at phytochemicals and what they are, I was able to understand how a mere fruit could help combat something such as arthritis. One thing that always plagued me about the açaí berry is how it has been mainstreamed into so many diet pills and put in the same category as fen-fen, hoodia and green tea. How could a simple berry be the weight loss cure America has been waiting for? When examining Cyanidin I found out that it is believed to have weight-loss properties within its chemical make-up. This was astonishing as I never figured there would be some truth to what I thought was a sheer scam. What was even more remarkable to me is that Cyanidin is one of the most dominant phytochemicals within the açaí berry. It was very exciting to also find out how antioxidants work. I always knew they were good for you but never knew why. Discovering that they help stop free radicals from causing harm to you and causing pain to your body was quite extraordinary. Seeing how proanthocyanidin took this role on as a very strong antioxidant showed me how until you know why something is healthy for you, you should not just take it as fact. To think that cancer can be caused by the continuous production of these free radicals is quite severe, and the fact that this berry has the capabilities to stop such a chain reaction from occurring is quite powerful. Also uncovering that the açaí berry had just as much oleic acid in it as olive oil itself was quite interesting, knowing how good olive oil is for the body. Finding out that fatty acids could help aid one when it came to brain function was quite intriguing. When researching beta-sitosterol it was shocking for me to find that it helped aid in ridding the body of cholesterol. High cholesterol is such a problem now, especially with obesity on the rise that it was a great service to find this out. I actually started my research with a question in mind being “could a berry (açaí that is) a day keep the doctor away?” Simply meaning, does this fruit have qualities to help people maintain a healthy lifestyle and get the most bang for their buck?

Upon concluding my research I came to the decision that “yes” in fact consuming this fruit will help one to live a healthy life, of course alongside a healthy diet as well as exercise. I highly doubt that if you ate these berries alongside a meal of a hamburger and fries that your body would be able to use all the nutrients that the açaí has to offer. I feel that this fruit does deserve the title “super food” or “miracle berry” based on the fact that my research found nothing but positive and beneficial properties within this fruit. I feel that research with the açaí berry has only just begun. If the cure for cancer lied within the confines of something that was a little bigger than a blueberry, how remarkable would that be? I learned a lot from this paper and feel pride in being able to share the wonders of such a small but complex drupe. Who would have thought that within a one inch radius we can find ways to help cure such health problems like arthritis, cardiovascular disease, diabetes, obesity, and so much more. It was highly enjoyable to see that something organic and pure can be constructed by the ultimate master chemist, Mother Nature herself.
Bibliography


TOPICAL & ORAL ANTIOXIDANTS AND DERMAL AGING
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ABSTRACT

The language of beauty has always been filled with ludicrous promises and grand declarations. Unfortunately, very few of these claims are true. Even though some over-the-counter (OTC) cosmetic products can do the skin some good, scientific studies continue to indicate that antioxidant therapy is most crucial for healthy and youthful skin.

The skin is exposed to many environmental factors which are potentially destructive and speed up the aging process, leading to premature aging of the skin. The leading cause of premature skin aging is ultraviolet (UV) wavelengths of light, and the formation of free radicals from the process of energy metabolism. The use of oral and topical antioxidants is very vital to prevent premature skin aging. This paper will attempt to give an overview of the principle antioxidants including: vitamins C and E, coenzyme Q10 (CoQ10), lycopene, green tea, alpha and beta hydroxy acids, alpha lipoic acid, pycnogenol, and niacinamide.

Vitamin C:

Also known as ascorbic acid, vitamin C is not synthesized in humans and is provided by diet such as citrus fruits or by pharmacologic means. Vitamin C is a very strong antioxidant, found in its reduced form as ascorbic acid but could also be found in its oxidized form as dehydro-L-ascorbic acid that easily reverts to the ascorbic form. Vitamin C is fat-soluble; hence, it is easily absorbed into the skin. The recommended daily intake is 1000mg (twice a day).

Topical vitamin C is also very effective in the prevention of sun damage by reducing sun burn cells with exposure to UV irradiation. Sunscreens are efficient in the protection against UV rays. Sunscreens that have vitamin C added to them have shown to be more effective in skin protection from UVA and UVB irradiation. Ascorbic acid is a requirement for collagen synthesis in human skin. Collagen is the chief constituent of connective tissue that supports the skin; and the skin requires constant synthesis of collagen to stay firm and youthful (LE 2003). Vitamin C esters stimulate the growth of fibroblasts; which are cells that help produce collagen and elastin in human skin. The reduction of the appearance of wrinkles and fine lines as one ages is achieved from the hydrating effects of vitamin C which is comparable to similar effects of retinol in topical formulations. Unlike ascorbic acid, however, vitamin C has an ester that is relatively more stable compared to ascorbic acid. The ester bond could be achieved by the addition of palm oil to vitamin C. For this reason, vitamin C can be mixed into creams and lotions and it could stay potent for long periods of time without any form of degradation occurring (Perricone 2001).

Vitamin C -3D structure
Vitamin C - 2D structure - m.p. 190-192 °C, C6H8O6

Vitamin E

This is considered a very good antioxidant in conjunction with vitamin C; both of which have been shown to be very effective in controlling photo-damage. Vitamin E is also used as a preventative for heart disease, and breast cancer.

The recommended dose for a young patient is 200 IU a day, and 400 to 800 IU a day for patients in their forties and fifties. The most active form of vitamin E in humans is Alpha-tocopherol, which is lipid-soluble. Tocopherols could be found in foods such as vegetables, seeds, and meat.

Vitamin E Chemical Structure, C26H44O2

A topical application of tocopherol in humans has been shown to exert photo-protective effects by reducing the number
of sun burn cells, inhibiting carcinogenesis, and reducing UV-induced skin damage. Experiments have demonstrated that using 5% to 8% of tocopherol cream on the face showed significant improvement in photo-aging compared to a placebo (Bogdan and Baumann 2008). This was achieved by the inhibition of human macrophage metalloelastase, which is involved in the degradation of elastin in the skin.

Another form of vitamin E is tocotrienol, also known as HPE. It has all the properties of tocopherol, but it is 40 to 50 times more effective at repairing skin damage by banishing free radicals (Perricone 2001).

**Coenzyme Q10 (CoQ10):**

Also known as ubiquinone, CoQ10 is a benzoquinone where Q refers to the quinone chemical group, and 10 refers to the isoprenyl chemical subunits. Daily recommended dose is 30—100mg.

This fat-soluble vitamin-like substance is present in most eukayotic cells, primarily in the mitochondria. It is a component of the electron-transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP (Wikipedia 2009). The presence of CoQ10 in plasma membranes provides protection against free-radical activity, as well as increasing energy production in aging cells, thus preventing premature aging of the skin.

CoQ10 is found in all human cells, as well as in foods such as fish, red meat, salmon, nuts, and shellfish. CoQ10 is a potent and popular antioxidant that is a major component of numerous over-the-counter cosmetic products because of its fundamental characteristic of being non toxic. The risk factor of using CoQ10, nonetheless, is that there is a possibility of developing contact dermatitis, which is also a cutaneous side-effect for vitamin E topical cream (Bogdan and Baumann 2008).

Structure of ubiquinone: (Wikipedia 2009).
LYCOPENE

This is a powerful antioxidant found in red fruits and vegetables as a carotenoid. Lycopene is included in numerous cosmetic products. In plants, algae, and other photosynthetic organisms, lycopene is an important intermediate in the biosynthesis of many carotenoids, including beta carotene, responsible for yellow, and orange or red pigmentation. Structurally, it is a tetraterpene assembled from eight isopren units, composed entirely of carbon and hydrogen, and is insoluble in water. Lycopene’s eleven conjugated double bonds give it its deep red color and are responsible for its antioxidant activity (Wikipedia 2009).

Molecular formula: C_{40}H_{56}

Molecular mass: 536.87 gmol^{-1}

GREEN TEA

Besides being a very popular beverage, green tea is one of the most studied antioxidants. Green tea is extracted from the Camellia sinensis plant. Green tea is composed of four major polyphenolic catechins, with EGCG (Epigallocatechin 3-gallate) being the most abundant. These green tea polyphenols, otherwise known as GTP, possess antioxidant, anti-carcinogenic, and anti-inflammatory capabilities. GTP could be administered both orally and topically. There are studies of in vivo and in vitro topical application of GTPs, showing suppression of chemo and photo-carcinogenesis in mice. In human skin, GTPs have shown to reduce the appearance of erythema, and sun burn cells from UV light exposure. There is an increase of green tea extracts used for cosmetic products in numerous OTC products today for photo-protection, in combination with sunscreens (Bogdan and Bauman 2008).

ALPHA AND BETA HYDROXY ACIDS

They were first considered as master exfoliants in the eighties, until much later when scientists proved that they were actually antioxidants (Perricone 2001). Alpha hydroxy acids are derived from foods, with the most popular of them being glycolic acid. Glycolic acid is derived from sugar cane, while the other alpha hydroxy acid, lactic acid, is derived from milk. When applied to the skin, glycolic acid helps to get rid of the dead cells (exfoliate), thus rendering the skin with a more youthful appearance. Lactic acid gives the skin a healthy glow. The difference between alpha and beta hydroxy acids is that alpha hydroxy acid is water-soluble, while beta hydroxyl acid is lipid-soluble. Alpha hydroxy acid is used on thickened, sun-damaged skin, while beta hydroxy acid is best used for oily skin with blackheads. The composition of alpha and beta hydroxylic acids in cosmetic products has been proven to relieve dryness, fine lines, and wrinkles by stimulating the production of collagen fibers akin to vitamin C. These acids have been used in moisturizers, eye creams, cleansers, sunscreens, and foundations. It is recommended that alpha hydroxy acid be used in combination with a sunscreen for more effective results.
ALPHA LIPOIC ACID

Lipoic acid is an organo-sulfur compound; one enantiomer of which is an essential cofactor for many enzyme complexes. This yellow solid is a carboxylic acid and features a cyclic disulfide, or dithiolane ring, a functional group (Wikipedia 2009). This antioxidant is very effective in fighting free-radical damage inside and outside the body. Lipoic acid is 400 times more potent than vitamins C and E and improves the levels of these vitamins in the body. For preventative purposes, alpha lipoic acid is used as an anti-inflammatory. The recommended daily dose for people forty and older is 100mg. When taken both orally and topically, it prevents glycation (sugar damage) of protein; this is achieved by preventing the attachment of sugars to collagen, thus preventing premature aging of the skin.

Structure of alpha lipoic acid (Wikipedia 2009)

NIACINAMIDE

Nicotinamide, also known as niacinamide and nicotinic acid amide, is the amide of nicotinic acid (vitamin B₃). Nicotinamide is a water-soluble vitamin and is part of the vitamin B group. Structure: (Wikipedia 2009)

Niacinamide has been known for antioxidant and anti-inflammatory properties, depigmenting, and immunomodulant properties. The use of niacinamide has laudable results such as
improvement on skin texture as well as skin tone; the reduction of fine lines, wrinkles, and hyper-pigmentation. Many cosmetic products have some percentage of niacinamide added to them as they happen to be well tolerated by many consumers.

PYCNOGENOL

Pycnogenol can be extracted from the bark of the French maritime pine tree (Pinus pinaster). It contains bioflavonoids, phenolic compounds, and procyanidins, which act as extremely potent free-radical scavengers. Pycnogenol is obtained by oral supplementation, and by topical application, with addition in several cosmetic formularies.

CONCLUSION

Anti-aging is a multifaceted phenomenon. The primary and immediate defense against skin damage from UV light is the antioxidant capacity of the skin. Based on scientific studies with documented and credible data, I believe that combining different antioxidants will result in a more synergistic effect, and thus will prevent free-radical activity and hinder premature aging of the skin. There is also reason to believe that using a combination of oral antioxidants and topical application of antioxidant additives in cosmetic products will greatly improve skin tone, wrinkles, texture, suppleness, and bring about an overall youthful appearance of the skin.

I must emphasize the role one’s life-style habits play in one’s general health and consequently, the health of the skin. A sedentary lifestyle will increase the aging process for most people, including the skin. A moderate amount of exercise three times a week, ranging from twenty to thirty minutes per exercise session has been recommended for keeping the body fit. This has been a challenge for me in particular, because I have to the sacrifice time, energy, and money to get my exercise routine going. However, the benefits I will reap as far as my overall health, and most especially the health of my skin is concerned, motivates me to do so. Of course, using antioxidants, and sunscreens are major factors I integrate into my health routine, thus staying proactive about premature skin aging.
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Malignant Melanoma
Laurie Bachand
April 24, 2009
Abstract

This paper will focus primarily on the recent advances in genomic research that have lead to significant discoveries in gene pathways linked to an increased risk of developing malignant melanoma. The causes and stages of this cancer are outlined before exploring how recent discoveries in genomic research have redefined prevention, and may significantly change the future path of diagnoses and treatment.

Malignant Melanoma

Tan on Demand, The Tan Factory, and Jamaea Mc Tan, are only a few of the thousands of tanning companies enticing the public with catchy lines promising youth, beauty, and self confidence, through a sexy glow. Even though the business names are borderline vacuous and their slogans far from realistic these companies are still thriving. In fact, almost 30 million Americans use tanning salons every year (Gorgos 2006). In 2004 there were approximately 55,000 individuals diagnosed with cutaneous melanoma and approximately 7,900 deaths occurred from metastatic disease in the United States alone (Sternemann 2006). The most disconcerting aspect of this disease is its prevalence among the younger generation and continued increase with age (Appendix A). According to the Surveillance, Epidemiology and End Results program, of the National Cancer Institute, between 1975-2000, melanoma was the second highest cancer type diagnosed in individuals between the ages of 15 to 29 (Herzog et. al 2007). While understanding the characteristics and development of this disease are essential in combating against mortality; prevention, in all aspects, is paramount to the overall suppression of malignant melanoma.

While the skin predominantly serves a positive function in being the protective covering that provides our body with its first line of defense against the environment, there are aspects of this organ that can go awry. The epidermis and the dermis make up the two distinct regions of the skin (Mariel 2007 p.152). In general, the epidermis is composed of two main layers, the outer epidermis and the inner epidermis, with the innermost layer containing the pigment producing cells known as melanocytes (Panno 2005 p.16). Melanoma is the uncontrolled growth of these melanocyte cells in a specific region of the body (Poole 1998). The accumulation of these abnormal cells will develop a noticeable change on the surface of the skin either in its growth or the appearance of a mole (Malignant...2002). Most melanomas arise spontaneously, however, it can develop from preexisting moles (Mariel 2007 p.166). The early signs of melanoma can be detected easily using the “ABCD system:” asymmetry, border, color, and diameter. Moles that are asymmetrical, have irregular borders (edges) or color, or are greater than 5–6 mm (about 1/4 inch) in diameter are suspect (Melanoma 2009). Once a suspicious lesion is detected it is imperative that action is taken before growth persists.

Melanoma has two primary growth phases. It begins in the radial stage, residing primarily in the epidermis with only slight invasion of the underlying dermis, and is characterized but an outward enlargement of the infected area (Poole, 1998, p.16). The next stage of growth is vertical growth where the melanoma cells penetrate the dermis, flourish, and begin forming a tumor, or raised area of abnormal cells, on the surface of the skin (Pope 2005 pg. 20). Anatomical levels of progression are assigned using the Clark classification system (see Appendix B) depending upon how many layers of the skin are affected (Melanoma...2002). If the cancerous cells penetrate through the epidermis, into the dermis layer, it obtains access to
blood and lymph vessels and the cancer can spread rapidly throughout the body (Poole, 1998, p.16). A melanoma tumor with over a 4 mm thickness presents a high risk of metastasis and a bleak chance for survival (Mariel 2007 p.166). Tumors of this caliber have a survival diagnosis of only 6 to 9 months (Chin 2006). Early detection is, therefore, imperative in increasing the chance of survival.

This type of cancer may be superficial and detectable with the naked eye, however, one of the main issues with the detection and diagnosis of malignant melanoma arises in its appearance. Many times melanomas can resemble benign lesions which increases the potential for misdiagnosis or delays in individuals going to the doctor (Sekulic 2008). First, regular self-examinations are imperative and, in any case of doubt, a trip to the doctor is necessary (Poole 1998). Yet, you must be cautious even with your primary care physician. Little time is spent in medical school teaching the technique of skin examination and few practitioners are sufficiently skilled in conducting thorough examinations and proper diagnosis (Pope 2005). In fact a case study, presented at the Poster Discussion Session of the 2004 American Academy of Dermatology Annual Meeting, analyzed the magnitude of discrepancy between primary care and dermatologists. In this case study:

216 physicians, 47% of which were dermatologists, were asked (A) the likelihood that the lesion should be biopsied (B) the likelihood that the lesion is a melanoma. Primary care physicians were asked the same question, however, for A they were asked if the lesion should be referred to a dermatologist. The results of the case study showed that the variance for the biopsy/refer question was 1.5 times greater for PCPs than for dermatologists, and over 2.5 times greater for the diagnosis question. (Chen 2005)

Considering the fact that malignant melanomas may be so easily overlooked, understanding the risk factors associated with developing malignant melanoma is the first step towards executing successful prevention.

First and foremost, environmental aspects play a significant role. Frequent sun tanning, without adequate protection, is known to be the greatest cause of skin cancer (Panno 2005). When the skin is exposed to excessive UV radiation, DNA bases become damaged and lesions are formed as surrounding pyrimidine bases link to the damaged chain (Mariel 2007 p165). Genetic variation also result, from excessive sun exposure, in the gene BRAF (Melanoma 2009). Mutations in this gene have been found in many tumor types, however, it has the highest incidence, 27-70%, in melanomas (Chin 2006). This gene is instrumental in the regulation of cellular signals, from the cell surface to proteins that ultimately communicate with the nucleus, which stimulates cell differentiation and apoptosis (Melanoma 2009). Apoptosis is defined as the “programmed cell death” which the body utilizes to naturally dispose of damaged, unwanted, or unneeded cells (Apoptosis... 2009). Other environmental aspects have begun to merit attention in regards to their influence on development of melanoma. For example, the effects of paraben esters, found in many cosmetics and topical agents, have been studied, and, while there is evidence of a link to other forms of cancer, no concrete link has been made to malignant melanoma at this time (Darbre). In addition to the effects imposed by the environment, purly genetic mutation factors also increase the risk of diagnosis.

Current research findings are uncovering more pronounced genetic associations linked to an increased risk of malignant melanoma. The MCIR gene was one of the first to be recognized as dramatically predisposing individuals to malignant melanoma without any excessive sun exposure (Landi 2006). Epidemiologists had previously suspected that skin types that are sensitive to the sun and that have the propensity to develop freckles were risk factors in
melanoma (Pope 2005). Yet, now there is definitive genetic proof. According to the Genetics Home Reference guide, MC1R is a gene that codes for the melanocortin 1 receptor, located on the surface of the melanocytes, which plays a vital role in normal pigment formation. Thus, a mutation to this gene causes alterations in pigmentation and susceptibility to UV radiation (MC1R...2009). It is no surprise that this gene alteration has been noted to coincide with the increased BRAF variations (Melanoma 2009). Other genetic links point toward familial inheritance.

It had been hypothesized, before genetic testing, that a family history of melanoma increased the risk in individuals. This hypothesis was confirmed when homologous deletions, centered on the CDKN2A gene, located on chromosome 9p21, were seen across the genomes of large melanoma prone families (Chin 2006). The CDKN2A gene is commonly referred to as the INK4a/ARF locus (Jones 2007). It resides at the center of two critical cell cycle regulatory pathways, the p53 pathway and the retinoblastoma (pRb) gene pathway (Robertson 1999). This particular gene codes for two cell cycle regulatory proteins, p14 ARF and p16 ARF, which bind to CDK4 and CDK6 kinases, and eventually act to suppress tumor cells by blocking cell proliferation (Jones 2007). If mutations arise in the coding region of the INK4a gene, as well as in noncoding regions, the mutant cell regulating genes will not bind to CDK4 and CDK6 are unable to cause cell cycle arrest. Appendix C outlines this pathway disruption that eventually leads to an overgrowth of abnormal cells.

Aside from inherited genes are other pathways specifically stimulated in the melanoma process. Once such genomic pathway, hyperactive melanoma cases, is the PI3 kinase-AKT pathway (Chin 2006). The AKT pathway is found to deregulate apoptosis in 70% of melanomas and cause systematic toxicity or increase metastasis (Madhunapantula 2007). Not only is this pathway evident, but further studies have found another substances activated by AKT. The PRAS40 substrate was identified in a recent case study where researchers:

demonstration that PRAS40 could be phosphorylated, in vitro, by Akt at the same location where this pathway is also phosphorylated after activation by insulin.

Researchers also showed that activation of an inducible Akt was sufficient enough to stimulate PRAS40 phosphorylation. (Kovacina 2003).

From this point, new research was conducted to validate the role of PRAS40 in melanoma metastasis. This was accomplished just 4 years later in a case study conducted by SubbaRao V. Madhunapantula. Through the confirmation of PRAS40 as a component in melanoma growth, new therapies can be investigated to target this particular substrate rather than the entire pathway (Madhunapantula 2007). Researchers are consistently searching for more answers and, recently, discovering further gene variations.

Kevin Brown, Associate Investigator at Translational Genomics Research Institute, identified the most recent gene that functions to increase risk of malignant melanoma. In May of 2008, the Nature Publishing Group published the article Common Sequence Variants on 20q11.22 Confer Melanoma Susceptibility that outlines the results of his case study. In a personal interview, he explained the process through which his team conducted their research. The team began by conducting a genome wide association study on 864 melanoma cases and compared the DNA sequences obtained with 864 control cases, presenting no melanoma, to find certain DNA sequences that show up more frequently in those who have melanoma than those who are healthy. Predominant similarities can indicate that either those specific sequences, or ones close by, may be responsible for contributing to increased risk. Out of the differences they found, there were significant evidence for a new location, unidentified in previous studies, on
chromosome 20q11.22. Dr. Brown and his team then, looked at those sequences across another 1200 cases and 1200 control samples to validate the genomic link. The replication process, in additional samples, validated that the chromosome 20 regions does have a genuine connection to increased risk of melanoma. While the genetic link may not be of profound, immediate implication to the individual, these advances are slowly altering the paths of treatment.

Treatments for early stages of melanoma differ from the late stage treatments in their makeup and effectiveness. The most widely used treatments currently include surgery, chemotherapy (Melanoma 2009). Melanomas treated at the early stages of radial growth are almost 100 percent curable (Poole 1998 p.27). Surgical removal is regarded to be the most effective treatment for malignant melanomas, since it can cure the majority of patients with less advanced tumors and controls local disease (Sternemann 2006). A study conducted in March 1992, by Dr. Guerry, found that early melanoma lesions take a few years to advance into the vertical growth stage, when it has an increased risk of metastasize, so there is adequate time for early detection (Pope 2005). Once the early stages pass, however, more aggressive treatments are implemented.

Chemotherapy is often times the second step in treating cancer after surgery. According to the American Cancer Society, chemotherapy is not very effective in the treatment of melanoma; however, it may still suppress some symptoms and may extend the life of the patients. The ACS provides a list of the common chemotherapy drugs, see Appendix C, which target cancer cells and kill or inhibit their growth (Cancer...2008). Reviewing this structures it is important to note the metal ion present in the drug Cisplatin. It has been known, for quite some time, that deoxyribosenucleic acid binds to heavy metals, thus, this characteristic helps the effectiveness of Cisplatin (Felsenfeld). This efficiency, however, becomes one of the major problems arising with chemotherapy drugs in that there is absolutely no control over which cells they attack (Brown). Another issue is the inability to determine the exact amounts that, when administered, will afford the highest effect upon the abnormal cells and minimal effect on normal, healthy cells (Longo). Because these treatments are not efficient in the treatment of malignant melanoma, researchers have been implementing their knowledge in the area of genomics to create better options.

One alternative form of treatment focuses on boosting the body’s own defense mechanism. Known as immunotherapies, these treatments include recombinant interferon alfa proteins, that work to bolster the immune recognition of tumor agents (Chin 2005). As described by Dr. Kevin Brown, all cells, including those of tumors, have proteins that surround their outer surface and are detectable by the immune system. In the National Cancer Institute Handbook, on melanoma treatment, “interferon alfa is a therapeutic peptide that binds to the specific cell-surface receptors of tumors and aids in the inhibition of growth and alteration of cellular differentiation.” The National Cancer Institute is conducting further studies to determine the effectiveness of this treatment on late stage melanomas.

On Dec. 19, 2008 the Translational Genomics Research Institute (TGen), Scottsdale Healthcare and Mayo Clinic, began testing a new drug that could help cancer patients by also stimulating the immune system. "VTX-2337 is a new, novel, small molecule aimed at stimulating the immune cells in the blood, lymph nodes, and in and around the tumor. It represents an exciting new class of agents for cancer therapy with good preclinical evidence of activity," Dr. Ramanathan said in a recent TGen press release (Yozwiak 2009). This new treatment will be used in combination with standard treatments to enhance the immune system
and provide more positive outcomes (VentiRX 2008). Other trials have also produced optimistic results in helping the immune system.

Xiao-Tong Song, of the Baylor College of Medicine in Houston, and his colleagues performed significant research on creating a new vaccine that can bypass the tumor defense mechanisms (Berry 2008). His work was published in Science News in 2009 and explained that they extracted dendritic cells from the bone marrow of mice, exposed them to an engineered virus that would block the cells from creating a specific protein A20, and exposed them to a typical cancer molecule. Blocking the A20 response showed to boosted dendritic-cell activity. They then infected the cells with melanoma and injected these cells back into the mice. Their results showed the cells producing an over activated signaling for cells that attack tumor cells in spite of the defense mechanisms of the tumors. Louis M. Weiner of the Lombardi Comprehensive Cancer Center at Georgetown University in Washington, D.C. commented, in the article, that this achievement "provides us with a new understanding of how to manipulate dendritic cells to achieve a more active immune response" (Berry 2008). With this discovery, and others, finding direct links to genes, pathways, and proteins have some type of effect on the development of melanoma researchers will have new questions to answer.

The next primary answer needed in the cure of malignant melanoma is how to regulate the known pathways. I believe that we have only begun to see the positive advances that will arise in cancer prevention and treatment. Soon, doctors will be able to identify specific genes that an individual possesses and be able to accurately predict their level of risk in developing this disease. Knowing every possible combination of factors, in addition to environmental conditions, will allow education to expand and increase the awareness of the public. Dr. Brown hypothesized that, with the technology we have to sequence genomes, there will be significant advances in tumor research that will allows us to know the specific differences between individual tumors. I believe with this knowledge researchers will be able to formulate personalized treatment options. While there may not be a definite cure in the near future, we will be able to significantly reduce the occurrence of malignant melanoma.
Appendices

Appendix A

![Graph showing incidence per year per million for different age groups.](image)

**Figure 5.1: Incidence of Malignant Melanoma Relative to All Cancer, SEER 1975-2000**


Appendix B

![Diagram showing levels and thicknesses of melanomas.](image)

**Figure 23. Levels and thicknesses of melanomas.**

Levels describe the anatomic layer of the skin into which the melanoma has penetrated. All level I and most level II melanomas are pure radial growth phase melanomas and do not metastasize. The brackets show where tumor thickness is measured.

Appendix C


Appendix D

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Description</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dacarbazine (also called DTIC)</td>
<td>May be used either alone or in combination with other chemotherapy drugs such as carmustine (also known as BCNU) and cisplatin. The combination of these 3 drugs, together with tamoxifen (a hormonal therapy drug) is called the &quot;Dartmouth regimen.&quot;</td>
<td><img src="structure_image.png" alt="Structure Image" /></td>
</tr>
<tr>
<td>Drug</td>
<td>Description</td>
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<td>--------------</td>
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<td></td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Used in a chemotherapy combination with vinblastine, and DTIC for treating melanoma</td>
<td></td>
</tr>
<tr>
<td>Temozolomide (Temodar)</td>
<td>A drug that works similar to DTIC, but it can be given in the form of a pill. It may be given by itself, although some studies have shown the drug to be more effective when combined with interferon.</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>A drug sometimes used to treat melanoma, either alone or combined with drugs such as cisplatin or carboplatin.</td>
<td></td>
</tr>
</tbody>
</table>

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VentiRx Pharmaceuticals Commences Phase I Clinical Trial Of VTX-2337, A Novel TLR8 Agonist For The Treatment Of Oncology (05 Dec 2008) Available at http://www.medicalnewstoday.com/articles/131866.php

Hydrogen:

What a Concept
Abstract
Hydrogen is the alternative fuel of choice right now in the United States and many car manufacturers have begun producing cars that run exclusively on hydrogen. With the current emphasis by the Barack Obama administration on alternative fuels and the car companies seeing rising sales of alternative fuel cars, hydrogen may soon be here to stay. Though it is very popular right now, the real question, however, is whether it is a truly viable alternative to oil or the same problem with a different face.

INTRODUCTION:

After his election in 2008, Barack Obama promised to transform the United States into a more economic and environmentally conscientious country. One of the goals he proposed was to transform cars so that they are less dependent on oil and more fuel efficient, thereby also becoming more safe for the environment. One of his proposals was to change from oil to alternative fuels, such as hydrogen.

This paper examines practicability of using exclusively hydrogen fueled vehicles and whether it truly is a viable alternative to oil and the answer to stopping car pollution. Part one of this paper explores hydrogen as an alternative fuel, what it is and where it is derived from. Part two focuses on cars and whether or not it is scientifically feasible or possible for them to operate on hydrogen fuel. Part three examines whether hydrogen is really a viable alternative for oil and whether it is scientifically possible, environmentally sound, and economically feasible. The conclusion states that if implemented properly, hydrogen-fueled vehicles are a progressive and efficient addition to our roads.

BACKGROUND:

In 2007, there were 1.8 million alternative fuel vehicles sold in the United States, indicating an increasing popularity of alternative fuels. Many people, including many governments, have become more and more concerned about the effects of increased anthropogenic greenhouse gases in the air and the burning of fossil fuels, which are known to increase greenhouse gas concentrations in the atmosphere and thereby contribute to global warming, thus resulting in more and more focus on finding viable alternative fuels to gas powered cars.

In addition to the environment, there have also been concerns about the cost of oil and the notion that it is something that may not be around forever. As less and less oil is produced, it begins to cost consumers and their respective governments more and more to get access to it. According to the Hubbert peak theory, when the production levels peak, demand for oil will exceed supply and without proper mitigation this gap will continue to grow as production drops, which could cause a major energy crisis. Furthermore, most of the production of oil is in the middle and far east and there is a genuine concern...
worldwide that fuel shortages could intensify the unrest that already exists in those regions, leading to further conflict and war and U.S. dependency on foreign regimes.

Hydrogen gas has emerged as a leading alternative to oil and many car manufacturers have turned to it to fuel their vehicles. Honda even began producing a car called the Honda Insight that is fueled exclusively by hydrogen and is currently doing a test run in Los Angeles. It released about 200 test cars in the Los Angeles, California area in 2008 to see if it will work. As a result, hydrogen has become a very popular alternative to oil, though it is still unclear whether it will prove to be a lasting alternative.

PART ONE: HYDROGEN: WHAT IT IS AND WHERE IT COMES FROM

A. How is hydrogen produced?

Hydrogen is the most abundant element in the universe, however, it is always bonded with something else like oxygen (to make water) or carbon. Hydrogen is all around us, but to use it, we must first separate the hydrogen from the other things bonded to it. This is not that difficult of a task and can be done rather easily, thus allowing it to be made from a variety of local resources like water, plants, coal, natural gas, and even algae.

Diagram 1: Hydrogen Production

Another advantage to making hydrogen gas is the amount you make. When we make most fuels today, it's best to make very large quantities in refineries but with hydrogen, you can just as easily make very small amounts, enough for one camera or cell phone, or very large amounts that could supply an entire town. Today, in the United States, over 95% of the hydrogen that is made in very large quantities from natural gas, mostly to make fertilizer and to help make gasoline cleaner by removing impurities like sulphur. As hydrogen moves from these large industrial uses to something that you and I commonly use to fuel our businesses, homes, electronics and vehicles, we expect other resources besides natural gas to be used and that it will be made in a variety of amounts depending on how much is needed.
B. How does an electrolysis produce hydrogen from water?

In order to extract hydrogen from oxygen, you can use an electrolysis which in turn uses an electric current to separate water into its separate components, i.e. hydrogen and oxygen. The electricity enters the water at the cathode, a negatively charged electrode, passes through the water and exists via the anode, the positively charged electrode. The hydrogen is then collected at the cathode and oxygen is collected at the anode.

Furthermore, this method of electrolysis does not require significant amounts of water. The hydrogen extracted from a gallon of water using a hydrogen generator, or "electrolysis," can drive a hydrogen fuel cell vehicle as far as a gasoline vehicle travels today on a gallon of gasoline. (For comparison, when making a gallon of gasoline about 3 gallons of water are used).

Using a Proton Energy System's H6m electrolysis, you can make 0.38 kilograms of gaseous hydrogen per gallon of water. (An electrolysis uses electricity to make hydrogen from water.) The Honda FCX Clarity has a combined EPA estimate mileage of 72 miles/kilogram of hydrogen. Therefore, the FCX Clarity will drive about 27 miles on the hydrogen produced from one gallon of water. The average fuel economy for light duty vehicles in the US is 21 miles/gallon of gasoline.

Reference Chart:

| 1 gallon water = 0.38 kg hydrogen > 27 miles in the FCX Clarity |
| 1 liter water = 0.10 kg hydrogen > 12 kilometers in the FCX Clarity |

\[ H_2O \xrightarrow{Heat} H_2 + \frac{1}{2}O_2 \]
C. How much energy is required to produce hydrogen via electrolysis of water?

The energy required to produce hydrogen at atmospheric pressure via electrolysis (assuming 1.23 V) is about 32.9 kWh/kg. A kilogram is about 2.2 lb. For 1 mole (2 g) of hydrogen the energy is about 0.0660 kWh/mole. Compressing or liquefying the hydrogen would take additional energy. One company produces hydrogen through electrolysis at about 7,000 psi at an energy usage of about 60 kWh/kg H₂ (2).

Because a Watt is Voltage x Current, this is equivalent to Power x Rate x Time. The power in this case is the voltage required to split water into hydrogen and oxygen (1.23 V at 25°C). The rate is the current flow and relates directly to how fast hydrogen is produced. Time, of course, is how long the reaction runs. It turns out that voltage and current flow are interrelated. To run the water splitting reaction at a higher rate (generating more hydrogen in a given time), more voltage must be applied (similar to pushing down on the accelerator of a car; more gas is used to make the car go faster.) For commercial electrolysis systems that operate at about 1 A/cm², a voltage of 1.75 V is required. This translates into about 46.8 kW-hr/kg, which corresponds to an energy efficiency of 70%. Lowering the voltage for electrolysis, which will increase the energy efficiency of the process, is an important area for research.

The electrolysis process discussed here can be done with high pressure but also with high temperature using nuclear reactor.

However there are a few more ways to commercially produce hydrogen:

from natural gas: \[ \text{CH}_4 + \text{H}_2\text{O} \rightarrow \text{CO} + 3 \text{H}_2 + 191.7 \text{ kJ/mol} \]

from carbon monoxide: \[ \text{CO} + \text{H}_2\text{O} \rightarrow \text{CO}_2 + \text{H}_2 - 40.4 \text{ kJ/mol} \]

different ways are less efficient and not used in this industry such as the chemical way:

\[ \text{Al} + 3 \text{H}_2\text{O} \rightarrow \text{Al(OH)}_3 + 1.5 \text{H}_2 \], in this case using the aluminum metal to produce aluminum hydroxide and hydrogen.
PART TWO: HYDROGEN AND CARS

A. How hydrogen vehicles work

Currently, there are two main types of hydrogen powered vehicles: fuel cell and hydrogen internal combustion engines. Fuel cell vehicles are electric cars in which hydrogen is pumped into the tank of the car and hydrogen gas then goes into the fuel cell where it is electrically converted into electricity. There is no combustion, moving parts, nor emissions other than water vapor. The car runs on electricity, which is also approximately 2-3 times more energy efficient than a gasoline engine. Hydrogen vehicles use a regular combustion engine modified to use gaseous hydrogen instead of liquid gasoline (much like a natural gas vehicle is modified). They burn hydrogen, but since there is no carbon in hydrogen, there are no CO₂ emissions and only trace amounts of NOx (oxides of nitrogen—the air we breathe is 79% nitrogen). Hydrogen vehicles are typically about 30% more efficient than comparable gasoline vehicles. Both types can be hybridized for additional gains in efficiency, by adding an electricity storage device like a battery or capacitor⁴.

B. Current State of Production of Hydrogen Powered Cars

Currently it seems as if every major automaker is developing hydrogen fuel cell vehicles. Most of the car makers seem to prefer the internal combustion engines instead of fuel cell alternatives. Also, some car makers have discovered that it is possible for existing cars to be converted to run on hydrogen and several major car companies are exploring those options as well. But in the end it comes down to whether or not car companies can come up with advanced hydrogen storage systems so that hydrogen cars can easily re-fuel or not. This is what will determine whether this trend catches on or not. It would also help to accelerate the introduction of truly clean fuel cell vehicles⁵.
PART THREE: VIABILITY OF HYDROGEN AS AN ALTERNATIVE FUEL

A. Viability of hydrogen-powered cars

The sustainability of a fuel cell electric vehicles will basically come down to whether for not people are willing to change and whether the governments of the world choose to support hydrogen powered technology. In many ways, these types of cars are better suited to modern vehicles that increasingly use electrical systems in place of mechanical and hydraulic to steer, brake, and control the various functions of the vehicle. Also, in a fuel cell vehicle, the entire powertrain can be consolidated into a flat "skateboard" chassis, providing automakers much design freedom in latching all sorts of different vehicle bodies on to the chassis – without having to work around a protruding, heat-producing engine and large mechanical driveline. A fuel cell is also 2-3 times more energy efficient than a gasoline engine. Other vehicles that use hydrogen in a regular combustion engine are also very viable. They use existing engine technology, modified to use gaseous hydrogen. Hydrogen vehicles are about 30% more efficient than comparable gasoline vehicles and produce ultra-low emissions, with no CO₂.

B. Safety Concerns

Most fuels have high energy content and must be handled properly to be safe. Hydrogen is no different. In general, hydrogen is neither more nor less inherently hazardous than gasoline, propane, or methane. As with any fuel, safe handling depends on knowledge of its particular physical, chemical, and thermal properties and consideration of safe ways to accommodate those properties. Hydrogen, handled with this knowledge, is a safe fuel. Hydrogen has been safely produced, stored, transported, and used in large amounts in industry by following standard practices that have been established in the past 50 years. These practices can be emulated in non-industrial uses of hydrogen to attain the same level of routine safety (National Hydrogen Association). Hydrogen has a wider flammability range, but because it is lighter than air (50 times lighter than gasoline vapors and even lighter than helium) and diffuses 12 times faster than gasoline vapors do, it is very difficult for hydrogen gas to find a suitable ignition source in an open environment, like a fueling station. Thus, it is still safer than gasoline.

Furthermore, hydrogen fuel stations are designed as "closed" systems, meaning that the fuel is not exposed to the atmosphere - unlike gasoline which can be spilled fairly easily during refueling. This closed system design approach keeps hydrogen always within proper containment and does not allow oxygen or air to mix with the fuel, thereby eliminating one of the required combustion elements needed to create a fire. This further mitigates hydrogen's low ignition energy property, compared to gasoline, by never allowing a spark or ignition source to have any ability to interact with the hydrogen gas.
Furthermore, breathing a small amount of hydrogen is not harmful to humans, animals, nor the environment. Hydrogen is a non-toxic element. Like other commonly-used gases, hydrogen displaces, or pushes away, oxygen. However, if the situation was where a person was breathing so much hydrogen (so much that is would displace the oxygen) and very little oxygen, problems could result. But this is highly unlikely since hydrogen disperses (rises and spreads out) very quickly, there’s a very low risk of breathing too much.

C. Cost of Production

The estimated costs for producing and delivering hydrogen to the fueling station using today’s technologies vary from $2.10/gallon of gasoline equivalent (gge) to $9.10/gge. These hydrogen costs do not include highway taxes and do include the increased fuel efficiency of fuel cell vehicles compared to gasoline-powered hybrid electric vehicles. That is, the driver of a fuel cell vehicle would pay the same amount to travel 100 miles on hydrogen as the driver of a gasoline-powered hybrid electric vehicle would pay for gasoline if the price was between $2.10/gallon to $9.10/gallon to travel that same distance. Projected costs using future technology if current R&D efforts are successful would reduce the cost of hydrogen to the range between $1.75/gge to $4.25/gge. Thus hydrogen is expected to be competitive with gasoline per mile driven.

In addition, some NHA member companies are projecting that they can produce and deliver hydrogen economically to fueling stations at costs as low as $1.20/gallon of gasoline equivalent, again untaxed. After adding the average US highway taxes (federal and state) of $0.43/gallon, hydrogen would still be less expensive than gasoline per mile traveled.

Furthermore, while it may take more energy to produce and deliver hydrogen than it takes to produce and deliver gasoline or natural gas, the hydrogen fuel is then used more efficiently than the current alternatives. Most hydrogen internal combustion engines are about 25% more efficient than their gasoline counterparts and fuel cells are 100-200% (2-3 times) more efficient.
CONCLUSION:

In conclusion, hydrogen powered vehicles are a very viable alternative to gasoline powered vehicles. They are efficient in many ways, however, there are also drawbacks to having them. Liquid hydrogen can still be difficult to store and transport, fueling stations have not yet been established, and it would take a great deal of time and effort to get all of the millions of people in the United States and throughout the world to switch over. Nevertheless, in the end, hydrogen vehicles have proven to be more efficient, safe, and cost effective than gasoline or diesel powered vehicles. They do not pollute the environment as much as gasoline powered or diesel powered cars. I also believe we should put our efforts in finding a way in which we can recycle existing vehicles and convert them to the future format. Thus, as soon as the U.S. government can establish more fueling stations and make hydrogen cars a more affordable and effective alternative to gasoline, hydrogen cars will become not just the future, but the present.
Index:


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8. National Academy of Engineering, "The Hydrogen Economy: Opportunities, Costs, Barriers, and R&D Needs"(2004), Fig. 5-3.

9. National Academy of Engineering, "The Hydrogen Economy: Opportunities, Costs, Barriers, and R&D Needs"(2004), Fig. 5-3.

10. National Academy of Engineering, "The Hydrogen Economy: Opportunities, Costs, Barriers, and R&D Needs"(2004), Fig. 5-3.
Organic Vs. Inorganic
By: Dawn Compton
April 2009
Over the past two decades food industries in the United States have been expanding with the production of organically grown produce. Reports show that the consumer has become more skeptical of how the food is being farmed, and what the farmers are adding to the produce. The term organic has no legal meaning, only that the organic farmers do not use chemicals and pesticides on the plants. The conventional foods in our everyday market are farmed with pesticides, hormones and antibiotics used to keep the livestock healthy and could pose a health risk for the consumer. In this article scientists will tell how different synthetic chemicals and irradiated foods affect the body and its aging process, the benefits of consuming organic produce and livestock, and the pros and cons of continuing consumption of regular conventional foods with pesticides. First the consumer must know the different levels of organic. There is one hundred percent organic label that is USDA certified that is on most fruits, vegetables, eggs, and other foods that are one ingredient. The next level is the organic which is only ninety five percent made with organic ingredients and can still have the USDA certification label. The third level is the “made with organic ingredients”; these foods are at least seventy percent organic and cannot have the USDA certification label. The rest of the foods that fall under seventy percent will not be organically approved by the government and FDA.

There are many benefits of eating organic foods compared to conventional foods that the consumers in the United States believe can benefit from. Most believe that there is more nutritional value in organic produce and will slow down the aging process from the antioxidants in organic farming. Some consumers believe organic food tastes better and that it may keep people at low risk of some cancers. On most conventional fruits and vegetables there are pesticides, hormones, sewer sludge, and irradiation added to the crops to help with growth rate, size, and to keep the crops healthy. There has been research conducted in finding the differences in nutritional values, along with the affects of the bodies aging process after repeated consumption of the chemicals on conventional foods.

The first health related benefit of organic produce is the high-level of antioxidants that are in the fruits and vegetables in comparison to conventional produce. An antioxidant is a nutrient such as vitamins and minerals that the body uses to keep from skin damage and breakdown. Reports show that the antioxidants are known to prevent diseases such as Alzheimer’s disease that is common in elders; some cancers, Rheumatoid arthritis, heart disease and cataracts. There are many different types of antioxidants that are vital to the human development such as, Vitamin E, Vitamin C, Beta-Carotene, and Selenium. The selenium antioxidant is similar to the elements magnesium and zinc. There are certain enzymes that make up an antioxidant that are crucial in defense of the free radical. The free radicals are molecules or active atoms that are charged due to the deficiency or an excess number of electrons. These enzymes will play an important roll in primary line of defense in destroying free radicals. SOD first reduces (adds an electron to) the radical superoxide (O2-) to form hydrogen peroxide (H2O2) and oxygen (O2). 2O2- + 2H → SOD→ H2O2 + O2 Catalase and GPx then work simultaneously with the protein glutathione to reduce hydrogen peroxide and ultimately produce water (H2O). 2H2O2 → CAT→ H2O + O2 H2O2 + 2glutathione → GPx→ oxidized glutathione + H2O. (The oxidized glutathione is then reduced by another antioxidant enzyme -- glutathione reductase.) Together, they repair oxidized DNA, degrade oxidized protein, and destroy oxidized lipids (fat-like substances that are a constituent of cell membranes).
These free radicals are abundant in the pollution, sun rays, smoke, and alcohol. They break down the skin on humans by grabbing onto the body and donating excess electrons. Certain enzymes that are in the antioxidants will help protect against these harmful free radicals. Other types of secondary enzymes will keep humans from further skin damage. There may be enough evidence to support that the higher amounts of consumed antioxidants can slow the aging process. This evidence proves that the organic produce can benefit higher than that of conventional.

The antioxidants are produced in fruits and vegetables when the plant undergoes stressors while it is growing, either from the weeds, insects or plant pathogens. This may be the fungicides, or herbicides that are put on the plant to control pests that increase the levels of antioxidants present in the organic produce. The fruit and vegetable plants that are grown with pesticides, hormones and other chemicals keep the plant from undergoing these stressors and the plant never produces as much antioxidants as the organic plants grown with botanicals, and animal and crop wastes. There is an average of thirty percent difference in the antioxidant levels from conventional to organic. Studies have shown that there is 27% more Vitamin C, 21% more Iron, 29.3% more magnesium and 13.6% more phosphorous in organic produce. There is supportive evidence that there are higher percentages also of some other specific vitamins, flavonoids or antioxidants in organic foods. Another study with strawberries, organic and conventionally cultivated has a higher percentage of antiproliferative activity against breast cancer and colon cancer. This significant difference is all affected by how the farming techniques are done. By the use of compost, cover crops, slow release forms of nitrogen can increase these certain vitamins that are not significantly abundant in conventional foods. Most of these vitamins and antioxidants are found in the outer layers or peal of the fruits or vegetables. That is why when the conventional foods are found to not have as much of these vitamins it is because of all the pesticides and chemicals that are sprayed on the exterior of the fruit or vegetable plant. Consumers may wash the outside or even peel off the outer layer of the fruit or vegetable and completely remove the vitamins and minerals of the plant. Another farming technique that organic farmers use is the low pressure; low temperature processing that keeps the antioxidants in the fruits and vegetables. The conventional produce farming uses a high temperature and high pressure processing that squeezes and burns out the nutrients in the fruit or vegetables. Organic farming is an old agricultural way that farmers did before the discovery of petroleum-based chemicals before the end of World War 2. The famers are now starting to return to the old agricultural ways of farming.

One reason why organic produce may be favored over conventional produce is the result of lower nitrate levels found in organic produce. Nitrates are naturally occurring in most earth grown foods and can be harmful to the body as it breakdown into nitrites. There were eighteen studies conducted that proved that there were higher nitrate levels in conventional foods than that of organic foods. There were one hundred and twenty seven cases of the nitrate levels being higher in conventional foods than organic. There were forty three cases of organic produce where the nitrate levels were larger and 6 cases of no difference in nitrate levels. This concludes that the range of ninety seven percent to eight hundred and nineteen percent organic is a dramatic difference of the levels of nitrates present in produce. Other naturally occurring toxins that are similar to nitrates are more prevalent in conventional foods than organic. For example,
glycoalkaloids that are naturally occurring that come from tomatoes, and potatoes. Celery plants can be known to have a naturally occurring toxin that can cause contact dermatitis and possibly a human carcinogen. There are many other naturally occurring toxins that range from corn to peanuts. There have been studies conducted for both conventional and organic produce for levels of naturally occurring toxins. The studies found that organic plants may produce these toxins when they are under stressors when using pesticides may lessen the toxins. Other studies show that there is an increase of toxins after the use of pesticides. This study has not yet completely been determined. Another larger reason for consumers to eat organic is the potential risks involved in consuming pesticides.

Pesticides have been around since the end of World War 2 and ever since then farmers have not been “organic” farming. The petroleum based chemicals which later turned into pesticides was the best option for the farmers. The chemical ammonium nitrate became used as a fertilizer and the organophosphates as an insecticide. The reason farmers used these pesticides were to warn off pests that invaded there crops. There are different types of pesticides that target and control the pests. There are fungicides that kill most fungi including molds, mildews, blights and rusts. There are Herbicides that control the growth of weeds and other unwanted plants. There are food traps that attract rodents or insects that are called attractants. The insecticides are targeted for the arthropods. Finally, there are biopesticides that is derived from natural materials as bacteria, plants, and animals. There is a list of other pesticides that are used for other farming produce. One of the first types of chemical pesticide is the organophosphates that attack the nervous system of insects. This also would have the same affect on humans if high-levels were ingested. This pesticide was developed in the 19th century and has not been persistent in the environment. Next, the pesticide Carbamate will attack the nervous system by disputing a neurotransmitter, acetylcholine. The effect on the neurotransmitter is reversible. Thirdly, Pyrethroid is a modified pesticide that is a naturally occurring pesticide pyrethrin. This pesticide has been modified because of its instability that occurs in the environment. The final chemical pesticide which is an insecticide is Organochlorine; this is no longer used and has been taken off the market due to its environmental effects and persistence.

There have been reports done by the EPA that show a list of released pesticides this year has been under screening for possibly disrupting the endocrine system or humans and mammals. The endocrine system controls the bodies’ growth, reproduction and metabolism. “Endocrine disruptors can cause lifelong health problems — especially for children,” said EPA Administrator Lisa P. Jackson. “Gathering this information will help us work with communities and industry to protect Americans from harmful exposure.” The EPA will issue a screening this summer of sixty seven of the pesticides for Endocrine Disruptor Screening Program (EDSP), and this will eventually lead to screenings of the registered pesticides. The EPA has been regulating the approval of new pesticides on the bases if they pose a risk to humans, animals and the environment. The EPA does a cumulative risk assessment designed to evaluate the exposure risks to multiple pesticides, and how they react in the human body. There are also limitations that are set up for workers that use the pesticides. The proper protective gear and limits to protect the environment must be taken to allow approval of the pesticide. While pesticides seem to be an increase health risk for human in conventional foods, the irradiated foods that are conventionally grown are also posing a health risk for consumers.
Irradiated foods are the exposure of foods to ionizing radiation which is also known as ionizing energy. Irradiated foods are known to kill harmful bacteria and certain organisms that grow in most meat products. The FDA has approved the process of irradiation, and is said to be safe and prevents illnesses like mad cow, salmonella and e coli. Although there are research in irradiated foods having other long-term affects on humans. Irradiated food is ionized with gamma rays, x-rays and beams of high energy electrons. All foods must be properly packaged after irradiation and kept at a proper temperature the meat will be at low risk of contamination of pathogens. Most meats that are left un-irradiated that are cooked at a high enough temperature will remove the harmful bacteria growth. The organic meats are left un-irradiated and have a labeled recommended temperature of cooking on the package. This is part of the organic labeling process for the FDA. Although, the irradiation is being used as a sterilizer, it can also allow foods to sit at room temperature for a longer time period than organic un-irradiated foods. Irradiated fruits will delay ripening of most fruits such as, bananas, mango, papayas and tomatoes will allow a longer shelf life than those fruits that are not irradiated. At a medium dosage of irradiation strawberries, blueberries and raspberries will have an extended shelf life. The irradiated foods will not become radioactive no more than the x-rays people get at the dentist or the airport x-ray scanner. This may be enough for a consumer to believe it is unsafe when you are eating these foods day in and out.

Consumers and researchers believe that there may be fewer nutrients in the foods after the irradiation. Resources tell that there is little to no change in the nutritional value from irradiated foods to non-irradiated foods. A component that may affect the nutrition in foods may be due to cooking, freezing, thawing and canning. Most of the vitamins and minerals in foods are resistant to the irradiation as niacin, vitamin D, and riboflavin. Although there are fairly sensitive vitamins like vitamin A, B1, (thiamine), K and E, which are significant nutrients the body needs to function. This factor depends on whether the vitamins are soluble in fat or water, and the atmosphere or where the irradiation took place. For example, a dry egg that was irradiated lost 5% of vitamin B1. Also with Vitamin C in vegetables and fruits are often affected after irradiation with the ascorbic acid. There may be enough evidence to support that there is no great significance in nutritional values from non to irradiated foods. “Irradiation of any food commodity up to an overall average dose of 10 kGy introduces no toxicological hazard; hence, toxicological testing of food so treated is no longer required”, The JECFI stated. Investigations in 1981 still support JECFI’s hypothesis on the irradiated foods posing no health risks. The investigations were done in China with twenty one males and twenty two females ate a diet of seventy one percent irradiated foods for a period of fifteen weeks. Since this investigation there has been no supportive evidence of health complications.

In 1993, there was an outbreak of E. coli that came from under cooked hamburgers being served at a restaurant that was on the west coast of the United States. This outbreak caused hundreds of illnesses and deaths of children and adults. Ever since then the consumers were aware of these possible threats and the demand for irradiation began to increase. The national and regional supermarkets began marketing these irradiated ground beef patties. Since the outbreak there have been fewer cases of E coli illnesses due to the surge of irradiated foods. The poultry was approved by the FDA shortly after the outbreak of 1993. Although fish and seafood have not, there are two petitions pending the approval of shrimp and mollusks. The increase risk of not having the seafood approved might possibly reach an outbreak in Salmonella in shrimp and Vibrio vulnificus in clams and oysters. The use of irradiation will continue to grow and will
be a popular demand for all kinds of foods that can spoil. Organic farmers do not use irradiation, but use other measures to keep the produce and livestock healthy and disease free. The biggest reasons for consumers to purchase organic foods is seventy percent of the avoidance of the pesticides, sixty eight percent for freshness, sixty seven percent for nutrition and health, and fifty five percent to avoid modified foods. The larger percentage of why consumers prefer organic is how it is farmed and processed. There are no synthetic chemicals or modifications done to the farming. The biological pest control is achieved by crop rotation, the use of pest management techniques, and the planting of pest-deterrent species. Since the process of the farming can be timely, the products tend to be more expensive than conventional foods. The use of composted organic materials has replaced the use of pesticides. Organic farming relies on green manure, biological pest control, cultivation, crop rotation and strictly excluding the use of synthetic fertilizers and pesticides. These methods of farming are regulated and strictly enforced.

"Organic agriculture is a production system that sustains the health of soils, ecosystems and people. It relies on ecological processes, biodiversity and cycles adapted to local conditions, rather than the use of inputs with adverse effects. Organic agriculture combines tradition, innovation and science to benefit the shared environment and promote fair relationships and a good quality of life for all involved." International Federation of Organic Agriculture movements. Organic farmers use fertilizers that are processed with mineral powder such as rock phosphates and greensand and seed meal. Agriculture relies on the one meter topsoil that tends to deplete more rapidly than it's replaced and causes some pesticides are known to keep the till from eroding. Methods such as these will help the control erosion and enrich the soil. The technique use to improve fertilization, pollination, season extension and water conservation is introducing beneficial organisms to the crops. Weeds are mechanically controlled by the farmers and the use of mulches and cover crops. Although picking weeds is the natural way of farming, it can get costly with the laborers. An idea of using ducks and fish to eat the weeds was used in the agricultural days. Research has shown a small amount of pesticides being used to the standard regulations.

![Tractors used to spray pesticides on crops.](image)

There are three main pesticides farmers still use in organic farming. One is pyrethrum that is used is large amounts of the conventional produce, the other is rotenone, copper and sulphur. Both of which are not used in the farming of conventional foods. Farmers may face challenges if there were the removal of all pesticides. Pest resistant modified crops have been proposed as another way to replace pesticides. Two different studies have been done on children with some being on an organic diet and the other on conventional food diet. There has not yet been completed health results found on this case, but the study concluded, "It is intuitive to assume that children whose diets consist of organic food items would have a lower probability of
neurologic health risks.” Most organic studies are found to have an increase level of vitamin C. As with meat and milk, there is an increase in the fatty acids, and carbohydrates are found to have no difference with the conventional produce. A study showed in 2007 that the organic milk is associated with a decrease risk of eczema. The organic farming in the United States has continued to grow in demand in the past twenty year. The farmers markets in the United States have grown from 1,775 in 1994 to 4,385 in 2006. Although, with the rising food prices in the past year the demand for organic produce may experience a falling demand.

In conclusion to this article, the popularity of organic foods will continue to grow, the organic food sales of 2005 were thirteen point eight billion dollars spent buy consumers. The popular of organic food for consumers are the more nutritious produces, the safe environment affects, the workers safety and animal welfare. There are many pros to eating organic produce, first being that the vitamins and minerals are more abundant in the produce. The levels of antioxidants in these organic fruits and vegetables show a thirty percent difference in conventionally grown foods. There is an increase level of Vitamin C, and riboflavin’s that make the conventional foods second pick to those who want more nutrient rich foods. Studies prove there are decreases of nitrate levels in organic produce that are proved to be higher in the conventional produce due to its high toxicity of the residue of the pesticides. The organic farmers only use a small amount of pesticides that is regulated to keep the crops manageable from invaders. These pesticides include two of which that are natural elements like copper and sulphur and one being used also in most conventional production of foods.

The one thing about organic that may pose a problem that is found in this article of research is the produce, meat, milk and eggs are not irradiated. This means the shelf life of the produce; milk and eggs are shorter than those of the irradiated conventional foods. No research concluded that irradiation was a health risk and irradiation demand will continue to grow. But the organic meat has a label of recommended temperature that will remove all microorganisms just like irradiation would. As for the produce, there is a shorter shelf life, but there are less pesticides being put on the produce and allow for the fruit and vegetables to be hardly washed or peeled. In this article of research the organic pros are stronger than the cons. With conventional foods there may be a higher risk of continuing consumption of these harmful chemicals and modified foods. The research show there has been more health concerns and news of people eating pesticide residues than eating the organically grown foods.
Bibliography


   Answers Corporation.

OxyContin: Good or Evil?

Kerri Dusel

April 24th, 2009
According to Dictionary.com addiction is "the state of being enslaved to a habit or practice or to something that is psychologically or physically habit-forming, as narcotics, to such an extent that its cessation causes severe trauma"¹. One of the most addicting prescription drugs around is Oxycontin. People will do just about anything to get their hands on some Oxycontin. Oxycontin is a strong semi-synthetic opioid analgesic medication. Oxycontin is used for chronic, long lasting pain commonly associated with terminal illness or cancers. But, these days Oxycontin has gotten into the wrong hands, and has become an extremely addictive, expensive street drug that has killed many people from overdose.

Oxycontin is the extended release version of Oxycodone Hydrochloride. Oxycodone Hydrochloride has a chemical formula of C₁₈H₂₁NO₄ • HCl and a molecular weight of 351.82 g/mol. Oxycodone has a melting point of 218-220°C. Oxycodone Hydrochloride was first made in 1916 at the University of Frankfurt in Germany, by Freund and Speyer. Freund and Speyer derived Oxycodone Hydrochloride from Thebaine. According to the Drug Enforcement Agency (DEA), "Thebaine is a minor constituent of Opium"². The DEA also goes on to state that Thebaine is similar to Codeine and Morphine, but they have one major difference. The difference is the type of effect they have on the user. Codeine and Morphine are depressants and the Thebaine is a stimulant meaning that the Thebaine will make you happier than if you were to take Codeine or Morphine. Thebaine is not used for any purpose, other than making other types of medications. Some of those medications include Oxycodone, Naltrexone, Naloxone, and Buprenorphine, which will be talked about later.

Even though Oxycodone Hydrochloride was first synthesized in 1916, it was quickly turned around and clinically used in 1917. But it wasn’t introduced to the United Stated market until about 1939. Oxycodone Hydrochloride got extremely popular and it became the illicit drug of choice in the 1960’s. In 1960 Oxycodone Hydrochloride was added to the “Dangerous Drugs (Amendment) Ordinance because people were abusing the medication. In the Controlled Substances Act of 1970, Oxycodone was placed on the second highest classing for the potential of abuse. The only other class that has a higher risk for abuse is CI (class one). Medications that
are in the CI class are marijuana, heroin, and drugs that have no medicinal value. Also CI medications are not prescribed in the United States since they don’t have any medicinal value. Although people have argued that marijuana does have medicinal values, the government still has sided against making marijuana legal. Medications that are in the CII class include Oxycodone Hydrochloride, Oxycontin, Percocet, Methadone, Opium Tincture, Ritalin, and Adderall, just to name a few.

It took about 79 years from when Oxycodone Hydrochloride was first synthesized to make an Extended Release version of the medication. The patent for an extended release version was given in 1993. In 1995 the drug manufacturer Purdue Pharma came out with the first Extended Release Oxycodone Hydrochloride (Oxycontin), which was approved by the FDA (Food and Drug Administration). The Extended Release version of Oxycodone Hydrochloride was first marketed in the United States in 1996. Oxycontin comes in several different strengths. These strengths include 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, and 160mg. In May of 2001 Purdue Pharma voluntarily stopped making its 160mg Oxycontin tablet. Purdue says that it wasn’t because of pressure from the DEA or others. Purdue Pharma just decided to suspend the manufacturing of it on for their own reasons. In 1996 alone (the first year Oxycontin was released in the US) made about $40 million dollars and every year since 2000 Purdue Pharma has raked in over one billion dollars per year. In 2004, the generic formulation of Oxycontin (Oxycodone ER) was approved. There were some issues with the generic patent and was and still is difficult to get the generic form distributed. Some people say that Purdue Pharma purposely made it harder for the generic companies to get the “okay” to manufacture the generic
(Oxycodone ER). Purdue would do this, so that they could reap all the benefits of the brand price of Oxycontin. Oxycontin, because of the Extended Release formula, can not be crushed or diluted or tampered in any way. Tampering with Oxycontin then taking it can cause the person to overdose. It does this because it is not slowly released over time (like it’s supposed to be) when it is crushed or chewed. All of the medication will release at once causing the patient to get an extreme amount of the medication at one time, causing them to overdose.

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<th>Year</th>
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<tr>
<td>4000B</td>
<td>Earliest recorded opioid use</td>
<td>1729</td>
<td>Emperor Cheng of China bans opium except for medicinal use</td>
<td>1995</td>
<td>Oxycontin approved by the FDA</td>
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<td>3400B</td>
<td>Sumerians call opium the “Joy plant”</td>
<td>1803</td>
<td>German scientist refines opium into Morphine</td>
<td>1999</td>
<td>Percocet approved by the FDA</td>
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<td>1300B</td>
<td>Opium use in Egypt spreads to Greece and the rest of Europe</td>
<td>1853</td>
<td>Hypodermic needle invented, Opium injection begins</td>
<td>2000</td>
<td>Drug addiction treatment Act is approved in the US</td>
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<td>460BC</td>
<td>Hippocrates recognizes the medicinal benefits of opium</td>
<td>1874</td>
<td>Heroin developed</td>
<td>2001</td>
<td>Subutex approved in Australia for Opioid Dependence</td>
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<td>330BC</td>
<td>Opioid use spreads to Persia, India, and China</td>
<td>1924</td>
<td>Nonmedical opioid use banned in the US</td>
<td>2002</td>
<td>Suboxone approved in the US</td>
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<td>400AD</td>
<td></td>
<td>1965</td>
<td>Heroin users in the US reach about 750,000</td>
<td>2003</td>
<td>Number of Americans abusing or addicted to heroin/opoid painkillers totals 1.6 to 2.4 million</td>
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<td></td>
<td>1970</td>
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<td>1300</td>
<td>Opium disappears from Europe during the Inquisition</td>
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<td>1527</td>
<td>Paracelsus reintroduces opium to Europe for medicinal purposes</td>
<td>1984</td>
<td>Vicodin Approved by the FDA</td>
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The mechanism of action for Oxycontin is unknown. Oxycontin does have effect on the opioid receptors of the brain and the spinal cord. Oxycontin does not eliminate the sensation of pain but decreases discomfort by increasing tolerance to pain"\(^3\). Not only does Oxycontin increase the tolerance of pain, but it has other effects on the person taking it when it is crushed, chewed, or injected. If Oxycontin is crushed, chewed or injected it can cause such feelings as euphoria, relaxation, calmness, and a stoned/high feeling. Drug abusers do this, because it is said to have feelings much like Heroin. Oxycontin is crushed to snort or ingest it, and it is diluted in water to inject it. When pharmacies are robbed, the most commonly asked for medication is Oxycontin. It is stolen not only for it’s street value, but for the temporary high that is creates. The NIDA reports that Oxycontin abuse rates are higher than Heroin abuse rates. Oxycontin is such a powerful pain medication that “a 5mg tablet of Oxycontin has as many active ingredients as 1 Percocet. So, chewing or snorting a 40mg tablet of Oxycontin is similar to taking 8 Percocets at once. An 80mg tablet of Oxycontin is like taking 16 Percocets all at once”\(^4\).
There are many symptoms of Oxycontin overdose. Some of these symptoms include respiratory depression, seizures, dizziness, weakness, loss of consciousness, coma, confusion, small pupils, reduced vision, nausea, and vomiting. You can’t just stop taking Oxycontin immediately. You have to gradually decrease the dose until you’re down to nothing. If you just suddenly stop taking Oxycontin, withdrawal symptoms will be noticed. Withdrawal symptoms include tiredness/fatigue, constant yawning, hot/cold sweats, heart palpitations, joint/muscle ache, nausea, vomiting, uncontrollable coughing, diarrhea, insomnia, watery eyes, and depression. These withdrawal symptoms can be seen as soon as six hours after the last dose and these symptoms can last for up to a week. Also, these symptoms are similar to Heroin withdrawal.

Having asthma, COPD, sleep apnea and other breathing disorders would limit a person from taking Oxycontin, since Oxycontin slows the respiratory system down. Also a person shouldn’t take Oxycontin if they have liver/kidney problems, underactive thyroid, epilepsy, low blood pressure, Addison’s disease, enlarged prostate, mental illness or a history of drug/alcohol addiction. If you have an underactive thyroid it causes you to be more tired than you should be, and taking Oxycontin with this condition would just make you even more tired. Also, with epilepsy you can have seizures all the time and taking Oxycontin can increase the quantity of seizures you have. Kidney problems would be a bad thing to have while taking Oxycontin because Oxycontin is excreted through the kidneys. Having a history of addiction to alcohol or other drugs is not good, since Oxycontin is very addictive. Taking Oxycontin would just make a person addicted to it if they have that kind of past. Also Oxycodone shouldn’t be taken while pregnant or nursing. Oxycodone is listed as a class “C” medication and class C medications shouldn’t be taken while pregnant. Oxycodone has also been secreted in breast milk, so if a baby is nursing they could feel the effects of Oxycodone.

Oxycontin has many “nicknames” on the street. Some of the nicknames are “OC”, “Oxy”, “OX”, “Blue”, “Oxycontin” and “Hillbilly Heroin”. Hillbilly heroin is the name of Oxycontin in the Appalachian Mountains, where Oxycontin is everywhere and just about everyone takes it. No matter what it is called, it is all the same stuff, Oxycontin. If people don’t try and steal it from pharmacies they get it other ways. Some people buy it off the street and some people just doctor hop. Doctor hopping is when a person goes to several different doctors to get the medications they need, including Oxycontin. But if you go to the same pharmacy all the time, the pharmacist will usually catch it, and notify all of the doctors involved, which leads the person to not only go from doctor to doctor, but also go pharmacy to pharmacy. Some states have a “prescription monitoring program” to see who is getting Oxycontin prescriptions and other prescriptions and how often. The states included in this monitoring program include California, Hawaii, Idaho, Illinois, Indiana, Kentucky, Massachusetts, Michigan, Nevada, New Mexico, New York, Oklahoma, Rhode Island, Texas, Utah, and Washington. There is also a program called DAWN (Drug Abuse Warning Network). “The New Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug-related hospital
emergency department (ED) visits and drug-related deaths to track the impact of drug use, misuse, and abuse in the U.S. This program isn’t in all states, not even in all the states that are listed above, but it has a lot of different people using it. Some of those people include Federal agencies, communities and the private sector, and members of the network. DAWN does all kinds of different drugs like illegal drugs, prescription and OTC medications, alcohol and dietary supplements.

Purdue Pharma marketed Oxycontin as a “less addictive” pain medication, but soon they found out that wasn’t true. In 2007 Purdue Pharma was required to pay millions of dollars because they lost one of the many lawsuits against them. The lawsuit was saying that Oxycontin was much more addictive than the company had let on. Purdue Pharma realized they were wrong, and agreed to pay about $600 million dollars. Some of the top executives at Purdue Pharma also had to pay fines out of their own pockets, some totaling around $34 million dollars.

If a person is addicted to Oxycontin or any medication they need to get help as soon as possibly, preferably now. No one treatment is appropriate for everyone and the drug addiction is not the thing you’re treating, it’s the patient. So the treatment must be changed based on the changing of the persons needs. Staying in the treatment program for just a few days is not enough. The person with the addiction needs to stay in the treatment program for as long as the program lasts, or longer. Also, treatment is for the rest of a person’s life, they must follow through everyday to get better. It’s not just saying that “I’m a drug free person”, a person must attend some sort of counseling and have behavioral therapy to get through their addiction. Also a doctor can prescribe some different types of medications to combat the person’s addiction. Some of those medications can be Subutex, Suboxone, or Naltrexone. Subutex consist of a compound called Buprenorphine Hydrochloride, which is an Opioid agonist-antagonist analgesic used in treating opioid dependency. Suboxone is very similar to Subutex,
except that it has one more component. Suboxone is made up of two compounds, Buprenorphine and Naloxone. Naltrexone is the third medication that can be used to treat opioid dependency. There are other medications out there that can help with opioid dependency, but those three are by far the most popular. "In 2006, 23.6 million persons aged 12 or older needed treatment for an illicit drug or alcohol use problem (9.6 percent of the persons aged 12 or older). Of these, 2.5 million (10.8 percent of those who needed treatment) received treatment at a specialty facility. Thus, 21.2 million persons (8.6 percent of the population aged 12 or older) needed treatment for an illicit drug or alcohol use problem but did not receive it."6 Also, Purfue Pharma is looking to make the extended release Oxycodeone less addictive. So they are coming up with alternate medications that are less addicting that Oxycontin. A company called Pain Therapeutics is also investigating a new medication to be a replacement for Oxycontin. "Oxytrex (oxycodone + ultralow-dose naltrexone) is an investigational drug shown here to minimize physical dependence while providing strong analgesia with twice-daily dosing."7 This is still in clinical trials and has not been approved by the FDA yet.

There are many famous people that have been addicted to opioid prescription and non prescription drugs. Some of the famous people that have been addicted and are still alive are Jack Osbourne (Oxycontin), Cindy McCain (Hydrocodone), Courtney Love (Oxycontin) and Rush Limbaugh (Hydrocodone/Oxycontin). A few of the unlucky celebrities that didn't make it through their addictions are John Belushi (Heroin), Chris Farley (Morphine), Howard Hughes (Codeine), River Phoenix (Heroin) and more recently Heath Ledger (Oxycodone/Hydrocodone). Famous people think that they can buy anything they want, but apparently they don't realize the consequences of their actions. They also don't seem to learn from other peoples mistakes (mistakes from their own peers).

I believe that Oxycontin is an evil medication. I believe that Oxycontin should not be on the market, in any strength, anymore. I believe that Oxycontin is far too addictive and dangerous for anyone to be taking. I work in a pharmacy, and I have seen too many stores get robbed for Oxycontin. I have also seen many forged prescriptions for Oxycodone and Oxycontin. I have seen my store have thefts in the pharmacy from employees that work in the front of the store. I can't believe that people would risk their life, their job, their friends, basically everything for a little high, or a little bit of money. The whole thing just boggles my mind. Prescription pads have been stolen from doctor's offices just to get their Oxycontin. I don't think that anything that addictive should be mass produced and sold. It kills people?! Do people not understand that? You crush a 160mg tablet (even though it's not currently being made) and snort it and you can die! Why would anyone want to do that? I think that a lot of states are doing a good thing by
making a “prescription monitoring program”, but what about the other 34 states that aren’t doing a program like that? Since we have a uniform “Controlled Substance Act” that we all use throughout the United States, there should be a uniform “prescription monitoring program”. Now all those people have to do, that don’t want to be monitored, is just go to another state that doesn’t have a program. Most people that take narcotics on a regular basis (I’m not talking about a small amount of Vicodin for a toothache), but people that are on serious pain medications 24 hours a day, seven days a week, 365 days a year, cannot be trusted. The reason why is because, what happens when the doctors prescribing these medications decide the patient doesn’t need to have them anymore? The patient will just start going to different doctors until someone will keep writing those prescriptions for them. When you type in “Oxycontin” into an internet search engine like Google or Yahoo not just overviews of the medication come up. It also pops up a lot of different stories of pharmacies that have gotten robbed or the names/cases of people that had to go to court because of their misuse of Oxycontin. Those people deserve to go to jail for misusing (either illegally taking or selling) any medication. Those people are ruining it for the people that truly, actually need the medication to get by from day to day. But still I think that the manufacturing of such a powerfully addictive medication should be banned. If the medication is not banned (which I’m sure it won’t be) then there should be a higher security when it comes to getting Oxycontin. The DEA should be notified every single time an Oxycontin or Oxycodone prescription is written, filled, picked up, or anything that has to do with those medications. We do have one small way of telling if the medication is going to the right person. We check “positive ID” when the patient picks up the medication. But anyone could get a fake ID just for their habits. Like I have said, if the people want a specific kind of medication, they will find a way to do it. One more thing the pharmacist (at my store) does to make sure the patient isn’t over taking the medication. The pharmacist checks the patient’s profile. We can see anybody’s profile at any Walgreens Pharmacy, but the downfall to that is that people don’t always just go to Walgreens, or one pharmacy for that matter. Jane Doe could go to every pharmacy on all four corners of a street, get Oxycontin 30mg, pay the cash price at three pharmacies and use their insurance at one pharmacy. No one would know how many times a person would fill a medication(s) if they go to different stores. As long as the patient goes to different doctors to get the same medication and goes to different pharmacies no one would have a clue. And trust me people do it all the time! When the person starts to get in too deep, they start to forget which pharmacy they went to with which doctor then they get messed up. If that happens at my store and the pharmacist notices it, the pharmacist will call the doctors to let them know what’s going on.

As long as any addictive medication, such as Oxycontin, is still on the market there will always be someone out there trying to get it anyway possible. These people abuse it and make it harder for other people that truly need it to get it. Hopefully people will start learning that these medications are dangerous and are not there for pleasure, but to help those that need it. Maybe with more research and more restrictions it will make it harder for people to get Oxycontin, or maybe eventually it will be taken off the market completely.
CITED


NOT CITED, BUT USED FOR INFO/PICTURES


Benefit and Side effects of Diet pills

Prepared for
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Prepared by
Shiva Far
April 24, 2009
Abstract

Diet pills have become increasingly popular over the last decade, but alarmingly, most consumers know little about their chemistry. The aim of this paper is to provide a general summary of the various over-the-counter weight-loss products available in the market. The term ‘diet pills,’ for the sake of this study includes weight-loss products in solid, gel, and liquid state. Diet pills can be classified into three main categories: 1) Metabolic enhancers, 2) Water-pills and 3) Appetite suppressants.

1. Metabolic enhancers

For mammals the rate at which the body processes ingested food into energy depends on activity-level, feeding behavior, and physiology (Cortes et al., 2009; Liow et al., 2008). In alpine and polar environments, mammals tend to be short and stocky, metabolic rates are slow, and reserves of fat are substantial. Mammals in hot-arid regions typically tend to have a more lean physique which allows them to dissipate heat. Such mammals also have higher rates of metabolism. The earliest human fossils are associated with hot semi-arid savannahs of East Africa (Su and Harrison, 2008). Therefore, it is likely that our earliest ancestors had lean muscular physiques. Dental morphology of these fossils and associated stone tools show a preference for nutritious roots, tubers, and animal protein (White et al., 2000). Unlike our ancestors, most modern humans in western societies have sedentary life styles. Our diets are enriched in carbohydrates and saturated fats. Therefore, it is not surprising that most modern humans in western societies consume more calories than they burn. Lack of strenuous physical activity has resulted in slower metabolic rates. These factors combined result in weight-gain.

In 1998 a brand new weight-loss product was introduced into the market with a promise that these pills along with a balanced diet would ensure significant decreases in body fat. The product was called Metabolife, and was the first over-the-counter popular weight-loss supplement. The product was an immediate success, and kiosks selling Metabolife could be found in all major malls across the United States. The pill contained a ‘proprietary blend’ of Ma Huang, Guarana, Ginseng and other herbs along with a dosage of multivitamins and minerals. Ma Huang is an herb of the Ephedraceae family. These plants are common in the high-mountain-deserts of the Andes and Himalayas and have been used for centuries by the locals as stimulants. Reynolds (1989) suggested that plants contain natural ephedrine which is a sympathomimetic amine, and is chemically similar to methamphetamine (Fig. 1, Fig2) Ephedrine increases nerve cell activity, and increases the body’s release of both Dopamine and Serotonin. Guarana is a natural source of caffeine and increases heart-rate. Ginseng is yet another stimulant that has been known to increase energy levels. Together, these substances enhance metabolic rates and facilitate weight-loss. Due to the success of this product, several
Figure 1.0 Molecular structure of Ephedrine, the most common ingredient in most metabolic enhancers.

Figure 2.0 Molecular structure of Methamphetamine, the most common compound in the drug ‘Crystal Meth.’ Note the similarity to the Ephedrine molecule shown in figure 1.

Figure 3.0 Molecular structure of the amino-acid L-Carnitine, a common ingredient in many metabolic enhancers.
brands followed this approach. The most successful of these were the products *Ripped Fuel*, *Xenadrine* and *Hydroxycut*. Not only did these brands contain ephedrine, they increased the dosage to a point that users would experience obvious shivering and trembling. Individuals prone to anxiety, depression and heart problems noticed that the use of these supplements made their symptoms worse. At this point the U.S Food and Drug Administration (FDA) stepped-in and decided to regulate the dosage of ephedrine and caffeine in these supplements. *Hydroxycut* and *Xenadrine* are still sold in stores across the U.S., however, the current dosages of ephedrine and caffeine are mild as compared to their original formula.

A major ingredient used in metabolic enhancers, and as a stand-alone-product is the amino acid L-Carnitine (Fig 3.0). The amino acid is used to breakdown lipids to release metabolic energy.

2. Water-pills

Water-pills induce diuresis which is the removal of fluids from the body through urination. Therefore although they can be used to reduce water-weight in an individual, they do not facilitate fat burning. Natural diuretics which make most over-the-counter water-pills contain caffeine, cranberries, watermelon and vinegar. These pills are exceedingly popular with female consumers who wish to lose weight in a short period of time.

3. Appetite suppressants

Appetite suppressants can potentially prevent hunger and reduce the amount of calories consumed by an individual. The most common ingredient in most appetite suppressants is the amino acid L-Phenylalanine (Fig. 4.0). Because of their side effects, which include insomnia, nervousness, and anxiety, they are only recommended for individuals who want to lose significant amounts (>5 KG) of weight. Hoodia is a slow growing succulent plant, used traditionally as an appetite suppressing survival food in the deserts of South Africa and Namibia, and somewhere someone got the bright idea that if it works for desert-dwelling aborigines like san people in Africa, it might be just the drug for pudgy North American couch potatoes trying to stave off that last “litre of Haagen Dazs”. As a result, Hoodia, has suddenly become one of the hottest diet trends to hit the lucrative weight loss scene with promoters like Anna Nicole Smith, former play boy playmate of the year and dubious cultural icon, who shills for Hoodia based pill called Trimspa X32. No one really knows whether Hoodia actually works. Over fifty hoodia diet pills studied were found to be fake.
I did some research on hoodia for my knowledge, there are no published human clinical trials demonstrating its appetite-suppressing effects. But some scientists believe, Hoodia, "cause the glucose sugar-sensing nerve cells in the brain to send the message that the blood sugar levels are good, and thus there is no need to eat at the moment, in other words, the nerve cells are telling the brain the person is full and not hungry. And there seems to be some evidence that this claim is true, when pure Hoodia is ingested in sufficient quantity."
Figure 4.0. Molecular structure of phenylalanine, an appetite suppressant.
Conclusion;

Many people who they have a weight problem search for a useful and good diet pill, something they can swallow down with a glass of water and watch the pounds fall off. But, there are some risks with taking those diet pills, and they do not produce the results that people are looking for. Most of diet pills are essentially an upper, which speed our metabolism and causes us to not be hungry since our body is getting energy from upper. Increasing metabolism rate dose cause to lose weight, because our body burns energy more quickly, but diet pills cause our body to consume itself. “Most of the diet pills that really work are composed mostly of an amphetamine derivative, which we may recognize from the drug like methamphetamine, like meth”. These die pills have many side effects that can be really harmful, especially for teens. These diet pills are a good diet plan to treat obesity. These pills can drop some weight really quickly but, they cannot keep the weight from coming back, just only healthy lifestyle choices, like developing good diet plan and exercise program, can prevent weight from coming back, these diet pills are just can be effected for the people with obesity because it essentially gives them a jump start to losing weight. There is a sad fact about diet pills is that many of the users of diet pills are young women whose weight is in an ordinary range, but they wish to become even thinner. So, most of diet pills are junk, they may be a good diet pill out there. Some herbs are reported to help that fat melt away, but they are not a long term fix. Using diet pills only treat the symptoms of a weight problem, not the cause. “diet pills are the symptom of a large problem in western culture”. A truly good diet pills would be one that motivated people to develop healthy eating habits and activity levels since this is the only effective way to lose weight and keep it off, so diet pills do not truly help many people, and, in truth, end up causing more problems than they solve. So using diet pills to lose weight will only disappoint us. There are numerous varieties of slimming pills that are available to consumers and none of them have proven to be effective. There has even been evidence that many diet pills can actually cause harm to those who use them. There are so many diet pills that make false claim about boosting our metabolism. The amount of energy we expend determines how quickly our body burns calories. The ingredients of diet pills that claim to alter our metabolism can alter our heart rate, and are unsafe for any person. If we want use diet pills, we should first consult our doctor and instead of relying on pills to lose weight, we should focus more on adjusting our eating habits and doing more exercise.
References


Hashimoto Disease

Leila Farmahiny

Dr. Mancini
Hashimoto diseases

Abstract

In therapeutic terms, the suffix -itis means inflammation; thyroiditis is soreness of the thyroid gland. There are five comparable kinds of thyroiditis. Although each diverse type of thyroiditis may cause unlike symptoms, many times they can be similar. Hypothyroidism is caused by an under active thyroid gland. The thyroid gland produces special cells but when thyroid cells, are attacked, the cells die. Without thyroid cells, the thyroid gland is no longer capable of producing enough thyroid hormone to maintain the body’s normal metabolism. The result is hypothyroidism, which is also known as Hashimoto thyroid.

What is Hashimoto thyroid?

In 1912, Hashimoto found a patient with a disorder of the thyroid. He found that the cause of the thyroid was diffusion of lymphocytes and change in some cell. It was discover that the thyroid secret two hormones, T3 (triiodothyronine) and T4 (thyroxine). These hormones are released into the bloodstream, controlling the rate of all the body’s or metabolism. In hypothyroidism the yield of these hormones is reduced, follow-on in reduce of metabolism. This causes a variety of symptoms. Hashimoto’s was caused by processes that damaged glands and lead to an inadequate production of thyroid hormones. The disease was named after Hararu Hashimoto, who discovered the disease. It is also referred to as chronic thyroiditis. This disease falls under the category of autoimmune diseases. Hypothyroidism is most common form of Hashimoto in North America. Mostly women between the ages 45 to 65 are affected by it. A review of crug therapy by Joanne M. Yasuda, Pharm D from Pharmacy time’s research, show’s this disease affected on women more than men’s.

<table>
<thead>
<tr>
<th></th>
<th>Unsuspected Hyperthyroidism, %</th>
<th>Unsuspected Hypothyroidism, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All women</td>
<td>&lt; 0.6</td>
<td>&lt; 0.6</td>
</tr>
<tr>
<td>Women, &gt;60 years</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Women, 40-60 years</td>
<td>0.45</td>
<td>0.5</td>
</tr>
<tr>
<td>Men, &gt; 60 years</td>
<td>0.13</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Table 1. Prevalence of Thyroid Disorders

Antibodies are produces substance cell in body, which are protection chemicals. They are usually made only to deal with unknown substances such as viruses, other microorganisms, and microgametophytes like pollen. In hypothyroidism, the antibodies and the cells that make them are intended for adjacent to the body’s own cells, in this case the thyroid cells. This is called auto-immune construction, and is almost not viable to check or overturn, so once thyroid cell injure occurs in this way, it is usually enduring. Figure1-1 show’s how Hashimoto thyroid generated.
Hashimoto's disease is similar to Graves' disease in that it occurs with about the same frequency and with the same prejudice, top age of arrangement and family history of thyroid disease or associated with autoimmune diseases.
What is the cause of Hashimoto thyroid?

Hashimoto's thyroid, like most autoimmune diseases, results from the combination of genetic and ecological triggers. An autoimmune disease causes the body to inappropriately attack the thyroid gland. However, the reason causes of this process are still unknown. Hashimoto's is also connected with a group of other autoimmune conditions, such as type I diabetes and celiac disease (digestive diseases). A patient's blood sample would show an increased number of antibodies to the thyroid peroxides enzyme but T3 and T4 hormone still show's normal. This enzyme is found within the thyroid gland. The patient's thyroid is destroyed and ultimately rendered hypothyroid. Some patients are affected by a phase of hyperthyroidism, in which case it is termed 'Hashitoxicosis', but the level hormone of hyperthyroidism is usually lower than Graves' disease.

Hashimoto is also related with primary thyroid atrophy and termed major of myxedema. The relationship between Hashimoto's disease and myxedema seem make it highly possible that non-goitrous myxedema is simply an end-stage of autoimmune construction of leaving only fibrous remnants. A role for antibodies to the TSH receptor that block the actions of TSH has also been proposed. Psychological and physiological stress can include various immunological changes. Stress also directly affects both the nervous and endocrine systems. Stress can be one of the environmental factors for thyroid autoimmunity.
Figur 1-3 differdrn between hypothyroidism hypoethyroidism

What is symptom of Hashimoto thyroid?

Hashimoto thyroid does not have any immediate symptoms. This disease progresses very slowly, so it may take many years to show symptoms or to show thyroid damage. The symptoms are actually similar to an underactive thyroid gland. Hashimoto’s evolves slowly as the gland loses the ability to produce the thyroid hormone, which is known as the hypothyroidism. This disease is not stable on a day-to-day basis and can even cause fluctuation between both hypothyroidism and hyperthyroidism. This back and forth cycle can cause a variety of symptoms. Some examples include anxiety, insomnia, weight loss, weight gain, depression and even a lowered temperature. When hypothyroidism becomes more advanced and more severe, the patient will develop puff around the eyes, a slowed heart rate, and lowered body temperature. It is difficult to diagnose a patient with Hashimoto’s until the disease has become advanced. Other symptoms such as heavy menstrual periods and a reduced sex coerce occur more often in those that have hypothyroidism.
Figure 1-4 is Pathology severe Hashimoto's thyroiditis; the normal thyroid follicles are small and greatly compact in number.

**Treatment of Hashimoto thyroid**

A Hashimoto disease has no particular treatment. Doctors can treat it with a low dose of thyroid function. Thyroid medication can substitute the hormone. How long the patient can take medication depends on thyroid level. Hormone replacement therapy usually improves the goiter condition. However, if goiter does not improve, surgery may be required. There are many different tablets for treatment, like synthroid, whose generic name is levothyroxin, or amour thyroid. They are different strengths, and it is important to take them every day. If the dose is not enough, the thyroid gland may continue to enlarge and symptoms of the hypothyroidism will persevere. This is because another side effect like increased serum cholesterol level, or risk for heart disease. On the other hand, if doses too strong, it can cause symptoms too, such as increased risk of development of osteoporosis.

Synthroid (levothyroxine sodium tablets, USP) is one of the medications using for this disease. Synthroid is contain synthetic crystalline L-3,3',5,5'-tetraiodothyronine sodium salt [levothyroxine (T4) sodium]. Because synthetic T4 is exactly produced in the human thyroid gland. Levothyroxine (T4) sodium has an empirical formula of C15H10I4N NaO4 • H2O, molecular weight of 798.86 g/mol (anhydrous), with structural formula as shown:
Synthroid, like some other drugs has side effects, if the patients use too many doses. Too much thyroid hormone causes symptoms of a hyperthyroidism. Some of these symptoms can be unsafe. These side effects include: an increased appetite, feeling hot and sweating, insomnia, high heart rate, chest pain, difficult breathing and hair loss. Also sometimes Synthroid, like some other medications, can also cause allergic reactions. The signs of an allergic reaction include an unexplained rash on body hives, itching and swelling around lip, and throat.

Armour Thyroid (thyroid tablets, USP) is a natural preparation derived from porcine thyroid glands and has a strong, characteristic odor (T<sub>3</sub> liothyronine is approximately four times as potent as T<sub>4</sub> levothyroxine on a microgram for microgram basis). They provide 38 mcg levothyroxine (T<sub>4</sub>) and 9 mcg liothyronine (T<sub>3</sub>) per grain of thyroid. The inactive ingredients are calcium stearate, dextrose, microcrystalline cellulose, sodium starch glycolate and opadry white.

Armour thyroid has the same sideeffect as synthroid. Some patients in the U.S. who do not take levothyroxine sodium (the generic name for Synthroid) are prescribed either Armour Thyroid or Thyrolar as an alternative, two drugs produced by the same manufacturer, Forest Pharmaceuticals. There is a difference between Armour Thyrolar and the levothyroxine sodium drugs. Mostly, Armour and Thyrolar are drugs provide both T4 and T3 thyroid hormones, in its place T4, as levothyroxine sodium drugs like synthroid do. An endocrinology practice believes that T4-only drugs are the only correct thyroid hormone substitute drugs. The current opinion is that everyone converts all the T4 needed into T3 automatically, and that drugs such as Armour and Thyrolar are obsolete and old-fashioned at best. Some doctors are even intense about this, and pledge that Armour has consistency problems or is dangerous, considering the fact that it was the primary thyroid substitute hormone drug for years, until Synthroid came on the market. Also, in terms of steadiness problems, the levothyroxine sodium drugs have recently come under heavy FDA fire for problems with stability and influence. A review of drug
therapy by Joanne M. Yasuda, Pharm D from Pharmacy time’s show’s how much a patient can use those drugs.

<table>
<thead>
<tr>
<th>Generic Name (Trade Name)</th>
<th>Thyroid Hormone Component(s)</th>
<th>Equipotent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desiccated thyroid</td>
<td>Natural $T_3$ and $T_4$</td>
<td>1 grain*</td>
</tr>
<tr>
<td>(Armour Thyroid, others)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liotrix (Thyrolar, Euthyroid)</td>
<td>Synthetic $T_3$ and $T_4$</td>
<td>12.5–15 mcg $T_3$, 50–60 mcg $T_4$</td>
</tr>
<tr>
<td>Liothyronine (Cytomel, others)</td>
<td>Synthetic $T_3$</td>
<td>15–37.5 mcg</td>
</tr>
<tr>
<td>Levothyroxine (Synthroid, others)</td>
<td>Synthetic $T_4$</td>
<td>50–60 mcg</td>
</tr>
</tbody>
</table>

$T_3$ = triiodothyronine; $T_4$ = thyroxine.
*1 grain (60 mg) desiccated thyroid = 60 mg $T_4$.

Table 2. Equipotent Doses of Thyroid Hormones for Replacement Therapy

Other associated disorders

Hashimoto’s thyroiditis is a common disorder of the protected system which affects the thyroid gland. However, much less often, the protected system can also harmfully affect practically any other part of the body, causing it to break down, and this propensity runs in families. Although the part of patients with Hashimoto’s thyroiditis and their genetic family will never become aware of any other autoimmune situation, they do have a statistically increased risk of emergent, subsequent disorders: Type 1 Diabetes type 1 (insulin-dependent), Graves’ disease (hyperthyroidism), Rheumatoid arthritis Pernicious anemia (incapability to attract vitamin B12, potentially causing anemia and neurology problems), Addison’s disease (adrenal failure; the adrenal gland provides cortisol to handle stress and illness), Premature ovarian failure.

Conclusion

Hashimoto’s thyroiditis is most ordinary, painless, distributed by the thyroid gland, affecting in middle aged women, particularly older women, and tends to run in families. The gland usually has a tough surface and sometimes feels lumpy. In about 50% of people with Hashimoto’s thyroiditis, the thyroid becomes underactive. In most of the rest, the thyroid remains normal. In a small number of people, the gland initially becomes overactive, after which it usually becomes underactive.

Hashimoto’s disease also produces antithyroid peroxides antibodies (anti-TPO) that cause an irritation of the thyroid gland. The end result is goiter constitution in many, and hypothyroidism is usually the end cause of long-standing Hashimoto’s disease.
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Epilepsy: An Overview of the Disorder and its Medicinal Treatments
Kristen Foster
Paradise Valley Community College
April 24, 2009
Abstract

Epilepsy is a neurological disorder that is prominent worldwide. There are four types of seizures: simple partial seizures, complex partial seizures, tonic-clonic seizures, and petit mal seizures. These four types differ by the location of the brain affected, symptomatology, duration, and etiology. There are several medicinal treatments for epilepsy, which are classified into several categories, four of which will be discussed: hydantoins, barbiturates, benzodiazepines, and succinimides. These categories differ in structure and mechanism of action.

Introduction

Epilepsy is a neurological disorder that affects millions of individuals in the United States each year. It is most often seen in young children, usually under the age of 15, and individuals over the age of 60; however, it can occur at any age. Epilepsy occurs when the nerve cells in the brain become over-activated and fires electrical currents uncontrollably, therefore causing a seizure. There are several types of seizures which are classified into categories depending on the location of the seizure and the amount of the brain that is affected. Primarily, seizures are classified as either partial or generalized seizures. Partial seizures occur only in a specific part of the brain, usually located in one hemisphere. Generalized seizures occur in both hemispheres of the brain.

Partial and generalized seizures are then divided into subcategories based on the symptoms that the individual experiences. There are two types of partial seizures: simple partial seizures and complex partial seizures. Typical symptoms that occur during simple partial seizures are confusion, jerking movements, or tingling. Individuals experiencing complex partial seizures exhibit loss of consciousness, involuntary behavior, and loss of judgment. In addition, there are two forms of generalized seizures. Firstly, there is tonic-clonic seizures, which are also known as grand mal seizures. During tonic-clonic seizures, patients initially experience a tonic phase where the muscles contract and they are immobilized, which is followed by the clonic phase where the muscles relax and stiffen continuously. The second type is absence or petit mal seizures, which is exhibited by a momentary loss of consciousness. Table 1 summarizes the different types of seizures and their symptoms.

Epilepsy types also vary in the location of the brain that is affected. Seizures can occur in the temporal lobe, frontal lobe, occipital lobe, and parietal lobe of the brain. The symptoms that patients experience also vary depending on the location of the seizure. Complex and simple partial seizures typically occur in the temporal lobe, as well as some tonic-clonic seizures. These seizures typically effect the limbic system within the temporal lobe, which is responsible for memory and emotions. Complex partial seizures and tonic-clonic seizures can also occur in the frontal lobes. There is no specific seizure type that occurs in the parietal lobe; however, patients with seizures in the parietal lobe experience visual and sensory sensations, including hallucinations, vertigo, or numbness or tingling. Seizures that occur within the occipital lobe also are an undetermined type. Symptoms that occur with seizures in this location affect the visual system causing blindness, eye fluttering, or hallucinations.
<table>
<thead>
<tr>
<th>Seizure Type</th>
<th>Simple Partial</th>
<th>Complex Partial</th>
<th>Tonic-Clonic (Grand mal)</th>
<th>Absence (Petit mal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>90 seconds</td>
<td>1 to 2 minutes</td>
<td>1 to 2 minutes</td>
<td>2 to 15 seconds</td>
</tr>
</tbody>
</table>
| Symptoms     | • No loss of consciousness  
               • Jerking on one side of the body or limb  
               • Confusion  
               • Lip smacking  
               • Repetitive motions  
               • May wander  
               • Loss of consciousness | • Body falls, stiffens, and jerks  
               • Loss of consciousness  
               • Loss of bladder and bowel control  
               • Fatigue and confusion  
               • Cry out, bite tongue, turn pale, or stop breathing | • Staring  
               • Eye blinking and twitching  
               • Lip smacking  
               • Jerking of the hands |

Causes

Epilepsy has been found to have several known etiologies; however, the actual cause of epilepsy has been found in only 28 percent of patients diagnosed with epilepsy.⁷ One known cause of epilepsy is damaged ion channels within the brain. Ion channels transmit electrical currents from one nerve cell to another. However, when the ion channel is damaged it causes the nerve to misfire and epilepsy occurs. Another cause of epilepsy is a chemical imbalance of the neurotransmitters in the brain. Neurotransmitters are the chemical messengers that transmit messages from nerve cell to nerve cell. The three neurotransmitters that are known to play a role in epilepsy are gamma aminobutyric acid (GABA), serotonin, and acetylcholine.⁷ Other causes of epilepsy include: genetic syndromes, fever, vaccinations, brain tumors, head trauma, brain abnormalities, and stroke.⁷

High fever is associated with febrile seizures, which occurs before epilepsy is developed.⁷ There also has been an association between epilepsy and vaccinations, specially the diphtheria-tetanus-pertussis vaccine; however, it has not been determined if epilepsy was a preexisting condition prior to the administration of the vaccine that consequently showed its symptomatology after the vaccine was given.⁷ Abnormalities in the brain structure can also cause seizures. Such abnormalities include: shunts used to treat hydrocephalus, hippocampal sclerosis, and cavernous angiomas. Hydrocephalus occurs when cerebral spinal fluid accumulates in the brain and causes swelling of the brain. A shunt is used to drain the fluid, which can result in seizures after the shunt is inserted into the brain. Hippocampal sclerosis is when the tissue of the brain becomes hardened causing loss of nerve cells. Cavernous angiomas are abnormal blood vessels that put pressure on nerve tissue, ultimately leading to seizures.⁷

Diagnosis

Epilepsy is diagnosed by a physician through a thorough physical examination, by obtaining the medical history from the patient, and through the use of diagnostic tools.⁸ A detailed medical history will include all the important information pertaining to the epileptic attack. The
history should include information on when the attack began, any recent illnesses, any uses of medications or drugs, any new life stressors, what symptoms were experienced, duration of the attack, were there any mental or cognitive impairments during or after the attack, and what activities were being performed before and after the attack.\textsuperscript{8}

Several different diagnostic tools are used in the diagnosis of epilepsy. Electroencephalograms (EEG) are often used in the diagnosis of epilepsy. An EEG measures the brain waves and indicates normal and abnormal brain activity.\textsuperscript{1} Computerized tomography (CT) scans are used to obtain images of the bony structure and soft tissue of the brain. Abnormalities of the brain can be seen through the use of a CT scan. Another diagnostic tool is a Magnetic Resonance Imaging (MRI), which is used to determine the proper treatment for epilepsy.\textsuperscript{1} Positron emission tomography (PET) can also been used to find brain abnormalities, such as damaged or scarred lesions on the brain.\textsuperscript{1}

Treatment

There is several different types of medications that are available for the treatment of epilepsy. Research has shown that more than half of the patients diagnosed with epilepsy have complete control over their seizures and 20 to 30 percent show a reduction in frequency of epileptic attacks.\textsuperscript{2} The types of medications used to treat epilepsy are known as anti-epileptic drugs or anticonvulsants.\textsuperscript{1} The most preferred type of treatment is monotherapy, or the use of only a single medication. In some cases, patients with seizures that are not controlled by only one medication, therefore, they are treated with polytherapy or multiple medications.\textsuperscript{2} There are several categories of anticonvulsants, which most medication are placed into. The types of anticonvulsants include: hydantoins, barbiturates, benzodiazepines, and succinimides.\textsuperscript{1} Other categories, which will not be discussed, are oxazolidinediones and adjuvants to anticonvulsants.\textsuperscript{1}

Hydantoins

Hydantoins are a class of anticonvulsants used to treat partial and tonic-clonic seizures.\textsuperscript{9} There are three types of medications that are hydantoins: ethosuximide, fosphenytoin, and phenytoin. These three medications are derivatives of hydantoins; therefore, they have similar chemical and physical properties, mechanisms, and pharmacokinetics.\textsuperscript{7} The basic structure of hydantoins consists of a heterocyclic compound containing two amines and three carbon atoms with two of the carbon atoms (carbon number two and four) double bonded to an oxygen atom. The structure of hydantoin provides the backbone for the structures of its derivatives. The molecular formula for hydantoins is $C_{3}H_{4}N_{2}O_{2}$.\textsuperscript{10} Figure 1 shows the basic structure for hydantoins.\textsuperscript{10}

![Figure 1](image-url)
Mechanisms

Hydantoins act on the motor cortex, which is located within the cerebral cortex.\(^9\) Hydantoins also reduce the activity within the brain stem. It affects the neurons within the brain causing them to release more sodium. Seizures occur when the nerve cells within the brain become overactive by excess stimulation causing the nerve cells to firing uncontrollably. The overload caused by the stimulation tends to reduce the sodium gradient causing the nerve cells to fire.\(^9\) Therefore, hydantoins are effective in preventing seizures by increasing the amount of sodium released. The mechanism of action for phenytoin is the same as hydantoins. Fosphenytoin eventually has the same mechanism of action as phenytoin since after it is administered, the body converts it to phenytoin.\(^9\)

Pharmacokinetics

Hydantoins have a high binding ability to proteins in the circulatory system.\(^9\) Specifically, phenytoin has a 90 percent binding protein and fosphenytoin has between 95 to 99 percent binding ability, meaning that 95 to 99 percent of the medication will bind to a protein receptor. Ethotoxin has a lower binding ability, with only 46 percent of the medication will bind to a protein. The maximum absorption length or the time in takes for 100 percent of the medication to be absorbed varies depending on the medication.\(^9\) Ethotoxin has a time frame of two to four hours, whereas phenytoin will be absorbed within one and a half to three hours for chewable tablets and oral suspension and four to 12 hours for capsules. Fosphenytoin will be absorbed within 30 to 60 minutes depending on whether administered intramuscularly or intravenously.\(^9\) Hydantoins are excreted through the urine and feces.\(^9\)

Side effects

There are several side effects related to the use of hydantoins.\(^9\) This class of medication has been know in cause hypotension, or low blood pressure, when the dosage is too high. They have also been found to be linked to lymphadenopathy, or diseases that occur in the lymph nodes. Such diseases can include Hodgkin disease, lymphoma, or lymph node hyperplasia.\(^9\) These medications can also liver toxicity. Other side effects can include: skin rash, itching, burning, or tingling of the skin, hyperglycemia, softening of the bones, and fertility problems.\(^9\)

Barbiturates

Barbiturates are another class of anticonvulsants that are effective in treating epilepsy.\(^11\) Phenobarbital, Primidone, thiopental, and methohexital are derivatives of barbiturates. These anticonvulsants are one of the first medications used for the treatment of epilepsy in infants and children.\(^1\) Barbiturates are effective in treating tonic-clonic and partial seizures.\(^1\) The basic skeletal structure of barbiturates is a heterocyclic ring containing four carbon atoms, two amines, and three carbonyl atoms bonded to carbon number two, three, and six. There is also two alkyl groups bonded to carbon number five.\(^12\) Figure 2 illustrates the skeletal backbone for barbiturates and the structure for Phenobarbital.\(^12\) The type of alkyl group that is bonded to carbon five determines the effectiveness and the duration of the medication. The more carbons that are present in the alkyl group decreases the effectiveness of the medication. In order to maximize the
effectiveness of the medication, short carbon chains or phenyl groups should be used.\textsuperscript{12}

![Diagram](image)

**Figure 2\textsuperscript{12}**

**Mechanisms**

Barbiturates are effective anticonvulsants because they work by suppressing the central nervous system.\textsuperscript{11} Since barbiturates suppress the central nervous system, they are also commonly used as anesthetics. This class of medications exhibits similar mechanisms of action to that of alcohol.\textsuperscript{12} They depress the central nervous system causing sedation and hypnotic sleep. Barbiturates are used less commonly since benzodiazepines are safer and produce less sedation.\textsuperscript{12}

**Pharmacokinetics**

When a barbiturate is administered, it immediately crosses the blood brain barrier and diffuses from the brain to the rest of the body.\textsuperscript{11} Typically, these medications are short acting due to their lipid solubility. Barbiturates are also immediately acting, meaning that some derivates start taking effect within eight to ten minutes if administered rectally or 30 to 40 seconds if administered intravenously.\textsuperscript{11} The time frame it takes for the plasma levels to have absorbed 50 percent of the medication is between three to eight hours; this level is known as the plasma half-life. These medications are excreted through the urine.\textsuperscript{11}

**Side Effects/Contraindications**

Barbiturates should not be given to patients who have been diagnosed with cardiovascular disease, hypotension, asthma, liver or kidney disease, or anemia. Patients with lesions in the lower bowel, gastrointestinal bleeding, rectal inflammation, or who have had rectal surgery should not be given barbiturates through rectal suspensions.\textsuperscript{11} The common side effects of barbiturates includes: pain, swelling, or necrosis at the injection site, respiratory problems, apnea, or hypotension may also occur.\textsuperscript{11}

**Benzodiazepines**

Benzodiazepines are antianxiety medications that have also been found to be effective in treating generalized and partial epilepsy.\textsuperscript{1} Benzodiazepine derivatives include: diazepam, lorezepam, oxazepam, and clorazepate.\textsuperscript{13} The structure of benzodiazepines and its derivatives are very similar, all having the same parent backbone. The molecular formula for benzodiazepine is \( C_9H_8N_2 \) with a molecular weight of 144.17 grams per mole.\textsuperscript{14} The basic structure for
benzodiazepines is a benzene ring connected to a diazepine ring. Benzene rings are composed of six carbons and three double bonds. Diazepine rings contains seven members, with five of those members being carbon atoms and two nitrogen atoms, and three double bonds. Figure 3 represents the basic structure of benzodiazepines.

![Figure 3](image)

**Mechanisms**

Benzodiazepines bind to specific benzodiazepine receptor sites located within the brain. The two benzodiazepine receptor sites that have been found are BZ₁ and BZ₂, which are associated with different cognitive functions. BZ₁ has been found to be linked with sleep mechanisms and BZ₂ receptors effects memory, motor, cognitive, and sensory functions. Once the benzodiazepine binds to one of the receptors, it causes inhibitory neurotransmitters, specifically gamma-amino butyric acid, to be released. Benzodiazepines are used as anticonvulsants because they effect the brain stem. They are effective by decrease the brain activity by decreasing the spike and wave discharges that occur during epilepsy.

**Pharmacokinetics**

The benzodiazepine derivatives all vary in their absorption, distribution, and metabolism depending on the type of medication. All of the derivatives have a protein binding ability between 80 and 98 percent; specifically, diazepam has a 98 percent protein bind ability, lorazepam has a 85 percent binding, and oxazepam has a 97 percent binding ability. The time it takes for the plasma levels to have absorbed 50 percent of the medication also varies between derivate.

Diazepam is absorbed with 30 minutes to two hours, whereas lorazepam and oxazepam take two to fours hours to be absorbed. Most benzodiazepines are metabolized within the body to active metabolites, causing a longer half-life, which means they stay effective longer. Only a few of the derivatives, such as alprazolam, lorazepam, and oxazepam, are broken down to inactive compounds which has a short duration. Benzodiazepines are typically excreted through urine.

**Side Effects/Contraindications**

Benzodiazepines should not be given to patients with glaucoma, liver disease, or children under the age of six months. These medications should not be used during pregnancy or lactation since they can cross the placenta and are excreted in breast milk. These medications have been shown to affect cognitive function, such as causing anxiety, insomnia, hallucinations, excitement, anger, and mania and hypomania. It has also been found that when used in patients with multiple forms of epilepsy, it has brought on tonic-clonic seizures; therefore, another anticonvulsant should be used in combination with a benzodiazepine to control seizures. The most frequently
experienced side effects are drowsiness and dizziness.\textsuperscript{13}

**Succinimides**

This class of anticonvulsants are used to treat absence seizures.\textsuperscript{15} Succinimides should not be used when other types of seizures are present.\textsuperscript{1} Medications that are considered succinimides include: ethosuximide and methsuximide.\textsuperscript{1,15} The backbone structure of succinimides is a heterocyclic ring containing four carbon atoms, a nitrogen atom, and two carbonyl groups bonded carbon numbers one and three. Ethosuximide has this skeletal structure with a methyl group and ethyl group attached to carbon number four. The molecular formula for ethosuximide is \( C_{7}H_{11}NO_{2} \) with a molecular weight of 141.17 grams per mole.\textsuperscript{16} Figure 4 illustrates the structure of ethosuximide.\textsuperscript{16} Methsuximide is similar in structure to ethosuximide, except that it contains a methyl group bonded to the nitrogen and another methyl group and a phenyl group bonded to carbon number three. It has a molecular formula of \( C_{12}H_{13}NO_{2} \). Figure 5 represents the structure of methsuximide.\textsuperscript{17}

![Figure 4](image)

![Figure 5](image)

**Mechanisms**

Succinimides appear to work within the motor cortex by depressing its function. These medications decrease abnormal brain activity that occurs during loss of consciousness.\textsuperscript{15} In some patients with epilepsy, certain stimuli, such as environmental pressures or flashing lights, can trigger a seizure to occur. Typically, these patients have a lower threshold in their central nervous system, so any stimulation can potentially trigger a seizure. Succinimides increase that threshold, so when the seizure-provoking stimuli are present, seizures are less likely to occur.

**Pharmacokinetics**

This class of medications are absorbed relatively quickly. The serum will absorb 50 percent of the medication within three to seven hours for ethosuximide and one to four hours for methsuximide.\textsuperscript{15} These medications are metabolized to inactive metabolites and have a short duration. Succinimides are usually excreted as inactive metabolites through the urine.\textsuperscript{15}
Side Effects

Succinimides has been found to cause lupus and abnormal liver and kidney functions.\textsuperscript{15} They also have been found to increase the occurrence of tonic-clonic seizures if the patients suffers from more than one type of seizure disorder. There are multiple side effects that occur with succinimides. Common side effects include drowsiness, dizziness, headache, blurred vision, and headache. The side effects can also occur in the gastrointestinal tract, typically causing nausea, vomiting, cramps, weight loss, and constipation.\textsuperscript{15}

Conclusion

Epilepsy affects millions of individuals worldwide.\textsuperscript{1} Epilepsy can cause several life changes that can be devastating to the individual. The four types of seizures are: complex partial seizure, simple partial seizure, tonic-clonic, and absence seizures.\textsuperscript{2} The different types of seizures are exhibited by different symptomatology, duration, and location of the brain that is affected. There are several different categories of anticonvulsants that are used to treat epilepsy. A few of the categories are hydantoins, barbiturates, benzodiazepines, and succinimides. Each class of medication are effective in treating the different types of epilepsy.\textsuperscript{9}

I personally have witnessed an individual experience epileptic attacks and they are rather frightening to observe. In addition, I have seen the life difficulties that have arose due to these epileptic attacks. Epilepsy can severely affect an individual’s life by preventing them from working, driving, or doing normal daily activities. Due to medical advances and the development of medications, these individuals are able to lead normal, healthy lives. I think it is important to have a basic knowledge and understanding of the treatments that are available for illnesses that may affect you or your family.
References

Hormone Replacement Therapy in Women:
The Facts, Myths and Considerations of Bioidentical Hormones in Treating Menopause and Female Sexual Dysfunction.

Kendra Gray
March 27, 2009

Hormone therapy has received a lot of media attention, particularly for post-menopausal women and women with sexual dysfunction. However, there is considerable confusion as to treatment options for women. FDA vs. Compounding Pharmacies, gender bias within the pharmaceutical company and a lack of consistent vocabulary for the issues being debated have left the public and practitioners more confused and misinformed than ever before. This paper attempts to present a fair and balanced discussion of the relative merits of each side of the story and provide a baseline vocabulary for a continuing debate.

The North American Menopause Society (NAMS), a non-profit organization whose membership includes leaders in the field from clinical and basic science experts from medicine, nursing, sociology, psychology, and more are uniquely qualified to provide information that is both accurate and unbiased, and not for or against any point of view are considered one of the top authorities on menopausal issues. NAMS states that menopause is “a normal, natural event—defined as the final menstrual period and usually confirmed when a woman has missed her periods for 12 consecutive months (in the absence of other obvious causes).”

Menopause is associated with reduced functioning of the ovaries due to aging, surgical removal, or damage such as that seen in some cancer patients. Although menopause is a natural occurrence marking the termination of the female reproductive cycle, the symptoms associated with these changes, ranging from hardly noticeable to severe, can interfere with a woman’s life. Signs and symptoms include amenorrhea, reduced fertility, hot flashes, sleep disturbances, headache, memory & concentration changes, mood swings, depression, anxiety, vulvovaginal symptoms, changes in sexual function and other concerns.

There are five further classifications of menopause according to NAMS: natural, perimenopause, induced, premature and post menopause. Natural menopause occurs spontaneously and permanently. Its onset generally ranges from 40 to 58 in the western world with the average age approximately 51. Genetics has been shown to influence the timing of menopause; women experience menopause around the same age as their mother or sisters. Smoking has been shown to cause menopause to begin approximately two years earlier when compared to nonsmoking individuals. Perimenopause is the intermediary time of 6 years or more immediately prior to natural menopause when changes begin, and includes 1 year after menopause. Induced menopause is caused by a medical or surgical
Sexual dysfunction in women can be classified into four categories: desire disorders, arousal disorders, orgasmic disorders, and pain disorders. Hypoactive disorders are a subclass of desire disorders and can be connected to estrogen and testosterone insufficiencies. Although Nancy Philips, author of Female Sexual Dysfunction, claims in peri- and postmenopausal women the relationship between hormones and sexuality is unclear, she admits estrogen replacement therapy has been shown to correlate positively with sexual activity, enjoyment and fantasies—"the latter thought to represent desire." NAMS' position statement is that endogenous testosterone levels (those produced within the self) have not been clearly linked to sexual function in postmenopausal women. [See Addendum 1: Supplemental Mean Plasma Steroid Levels in Healthy Women]

Published evidence from randomized controlled trials, although limited, indicates that exogenous testosterone, both oral and non-oral formulations, has a positive effect on sexual function, primarily desire, arousal, and orgasmic response, in women after spontaneous or surgically induced menopause. [See Addendum 2: Testosterone vs. Age in Women] Unfortunately there are no FDA approved testosterone therapies for women despite what seemed to be a perfectly safe option, Intrinsa, developed by Proctor and Gamble and currently in use in Europe. The acknowledgment by the FDA of a need for a product that treats hypoactive sexual desire disorder in surgically menopausal women is a small step towards the recognition of sexual dysfunction in women's health. With anywhere from 25% to 63% of women (in contrast to only 10% to 52% of men) experiencing sexual dysfunction, it is distressing that so little is being done to help this population.

The reason that this issue appears to be neglected is multifold, including the intricacies that are involved with gender differences in sexual response, the lack of research, and general gender bias in relation to women's sexual health. At the end of 2003, the FDA
approved its third drug, Cialis® (tadalafil) for erectile dysfunction. The side effects of male enhancement drugs range from blindness, hearing problems, heart attack and death. According to the National Institutes of Health (NIH) some side effects associated with Viagra include headache, upset stomach, diarrhea, dizziness or lightheadedness, flushing (feeling of warmth), and stuffy nose. In comparison, testosterone therapy in women, can cause hirsutism, (facial hair growth) and acne; these are hardly side effects worth warranting denial for a product to help women cope with a disease in which men are getting plenty of assistance with more severe side effects.

The problem lies not only in gender bias but misdirected fear. There exists today much controversy and confusion over hormone replacement therapy, bioidentical hormones, and menopausal hormonal therapy. This stems largely to the 2002 abrupt termination of the trial of Estrogen Plus Progestin by The National Heart, Lung, and Blood Institute of the National Institutes of Health due to increased breast cancer risk, and lack of overall benefit. “The large multi-center trial,” a component of the Women’s Health Initiative, found increases in coronary heart disease, stroke, and pulmonary embolism in study participants on estrogen plus progestin compared to women taking placebo pills. Originally the study was scheduled to run until 2005. Prior to the trial, the FDA had already approved use of menopausal hormonal therapy products such as Premarin® and Prempro™ for treating moderate-to-severe hot flashes and night sweats, moderate-to-severe vaginal dryness, and prevention of osteoporosis associated with menopause. However, due to the trial physician instructions were changed to make additional disclaimers noting “serious risks [for] postmenopausal women who use or are considering using estrogen or estrogen with progestin treatments” and strongly recommend discussing their personal risk factors and options with their healthcare providers.

This lack of clarity in the industry is due to semantic ambiguity: what are bioidentical hormones, what are synthetics, and what is natural? The confusion with these terms further becomes adulterated with media, healthcare providers and consumers’ misuse. The results of the Women’s Health Initiative caused such sensationalization and a scare about hormone therapy in women that 70% of women who were taking hormone therapy discontinued it, and 26%
of women lost confidence in medical recommendations in general.¹ The Women’s Health Initiative trial of combined estrogen and progestin (as Prempro) reported blood clots, heart attacks, strokes and breast cancer.⑤ Concerned physicians stopped recommending hormone replacement therapy in many cases, leaving their patients searching for answers. Desperate for solutions, the women of America sought alternative remedies and found themselves tuned into Oprah, Susanne Summers, Robin McGraw and Michael Platt who found the "The Juice of Youth and "natural" miracle cure for the sometimes debilitating symptoms of hormone loss. Compounding pharmacies began increased marketing of these options for patients who were understandably concerned about taking Premarin® or Prempro™ after the reported Women's Health Initiative risks and were idolized for offering a solution. FDA approved hormones that were and are proven to be bioidentical and have less severe side effects were ignored; a classic case of throwing the baby out with the bathwater.

Dr. Joanne Pinkerton, MD professor and Vice Chair, Department of Obstetrics and Gynecology, and Director of The Women’s Place Midlife Health Center at the University of Virginia Health directly challenges the media and celebrity interpretation of bioidentical hormones with her 10 erroneous beliefs patients have about compounded hormones (Figure 1.1)¹² Her opinions are further supported by The North American Menopause Society. In a consumer education publication NAMS have confirmed that the term “bio-identical hormones” or “natural hormones” is used differently by consumers, the media, and healthcare providers. They state that scientists and healthcare providers define bio-identical hormones are those that are chemically identical to the hormones produced by women. “A woman’s body can make various estrogens (such as 17-beta-estradiol, estrone, and estriol) as well as progesterone, testosterone, and other hormones. Thus, bio-identical hormone therapy can mean a medication that provides one or more of these hormones as the active ingredient.”¹³

Hormones have been produced to be chemically exact duplicates of some of these naturally occurring, bio-identical hormones. The significance of this is that there are well-tested, government-approved, brand-name hormonal prescription drugs. Several drugs contain 17-beta-estradiol (Estrace and generic oral tablets, Estrace vaginal cream, all the estrogen skin patches, and now topical gels). There are two progesterone products (Prometrium oral capsules and Crinone vaginal gel)¹³,¹⁴ Figure 1.2.
With the fear over “synthetic hormones”, lab created, or “natural hormones” there is still more to sort out. Synthetic hormones are thought of as lab created chemicals. In the examples given in Figure 1.2, the hormones are lab created but are exact carbon copies of the naturally occurring molecule that ovary the human body [ovary] creates. In contrast, Premarin®, Prempro™ and Provera are intentionally different; they are manufactured and patented by pharmaceutical companies and are not the exact hormone molecule produced by the body. For example, Premarin is “a mixture of conjugated estrogens obtained exclusively from natural sources.” This is deceptive, as upon further reading and research the natural sources are sodium salts of water-soluble estrogen sulfates blended to represent the average composition of material derived from pregnant mares’ urine. It is composed of 17-alpha-estradiol, a seemingly small but grossly significant difference that changes the risk factors immensely.  

Persons who believe that all plant-based hormones are natural are incorrect. According to the American Cancer Society wild yams, the base for many synthetic hormones, cannot supply the body with progesterone. The yam does, however, contain the chemical diosgenin, which can be converted into progesterone through a “lengthy process” in the lab. Thus in many cases the “natural” yam hormones are actually chemically altered and may or may not end up being synthesized to a bioidentical estrogen in the examples given above. Additionally, all bioidentical hormones—both individually compounded formulations and pharmaceutical products—come from the same soy or wild yam precursors before they are chemically converted to the different hormones.

Lack of education has many people believing that compounded hormones, or those custom mixed at compounding pharmacies, are the only safe hormones available. Others claim that big drug companies do not make bioidentical hormones because they cannot patent the natural molecule and make money on them. Both of these assertions are incorrect. Compounding pharmacies, according to The International Academy of Compounding Pharmacists, are “the long-established tradition in pharmacy practice that enables physicians to prescribe and patients to take medicines that are specially prepared by pharmacists to meet patients’ individual needs.” NAMS’ position on compounding pharmacies is that “concern arises with the bioidentical hormone medications that are ‘custom-compounded’ (custom-mixed) recipes prepared by a pharmacist following an individual prescriber’s order for a specific patient. These medications do not have FDA approval because individually mixed recipes have not been tested to prove that the active ingredients are absorbed appropriately or provide predictable levels in blood and tissue. Further, there is no scientific evidence about the effects of these compounded medications on the body—both good and bad.” Custom-compounded hormones do provide certain benefits, such as individualized doses and mixtures of products and dosage forms that are not available commercially. Another example is the case of Proveritum, a FDA approved human bioidentical hormone, which contains peanut oil; a woman with peanut allergy may be forced to a compounding pharmacy for a similar alternative. Risks to the consumer are real as compounds do not have government approval because individually mixed recipes have not been tested and verified that they are absorbed appropriately, provide predictable levels in blood and tissue, are consistent amounts of medication, and are sterile.
Expense is also an issue, as many custom-compounded preparations are viewed as experimental drugs and are not covered by insurance plans. Furthermore, women are willing to pay out of pocket, unaware that there are safe alternatives that their insurance company will cover.\textsuperscript{12,19} Interestingly, Wyeth, maker of Premerin\textsuperscript{R} and Prempro\textsuperscript{TM} filed a “Citizens Petition” with the FDA to restrict compounding and dispensing of bioidentical hormones (i.e., estradiol, progesterone, and testosterone) for women needing hormone therapy. This attempt to limit choices for women is discriminatory particularly given the lack of options and information for women at this time.\textsuperscript{18}

As recently as January 8, 2009 the FDA has taken action against compounded menopause hormone therapy drugs sending warning letters to seven pharmacy operations that the claims they make about the safety and effectiveness of their so-called "bio-identical hormone replacement therapy," or "BHRT" products are unsupported by medical evidence, and are considered false and misleading by the agency. The FDA is concerned that unfounded claims like these mislead women and health care professionals particularly when distributed for off label use such as for the treatment of Alzheimer’s disease, stroke, and various forms of cancer. According to the FDA the pharmacies on the warning list compound hormone therapy drugs that contain estriol as well as progesterone and estrogen. No drug product containing estriol has been approved by the FDA and the safety and effectiveness of estriol is unknown.\textsuperscript{20} As this article has already discussed the FDA warns “bio-identical hormone replacement therapy” (BHRT) is a marketing term and not an accurate description or definition of a product. A commonly held myth is that if bio-identical products were unsafe, there would be a lot of reports of bad side effects. Many people fail to understand that because bio-identical products are typically compounded in pharmacies, they are not required to report adverse events associated with compounded drugs.\textsuperscript{21}

Compounding pharmacies argue that they are regulated, just not by the FDA. The National Association of the Boards of Pharmacy and the United States Pharmacopeia, the national standard setting organization for pharmacy and pharmaceutical manufacturers, have established standards for compounding and the pharmacies are regulated on a state level. The International Academy of Compounding Pharmacists advertise that materials that make up the medications are all sourced from licensed FDA-registered manufacturers. Compounding pharmacies fill the

\textbf{Figure 1.3}

\textit{Route of Delivery Affects Risks and Benefits}

Bioidentical and foreign hormone products offer different benefits. The route of delivery for hormones can also change the response, side effects and risks. Consider the following examples (see references):

(a) transdermal 17-beta estradiol has been shown to have a lower risk of gallstone formation than oral estrogens, particularly CEE and ethinyl estradiol.

(b) Vaginal progesterone has fewer sedative and depressive side effects than either oral micronized progesterone or oral MPA.

(c) Oral micronized estradiol has less potential to stimulate formation of renin substrate and raise blood pressure than does oral CEE, and estradiol used non-orally can lower blood pressure significantly.

(d) Non-oral bioidientical testosterone has a lower risk of adverse lipid effects (i.e. decrease in HDL cholesterol) than does oral methyl testosterone.

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void by drug companies whose manufacturing is based on profitability. They provide many patients with unique health needs compounds they otherwise cannot find in correct dosages or forms. The critical issue is ultimately that patients and their families need a balanced, medically-sound approach to address all of these issues and enforcement of existing regulations to correct abuses without further restricting the choices of patients. Figure 1.3 illustrates the critical need for compounding pharmacies as they allow for patients with different risk profiles who may be having adverse side effects with one method of delivery to find the therapy regimens to meet their needs.

It should also be mentioned that bio-identical hormones are not always better, safer or ideal. For example, women requiring contraceptive benefits from their hormone therapies need a stronger synthetic, ethinyl estradiol, which is used in birth control pills worldwide, and other progestins, synthetically manufactured and not a human bioidentical. In the case of contraceptives higher potency of chemically different estrogens and progestins are preferred as they have the ability to reliably suppress ovulation and are more effective. Bioidentical 17-beta estradiol and progesterone do not suppress ovulation enough to provide reliable contraception. “In fact, bioidentical estradiol and progesterone are used in fertility treatment for cycle management to enhance fertility.” Endometriosis is another example of synthetic, non-bioidentical progestins being superior because they are more potent than progesterone and better suppress pelvic pain from bleeding of endometrial tissue in the pelvis. The progestins also suppress growth of endometriosis and help prevent further pain and pelvic damage.

Pharmaceutical companies, compounding pharmacies and healthcare providers have their roles and opinions as to what is best. Undoubtedly, the ideal is to have these groups working collaboratively and synergistically to offer options and solutions to the people they claim to serve. There is no single panacea or product that will work for all women and their needs. Individual risk factors need to be taken into account and healthcare providers and their patients should work collectively to decide on what is ideal. As diverse a population exists, there must equally be diversity of treatment options. There are strengths and weakness to both synthetically manufactured human bio-identical hormones as well as a proper place for synthetic non-bioidenticals. The FDA has a responsibility to monitor drugs and therapies for safety and effectiveness, but ultimately the patient should have the right to determine what they feel is best for their health and be able to have the option of using compounding pharmacies if they feel the benefits outweigh the risks. Patients need to take ownership of their health and educate themselves using reliable sources. Although celebrities are great at marking products they are not physicians. If they are benefitting financially from what they are advocating skepticism and caution should be used. Patients should have a take-charge attitude about their health and be proactive. As their own advocates, when speaking to their healthcare provider about what they see in the media, patients should be fully aware of the side effects and contradictions in terms of treatments and prescriptions they are requesting. They must also be fully responsible of the consequences for failing to follow physician recommendations.
### Related Molecules†

<table>
<thead>
<tr>
<th>Compound</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genistein</strong></td>
<td>Isoflavone and phytoestrogen with antineoplastic activity.</td>
</tr>
<tr>
<td><strong>Coumestrol</strong></td>
<td>Coumestans are estrogen-like substances (phytoestrogens) made by some plants. Coumestan may have anticancer effects.</td>
</tr>
<tr>
<td><strong>Trans-resveratrol</strong></td>
<td>Isoflavone and antioxidant and a type of polyphenol.</td>
</tr>
<tr>
<td><strong>Biochanin A</strong></td>
<td>Isoflavone found in soy products. Soy isoflavones (estrogen-like substances made by some plants) are being studied to see if they help prevent cancer.</td>
</tr>
<tr>
<td><strong>Estradiol</strong></td>
<td>A form of the hormone estrogen.</td>
</tr>
<tr>
<td><strong>Diethylstilbestrol</strong></td>
<td>A synthetic form of estrogen, a female hormone. It was prescribed between 1938-1971 to help women with certain complications of pregnancy. Daughters of women who took DES have been linked to uncommon cancer of the vagina or cervix, and in increased risk of breast cancer.</td>
</tr>
<tr>
<td><strong>Ipriflavone</strong></td>
<td>Synthetic isoflavone. Proposed inhibitor of osteoclasts found to induce lymphocytopenia in a significant number of women.</td>
</tr>
<tr>
<td><strong>Tamoxifen</strong></td>
<td>A drug that interferes with the activity of estrogen, a female hormone. Tamoxifen has been used for more than 30 years to treat breast [and other cancers] in women and men.</td>
</tr>
<tr>
<td><strong>Enterolactone</strong></td>
<td>Lignans. Produced by the intestinal microflora from precursors in plant foods and has been implicated in protection against cancer.</td>
</tr>
</tbody>
</table>

†Drawings Courtesy of Sigma-Aldrich Retrieved March 23, 2009 http://www.sigmaaldrich.com/
Addendum 1
Mean Plasma Steroid Levels in Healthy Women

<table>
<thead>
<tr>
<th>Reproductive Age&lt;sup&gt;a&lt;/sup&gt; (n = 15)</th>
<th>Naturally Menopausal (n = 18)</th>
<th>Oophorectomized (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrone (pg/ml)</td>
<td>58</td>
<td>49</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>40</td>
<td>20&lt;sup&gt;**&lt;/sup&gt;</td>
</tr>
<tr>
<td>Testosterone (ng/dl)</td>
<td>44</td>
<td>30&lt;sup&gt;**&lt;/sup&gt;</td>
</tr>
<tr>
<td>DHT (ng/dl)</td>
<td>30</td>
<td>10&lt;sup&gt;**&lt;/sup&gt;</td>
</tr>
<tr>
<td>Androstenedione (ng/dl)</td>
<td>166</td>
<td>99&lt;sup&gt;**&lt;/sup&gt;</td>
</tr>
<tr>
<td>DHEA (ng/dl)</td>
<td>542</td>
<td>197&lt;sup&gt;**&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Mean value during early follicular phase

**P<0.01 for comparison with reproductive age

<sup>p</sup>P<0.05 for comparison with naturally menopausal

Adapted from Vermeulen, *J Clin Endocrinol Metab* 1976;42:247

Addendum 2
Total Testosterone vs. Age
Age in Normal Women

![Graph showing correlation between age and total testosterone](image)

R = -0.54
P < 0.003

Adapted from Zumoff et al. *J Clin Endocrinol Metab* 1995; 80: 1430
References


Green Chemistry and the Pharmaceutical Industry:
How Green Chemistry is Impacting the Next Generation of Pharmaceuticals

Scott Harvey

Organic Chemistry II
Instructor: Dr. Hank Mancini
04-02-2009
Green Chemistry and the Pharmaceutical Industry:  
How Green Chemistry is Impacting the Next Generation of Pharmaceuticals

The nature of Green Chemistry involves the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. Green chemistry can be applied throughout the production process, including the design, manufacture, and use of a chemical product. When the costs of inefficient chemical processes and waste treatment are considered, the financial benefits of this approach become obvious. The pharmaceutical industry is hoping that Green Chemistry can not only provide a framework for producing drugs that limit their impact on the environment, but also cuts costs.

The pharmaceutical industry continues to maintain its position as one of America’s top industries despite billions of dollars in annual revenue disappearing as profitable drug patents expire. New pharmaceuticals are being developed to fill this void, but with a cost of over 1 billion dollars to bring a drug to the market, cost cutting strategies must also be implemented. The pharmaceutical industry is in general agreement that Green Chemistry must be a part of the solution. Green Chemistry can not only cut the cost of drug development, it can also lower the production costs of existing drugs. Green Chemistry is the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances. Green chemistry can be applied throughout the entire production process, including the design, manufacture, and use of a chemical product. Unlike many other green alternatives, Green Chemistry can be a fiscally responsible solution in addition providing a more sustainable way of producing drugs.

Based on a review of current literature, this study gives a brief explanation of some of the current scientific understanding of how Green Chemistry can impact the future of the pharmaceutical industry. By searching abstracts from current Chemistry and Pharmaceutical journals a large amount of research was found relating to both the principles of Green Chemistry and the ways that these principles can be applied to the pharmaceutical industry. Green Chemistry is the universally accepted term used to describe the movement towards more environmentally acceptable and sustainable chemical processes and products. The 12 principles of Green Chemistry are:

1. Prevention of Waste: Design chemical syntheses to eliminate waste and leave no chemicals to be treated or disposed of.
2. Atom Economy: Design chemical syntheses so that the final product contains the maximum proportion of the starting material.
3. Less Hazardous Chemical Synthesis: Design syntheses so that they produce little or no toxic effects on humans and the environment
4. Design Safer Chemicals: Design chemicals that have no toxic effects on humans.
5. Use Safer Solvents: Avoid using toxic solvents and separating materials
6. Design for Energy Efficiency: Design chemical syntheses that run at room temperature and standard pressure.
7. Use Renewable Feedstock: Use raw materials and feedstock that are renewable instead of the traditional fossil fuel feedstock.
8. Reduce Chemical Derivatives: Derivatives require extra reagents and produce waste.
9. Use Catalysts: Using catalysts rather than stoichiometric reagents reduces waste and catalysts can be recovered and reused.
10. Design for Degradation: Chemicals and products should breakdown naturally and should not pollute the environment.
11. Real-Time Analysis for Pollution Prevention: Create in-line monitoring systems to evaluate the efficiency of reactions in real-time.
12. Inherently Safer Chemicals for Accident Prevention: Design chemicals and products that limit the potential for accidents such as burns, fires, and explosions. [6]

The Green Chemistry Guidelines are meant to direct everything from research and development to production and post consumer degradation. As is the case with many environmentally friendly alternatives, the short-term cost of adhering to the Green Chemistry model is made up for in the long-term benefits. It is expected that more than $60 billion dollars of revenue will be lost to generic rivals in the next decade as profitable drug patents expire. [7]

In 1997 the Green Chemistry Institute was formed as a not-for-profit corporation meant to promote Green Chemistry, and in 2001, the Green Chemistry Institute joined forces with the American Chemical Society to form the American Chemical Society Green Chemistry Institute. [8] As the Green Chemistry movement gained momentum, the pharmaceutical industry, as one of the industries responsible for a large amount of toxic environmental waste, partnered with the ACS GCI to form the ACS GCI Pharmaceutical Roundtable. The current ACS GCI Pharmaceutical Roundtable membership consists of prominent pharmaceutical companies: AstraZeneca, Boehringer-Ingelheim, Eli Lilly and Co., GlaxoSmithKline, Johnson and Johnson, Merck & Co. Inc., Pfizer Inc., Shering Plough, and Wyeth. These nine companies have been leading the way in implementing the Green Chemistry guidelines into the production of Pharmaceuticals. [9] They have educated their workers and the public, influenced current research, and made Green Chemistry information more available to the public. Through their efforts the “Green Chemistry Movement” has received considerable press and become a major force in shaping the future of the pharmaceutical industry.

The ACS GCI Roundtable has put together a list of areas in need of advancement in order to make Green Chemistry a reality. Topping the list was the need for solvent replacements that can work in a variety of reactions and lessen or eliminate toxic byproducts. Solvents are used to
dissolve reactants, and also to extract and purify products. In the production of pharmaceuticals, the ten most commonly used solvents account for 80% of all solvents used and are by far the most environmentally damaging aspect of the drug production process. Many common solvents not only pose environmental hazards, but also have safety concerns for those who work with them. For this reason solvents must be captured, recycled, or incinerated at considerable financial costs to the manufacturer. The need for cheap and environmentally friendly alternative solvents created an area of research that has received much attention from the scientific community. Carbon dioxide has been recognized as a possible replacement solvent for years but its inability to dissolve many organic substances limited its usefulness. With the force of the green chemistry movement behind it new research has lead to the discovery of several uses for carbon dioxide that could have a significant impact on the way that drugs are discovered, developed, and delivered to the patient.

Professor C.A. Liotta of the Georgia Institute of Technology has developed the use of supercritical carbon dioxide as a solvent that could replace some of the traditional toxic solvents used in chemical processes. Carbon dioxide is the second cheapest solvent available (water is first) and is environmentally friendly. In its gaseous state carbon dioxide has limited use as a solvent, but when carbon dioxide is warmed to 31°C and compressed to 1,100 psi, it acts as a solvent that can work for some chemical reactions. At this temperature and pressure the carbon dioxide is said to be a supercritical fluid. Supercritical fluids are created by heating and pressurizing a substance to the point where the liquid density and the vapor density are equal, and it is at this point that the phase barrier is blurred. The properties of supercritical fluids are unique in that they can behave as both a liquid and a gas. Specifically, they can diffuse through solids as gasses can but can also dissolve substances like a liquid. It is this ability that gives supercritical carbon dioxide its unique abilities as a solvent. Although this research has provided new opportunities, there are also new complications that need to be overcome before we will see the widespread use of supercritical carbon dioxide as a replacement solvent. For example, supercritical carbon dioxide as a solvent is only useful for a small amount of reactions due to its inability to dissolve polar substances or large molecules (molecules containing more than 20 carbon atoms). Although the use of some traditional solvents, such as methanol, can
increase the solubility characteristics of supercritical carbon dioxide, there have been efforts to discover environmentally benign techniques for achieving the same results.

Recently, microemulsion research has provided a way for supercritical carbon dioxide to be a more useful solvent in large-scale industrial chemical processes. Microemulsions from carbon dioxide have unique characteristics that solve some of the problems of early supercritical carbon dioxide solvents. Specifically, microemulsions are small (5-100 nm), thermodynamically stable, and are capable of dissolving many polar substances in microemulsion fluids. Microemulsions consist of an aqueous phase, oily phase, a surfactant and a co-surfactant. The surfactant allows the oil and aqueous portions to become miscible and during this process extremely small droplets, or emulsions form. By utilizing the properties of microemulsions formed by carbon dioxide, many more polar species are able to be dissolved and the usefulness of carbon dioxide as a solvent is greatly increased. Further advancements have been seen in the development of surfactants that further improve carbon dioxide solvent potential in both the liquid and supercritical phase.

Professor Joseph DeSimone of the University of North Carolina at Chapel Hill has developed nonionic surfactants that improve carbon dioxide’s ability to dissolve polymer latexes. By incorporating CO2-philic and CO2-phobic molecules into polymer chains, DeSimone was able create polymers that would break apart in the presence of both supercritical and liquid carbon dioxide. Breakthroughs in surfactant modified carbon dioxide and supercritical carbon dioxide are giving chemists alternatives to traditional solvent and opening new avenues for future research. Although this research is continuing, there is hope that carbon dioxide can replace some of the 30 billion pounds of traditional solvents used each year worldwide.

Besides advancements in the use of carbon dioxide as a solvent, supercritical carbon dioxide has been used to improve the way that drugs are delivered into the body. Polymer drug coatings have been used for years to slowly deliver drugs into the body as the benign coating is dissolved by the body; however the traditional process involves high heat and harmful solvents and only works on small-molecule drugs. Since many new pharmaceuticals are large-molecule drugs that are susceptible to molecular breakdown when the traditional method for polymer coating is used, a new method for delivery of these drugs has been a necessary advancement. Besides the prohibitive nature of high heat processes, the cost of heating this process as well as the cost of solvent treatment, makes a non-toxic, low temperature alternative financially beneficial for the
pharmaceutical industry as well. Professor Steve Howdle of the University of Nottingham in Nottingham, England has used supercritical carbon dioxide to create polymer drug coatings at low temperature that allow sophisticated drugs to receive a slow-release polymer coating. Howdle’s method allows delicate pharmaceuticals to be wrapped in a polymer coating at low temperatures and introduced to the body in very controlled amounts. In his technique, supercritical carbon dioxide is used to soften the polymer at low temperature at which point the drugs can then be mixed in and the coating is added without molecular breakdown. The work of Professor Howdle has opened a new door for the delivery of breakthrough drugs and given new life to this area of research and should play a major role in the drugs that are available in the near future. Besides carbon dioxides use as a solvent, it has also been used to advance the instrumentation used in the drug production process. Supercritical fluid chromatography has been developed by Merck & Co. as a cheap and environmentally friendly alternative to other chromatographic instruments. Supercritical fluid chromatography provides faster analysis, cuts energy consumption, lowers manpower needs, and the carbon dioxide can be recycled.

In addition to the need for better solvents, the ACS GCI Pharmaceutical Roundtable also identified the need for more efficient chemical processes as an area that can immediately impact the environmental footprint of the pharmaceutical industry. Improving syntheses has always been used to lower production costs, but lately the focus of eco-friendliness has forced companies to create elegant new syntheses that cut the amount of waste put into the environment. BHC CO. used Green Chemistry to improve the process of manufacturing ibuprofen, the extremely popular non-steroidal anti-inflammatory painkiller. The conventional method for the production of ibuprofen involved six stoichiometric steps and used less than 40 percent of the atoms in the starting material. This process produced 60 percent waste, and the cost of treating
this waste was a substantial part of the total production cost of the drug. The new method involves only 3 steps and utilizes 80 percent of the atoms from the starting material. The green chemistry synthesis uses fewer solvents and produces less than one percent waste. The work of BHC Co. resulted in a process that produced significantly less waste and lowered the overall production cost of ibuprofen.\textsuperscript{[24]}

Pfizer has also demonstrated the utility of the Green Chemistry model in their production of setraline hydrochloride, the active ingredient in the popular antidepressant Zoloft.\textsuperscript{[25]} Pfizer manufacturing chemists Geraldine Taber, Juan Colberg, and David Pfisterer applied the principles of Green Chemistry to their production process and reduced the number of steps by half. In the first step alpha naphthol is reacted with ortho dichlorobenzene to give sertraline ketone in higher yields than the traditional method. The next step is the reaction of this ketone with methyl amine gives an imine, which can be reduced to give an amino compound. The amino compound is resolved with mandelic acid to give the final product, setraline hydrochloride. Another benefit of the new synthesis is that the only solvent used is methanol, a mild solvent, and prevents the need for other, more toxic solvents. The cost of developing the new synthesis has been offset by eliminating the other solvents which would need to be distilled, recovered, and treated.\textsuperscript{[26]} Overall, the improvement reduced the use of solvents from 60,000 gallons to 6,000 gallons per ton of sertraline produced and also doubled the yield. Overall, the amount of raw materials used has been decreased by 50 percent since the new synthesis was implemented in 1998.\textsuperscript{[27]}

The Green Chemistry principles of atom economy, reducing waste, and making safer chemical syntheses have been applied throughout a large number of pharmaceutical processes, as these are the most productive, profitable, and cheapest of the Green Chemistry guidelines.\textsuperscript{[28]} However, there remains a need to develop new renewable feedstock alternatives that do not rely on traditional petroleum based feedstock, as well as developing pharmaceuticals that naturally degrade after use. There are barriers, both inherent and perceived, to achieving these goals. Some of the barriers that continue to delay
widespread implementation of the Green Chemistry model throughout the pharmaceutical industry are:

- The belief that Green Chemistry implementation would be too expensive.
- The belief that meeting the Environmental Protection Agency regulatory guidelines is sufficient for preventing environmental damage.
- Lack of Green Chemistry Education.
- The need to share information that could help other pharmaceutical companies to become greener.
- The belief that Green Chemistry would impede the process of research and development.
- The belief that environmental damage is acceptable for such an important industry.
- The lack of communication between the industry the academic community and regulatory agencies.
- The lack of training within companies\(^{[29]}\)

The work of the ACS GCI Pharmaceutical Roundtable has addressed many of these barriers and the perception of Green Chemistry seems to be changing. Most importantly, Green Chemistry information is now more accessible than ever. The EPA has supported the Green Chemistry movement and has established a database for Green Chemistry research.\(^{[30]}\) This allows chemists, students, and the public to have access to information that can hopefully inspire more positive changes in the industry.

The University of Oregon is leading the way in applying Green Chemistry throughout their chemistry curriculum and has created a laboratory experience that stresses the importance of environmental responsibility.\(^{[31]}\) The proof that young people are ready to accept the responsibility of being environmental stewards can be seen in the 30 percent increase in enrolment for Organic Chemistry labs at the university. Students are responding to the possibility that they can help discover the answers to questions that affect all of our futures.\(^{[32]}\) The chemistry students graduating from the University of Oregon are prepared to enter the workforce with an understanding of the Green Chemistry model and have extra value to an employer as Green Chemistry continues to gain momentum. As is the case with the pharmaceutical industry, the University of Oregon has cut costs, produced less waste, and provided a safer laboratory for students to work in. Hopefully, the University of Oregon can help change the mindset in academia, to one that stresses the importance of environmental responsibility.

Through the work of chemists, progressive companies, regulatory agencies, academia, and the public, Green Chemistry awareness is growing, but currently less than 1 percent of chemical processes across all disciplines, adhere to the green chemistry model.\(^{[33]}\) As new breakthroughs
continue to influence the scientific community the relevance of environmentally sustainable chemical procedures will be adopted by those companies that are hesitant to commit to a new way conducting business. Hopefully, with the help of environmentally friendly researchers, Green Chemistry will become a cornerstone of all chemical production in the US, and someday, the world.
LIST OF REFERENCES


[8, 9] ACS Green Chemistry Institute Website http://portal.acs.org/portal/acs/corg/content?nfb=true&_pageLabel=PP_TRANSITIONMAIN&node_id=1400&use_sec=false&sec_url_var=region1&__uuid=db8fb8a8-7792-40da-8723-82d5d14b26e0 (Retrieved 14 April 2009)


Blood Pressure & Blood flow

Fluid Dynamics

by

Wessam M Hashem

4/24/2009
Blood flow inside the human body is studied using fluid dynamics, pressure, force, and the study of mechanics. The fluid dynamics of blood flow is a unique principle which is only understood by studying the specific and independent interactions between physical and systemic circulatory function. Physiology helps bring an understanding to the way the organs work and anatomy provides a model to the way the body is designed. Each organ or circulatory function plays a specific role in the way it can provide a certain mechanical property or an independent physiological process which will then be used to establish a desired response or action.

Throughout history many have developed models of the circulatory system. During the evolution of such studies many of the fundamental qualities of blood flow dynamics have been observed. Such information has lead to the modern understanding and interpretation of this study. Many of the original studies included much about structure of the vascular network, the heart and its vascular branching. This information was useful because it was the basis that which developed much of the current diagnostic equipment used to study blood pressure. It was known at the time that the heart served as the pump and the arteries and veins served as the transport conduits for nutrients and discharge of wastes. Little was known about how important topics such as mechanical modeling, pulse propagation, material elasticity and dimensional analysis could be applied as well.

The circulatory system includes the heart, arteries, capillaries, and the veins. All of these structures work together to perform the basic function of blood circulation. It has been recently suggested that the performance and efficiency of the system depends on the structural property, mechanical configuration and physical capacities of these organs. This idea has been considered because it is believed that the body has evolved to efficiently generate equilibrium between work energy production as it develops an effective response. The internal environment of the body is unique to its external surroundings. For this reason it is easy to assume all forces are local events which are independent to the body’s internal demands. However, the body is constantly learning how to communicate and adapt to the external environment. Therefore, the regulation and the development of the internal environment could not exist on its own. Neurological, chemical and even physical characteristics of the internal system must evolve to function at a level which can select and develop a response to nature. The combination of all these studies is used to examine the blood flow and its dynamic features.

The study of blood flow and circulation is a process in which the blood is pumped through the body. In order for this to occur there must be location at which this cycle initiates, where it ends and, how it happens. Starting with the anatomical structure of the human and mammalian species is an organ which serves as the central part of the circulatory system which is known as the heart. The heart is a four chambered muscle which is used to generate the initiation of an important force called pressure. The heart receives deoxygenated blood from tissues and other organs and it delivers fresh oxygenated blood to the whole body. The heart also pumps blood to and from the lungs where the blood is filtered. It is amazing to understand how the heart generates enough force to pump the blood through the entire body but also to generate enough energy to pump the blood back into its own chambers.

It important to discuss certain observations about the way the heart contracts. The hearts left ventricle is very muscular. It pumps the blood into the systemic system. This chamber is also longer and narrower than the right ventricle. The septum which separates the left and right ventricles is notable for its function to contract in association to the action of the left ventricle. The shape of the left ventricle is a conical. When this Ventricle contracts the diameter of the ventricular area is reduced more than in its longitudinal direction as compared to the right ventricle. The right ventricle pumps the blood into the pulmonary system. The nature of the right ventricular contraction is also believed to assist in the full contraction and emptying of the left ventricle. The upper atria chambers pump returning systemic and pulmonary blood from the atrial chambers into the ventricular chambers. The rhythmic cycle of the heartbeat is produced by electric signals produced by pace making nodes located inside the heart. The SA node signals the pace of the heartbeat while the AV node distributes and facilitates the signals propagation. Together this synchronization is the essential nature to the blood flows inside the hearts chambers.

Valves located inside the heart and the pulmonary artery and aorta are used to ensure a one way blood flow. The valves are designed to function to open and close in one direction. Atrio-ventricular (AV) valves separate the atria from the ventricles. They form a tight seal between the atria and ventricular chambers during ventricular contractions. The remaining valves prevent the blood from returning into the heart as the ventricles relax. These valves known as the semilunar valve located at the base of the aorta and the pulmonary valve which controls the flow of blood from reentering the right ventricle from the pulmonary trunk.
When the ventricles contract a pressure gradient is generated inside the ventricle chamber causing the AV valves to swing shut. The blood exits the ventricles by overcoming the pressure gradient in the arteries causing those valves to open allowing the blood to exit the heart. When the heart relaxes the reversal of the pressure gradient causes the semilunar and pulmonary valves shut and the AV valves to open to allowing the ventricles to be refilled with more blood. It is important to note that the resistance of the blood flow causes a pressure gradient which is different than the pulsation pressure gradient formed by contraction.

The cardiac system offers a basic understanding about how the force blood pressure and how blood flow is generated. The cardiac system causes a local change in the blood volume generated by its chambers. Fluids always travel from high to low pressure gradients until equilibrium is reached or if there happens to be an obstruction (ex. valve). Since the pressures of the blood are highest after fluid exits the heart, the majority of the blood volume is found in the veins which are the farthest away from this high pressure region. The heart is using a mechanical force to displace blood volumes between pressure gradients and the valves function as a secondary mechanism which in part regulate the blood flow.
To further understand the relationship between the cardiac cycle and the arteries, the cardiac rhythmic cycle must be examined and identified. This is practiced by observing qualitative data in relationship to the mechanical conditions presented during cardiac function. The first stage is known as the quiescent period; it is when none of the chambers are contracting. At this stage, blood is flowing into the atria and ventricle chambers. This is followed by atrial systole. During atrial diastole, the atria contract forcing about 31% additional blood volume into the ventricles. Isovolumetric contraction occurs when the ventricles begin to contract, causing the AV valves shut. At this point, the ventricles have not yet ejected the blood from its chamber and the volume in the ventricle has not yet changed. This is because the pressure in the ventricle has not yet overcome the blood pressure to open the aortic valve. The next phase is called ventricular ejection. This is the time when the blood exits the ventricle by overcoming the systemic blood pressure forcing the valves open and the blood is forced into the arteries. At rest, the heart expels about 54% of its blood contents but this could be up to as much as 90% under heavy work loads. During isovolumetric relaxation, the ventricular chambers are filled with blood causing them to inflate. The heart also contains a fibrous skeleton which elastically recoils the heart cavity sucking the blood back into its ventricles. It is also caused by the sudden purge of blood flow returning back into the ventricles from the arteries as these valves begin to close. Ventricular filling accounts for the phase when the AV valves are open and the blood passing through the atria is passed into the ventricles. It is important that both ventricles pump out the same volume of blood during each contraction. The right pulmonary ventricles only need to generate about 20% of the pressure compared to the systemic ventricle. This is because the pulmonary pressure is less than that of the systemic pathway. If the volume of blood output was to be different in each ventricle, then blood pressure would accumulate in the lungs and could lead to disease.

The stroke volume of the heart is discussed by the relationship of three events called preload, contractility, and after-load. Preload is a process by which the ventricular cardiac muscles react to a change in blood volumes presenting a systemic response to fluctuations caused by venous return. The blood flow is increased and more fluid is dumped back into the heart when the body is under heavy work loads. The preload is the tension generated inside the ventricular muscle tissue just before the heart begins to contract. If the return blood volume is increased, then the pressure (tension) is also increased which causes a stretch in the myocardium tissue (cardiac muscle). The myocardium is specialized to operate at a certain length. If the length of the myocytes is increased then the muscle begins to contract with more force. The result is a balance in the output generated by both ventricles. Any differences in blood volume exerted by one ventricle will eventually reach the other and it will respond accordingly by optimizing the contractile force.

Contractility is caused by preload. The stretching of the cardiac tissue results in an increase in the availability of calcium in the muscle tissue causing an increase in contraction. Calcium serves to connect the muscle filaments during contraction and also increases the duration of the action potential in myocardial tissue. The after-load is the increase in pressure in the either aorta that opposed the opening of the semilunar valves and reduces the heart's stroke volume. By determining the stroke volume it is possible to determine the work output of the heart and its ability to perform and respond to blood flow. The stroke volume depends on the heart's ability to eject ventricular blood. Mechanical changes in the static forces generated by the blood volumes in the heart are observed as work loads. The relationship between the hearts function and its response to such forces is determined by a systemic process in response to the required regulation of cardiac contraction. The load that is exerted on the heart is usually in a form of a mechanical response or function in an effort to resist, comply or to yield to any systemic condition presented to the heart. To understand how the ventricles eject blood through the body, the surrounding conditions and events must be examined to help identify the variables which encourage heart function. This information is obtained by monitoring blood pressure and heart rate.

The blood circulates through the body through a vascular system of arteries, capillaries, and veins. The arteries are the most muscular blood vessels. The wall of large arteries has a layer of collapsible tissue found between the internal lumen and the (middle) media layer (smooth muscle). The large arteries are elastic. They are considered conducting arteries because they expand when the ventricles pump blood into them (systole) and then recoil shortly after the ventricle relaxes (diastole). This elastic property decreases the effects of the fluctuations in blood pressure as they enter smaller arteries. This also contributes to adding additional force to the pump the blood further downstream. It is similar to the propagations found in waves when transmitting energy. Even the muscular layer in large arteries is filled with a network of elastic tissue and collagen forming a fibrous skeleton which help induce a rhythmic pulsation complementing the heart cycle.

Some of the pressure force generated during the contraction of the ventricles is absorbed by the large arteries blood volume capacity caused by and increase in their diameter. The elasticity of the arteries causes the artery wall to then return to its relaxed size causing a pulsating propagation of pressure along the length of the vessel. It helps reduce the work load on the heart by absorbing some blood pressure force by increasing its volume. The pressure is used to store the increase in the volume of blood as potential energy which is then released as energy with less impulse. This also converts mechanical energy into pressure then which then provides work energy.
Middle sized arteries have two layers of elastic lamina one inside the smooth muscle layer and one outside. They also have a thick muscular wall and the serve as the distributing conduits in the delivery of blood to specific organs and limbs. Their muscular property allows the vessels to contain and reserve large amounts of blood pressure. The small arteries are also known as resistance arteries. They have a large and muscular media layer which is proportionally thicker than that of the larger arteries. They also lack much of the elastic tissues also found among the larger vessels. They function as the controls for blood flow to certain organs and tissues.

![Artery and Vein Diagram](image)

In arterial branching, the diameter and size of the smaller arteries actually provides a greater volume capacity than that of the larger arteries. The smaller branches collectively generate a larger volume area than that of the larger artery. This quality is believed to reduce the pulsation effect of ventricular contraction. The larger area, along with the geometric branching of the arteries help dissipate the impulsive and turbulent effects of pressure propagation inside the vessels. There is a considerable relationship between geometric tapering effects of the vascular system. The tapering dimensions provide structural variance in utilizing blood volume. This feature is an anatomically a geometric influence. It also means that differences in blood volumes located in the arteries depend on mainly dimensional capacity. The stiffness of the descending arteries (peripheral or farther from the heart) increases as the arteries overall diameter is reduced but they also have a greater ability to dilate and contract. This help reduce the pressure pulsation and helps equilibrate blood velocity to more constant value. The arteries also have a thicker cell wall with a smaller interior radius. The reduction of collagen and elastic tissue found in the smaller arteries is replaced by a thicker layer of smooth muscle fibers. These qualities cause an increase in the bloods velocity and an increase in mechanical influence in the functioning of these arteries.

Stress and strain properties can be modeled by mathematical formulas used in physics and they are used to determine the elastic vs. mechanical relationships in reference related to structural composition and mechanical capability. This information is then used to determine the nature in the way the arteries and how other vessels function. The stress is measured quantity used by calculating the force exerted by pressure over the area of the artery. The strain is also a measured quantity obtained by measuring the stretched length longitudinal compared to the original length of the vessel. Strain in the radial dimension is calculated by the stretchable change in the radius vs. the radial diameter. This information is then used to determine how tension caused by pressure against the vessel wall (ranging in thickness) which can stretch the arteries. This also determines the nature of how the structural compositions (elastic or muscular) contribute to function. When the radial strain is observed to be half of the longitudinal strain, the material is considered incompressible. Arteries have a radial strain which is half of longitudinal strain and are thus considered incompressible while veins are collapsible. Therefore, and change in pressure over the wall thickness will show a relationship between the length and diameter of the arterial lumen. Because of this, when the artery is stretched, its internal volume remains the same. The layers of the tissue content in the artery wall contribute a differential and constant character to provide independent and integrated function and increased reliability.

Veins form the network of vessels that return the blood to the heart. They are usually larger in internal diameter than that of similar sized arteries. This is because they lack much of the media muscle layer and elastic tissue. They also have less blood pressure because they are
farther away from the heart. The systemic veins contain over fifty percent of the total blood volume in the body. The smaller veins receive branches and dump return blood into larger veins. The thin walled structure of veins allows them to expand easier than arteries. The veins also contain venous valves. These valves accommodate for the lack of blood pressure needed to direct the flow of blood back to the heart and also against the force of gravity. They are one way valve which eliminate the back flow of the blood and are only located in medium sized veins. The veins have a greater total number than the arteries which one of the reasons why they contain a higher blood volume for this quality they are referred to as capacitance vessels. The structural qualities and vessels and their components of the vascular system provide resistance, conduction, distribution, exchange and capacity to blood pressure and systemic circulatory function.

The veins are the main location of blood storage reserve. The also play an important role in the returning of the blood to the heart. This is known as venous return. The veins need to maintain a positive pressure gradient to ensure that blood is sufficiently returned to the heart and also to maintain equilibrium. The low blood pressure available in the venous system allows for a larger volume of blood. The veins regulate blood pressure in the event any blood loss has occurred. The veins account for the blood loss by decreasing the venous blood volume.

Differentiated cells known as sympathetic fibers in the vein tissue cause vasoconstriction when they are stimulated. This is caused in order to maintain normal blood flow. Compliance is a measurement of change in volume over the change in pressure. The veins are much less muscular than arteries and much less stiff. This provides the venous system with a large compliance measurement. Veins also rely and skeletal muscle tone in order to help increase venous pressure of the peripheral limbs and tissues of the body.

The vein wall is thinner than the artery. It also lacks the elastic and collagen material composition. This design is a complement to the low pressure environment they control. In veins, cross sectional areas are not considered circular. Veins often exhibit an elliptical shape. In theory, this configuration is not recommended for optimal blood flow. The amount of power required to deliver similar quantities of blood through an elliptical vessel as a cylindrical shape are about double in the amount of force that is required.

Venous return is an important factor which regulated heart output. During the preload cardiac cycle, the filament stretches and muscular stimulation is at optimal length if venous return is at normal pressure. Venous blood pressure returning to the heart is provided by factors that affect the pressures inside the veins. If skeletal muscle stimulation is observed it causes an increase in venous blood pressure and causes an increase in stroke volume of the blood inside the heart. This will also increases the intensity and length of the hearts contractions. One factor effecting venous return is the pressure gradient. Venous pressure forces the blood towards the heart. The change form a high to low pressure gradient forces the blood into the heart. An increase in blood volume will also increase the venous return blood. When the veins constrict, they reduce the amount of blood flow back to the heart and when the veins dilate it increases the amount of blood flow through. If skeletal muscle is active, it causes a decrease in the volume capacity, increases blood pressure in the veins and it increases venous return.

The respiratory pump is another mechanism which influences venous return. Breathing causes changes in the internal pressures observed between the lower abdominal and upper thoracic cavities. The inferior vena cava is the largest vein in the body and it happens to pass through both of these cavities. When the body inhales, the diaphragm causes and increase in cavity pressure in the abdominal region and it also decreases the internal pressure of the upper thoracic cavity. This pressure difference causes fluctuations in the blood flow through the vena cava. The blood flow is resistant to backward flow due to the venous valves. Inhalation causes a blood pressure increase in the abdominal cavity and a decrease in the thoracic cavity providing a pressure gradient to assist the directional blood flow to the heart. This pump only applies to the central venous system.

Cardiac suction occurs during iso-volumetric relaxation and ventricular filling. During ventricular systole, the opening of the AV valves creates a pressure decrease in the atria causing some blood to be suctioned out of the vena cava and the pulmonary veins. Gravity and skeletal muscle contraction also affect the venous return of the blood to the heart.

The capillaries are the location for nutrient and waste fluid exchanges. Although they are extremely small in diameter their numbers and abundance allow them to cover a large interior wall area necessary to provide the most surface area available. They only consist of endothelium cells only and they get larger in diameter at the venous end than they are at the arterial end. Metarterioles are short vessels that are located in between the small arteries (arterioles) and the capillaries. They contain sphincter like muscles which open and close the entrance of the blood flow into the capillary beds. The capillary bed is also the location where the greatest drop in blood pressure is observed. The regulation of the blood flow to the capillary beds plays a very vital role in the systemic response to the body by adjusting blood flow and cardiac output.

The capillary bed is also referred to as the microcirculatory system, is an important system which facilitates the selective blood flow to certain organs and tissue. On average only twenty-five percent of the bodies capillary beds are supplied with blood at any given time. The reason for this is because there is not enough blood volume in the body to supply the entire vascular system at once. It is difficult to study the pressure of
Blood inside such tiny vessels, therefore, capillary exchange mechanisms are studied to define the mechanical blood properties at a given time and location. Components such as resistance, exchange, capacitance, and diffusion are studied to determine the structural and functional impact on blood flow through capillaries. Since the blood volume is so small in the capillary, the viscosity and concentration of the blood plays a role in flowing circulation inside the capillaries.

Concentrations of carbon dioxide and oxygen move across the capillary membrane from areas of high to low concentrations. Fluids are filtered out of the capillaries and they reenter the bloodstream by osmosis. One of the main causes of the drop in blood pressure in the capillaries is due to the friction generated as the blood passes these busy passages. Filtration and re-absorption mechanisms of capillary diffusion are differential to the type of tissues they supply. The capillary beds located in the kidneys absorb very small amounts. These capillaries are mainly used for filtration. In the lungs, the capillary function by operates mainly through absorption. These differential qualities of capillaries are due to membrane structure which provides selection to the type of capillary function.

The regulatory structures of the microcirculatory system consist of the arterioles, the pre-capillary sphincters and the metarterioles. Collectively, these structures reduce the arterial blood pressures to levels that optimize capillary action. The pre-capillary sphincters are controlled by local chemical/metabolic stimuli. The pre-capillary sphincters and the arterioles serve to regulate the amount of blood flow into the capillary beds. The arterioles are considered to be the most significant function of the vascular system which can affect cardiac output.

Blood flow to certain regions or tissues of the body do not change the overall blood pressure. Blood pressure is normally measured using mercury liquid as a control medium. The mercury is measured in millimeter displacements to any changes in pressure observed. Since the mercury liquid is dense, it causes little changes of pressure to cause the column of mercury to travel through a tube making it more convenient to measure. The pulsating nature of the heart cycle causes changes in measurable blood pressure. The pressure is measured by sphygmomanometer. Heart rate is measured in beats per minute. Systolic blood pressures are measures of the maximum arterial pressures observed during ventricular contraction. Diastole is measured as the minimum pressure inside the arteries generated between a heart beat.

The blood is observed as a Newtonian fluid. The nature of blood fluid flow is described to behave conditional to temperature and pressure. Although the blood does contain plasma cells and gases the measurable observations of mechanical blood fluid in motion can only be
provided by the large scale blood flow in the arteries and veins. Blood viscosity only has a significant impact when the diameter of the vessel size is small enough to obstruct the uniform passage of fluid pressure caused by particle or elemental interference. This results in a phenomenon known as a no slip boundary. In large vessels the velocity of the blood at the center of the vessel is faster than it appears in the areas where it makes contact with the vessel wall. When the vessel diameter is decreased the fluid portion (plasma) rather than the red blood cells and elemental composition of the blood become more resistant to velocity due to resistance of friction caused by his no slip theory. Therefore, in capillaries and the microcirculatory system facilitate the displacement of higher volumes of solid and gas content than that of it counter liquid ratio. This causes a decrease in blood viscosity in the smaller vessels.

Cardiac output, blood volume, and heart rate all contribute to pulse pressure. The arteries play an important role by moderating pulsation pressure to ensure a steady blood flow in capillaries. The arteries absorb much of the stresses of the high pressure fluctuations by dissipating the blood surge throughout the length and elastic features of the artery wall. By the time the blood reaches the capillaries and veins the blood is flowing at a steady speed. In closed circulatory systems, resistance of the blood flow is a force generated by the pressure along the vascular length of the vessels. The pressure and resistant forces are the key factors in providing blood flow circulation. Blood viscosity and vascular length and radius all contribute to resistance. A high blood viscosity is resistance to blood flow. Blood viscosity is an important regulatory factor used in treating diseased patients. Low blood pressures could cause decrease in physical and mental functions because it reduces the capacity and efficiency of the heart to maintain adequate circulation. High blood pressures usually lead to heart disease because it causes variable strain on the heart and all the vessels.

Blood flow velocities are the highest in the aorta. The velocity of the blood decreases gradually as it reaches the capillaries where it is lowest. In the veins the blood velocity increases to levels higher than the capillaries. It has been difficult to model the body's blood flow dynamics because most of the information used to calculate and measure blood circulation cannot describe the natural physiology of fluid dynamics inside the body. The constant local and systematic changes in body are difficult to measure at the specific and overall processes. The study of fluid dynamics is a field of study that can be used to study blood flow because it involves the utilization of a large array of data and conditions to analyze the collaboration of events which cause blood flow. With the varying structure and function of each vascular component it is often difficult to develop methods which define the interactive process which lead to circulation.

In order to understand the concepts behind the information used to describe blood flow and dynamics, certain principles must be extracted from fundamental and modern scientific practice. Such information is used to identify certain causes, and to explain how these events occur, and to provide additional information on how any why such information is necessary. For this reason three topics are should be used to identify all aspects of circulation. From a medicinal point of view the information and terminology is derived mainly from the biological and chemical study of physiology and anatomy. The technical study point is gathered using mathematics, and physics. There is however, a relationship between the analytical and subjective ideas that can emerge from each of these independent studies. Such ideas emerge through interpretations of the systematic processing of information used in problem solving, the integration of design and development, the ethics behind engineering, and even theory. These ideas cause much controversy but they are all important events when used to study science.

In the future, technology will improve the tools used to measure blood pressure and small scale fluid dynamics. Blood flow and the dynamics of circulation is a very important biological study. It has developed the latest innovations in bioengineering and in medicinal applications. This field of study has developed useful information for use in disease prevention to drug therapy. The application of new surgical materials and monitoring devices has improved the diagnosis and treatment of disease with greater accuracy. It can also help scientists develop and understand the ways in which the body fuctions between structural and mechanical mechanisms combined.
References:

RU- 486:
The Abortion Pill

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April 20, 2009
Abstract

The drug RU-486, commonly referred to as Mifepristone, is a steroid that prevents the progesterone hormone to continue a pregnancy. "Mifepristone is an anti progestin." Details of how the drug became legal in the United States, and how RU-486 works will be discussed. Advantages and disadvantages along with FDA controversies will be weighed.

Introduction

The right to take a life, or the right not to take a life, that is the question. "RU-486, also known as the "abortion pill", and Mifepristone, is a drug that induces miscarriages if taken in the first three months of pregnancy." This drug is used in replace of surgical abortion. The drug was first produced by researchers at Roussel Uclaf (the RU in RU-486), in France in the early 1980's. It became licensed in France as a form of abortion in 1988, and was made legal in the United States in September of 2000. Along with approval many different controversy surfaced about the drug.

![Mifepristone (RU486) Structure](image)

![RU-486 Pill](image)

Legal Status

Mifepristone was first banned in the United States by the Bush administration in 1989, due to safety concerns they had about the drug. At first, this decision was also approved by Roussel Uclaf. "In 1994, Roussel Uclaf gave the United States right to the drug in exchange for immunity from liability claims."
The production of this drug did not start immediately. "In 1996 the drug went into approval status, even though compilation of U.S. trial data was still incomplete." In September 2000, under the Clinton administration Mifepristone was approved by the FDA. "Under the Clinton administration the FDA took a very active role in effort to bring the drug into the U.S. In the course of carrying out the President’s directive, the FDA actively pressured French manufacturer Roussel Uclaf to submit a marketing application, allowed the Population Council to use data from foreign studies in its marketing application, rather than require the Council to wait until it was ready to submit data from American studies, and they submitted the application to an advisory panel stacked with known abortion activist and RU-486 supporters." It is now legal in fifty states, including Washington D. C. and Puerto Rico. "The FDA mandated that the drug be made available to women who are no more than 49 days pregnant (7 weeks from their last menstrual period)." Women who take the RU-486 pill are required to sign a form indicating they are aware of the risks associated with the drug for them and their baby. "Doctors prescribing RU-486 are required to be able to date pregnancies and diagnose ectopies. They also must be able, the FDA says, to provide surgical intervention in situations where there are incomplete abortions or severe bleeding, or to have in place arrangements for patients to obtain such services from other physicians who can perform these sort of surgical procedures." Instead of special training in use of the drug, physicians only have to sign a form indicating they have read and understood the prescribing information. They are also not required by the FDA to conduct ultrasounds to confirm the length of a pregnancy.

FDA Controversy

Many pro-life activist expressed that they believed Mifepristone was approved to quickly by the FDA. "The process of the application for RU-486 was complete in just six months, while other potential life saving drugs were taking up to seventeen months to be processed." These activist believed because RU-486 was one of the first drug in the nation’s history for specific purpose of taking a life of another human being, the FDA should have spent more time testing and regulating the drug. "Many groups in the U.S. campaigned against the approval of Mifepristone. These groups saw ethical issues with abortion and felt there were strong safety concerns regarding the drug, and adverse reactions associated with it, including death."

In the U.S. the drug is sold by Danco Laboratories under the trade name Mifepepx, in China. This too brought up controversy about the manufacturing of the pill. Many groups protested that the drug could not be properly over looked or guaranteed to be safe because it was being made in China. "They also claimed that China was cited by the FDA for tainted drugs, yet they still allowed the manufacturing of the RU-486 to be continued there. FDA ordered that a second drug, Misoprostol, be used in conjunction with the RU-486, because the RU-486 was not effective in computing an abortion alone." This too caused a new wave of controversy.
Many claimed that Misoprostol was a ulcer medication and its manufacturer warned the FDA that it did not recommend the drug for the use of abortion.

"Trails in the United States did not meet FDA’s standards. Ninety-Nine percent of the U.S. test subjects suffered some adverse event, and twenty-three percent of those were considered serious. Abortion was complete in only ninety-two percent of the test cases." "Nearly all the safety precautions the FDA recommended to protect women from being injured or killed by the Ru-486 were dropped from the final approval. These precautions included ultrasound diagnosis to verify the age and location of the pregnancy." Pro-life activist rallied that the FDA was not doing their part and putting women at health risks.

"Complications that were reported to the FDA demonstrated that RU-486 was a serious threat to the health and safety of women, these included two fatalities, and twenty other near fatal complications including, heart attacks, and bacterial infections." "In U.S. trials a total of 295 patients were classified as having failed abortions. Of these, 79 had ongoing pregnancies, and 126 had incomplete abortions." Protesters against the drug claimed that these facts alone would cause an ordinary drug to be removed from the market immediately.

**FIGURE 2**

Two surveys taken. One questioned Abortion and the other question on the RU-486 Pill.
How the RU-486 Abortion Works

“A RU-486 abortion usually takes between two days and two weeks. It also requires at least three visits to the doctor.”⁷ The drugs given for the abortion can not be bought at the pharmacy, but must be given by a doctor in the clinic. The first visit will start by the patient learning about the side effect and risks of the RU-486 abortion. “The doctor will then perform a pelvic exam to ensure that the pregnancy is no more than 49 days, and that the embryo is growing in the womb.

The doctor will then proceed to give the patient three tablets (200 mg each) of the RU-486 to be taken immediately.”⁷ Progesterone stimulates the uterine lining which nourishes the developing child. “When the RU-486 is taken it binds itself to the progesterone receptor wall of the uterus, thus blocking the effect of the women’s natural progesterone. This triggers shedding of the uterine wall, much like a normal period.”⁸ The child is now deprived of necessary nutrients, and starves to death. “The cervix is opened and mild contractions help expel the embryo.”⁸

The second visit will take place within two days of the first visit. On this visit the patient is given a second drug, Misoprostol to be taken at home. “This causes the cervix to soften and dilate. Strong contractions of the uterus begin. Deep cramps and heavy bleeding will occur in a time range of 2-24 hours.”⁹ During this time the embryo is being pushed out of the uterus. The last visit is usually about fourteen days after the initial visit. During this visit the doctor will determine if the procedure has been completed. If it is not complete further action is taken, which usually is surgical abortion.

During the time frame that RU-486 can be used, the baby is undergoing a rapid period of development. It is at about the fifth or seven week of pregnancy. The child is about 2mm long. “By this time the baby’s nervous system has begun to form, and their heart beat is likely to have already had its first beats.”⁹

“RU-486 is not recommended for all women who would like to have an abortion. The procedure maybe unsuitable for smokers aged 35 years and older, women with certain medical conditions such as heart disease, asthma or hypertension, and for pregnancies more than 9 weeks gestation.”⁹
Advantages and Disadvantages

Like most drugs, RU-486 has a list of both advantages and disadvantages that have been noticed by both patients and the providers. Many providers are reluctant to provide the pills due the extra expense involved in counseling and the expense of training. "The price of a RU-486 abortion, with Danco Laboratories charging $270 for a single dose of the RU-486 pill, is also an issue for providing clinics." 

"Originally the claim was that a RU-486 abortion would cost about the same as a standard first-trimester surgical abortion, but with the pill and additional cost associated with the mandatory three office visits, lab work, and extra time, there was no way a comparable fee could be charged." 

For Clients RU-486 offers more privacy, as the women can usually miscarry in her own home. Another advantage for the client is that no anesthesia is required. "Women who have taken the RU-486 stated that it is less stressful, clinical, and emotionally charged than surgical abortions" 

Disadvantages also occur for the clients using RU-486. For example, the procedure is time consuming with three mandatory visits. If the procedure does not work a surgical abortion would also be needed. Another disadvantage is that the RU-486 pill can take days to work, where as a surgical abortion only takes about a ½ hour.
Effects

Along with these disadvantages adverse events and side effects take place. “Most all women who have used the abortion pill have experienced at least one of the following side effects: heavy cramping, heavy bleeding nausea, headaches, vomiting, dizziness, fatigue, back pain, fever, and rigors.” The procedure can be very discomfoting and very painful. Deaths have occurred in recent years related to RU-486 abortions, 4 in California and 1 in Tennessee, are examples.” On November 15, 2004 the FDA reported having received 676 “adverse events” reports concerning Ru-486 abortions, including: 17 ectopic pregnancies, 72 cases of needed blood transfusions, and 7 serious infections.”

Conclusion

RU-486 carries a wide range of controversy. It is used to carry out an abortion in the first two months of pregnancy. Pro-choice groups believe the drug allows women to have an abortion with more privacy and comfort. On the other spectrum pro-life groups believe the RU-486 pill is harmful to women’s health and that it is wrong to take a life of another.

It is my own strong opinion that the RU-486 pill is ethically and morally wrong. I believe the pill makes getting an abortion too easy and is used in our society as a form of birth control. Abortions have increased in the United States since the approval of the abortion pill method. “In 2001 the increase was 1%, in 2002 it climbed 5.2%, 7.9% in 2003, and 9.3% in 2004.” We as humans do not have the right to take a life of another being. At 49 days this fragile child has begun to form a little nose, little ears, eye lids, and an upper lip. The child’s fingers are starting to separate into individual digits and with a simple swallow of a pill this precious life would be taken, and never to be seen, held, or to be given the option to form a life with dreams larger than we could imagine. That thought alone is unjust and cruel. It is the innocent murder of a child. Would it be any different to have a gun held to your head and have another human pull the trigger and take your life away from you in an instant? The intent from the beginning would be murder, and yet those criminals are sent to prison.

Taking an innocent life should never be a legal option. The option for women to have safe sex, the option for adoption, and or the option of celibacy, should be embraced in our society, but never should the option of a taking a life be acceptable. Not only is an innocent life being taken, but the purpose and the opportunity of great achievements to come from this amazing being are also taken as well. That child could be the next President of the United States, the first researcher to find a cure for AIDS, or a teacher who molds the minds of students class by class, but in a blink of an eye those opportunities are taken from that amazing creation, and this society as a whole.
Imagine the world without an Albert Einstein, a Shakespeare, an Abraham Lincoln, a Michael Jordan, a Barack Obama, or the very woman who gave birth to you. Imagine the difference in our world, if these lives were also taken before they even began.

Figure 4

Embryo at 7 weeks
Reference

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Lipodissolve

Lipo-Dissolve Uncovered

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April 24, 2009
Abstract

With America’s obsession to obtain the mirage of a “Perfect Body”, it is no wonder that many are turning to the latest diet fads, holistic supplements and trendy fitness routines all with hope of getting closer to reach this unobtainable goal. A new controversial medical treatment, Lipo-Dissolve, claims to “melt away” fat as some experts suggest it to be highly effective. Nicknamed “lunch time lipo”, Lipo-Dissolve is a medical procedure that signals intrigue for both the general public and medical professionals alike. Comparable to liposuction in that it is intended to eliminate unwanted fat deposits, Lipo-Dissolve claims to be a less evasive, more cost effective and a non-surgical fat-reduction method intended for localized, small volumes of unwanted fat.

Background

Lipo-Dissolve was a very popular medical treatment that began in the 1950s. A doctor from France developed a technique of directly injecting a chemical formula into the fat that is found around a specific organ that he was going to do an operation on. He realized that the chemical caused the fat to dissolve and this resulted in a direct course to the organ. The method was then developed to be used cosmetically and was introduced in the United States in the 1990’s. Lipodissolve is also known as mesotherapy, lipolysis, injection lipolysis or lipostabil.

Lipo-Dissolve is an injection-based procedure, which was created to enable the body to liquefy or soften the fat. Areas typically treated with Lipodissolve are the upper and lower abdomen, “saddlebags”, thighs, upper arms, fats pads under the eyes, the chin, and is also used in the treatment of cellulite, stretch marks and to improve the skings elasticity and increase collagen production lost with the natural signs of aging. Treatment usually consists of a series of injections in a grid formation into the subcutaneous fat deposits and connective tissue using thin needles. A mixture of the compounded drugs, mainly phosphatidylcholine and sodium deoxycholate, are administered by a physician in a dosage they deem appropriate for the individual patient. The ingredients used in lipodissolve may vary depending on the doctor and the area being treated. Other than the phosphatidylcholine/deoxycholate (PCDC), multivitamins, alpha lipid acid, enzymes and plant extracts are also mixed together into a solution and injected into the patient unwanted fat pockets. Some doctors may also add non-steroidal anti-inflammatory medications, antibiotics and hormones to the mix. These chemical cocktails typically are prepared in compounding pharmacies, which specialize in customizing formulations of drugs based on a doctor’s orders. Several treatments of the injections taking up to 45 minutes depending on the site of injection, with six to ten appointments ranging between four to six weeks apart, are often required to produce the optimal result. The cost for a Lipo Dissolve can range around $400 - $600 per treatment. There is little known downtime for recovery and the procedure can be preformed without anesthesia.
Main ingredients in Lipo-Dissolve

Phosphatidylcholine is a natural glycerolphospholipid made of glycerol, two fatty acids and a choline attached as a headgroup. They are a major component of biological membranes and can be isolated from foods, either egg yolk or soybeans, from which they are mechanically extracted or chemically extracted using hexane. Phosphatidylcholine, PC, is more common on the exoplasmic or outer leaflet of a cell membrane. Phosphatidylcholine is a fat emulsifier vital for cholesterol metabolism. PC is currently a dietary supplement taken in the oral form in the United States and is one of several ingredients used in some FDA-approved intravenous drugs. However, the FDA had not approved the combination of phosphatidylcholine with deoxycholate for the use as an aesthetic intravenous treatment to emulsify or remove fat. Phosphatidylcholines are such a major component of lecithin and the terms are sometimes used interchangeably. Lecithin is any of a group of yellow-brownish fatty substances occurring in animal and plant tissues, and in egg yolk, composed of phosphoric acid, choline, fatty acids, glycerol, glycolipids, triglycerides, and phospholipids such as phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol. Lecithin has low solubility in water and in an aqueous solution, the phospholipids can form either liposomes, bilayer sheets, micelles, or lamellar structures, depending on hydration and temperature. This results in a type of surfactant that is usually classified as amphoteric. However, lecithin extract consists of a mixture of phosphatidylcholine and other compounds. Phospholipase D catalyzes the hydrolysis of phosphatidylcholine to form phosphatidic acid (PA), releasing the soluble choline headgroup into the cytosol.

Medical researchers use this combination in experimenting with injection lipolysis, using injected phosphatidylcholine to try to break down fat cells combined with sodium deoxycholate, is a mixture known as Lipo-Dissolve, and as an alternative to liposuction.

Sodium deoxycholate, the active ingredient in the PC/DC formulas exist in nature and is referred to as a "secondary bile acid". Sodium Deoxycholate is produced in the intestine from the salts of glycocholic and taurocholic acid from the active nature of bacterial enzymes. Less than half of the sodium deoxycholate is absorbed by the intestine and is returned the liver where it is combined and is filtered into the gall bladder. Sodium deoxycholate is extracted from cattle bile in a high temperature alkaline process. Sodium Deoxycholate is used in purpose ranging from cell lysis (RIPA Buffer), liposome preparation, isolation of membrane proteins and lipids, preventing nonspecific binding in affinity chromatography and a cell culture media supplement. Sodium deoxycholate causes the fat cells to undergo a process called onciosis when injected into the fat layer. Oncosis causes the cell to swell, damaging the cell membrane that is unable to be healed and repaired by the cell itself in most instances. Sodium deoxycholate combined with phosphatidylcholine helps to prevent the rapid cell death and is less harsh. When the treatment area has a broader surface, the formula is spread out equally over the treated area, causing a smoother and even reduction of fat.
Phosphatidylcholine:

\[
\begin{align*}
&\text{CH}_2-OOCR' \\
&\text{R'}\text{COO-CH} \\
&\text{O} \\
&\text{CH}_2-O-P-O-\text{CH}_2\text{CH}_2\text{N(CH}_3)_2 \\
\end{align*}
\]

phosphatidylcholine

1,2-dihexadecanoyl-sn-glycero-3-phosphocholine

Pathway for the synthesis of phosphatidylcholine in animals and plants:

\[
\begin{align*}
\text{HOCH}_2\text{CH}_2\text{N(CH}_3)_2 & \xrightarrow{\text{ATP}} \text{O-P-O-CH}_2\text{CH}_2\text{N(CH}_3)_2 \\
\text{choline} & \xrightarrow{\text{ADP}} \text{phosphocholine} \\
\text{CTP} & \xrightarrow{\text{PPI}} \text{cytidine diphosphocholine} \\
\text{CDP-choline} + \text{R'}\text{COO-CH} & \xrightarrow{\text{CH}_2-OOCR'} \text{R'}\text{COO-CH} \\
\text{CH}_2\text{OH} & \text{O} \\
\text{sn-1,2-diacylglycerol} & \text{phosphatidylcholine}
\end{align*}
\]
Sodium Deoxycholate:

Alternative Names:  Deoxycholate, Sodium Salt  3,12 α-Dihydroxy-5β-cholan-24-oic acid, mono sodium salt

Molecular Weight (MW):  414.6

Formula: C₂₄H₃₉NaO₄

Clinical Trials:

There is conflicting results and information regarding the success and failure of the Lipo-Dissolve procedure. Due to the fact that the treatment is relatively new in the United States, is not FDA-approved and the lack of a standardized mixture and components of the lipotherapy varies with each administering Physician, results are not concrete. In a study recently completed by a group of Dermatologists, Thirty-seven female patients were studied for the treatment of localized fat in the gynoid lipotherapy. Each patient was treated on one side with injections of phosphatidylcholine/sodium deoxycholate and sodium deoxycholate on the contractual side. Four treatments were done every eight weeks. The overall reduction of the fat in the localized area proved to be 91.9%. Both treatments showed reasonable efficiency in treating the fat, with sodium deoxycholate having more pronounced side effect and a slower postoperative results, and phosphatidylcholine obtaining a later emulsification of fat. The possible weight loss results were ± 2 kg during the study, but it was concluded that a further study was necessary to determine results as being completely unbiased, recommending that a larger sample of nonslimming patients be used to permit the efficiency of the drugs. The side effects in the test were pain on injection, 78.4% PPC/DEOX and 100% with DEOX, bruising 83.8% PPC/DEOX and 91.9% DEOX, erythema, stinging/ burning, and swelling was 100% in both PPC/DEOX and DEOX mixtures.
Another study tested the cell viability and cell membrane lysis assays, performed on cell cultures and porcine skin after treatment with the phosphatidylcholine formula, isolated sodium deoxycholate. The results were a significant and comparable loss of cell viability, cell membrane lysis, and disruption of fat and muscle architecture was seen in cell cultures and tissue specimens treated with the phosphatidylcholine formula and isolated sodium deoxycholate. The conclusions were comparable to the effects created after treatment with laboratory detergents. The phosphatidylcholine formula typically used in subcutaneous injections for fat emulsification worked in the study primarily as a detergent causing nonspecific lysis of cell membranes. The results proposed that sodium deoxycholate was the major active component responsible for cell lysis. Detergent
substances may have a role in eliminating unwanted fat tissue. The study also concluded that physicians use caution administering the formula until sufficient safety data are available.

Complications with Lipodissolve:

Lipodissolve treatment is under attack by many plastic surgeons and dermatologists. The American Society of Dermatologic Surgery has issued warnings against lipodissolve treatments due to the lack of controlled studies to demonstrate its safety and efficacy. Overall, there is limited scientific evidence available on injection lipolysis for fat reduction. The studies that are available for review had low levels of validity for scientific studies and do not offer comparable formulations and dosages of the key ingredients necessary to compare the safety and efficiency of treatments.

Consumer rating sites report the majority of patients having received the treatment scored the procedure very low in terms of creating long-lasting weight loss. Also, no studies have demonstrated where the medication travels or how it may affect organs. New research does exist on the optimal ingredients, proper dosages or short-term side effects. The American Society for Aesthetic Plastic Surgery (ASAPS) reports that infection, disfiguring masses of inflamed tissue and tissue death can occur after lipodissolve, especially when the procedure is performed by common people. Some plastic surgeons are seeing indentations and depressions in the skin of people who have undergone lipodissolve. Such defects can be extremely difficult to correct. The individual ingredients in the injections are approved by the FDA but are not approved to be injected as a treatment for any kind of weight loss. Lipodissolve injections do liquefy fat, but where the fat goes is a growing concern. Potentially it could be filtered through the liver, creating a fatty liver. Such excess fat in the liver can result in inflammation and possible scarring and liver failure. The liquefied fat may also wind up in the blood vessels, where it could add to existing fatty plaque and increase the risk of heart attack or stroke.

Lipodissolve should not be used in pregnant women, nursing mothers or obese individuals, or in people with diabetes, autoimmune diseases, vascular complications or infections of any kind. It is not an appropriate treatment for large areas of fat. The relatively new procedure has caused problems in at least two states, Kansas and Nebraska. Both are currently in the process of enacting legislation to ban lipodissolve. Kansas has a temporarily ban on the product unless it is done as part of an FDA-approved clinical trial. Legislation in Nebraska is seeking to ban this procedure until it receives FDA approval. The state of Nevada is also considering such a ban. ANVISA, the Brazilian FDA, banned the use of phosphatidylcholine-based products for injectable fat removal because they have never been approved for cosmetic use. And Health Canada, the Canadian FDA, has ordered physicians to stop marketing and administering the products.
Conclusion:

The obsession to be thin and beautiful is a common threat for the majority of Americans. Diet pills, exercise programs and plastic surgery is a billion dollar industry that is in business to help people look their best and feel even better. With so many methods available to individuals who are looking for long-term weight loss results, new and improved products spring on the market daily. For some people, Lipodissolve may seem like a viable option, even without much scientific evidence to back it up. However, with the lack of research and no concrete evidence, I personally feel that there are better, healthier options to achieve a thin body. There is no quick fix or pain free method out there for weight loss, regardless of how pretty it is packaged or how many supporters are backing it. Healthy living is a lifelong commitment that can be a rewarding journey if properly managed and maintained.
References
