

# Journal of the Health Resource Center

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# Editorial Report

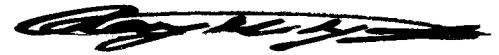
Ming-Yu Cheng

Since the early 1980s, the herbal market place has burgeoned beyond the expectation of health care professionals. In the United States, herbal products intended for promoting health were once relegated to health and natural food retail stores. The number of health food stores has tripled since then. Today, herb products can be found in every conceivable retail outlet where nonprescription drugs and personal care products are sold, including chain pharmacies, discount retail stores, supermarkets and even on counter displays at convenience stores or internet sites. Surveys also find that the majority of Americans rely on dietary supplements to maintain good health. As a result, the dietary supplement industry generates billions of dollars in sales annually, making it one of the most dynamic sectors of the U.S. economy.

In Europe, traditional medicines are categorized under the all-encompassing title of what is now termed complementary and alternative medicine (CAM). This includes several traditional herbal medicine systems, notably western-based and Chinese herbal medicine, acupuncture, and Ayurvedic medicine, all of which are rapidly growing in popularity. A recent British Broadcast Company survey found that 1 in 5 people in the United Kingdom now use CAM on a regular basis and that herbal medicine was the most popular form of self-treatment. A survey conducted in March 2001 of the European herb market values the trade at Euro 3.2 billion. The international market has been growing fast. Various sources estimated the 1999 in-

ternational market for natural products at between \$35 billion and \$45 billion.

Corresponding with these usage patterns, the Journal of the Health Resource Center, a publication of California State University Long Beach, Student Health Center, reports the development and available evidence on clinical efficacies of important herbal products including energy drinks, diet supplements, sexual supplements and anti-depression supplements. Reliability and validity of the studies on herbal medicine have been an issue during the process of researching and summarizing those findings. In addition, most of the clinical studies on herbal medicine are not double-blinded, nor are they representative samples, which has caused problems on interpreting study results. In conclusion, while the emerging interest in herbal medicine across western countries shows every promise of continuing its rapid development in the future, more well designed clinical studies based on representative populations and effective regulations on manufacturing and sales of supplements are essential to secure the safety of herbal medicine and the right of consumers.



# The Effects of Energy Drinks

Shafinaz Hussein

**With an increasingly demanding lifestyle, people are looking to just about anything to give them a quick pick-me-up, which is why the market for energy drinks is so lucrative. But many people, including authorities, are questioning the safety of these drinks in light of the death of several people who had been consuming energy drinks. A breakdown of the ingredients indicates that the energy enhancing effects are derived from stimulants, carbohydrates and vitamins B6 and B12. In moderation, these drinks may be relatively harmless. The trouble arises when they are consumed in excess, in combination with other stimulants and/or alcohol.**

Energy drinks have taken over the beverage market with a bang. Some like its taste and others want the energy it claims to give. Recently, three people who had been drinking Red Bull died. Two of them had Red Bull mixed with alcohol while the third had several cans of Red Bull after a workout and had died from kidney failure. Whether or not Red Bull is responsible for their deaths is still under investigation.<sup>8</sup> Red Bull is one of the many energy drinks available, which claims to increase stamina both mentally and physically, stimulate metabolism and improve reaction speed. The common ingredients found in these drinks include stimulants, amino acids, vitamins and carbohydrates. Detailed scientific research is lacking, but many argue that these energy drinks are just hype and that the effects are simply the results of the stimulant and carbohydrates. The manufacturers however claim that it is the unique combination of the ingredients mentioned above that gives it the kick.<sup>5</sup>

The most common stimulant added to energy drinks is caffeine. It is an alkaloid, which is an organic base obtained from plants and composed of nitrogen, carbon, hydrogen and commonly oxygen. Two sources of caffeine are coffee beans from the *Coffea* plant and guarana, which is a dried paste made from the crushed seeds of the plant *Paullinia cupana*. The caffeine content of guarana ranges from 2.5-5% while coffee beans range between 1-2%.<sup>6</sup> The amount of caffeine present in energy drinks range from 240-320 mg/liter. In comparison, cola drinks contain caffeine ranging between 33-213 mg/liter while coffees range between 210-340mg/liter.<sup>5</sup> Caffeine is a stimulant that stimulates the central nervous system to increase the heart rate, constrict blood vessels, dilate pupils and breathing tubes, in-

crease release of glucose from the liver and increase fluid excretion. These effects can be seen 15 to 30 minutes after ingestion. An excessive amount of caffeine can cause various kinds of side effects depending on the physiology and metabolism of the individual. The different levels of caffeine sensitivity, which is the amount of caffeine that will produce adverse effects, varies with each individual. The spectrum of side effects includes difficulty sleeping, confusion, increased urination and thirst, difficulty breathing, irregular heartbeat, diarrhea, vomiting and even death. Death normally follows heart arrhythmias and convulsions. Though caffeine is relatively safe when consumed in moderation, those with coronary heart disease should limit caffeine intake.<sup>20</sup> In a study at Duke University Medical Center, individuals who drank 4-5 cups of coffee per day experienced a 5 point increase in blood pressure. This may be a small value, but in the long run it places those individuals at a higher risk for heart disease or stroke.<sup>3</sup> High blood pressure also increases the risk for kidney disease leading to kidney failure. Those suffering peptic ulcers should also avoid caffeine since it stimulates the body to produce acids and pepsin into the stomach, which will aggravate the ulcers.<sup>17</sup>

The effects of caffeine on pregnancy and the fetus have been studied in animal and human models but not as thoroughly. Studies with rats indicate that caffeine at high doses is teratogenic, which means it produces deformed fetuses. At low doses, the pups showed inconsistent post weaning behavioral effects. Another study with primates exposed to caffeine resulted in stillbirths, miscarriages and reduced birth weights. In human models, however, the results have been inconsistent with regards to caffeine and its association with decreased birth weight, spontaneous abortions, delayed conception, pre-term delivery and congenital malformation. These adverse effects are

normally seen in those mothers who are high consumers of caffeine. Sudden Infant Death Syndrome was also seen to be associated with caffeine in a recent epidemiological study. It is concluded from these studies that caffeine consumption of less than 300mg/day by the mother during pregnancy will not produce any adverse effects on the fetus, however it is advised that mothers should avoid caffeine during pregnancy. Caffeine should also be consumed very minimally during breastfeeding since caffeine can be easily passed to the child through breast milk.<sup>5</sup>

Caffeine intake should also be monitored in children, especially hyperactive children since it stimulates the central nervous system. Studies in which children were given 10 mg per kg body weight had inconsistent results. Some children experienced no changes while others had changes in their mood, behavioral, cognitive and motor functions.<sup>5</sup> Caffeine may also have adverse effects on the child's nutrition since it suppresses the appetite and replaces important nutrients.<sup>20</sup>

With regards to exercise, caffeine has shown to increase performance in endurance exercises and other exercises lasting 5 minutes or more. Sprints and exercises lasting 90 seconds or less received no benefit from caffeine ingestion. Caffeine increases mobilization of fat for energy. This enables the body to spare glycogen, the primary source of energy, for later use, thus prolonging the duration of exercise.<sup>11</sup> These studies, however, were done on well-trained athletes; therefore the same effects may or may not be seen in the average person.<sup>18</sup> The amount of caffeine needed for those energy enhancing effects is about 1.5-3mg per pound body weight. Caffeine containing beverages, such as coffee or energy drinks should not be a form of fluid replacement during or after exercise since caffeine functions as a diuretic, which increases the volume of urine excreted.<sup>2</sup> The effects of caffeine in combination with taurine, which is an amino acid normally added to energy drinks, or other substances, have not been studied.<sup>5</sup>

Caffeine does not counteract the effects of alcohol, which is a depressant, as is commonly believed. Instead, it decreases the effects of alcohol. Caffeine increases the person's alertness, but the individual is still intoxicated and lacks coordination and motor skills. This produces a dangerous combination since the individual may feel that the alertness will enable him/her to operate machineries or drive safely.<sup>17</sup> Also, the individual may feel that he/she is well below his/her alcohol limit and may continue to consume even more alcohol placing that person at risk for alcohol poisoning or other adverse consequences.<sup>7</sup> Some consequences include dehydration since both substances are diuretics, which prevent the body from reabsorbing water.

Substances found in herbal supplements may also conflict with caffeine and produce negative results. Ma Huang, also known

as ephedra, is an ingredient commonly found in weight loss and energy supplements. It is a stimulant much like caffeine so when these two substances are present together the stimulatory effects of both may be magnified, leading to over stimulation and further complications.<sup>13</sup> Guarana may also be found in some supplements, which when mixed with caffeine may increase the stimulatory effects. These substances may also be added to energy drinks to provide more stimulatory effects, however it can lead to over stimulation and other adverse effects.

Illegal drugs or prescription drugs may also conflict with high levels of caffeine intake increasing the risk for over stimulation. For example, methamphetamine, also known as speed, is a strong stimulant that when mixed with caffeine may further increase the stimulatory effects on the central nervous system. Other stimulants include ecstasy, which is a combination of amphetamine and/or methamphetamine and hallucinogens, such as LSD. Some productions of ecstasy may contain caffeine as well to increase the stimulatory effects. Ecstasy also increases the risk for dehydration, hypertension and heart failure, all of which is aggravated by caffeine intake. Cocaine usage with caffeine may also increase convulsions or excessive nervousness. Marijuana and caffeine together may lead to dangerous rapid heart-beat. Among prescription drugs, those containing monoamine oxidase (MAO) inhibitors with caffeine may increase blood pressure to dangerous levels. Other drugs containing xanthines, sympathomimetics, oral contraceptives, cimetidine and isoniazid may increase the risk for over stimulation.<sup>7</sup> Over the counter caffeine pills such as No-Doz may also place an individual at risk for over stimulation when consumed with an excessive amount of energy drinks containing caffeine.

Sucrose and glucose are carbohydrates found in energy drinks. They are organic molecules that function in energy production in the cell as well as building blocks of cells. When glucose and sucrose are abundant in the blood, the body undergoes formation of glycogen, which is made up of large numbers of glucose molecules linked together. This serves as a storage molecule so that when there are low levels of glucose in the blood or there is a demand for glucose to be converted to energy, the body will undergo breakdown of glycogen to release glucose into the bloodstream. The glucose molecules are converted to ATP, the actual fuel molecules used by the body, through the mechanisms of glycolysis, Krebs Cycle and electron transport chain.

Energy drinks have higher than average amount of carbohydrates in comparison to other beverages, which gives the consumer a surge of energy that lasts a short while. Excessive amount of carbohydrate intake, whatever the source may be, can cause hyperglycemia, which is high blood glucose levels, in diabetic individuals. One of the consequences of this is glucosuria, which is the presence of glucose in the urine. This is

followed by excessive excretion of water into the urine causing the body to dehydrate. Combined with the diuretic effects of caffeine in the drinks, the individual may further lose water. In addition to this, glucose breakdown in the cells yields intermediates that are the starting materials for fat synthesis. With this, healthy individuals as well as those who are diabetic may experience increased body fat with excess carbohydrate consumption. This can lead to obesity over a long period of time if care is not taken.<sup>12</sup>

Taurine is an amino acid commonly present in energy drinks. Red Bull has about 400mg of this amino acid for every 100ml. The adult body is able to produce taurine from two other amino acids, methionine and cysteine, with the help of vitamin B6 also known as pyridoxine. Taurine has many roles in the body such as fat emulsification, fat absorption and detoxification.<sup>5</sup> It is a part of bile acids, which allow for the emulsification of fat globules into droplets and for the absorption of these droplets.<sup>1</sup> The fat droplets are broken down with the aid of lipase into glycerol and fatty acids, which are then converted into energy through glycolysis and beta-oxidation, respectively. If the blood already has enough glucose levels, then the fatty acids are re-esterified to glycerol and stored in adipocytes as fat.<sup>14</sup> Toxicity from taurine may result in diarrhea and peptic ulcers. Other than that, it poses no other harm.<sup>8</sup> Interactions of taurine with caffeine has not been thoroughly studied.<sup>5</sup>

Vitamin B6 or pyridoxine is a member of the B-complex family and is used in the normal breakdown of proteins, fats and carbohydrates for energy. It also helps to alleviate symptoms of depression and heart disease. High doses of it, 500-1000 mg/day, and rarely low doses, 250-500 mg/day, can cause nerve damage, which is reversible once the vitamin intake is ceased. The recommended daily allowance (RDA) is 1.3 mg/day for individuals between the ages 19 and 50 while for men and women above 50 years old, the RDA is 1.7 mg/day and 1.5 mg/day, respectively.<sup>15</sup> Red Bull has 250% of the RDA.<sup>4</sup> This is still well below the tolerable upper limit, which is 100 mg/day. Vitamin B12 is another member of the B-complex family. It functions in the conversion of energy from food and helps to reduce the risk for heart disease. Unlike B6, it poses no side effects at high doses because the body efficiently eliminates it through the kidneys.<sup>15</sup>

Inositol is an essential nutrient that forms inositol triphosphate, which functions in mediating the cell's response in the release of calcium from the calcium stores of the cells called endoplasmic reticulum. It improves neural transmission in those with nerve damage or numbness since calcium is an important component in neural transmission.<sup>19</sup> In addition to this, it is speculated that the body uses inositol to produce lecithin. Lecithin helps the body utilize fat by helping the transfer of fats from the liver to the cells. This helps in lowering cholesterol levels in the

body. Even though there are no reports of toxicity at any dosage levels of inositol and there are no recommended dietary allowances established for inositol, doctors would advise taking no more than 500 to 1000mg per day.<sup>21</sup> A can of Red Bull has 50mg of inositol, which is much less than the advice given by doctors.

Glucuronolactone is found in energy drinks. It is a metabolite produced by the body from glucose and serves as the precursor to glucuronic acid in the glucuronic acid pathway in the liver. Glucuronic acid functions in detoxification by binding to toxins and making them water soluble, which then allows for their elimination through the kidneys. This molecule also allows for the transport of hormones by binding to them and releasing them at target sites.<sup>10</sup> Glucuronolactone is easily absorbed by the body and according to toxicity studies done on animals, it has low acute toxicity at low levels. However, there is very little information available with regards to large consumption of this metabolite.<sup>5</sup>

## Conclusion

There are no thorough scientific studies that have been done on the interactions of the ingredients in energy drinks with alcohol, illegal drugs, prescription drugs and supplements. Further studies are also required for its effects relating to strenuous exercise and health complications. It seems energy drinks rely on caffeine, carbohydrates, vitamins B6 and B12 to provide the temporary energy enhancing effects. The amount of caffeine in a can of energy drink is about 1-2 cups of coffee. Whether or not this will produce any effects depends on the individual's tolerance. Carbohydrates are also abundant in these drinks; the amount is higher than the average drink. Vitamin B6 is also higher than the RDA value. The effects from these ingredients are only temporary.

Taurine does not function directly as an energy enhancer. It plays a role in fat emulsification and absorption, which can then be converted to energy. This non-essential amino acid can be obtained from the diet through meat and fish or be manufactured by the body from methionine and cysteine. So, the addition of it may not be significant relative to the daily diet. The other ingredients, inositol and glucuronolactone, have no effect on energy production.

Energy drinks may be harmless when consumed in moderation, however when it is consumed in excess it may result in over stimulation. Some energy drinks may add other stimulants besides caffeine such as guarana or ephedra, which can also lead to over stimulation when consumed in excess. Besides this, those combining energy drinks with other stimulants in supplements and/or drugs, whether it is over the counter, prescription or illegal, may find themselves with an increased heart rate,

heart palpitations and so forth. Alcohol and energy drinks will also produce dangerous physiological effects such as dehydration and possibly alcohol poisoning. The individual may also be at a higher risk for injuries or accidents. Consuming these drinks in moderation, 1-2 cans, might be relatively harmless, however before guzzling them down liberally, it might be wise to consult a doctor with regards to drug interactions and pre-existing health conditions.

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# Diet Supplement: Are you really SAFE?

Yumiko N. Lee

Corpulence and obesity are epidemics now because of the over-availability of the food and the low demands made on the metabolism by our sedentary culture. Obesity poses a threat to life, health, and well being. Drugs used for weight loss are generally called anorexiant. Most of those drugs will lose their effectiveness over time and they can be addictive and dangerous. The target population, dosage, and adverse effects from the consumption of anorexiant such as phenylpropanolamine, ephedra(Ma Huang) , chromium, meal replacement, laxatives, hydroxycitric acid, pyruvate, 5-HTP (serotonin), guarana, and some of prescription drugs are discussed in this paper. Finally, diet supplements are not substitutes for exercise or a healthy life style. People must be cautious when using any weight loss medications including herbal diets that are so-called “natural remedies.”

When you buy a product in a store, particularly something you eat, you naturally assume it's safe. Some government agency must have checked to make sure it's not harmful for you and your family. In 1994, Congress passed the Dietary Supplement Health and Education Act. This act removed dietary supplements from pre-market safety evaluations required of food ingredients and drugs. Drugs are tested for effectiveness and safety, but the 1994 legislation eliminated the FDA's authority to regulate the safety of nutritional supplements before they are on the market. The 1994 legislation also changed guidelines for marketing supplements<sup>1</sup>. Marketing representatives can make unproven claims, such as saying that a product “cures” cancer, as long as they are not selling the product at the same time.

Corpulence and obesity are epidemics now because of the over-availability of food and the low demands made on the metabolism by our sedentary culture. Weight loss is, indeed, so difficult to battle alone against a constant barrage of advertising, discrimination, and the insidious opposition of the body itself, that no one should be faulted or socially ostracized for failing or for giving up the effort altogether. On the other hand, obesity, still poses a threat to life, health, and well being, and the struggle against it is worthwhile.

According to a recent study, exercise, problem-solving skills and social support are the most important predictors of success in a weight loss program<sup>2</sup>. Successful weight loss and healthy weight management depend on long-term lifestyle changes such as reducing calorie consumption and increasing

physical activity. However, because these changes are difficult, easily obtained nonprescription weight loss products are an appealing alternative to the increasingly overweight U.S. population.

Drugs used for weight loss are generally called anorexiant. Most lose their effectiveness over time, thus requiring increased dosage, and they can be addictive and dangerous. None of these drugs deals with the underlying problems that may be causing the obesity. Unless specially instructed by a physician, people should use non-drug methods for losing weight.

People must be cautious when using any weight-loss medication, including over the counter diet pills and herbal or so-called natural remedies. Over-the-counter (OTC) diet pills that contain phenylpropanolamine (Acutrim, Dexatrim) have been known to cause severe high blood pressure and stroke if taken in doses of 75 mg or higher in the immediate-release form. The so-called “herbal-phen-fen” remedies (Herbal Phen-Fen, Phen-Trim, Phen-Cal) contain ephedrine, derived from the ephedra herb (also known as Ma Huang). Studies have reported severe side effects (rapid heart rate, high blood pressure, psychosis, and seizures) from OTC remedies that contain even small amounts of ephedrine. Eighteen deaths have occurred with its use since 1994, mostly from heart attack and stroke. Dietary supplements, teas, and laxatives that list the ingredient plantain may contain digitalis, a powerful chemical that effects the heart. Many dietary herbal teas contain laxatives, which can cause gastrointestinal distress, and, if overused, may lead to chronic pain, constipation, and dependency. In rare cases dehydration and death have occurred. Some laxative substances found in teas include senna, aloe, buckthorn, rhubarb root, cascara, and castor oil. Some fiber supplements containing guar gum has

also caused obstruction of the gastrointestinal tract.

## Phenylpropanolamine

Phenylpropanolamine, commonly known as PPA, is used as a nasal decongestant or as an appetite suppressant. It acts on many different parts of the body. PPA produces effects that may be helpful or harmful. This depends on the patient's individual condition, response, and the amount of medicine taken. PPA is the main ingredient in over-the-counter (OTC) weight loss aids Dexatrim and Acutrim, and because PPA is synthetic of ephedrine alkaloid with stimulant properties, it may reduce appetite by stimulating the Central Nervous System. (CNS)<sup>3</sup>

Until recently, PPA was considered to be a safe short-term weight reduction agent; however, many cerebrovascular and cardiac events as well as stroke were reported. Also, this appetite-reducing effect is only temporary, and is useful only for the first few weeks of dieting until new eating habits are established.<sup>4,5</sup> In November 2000, the Food and Drug Administration (FDA) issued a public health warning regarding phenylpropanolamine (PPA) due to the risk of hemorrhagic stroke. The FDA, supported by results of a research program, requested that manufacturers voluntarily discontinue marketing products that contain PPA and that consumers work with their healthcare providers to select alternative products.<sup>6</sup>

## Ephedra (Ma Huang)

More than three billion servings of weight management products containing the active ingredient ephedra, an herb also called Ma Huang, are consumed each day in this country in an attempt to beat the bulge. However, some products contain dangerous amounts of ephedra, which create many side effects. Ephedra products have stimulant properties and are purported to decrease weight when used in combination with caffeine through thermogenesis (rise basal metabolic rate and rise body temperature, so that calories burn at a faster rate) and appetite reduction. Ephedra stimulates CNS to raise blood pressure and increase heart rate.<sup>7,8,9</sup>

Ma-Huang is usually used for the disease of the respiratory tract with mild bronchospasms in adults and children over the age of six. Ephedrine became widely used as a nasal decongestant, a central nervous system stimulant, and treatment for bronchial spasm. Contraindication of this drug includes states of anxiety and restlessness, high blood pressure, angle-closure glaucoma, cerebral perfusion, prostate adenoma with residual urine volume, pheochromocytoma and thyrotoxicosis. The following side effects could occur as well; headache, irritability, urinary disorder, motor restlessness, nausea, sleeplessness, tachycardias, vomiting, and with higher dosages strong rise in blood

pressure and cardiac rhythm disorder.<sup>10</sup> Ma-Huang is the main ingredient of Metabolife.

### Overdose:

Adults should take no more than 150 mg every twenty-four hours. Doses of more than 100 grams (about 3 ounces) can be life-threatening. Symptoms of overdose include severe outbreaks of sweating, enlarged pupils, spasms, and increased body temperature. Death results from heart failure and suffocation. If you suspect an overdose, seek emergency treatment immediately.<sup>11,12</sup>

## Chromium

Chromium is an essential mineral the body needs in very small amounts, but it plays an important role in human nutrition. It is found in a variety of meats, seafood, dairy products, eggs, and whole-grain foods.

Chromium's most important function is to help regulate the amount of glucose in the blood by aiding the movement of glucose out of the blood and into cells. No recommended dietary allowance has been established for chromium, but Estimated Safe and Adequate Daily Dietary Intake is as follows; for adults (7 years and older) 50 to 200 mcg a day.

Recent evidence suggests that chromium supplements may help reduce fat in the body, probably through its effects on insulin.<sup>13</sup> However, there is very few evidence that chromium deficiency is widespread in the U.S. or any other country. Sellers of chromium picolinate have been fined by the U.S. Federal Trade Commission 32 times for making false claims about their products. But it is not likely they will stop because this supplement generates many millions in sales yearly. A settlement for a false claim seems to be just a cost of doing business for some companies.

Chromium appears to be safe when taken at a dosage of 50 to 200 mcg daily.<sup>14</sup> However, chromium is a heavy metal and might conceivably build up and cause problems if taken in excess. There have been a few reports of kidney damage in people who took relatively high dosages of chromium. A case of kidney failure appeared after taking 600 mcg per day for six weeks.<sup>15</sup>

Clinical studies show that chromium consumption does not support the body composition improvement.<sup>16</sup> In a recent study, chromosomal damage was induced both by the chromium picolinate salt and the ligand in hamster ovary egg germ cells, raising the possibility of mutagenesis and carcinogenesis. The effects were seen with concentrations that were achievable in the serum of humans who take the current recommended doses;

they were not seen with chromium nicotinate.<sup>17-20</sup>

Chromium is the main ingredient of OTC weight loss products such as Body Solution, Metabolife and Dexatrim Natural. The success of chromium picolinate is due to a well-orchestrated marketing campaign initiated by both Nutrition 21 (a supplement company in San Diego, CA) and their consultant chemist, Gary Evans, Ph.D (author of the book *Chromium Picolinate*). Nutrition 21 holds the chromium picolinate patent, but patenting laws do not require that claims for health products be valid. Independent research by the USDA Human Nutrition Research Centers in Beltsville, MD and Grand Forks, ND do not support the marketing claims made by Evans or Nutrition 21.

## Meal replacement

Like Slim Fast, Ensure and Advantage Bar, popular meal replacements are in the market to aid weight loss. Most of the meal replacement products contain multi vitamins along with carbohydrate and high fat to satisfy the appetite. This type of product is relatively balanced and rich in nutrients. However, meal replacements could help someone who participates in both a healthy diet and exercise at the products' disclosers state in order to lose weight effectively. In addition, multivitamins do not take any role in weight reduction at all though it could enhance your overall health in general for someone who is experiencing vitamin and mineral deficiency. Moreover, the quality of the product is in wide range. It is very important to follow the instructions of the product since some of the products do not contain sufficient amounts of nutrient for a meal. You may need to eat fruits or drink milk to balance the diet. Importantly, there are very few reliable clinical studies to confirm the effect of the meal replacement for weight loss<sup>1</sup>. Therefore, we do not know any side effects or adverse effects from consumption of this yet.

Hollywood 48 Hour –Miracle Diet is a very popular diet aid but it is a starvation diet method, if you read the instructions of this product. It is simply a fruit juice with a lot of vitamins! Please do not consider this as a miracle drink for you to lose weight. When you do not eat anything, you WILL lose weight. However, starvation diets are very dangerous to your system since there is no energy supply for your brain nor your heart. The degradation of protein will happen eventually.

## Laxatives

Laxatives are used to relieve constipation, but many people use it for weight control. It is used to induce diarrhea that lead to water loss in the body, which causes electrolyte imbalance. Stimulant laxatives uniformly achieve their desired goal by irritating the lining of the large intestine and the colon and causing contractions.

They are marketed under brand names such as Ex-Lax, Dulcolax, Senokot, Correctol, and Topcare, and are included in many grocery store or pharmacy brands. Many natural fiber products work very similarly as these products. The Food and Drug Administration reports that approximately 15-20 percent of adult consumers use laxatives. In addition, studies show that approximately 1 in every 5 persons with an eating disorder (anorexia or bulimia) is laxative dependent. Laxative use or abuse is a part of the standard diagnostic criteria for diagnosing an eating disorder. Approximately 4.18 percent of the population generally is laxative dependent.

Risks and dangers include, among others, dependency, electrolyte imbalance, dehydration, potassium loss, and kidney damage. Stimulant laxatives are further known to interfere with the absorption and/or effectiveness of other medications and can make the users severely dehydrated. Because these laxatives deplete essential minerals like potassium and calcium they create heart, bone, and kidney hazards. Further, in order to compensate for the resulting dehydration and essential losses of vitamins and minerals the body will retain fluids and cause weight gain up to 30 pounds.

Continuing the cycle of laxative use creates dependence, dehydration, potassium losses and electrolyte imbalances, which in turn cause dizziness and confusion and endangers the cardiac and renal systems. They can cause colon infection as well. There is protective mucus that lines the colon. Laxatives and enemas strip away this protective mucus leaving the colon vulnerable to infections. Finally, one of the most fatal dangers of laxative abuse is the risk of death. If this risk doesn't scare you, I'm not sure what will. Laxative abuse can upset your electrolyte balance and can damage muscles and tissues surrounding the heart. The heart can stop beating and without quick medical intervention, the individual can die.



## Hydroxycitric Acid (HCA)

Citric acid is a substance involved in the metabolism of carbohydrates. HCA (a modified form of citric acid) is believed by some to inhibit the enzyme that allows carbohydrates to be stored as fat. It is suggested that, in the presence of HCA, excess carbohydrates would be expended instead of being stored as fat. A decrease in appetite is purported to be a side effect of this process, which further promotes weight loss. HCA can be extracted from the *Garcinia* plant naturally, yet “natural” does not mean safe! Animal research indicates that HCA suppresses appetite and induces weight loss.<sup>22-25</sup>

According to Center for Science in the Public Interest, weight loss products containing HCA have been unsuccessful by a major pharmaceutical company due to toxicity findings. Also, there are no hard evidences to show that HCA does not prevent fat storage or promote weight loss. A double blind trial that provided either 1,500 mg of HCA or a placebo to 135 overweight men and women who also were on a calorie-restricted diet found after twelve weeks that the HCA supplementation did not produce a significant change in weight loss.<sup>26</sup> Uncontrolled and/or preliminary evidence from several other human trials suggest the possibility that weight loss might occur;<sup>27</sup> however, none of these studies is as methodologically strong as the negative trial previously mentioned.

A typical dosage of HCA is 250 to 1,000 mg 3 times daily. Supplements are available in many forms, including tablets, capsules, powders, and even snack bars. Products are often labeled *Garcinia cambogia* and standardized to contain a fixed percentage of HCA. The recommended amount of HCA intake is 1500 mg/day, yet optimal amount has not been known. No serious side effects have been reported from animal or human studies involving either fruit extracts or the concentrated chemical. However, formal safety studies have not been performed, and therefore, its safety remain unknown.

## Pyruvate

Pyruvate is used to aid weight loss by increasing resting metabolic rate<sup>28</sup>. Many marketing of supplement distribution claim that it can (1) reduce fat and weight, (2) improve exercise endurance, (3) reduce cholesterol, and (4) act as an antioxidant. However, few clinical studies are done to prove these claims. Pyruvate is a three-carbon (triose) ketoacid produced in the end stage of glycolysis. It can be reduced to lactate in the cytoplasm or oxidatively decarboxylated to acetyl CoA in the mitochondrion. Simply, it is a product of sugar metabolism. The stimulation of cell membrane by pyruvate will enhance the weight loss, yet long-term study has not been done. Gastrointestinal upset and diarrhea are the main side effects of this product. The recommended maximum intake is 44g/day.<sup>29</sup>

## 5-Hydroxytryptophan (5-HTP), Serotonin

5-HTP is a stimulant for the neurotransmitter, serotonin. 5-HTP is not found in foods to any appreciable extent. For use as a supplement, it is manufactured from the seeds of an African plant called *Griffonia simplicifolia*.<sup>30</sup>

The drug fenfluramin was one member of the Phen-fen treatment for weight loss. Although it was very successful, fenfluramine was later associated with damage to the valves of the heart, so it was removed from the market. Because fenfluramin raises the serotonin level, it seems reasonable to believe that other substances that affect serotonin might also be useful for weight reduction. Clinical studies have not yet confirmed the results of this theory yet.

In the body, serotonin is produced from the amino acid, tryptophan. Once released from the serotonergic neurons, serotonin acts as a neurotransmitter, attaching to various serotonin receptors. Stimulation of these receptors will result in numerous clinical effects. Serotonin is metabolized and inactivated by the enzymes monoamine oxidase and aldehyde dehydrogenase.<sup>30</sup> Serotonin stimulates the appetite center in the brain to aid weight loss by reducing the appetite. Appetite reduction and weight loss has occurred with doses of 600-900 mg per day.<sup>31,32</sup> However, there are many side effects by taking this product such as gastrointestinal upset, sleepiness, headache, muscle pain and anxiety. Liver damage is also reported from consumption of 5-HTP. The maximum recommended amount of 5-HTP is 900mg/day.<sup>33</sup> The theory behind taking 5-HTP as a supplement is that providing the one-step-removed raw ingredient might raise serotonin level. However, this plausible idea has not been proven.

## Guarana

Guarana is made from a dried paste of *Paullinia cupana*. It stimulates the central nervous system (CNS) to increase metabolic rate and it produces diuretic effects. Guarana is one of the ingredients of Pepsi-Cola in the United States. Guarana has a relatively high caffeine content, ranging from 2.5 to 5 percent. Guarana is listed on the Food and Drugs Administration's list as “Generally Recognized as Safe” (GRAS).<sup>34</sup> (Caffeine is also added to “cola” and “pepper” –type drinks, baked goods, frozen dairy dessert, soft candy, and the like). The consumption of Guarana could cause insomnia, irregular heart beat, elevate blood sugar, excess stomach acid, trembling, anxiety, palpitations, urinary frequency, and hyperactivity.<sup>34</sup> In 205 healthy postmenopausal women, caffeine consumption (three cups of coffee per day) was associated with bone loss in women with calcium intake of less than 800 mg per day.<sup>35</sup> A tablet of Guarana contains 30mg of caffeine. Adults should limit their consumption of caffeine to no more than 250 mg per day.<sup>36</sup> Pregnant women and children should be more conservative.

Approximate amounts of caffeine in some commonly used foods and beverages: <sup>37,38</sup>

Cup (6 oz) of boiled coffee	100 mg
Cup (6 oz) of instant coffee	65 mg
Cup (6 oz) of tea	10-50 mg
Bottle or can (12 oz) of cola beverage	50 mg
Cup (6 oz) of breakfast cocoa	13 mg
Bar (1 oz) of milk chocolate	6 mg
Tablet of caffeine	100-200 mg
Tablet of guarana (800 mg)	30 mg
Cup (6 oz) of mate	25-50 mg

FDA warns public with several phrases that pharmaceutical companies use to promote weight loss products. <sup>39</sup>

- “Fat Blockers” such as XENICAL purport to physically absorb fat and mechanically interfere with the fat a person eats. It will cause the loss of fat-soluble vitamins such as vitamin A, D, E and K as well as water from the body.
- “Fillers” such as fiber-products may absorb liquid and swell in the stomach, thereby reducing hunger. However, some products cause obstruction in the intestines, stomach, or esophagus.
- “Starch Blockers” promise to block or impede starch digestion. Not only is the claim unproven, but users have complained of nausea, vomiting, diarrhea, and stomach pains
- “Magic Weight Loss Earrings” and devices custom-fitted to the purchaser’s ear that purport to stimulate points controlling hunger have not proven its effectiveness.

## Rx weight reduction drugs:

There are many places where prescription drugs are sold online without a doctor’s office visit. Prescription drugs for weight loss are specifically for someone who really needs to reduce weight due to a medical complication. Prescription drugs are far stronger than OTC drug; therefore, the side effects are severe as well.

## Orlistat (Xenical)

**Use:** Orlistat is a prescription weight-control medication useful for the long-term treatment of significant obesity. It is a weight loss medication that targets the absorption of fat in the body rather than suppressing your appetite. <sup>40</sup> It is useful for long term use and has been shown to be effective for 1-2 years. <sup>41,42</sup> Dietary fats are inhibited from being absorbed and this allows about 30% of the fat eaten in a meal to pass through the gut undigested.

**Side effects:** Loose stools and increased gas or flatulence espe-

cially after meals containing high levels of fat. This medicine can cause changes in your bowel habits, such as fatty or oily stools, due to the elimination of undigested fat in your stool. <sup>43</sup>

## Sibutramine (Meridia)

**Use:** Sibutramine acts as a reuptake inhibitor of both norepinephrine and serotonin to regulate satiety. <sup>44</sup>

**Side effects:** Headache, dry mouth, drowsiness, constipation and difficulty sleeping may occur. <sup>45</sup> If these effects persist or worsen, notify your doctor promptly. Many drug interactions can occur.

Several studies show that Sibutramine intake significantly decrease the subjects’ weight compare to the subject with placebo. <sup>46-48</sup>

## Phentermine (Fastin)

**Use:** This medication is used as an appetite suppressant by increasing the level of norepinephrine. <sup>49</sup> It is used in conjunction with an overall diet plan to reduce weight.

**Adverse effects:** Dry mouth, sleeplessness, irritability, stomach upset or constipation may occur the first few days as your body adjusts to the medication.

Phentermine has not been studied as a monotherapy for longer than 36 weeks or approved for administration longer than a few weeks. <sup>50</sup>

## Axokine

**Use:** Re-set of “Set Point” at hypothalamus in the brain, therefore, the regaining/rebound of weight after weight loss can be prevented.

**Adverse effects:** Skin irritation at the injection site. Cough and vomiting were seen with excessive dosage.

In Nov, 2000, Double-blind placebo study of Phase II study has been done successfully. This product is still under investigation.

The optimal amount of this drug is 1 mcg/kg/day <sup>51</sup>

**TABLE 1. Differential product effects to human**

<b>Product</b>	<b>Use</b>	<b>Adverse Effect</b>	<b>Maximum Recommended Amount</b>
<b>Ephedra</b>	Reduces appetite, thermogenesis	Anxiety, restlessness, high blood pressure, glaucoma, headache, urinary disorder, nausea	150 mg/day
<b>Chromium</b>	Increases insulin effectiveness	Liver and kidney damages	200 mcg/day
<b>Meal Replacement</b>	Relatively low fat and balanced meal if the instructions are followed	May gain more weight when consumed with other food	None
<b>Laxative</b>	Induces defecation and urination	Dehydration, water retention and electrolytes imbalance, potassium loss, kidney damage, colon infection	None, must follow the instruction on the package
<b>Hydroxycitric acid</b>	Prevents conversion of fat from carbohydrate	Not known	1500 mg/day
<b>Pyruvate</b>	Increases carbohydrate utilization to cells	Not known	44 g/day
<b>Serotonin</b>	Stimulates appetite center in the brain to reduce appetite	Gastrointestinal upset, sleeplessness, headache, and anxiety	900 mg/day
<b>Caffeine</b>	Stimulates central nervous system to rise metabolic rate and increase diuretic effect	Insomnia, elevated blood sugar, irregular heart beat, excess stomach acid, anxiety, hyperactivity, frequent urination and palpitation, decrease calcium absorption	250 mg/day

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# Herb Power:

## Are there any useful supplements when it comes to treating sexual dysfunctions?

Martin S. Mach

Immense industries have sprung up around correcting sexual dysfunctions such as impotence and infertility. Remember Viagra or fertility clinics? Admittedly, the range of new brews and potions under the term of “herbal supplements” is bewildering when it comes to curing impotence or infertility, but there is little evidence (and often it is contradictory) that they have any benefit to public health. Traditional herbal and mineral supplements such as ginseng, yohimbe, ginkgo biloba, zinc, and newer trendy herbal products have been extensively used throughout the world for many symptoms, not just sexual dysfunctions. However, questions persist regarding the scientific evidence and efficacy of these products, as they remain unproven.

While Americans use supplements on a regular basis and supplements are main components in their health regimens, it might come as a surprise that in the age of Viagra and in vitro fertilization that Americans still use herbal treatments for sexual dysfunctions such as impotence or infertility. Reasons for using these products range from improving the chances of pregnancy to enhancing sexual arousal. However, many of the problems related to sexual dysfunctions may be more serious such as psychological or physiological difficulties--beyond the remedy of mere herbs. Other times a change in diet or the introduction of an exercise regimen is sufficient to bring about the desired outcome. Unfortunately, even with well-documented and practiced procedures such as in vitro fertilization the success rates are low. Frankly, the claim that herbs and other supplements are unnecessary and a waste of money may be true. Supplements listed in detail in this article are those that are most often recommended for sexual dysfunctions, are commonly listed in the ingredients of herbal supplements, and/or there have been attempts to scientifically prove the claims of these substances. Nonetheless, many substances have been suggested or tried as treatments for sexual dysfunctions but they have not been scientifically proven effective at this time. The bottom line is that there are no well-established natural treatments for these sexual dysfunctions.

Impotence, or erectile dysfunction (ED), is the inability of a male to attain or sustain an erection sufficient for intercourse. It can be a persistent condition; however, almost

half of all men experience impotence occasionally. Common non-herbal treatment options include the drug Viagra, mechanical devices that use a vacuum to produce an erection, drugs for self-injection, and implantation of penile prostheses. Impotence can have either physical or psychological (or both) causes. Although some doctors used to believe differently, most researchers and doctors now believe that a majority of men suffering from impotence have physical causes. Psychological counseling can be helpful, however, if the impotence is related to emotional factors. There are several physical contributors to impotence, including atherosclerosis, diabetes, pituitary tumors, hormonal imbalances, hypothyroidism, multiple sclerosis, smoking, chronic alcohol use, or what doctors sometimes call “venous leakage” of blood. Certain medications can also be the culprit. Common supplements and herbs that claim to be helpful in the case of impotence are **L-arginine**, **ginkgo biloba**, **ginseng**, **yohimbe**, and **zinc**. Many other herbs and supplements are reputed to improve sexual function, including ashwaganda, DHEA (dehydroepiandrosterone) suma, damiana, pygeum, choline, pantothenic acid, L-phenylalanine, L-tyrosine, nicotinic acid, and muira puama. However, there is as yet no real evidence that they work.

Male infertility, as defined by doctors is the failure of a couple to achieve pregnancy after a year of unprotected intercourse. In men, infertility is usually associated with a decrease in the number or quality of sperm. Infertility in men can be caused by anatomical defects to hormonal imbalances. There are a multiple possible underlying causes for this including biochemical, psychological, environmental, and the exact cause may be unknown or a mixture of variables. In about half of all cases, however, the source of the problem is never discovered. Some of the causes of infertility are responsive to natural medicine, whereas others are not. **Zinc**, **coenzyme Q10 (CoQ10)**, and **L-arginine** are natural treatments widely

recommended for male infertility. Many other substances have been suggested as treatments for infertility, including the herbs ashwaganda, pygeum, as well as supplements PABA (para-aminobenzoic acid), L-carnitine, beta-carotene, Vitamin C, Vitamin E, Vitamin B12, SAmE (S-adenosyl-L-methionine) and selenium. However, the evidence that they really work is negligible. The good news is that without any treatment, approximately 25% of supposedly infertile men bring about pregnancy within a year of the time they first visit a doctor, this is symptomatic of low fertility rather than infertility.<sup>1</sup>

Female infertility is defined by doctors the same way as male infertility, the failure to become pregnant after a year of unprotected intercourse. Common techniques designed to correct female infertility range from hormone therapy to in vitro (test-tube) babies. Although these methods have occasional successes, there is considerable controversy about the high cost and low rate of effectiveness of fertility treatments in general. Infertility in females can be caused by a variety of problems such as sex-hormone abnormalities, low thyroid function, endometriosis, scarring of the tubes connecting the ovaries with the uterus, or a host of other causes. Smoking, drinking alcohol, and even caffeine have been found to cause female infertility. Tubal disease and endometriosis (a condition in which uterine tissue begins to grow where it shouldn't) account for 50% of female infertility; failure of ovulation is the cause of about 30%; and cervical factors cause another 10%.<sup>2</sup> **L-arginine** has been studied for its effects on women's infertility and libido. Gross deficiencies of many nutrients including iron, B vitamins, Vitamin E, and beta-carotene reduce female fertility, but not much is known about the specific role most nutrients play. PABA, Vitex, Chasteberry, and ashwaganda are more exotic treatments recommended. As with infertile males, infertile women often eventually become pregnant with no medical intervention at all. There is no good published evidence that any dietary supplement can improve libido or sexual function in women.

## Arginine (L-arginine)

An amino acid found in many foods; it is needed to produce sperm. Also, it can raise levels of nitric oxide in the blood and body tissues that can increase blood flow, which is necessary for arousal. The best dietary sources of arginine are meat, nuts, eggs, milk and cheese.

There is some evidence that arginine helps some men. Most research shows that several months of arginine supplementation increase sperm count and quality<sup>3,4</sup> and also fertility.<sup>5,6</sup> Notwithstanding, some studies have reported that arginine helps few,<sup>7</sup> if any, infertile men.<sup>8</sup> Only two small studies have looked at whether arginine has any effect on sexual performance in humans. In both studies, the results

were less than impressive. In one study the results looked positive, however, the results in a subsequent study couldn't be duplicated.<sup>9</sup> In the second published study, researchers at Tel Aviv University in Israel gave 46 men with erectile dysfunction either 5,000 mg of arginine or a placebo every day for six weeks. Arginine made no difference in erectile function or sexual activity, performance, or satisfaction, according to questionnaires filled out by the men. What's more, the researchers could detect no increased engorgement of the arginine-takers' genitals.<sup>10</sup> Two unpublished studies have looked at ArginMax, a popular product that contains a combination of arginine, ginkgo, ginseng, a handful of vitamins, and (in the women's formula) damiana. In one study, 21 of 24 men with erectile dysfunction who took ArginMax for four weeks reported improvement in their ability to maintain erection during intercourse, compared to five of 24 men who were given a placebo. In the other study, 25 of 34 women who took ArginMax for four weeks reported that their sex lives were more satisfying, compared to 16 of 43 women who were given a placebo.<sup>11</sup> Until the studies are peer-reviewed and published, there is no way to validate the results.

Though there are conflicting, insufficient, or only preliminary studies suggesting a health benefit from arginine, nonetheless, many physicians of natural medicine advise 4 grams of arginine per day for several months to see if it will help infertile men. However, in research the amount varies considerably (2-30 grams per day).

Arginine appears to be free of obvious side effects, so far. Although, some doctors are concerned that increases in growth hormone triggered by arginine could overwork the pancreas. Occasional side effects reported with large doses of this dietary supplement include diarrhea. Those with kidney disease or liver disease should talk to their physician about taking this supplement. Those with herpes (either cold sore or genital herpes) should not use arginine supplements, because arginine can stimulate replication of the virus. Some preliminary research has shown high usage (30+ grams per day) of arginine can both promote and interfere with cancer growth.<sup>12-14</sup> No known drug interactions exist with arginine.

## Coenzyme Q10 (CoQ10 or ubiquinone)

Coenzyme Q10 is a vitamin-like compound that is present throughout the body. Coenzyme Q10 is primarily found in fish and meat. Coenzyme Q10 is a powerful antioxidant that protects the body from free radicals.<sup>15</sup> As a coenzyme, this nutrient aids metabolic reactions, such as the complex process of transforming food into ATP, the energy on which the body runs. Synthesis of sperm requires considerable energy. Due to its role in energy production, coenzyme Q10 has been studied in infertile men.<sup>16</sup> Preliminary research reports that supplementation of coenzyme Q7 a related molecule, increased sperm counts in a group of infertile

men. However, this supplement has little scientific support and/or minimal proven health benefit.

Adult levels of supplementation are usually 30-300mg per day, depending on the health of the individual. There are no known toxicities or significant side effects associated with coenzyme Q10. However, this supplement should not be used if you are pregnant or breast-feeding because the safety of coenzyme Q10 is unknown. Certain medications interact in a positive and/or negative way with coenzyme Q10. There have been reports that coenzyme Q10 may decrease the effectiveness of blood-thinning medications such as warfarin.<sup>17</sup> Be aware that there are some interactions between coenzyme Q10 and pharmaceuticals. Per the book "A-Z Guide to Drug-Herb-Vitamin Interactions", coenzyme Q10 should not be taken in conjunction with the follow-

combination of ginkgo and papaverine has reportedly been effective for treatment of erectile dysfunction.

Ginkgo may improve circulation, and several studies have shown that it can help with sexual function. But none of them compared the herb to a placebo, so there's no way to tell whether the improvement would have occurred no matter what the subjects were given. One study involving 30 men who were experiencing erectile dysfunction as a result of medication use (such as selective serotonin reuptake inhibitors and other medications), found that approximately 200 mg per day of ginkgo had a positive effect on sexual function in 76% of the men.<sup>21</sup> Unfortunately, this was not a blind study and we do not know how ginkgo would affect healthy men.



ing: (generic or Trade names listed) Adriamycin, Amitriptyline, Apo-Gemfibrozil, Atorvastatin, Blocadren, Cosopt, Coumadin, Desipramine, Doxepin, Doxorubicin, Elavil, Fluvastatin, Gemfibrozil, Imipramine, Inderal, Inderide, Lescol, Lipitor, Lopid, Lovastatin, Mevacor, Norpramin, Novo-Gemfibrozil, Pravachol, Pravastatin, Propranolol, Simvastatin, Sinequan, Timolide, Timolol, Timoptic, Tofranil, Tricyclic Antidepressants, Warfarin, Zocor.<sup>18</sup>

## Ginkgo Biloba (GBE or Maidenhair tree)

Ginkgo has been extensively used worldwide; a popular prescribed medical herb in Europe with hundreds of studies performed on this substance. Ginkgo biloba works by increasing arterial blood flow by reducing the stickiness of blood. Ginkgo has been used to treat and help some impotent men.<sup>19,20</sup> The

The average daily dose is 120 mg of dried extract in 2 or 3 doses orally (in clinical studies up to 240 mg were used as a daily dose or 40-80 mg 3 times a day). Ginkgo biloba is considered to be safe and side effects are rare. Ginkgo does not appear to alter heart rate and blood pressure or to change cholesterol and triglyceride levels. Mild gastrointestinal complaints could occur as side effects. Allergic skin reactions have been observed on rare occasions. Other hypersensitivity reactions are the occurrence of spasms and cramps, and in cases of acute toxicity, atonia and adynamia. Ginkgo has blood-thinning properties and therefore should not be used if you are taking anticoagulant (blood-thinning) medications or nonsteroidal anti-inflammatory medications (NSAID), such as aspirin, naproxen (Aleve) clopidogrel, dipyridamole, heparin, ticlopidine, or warfarin.<sup>22</sup> High doses of Ginkgo biloba could decrease the effectiveness of anticonvulsant therapy in patients taking carbamazepine or valproic acid to control seizures. If you are tak-

ing these medications, you should not use ginkgo without consulting your health care provider. Because ginkgo decreases platelet aggregation (stickiness), there is some concern that ginkgo may increase risk of intracranial (brain) hemorrhage.<sup>23</sup>

Ginkgo biloba may be beneficial during treatment with cyclosporine because of its ability to protect cell membranes from damage. If you are currently taking cyclosporine, you should consult your doctor before adding any new herbs or supplements to your existing medication regimen. The combination of papaverine and ginkgo may be effective for the treatment of erectile dysfunction in patients who do not respond to papaverine alone. Consult with your doctor about whether this is an appropriate treatment option for you. Although there has been one literature report of increased blood pressure associated with the use of ginkgo during treatment with thiazide diuretics, this interaction has not been verified by clinical trials. Nevertheless, you should consult with your healthcare provider before using ginkgo if you are taking thiazide diuretics. Additionally, there has been a report of an adverse interaction between ginkgo and trazodone, an antidepressant medication, which resulted in an elderly patient going into a coma. Therefore, you should not take ginkgo if you are taking trazodone for depression without consulting with your doctor first.<sup>24,25</sup>

## **Ginseng (*Panax ginseng*, *Panax quinquefolius*, *Eleutherococcus senticosus*)**

There are three different herbs commonly called ginseng: Asian, Chinese or Korean ginseng (*Panax ginseng*), American ginseng (*Panax quinquefolius*), and Siberian or Russian “ginseng” (*Eleutherococcus senticosus*). Siberian “ginseng” is actually not ginseng at all, but it is believed to function identically as ginseng. Dried, unprocessed ginseng root is called “white ginseng,” and steamed, heat-dried root is “red ginseng.” Amongst many claims for ginseng, the improvement of sexual performance is one, but there is as yet little direct evidence that it really works.<sup>26-28</sup>

Ginseng’s actions in the body are due to a multifaceted interplay of chemicals. The primary is composed of the ginsenosides, which are believed to increase energy, counter the effects of stress, and enhance intellectual and physical performance. Thirteen ginsenosides have been identified in Asian ginseng. Siberian ginseng contains eleutherosides. Other constituents include the panaxans, which help lower blood sugar, and the polysaccharides (complex sugar molecules), which support immune function.

There have been thousands of research papers published on ginseng. Unfortunately, nearly all involved animals that

received injections of ginseng extracts directly into the abdomen. There are only a few good double-blind human studies of ginseng taken by mouth. In experiments with animals, ginseng generates the release of nitric oxide. So does the anti-impotency drug Viagra. In the only published human study, 30 Korean men with erectile dysfunction who took 300 mg a day of Korean red ginseng for three months reported significant improvements in their sexual performance.<sup>29</sup> Thirty similar placebo-takers reported less improvement. However, one small study isn’t enough. Ginseng, especially American ginseng, is claimed to exhibit some estrogen-like activity and may improve vaginal lubrication in menopausal women.<sup>30</sup>

The typical recommended daily dosage of Asian ginseng is 1 to 2 grams of raw herb, or 200 mg daily of an extract standardized to contain 4-7% ginsenosides. Siberian ginseng is taken at a dosage of 2 to 3 grams whole herb or 300 to 400 mg of extract daily. Normally, a 2 to 3 week period of using ginseng is recommended, followed by a one to two week rest period. Finally, because Asian ginseng is so expensive, some products actually contain very little, often in an adulterated weaker form. Some products that claim to contain ginseng actually contain none.

Used in the recommended amounts, ginseng is generally safe and non-toxic. In certain instances, however, it may cause overstimulation and possibly insomnia.<sup>31</sup> Consuming caffeine or other stimulants with ginseng increases the risk of over-stimulation and gastrointestinal upset. Persons with uncontrolled high blood pressure should not use ginseng. Long-term use of ginseng may cause menstrual abnormalities and breast tenderness in some women. Ginseng is not recommended for pregnant or lactating women. Adverse affects include diarrhea, restlessness, nausea, vomiting, anxiety, tachycardia, hypertension and extreme nervousness. There is some evidence that ginseng can interfere with drug metabolism, specifically drugs processed by an enzyme called “CYP 3A4.”<sup>32</sup> One study reported that ginseng might increase the effects of digoxin, a medication used to treat heart conditions. You should consult with your doctor before using ginseng with digoxin in order to assure that it is appropriate for you to combine the two. There have been reports of a possible interaction between ginseng and the antidepressant medication, phenelzine, resulting in symptoms ranging from manic-like episodes to headache and tremulousness. Therefore, you should not use ginseng with phenelzine. There have been reports that Asian ginseng may possibly decrease the effectiveness of the blood-thinning medication, warfarin. If you are currently on warfarin therapy, you should refrain from taking Asian ginseng. Ginseng may block the effects of analgesic medications such as morphine. You should not use ginseng with morphine except on the advice of your doctor. There has been a report that Siberian ginseng increased levels of digoxin in the blood but did not cause toxic effects. However, you should consult with your health care provider before using Siberian ginseng if you are currently taking digoxin.

## **Yohimbe (*Pausinystalia Yohimbe*)**

Yohimbe is an over-the counter supplement made from the bark of a West African tree that has been traditionally used to treat fever,

coughs, and leprosy.<sup>33</sup> Additionally, yohimbe is often used for sexual disorders and as an aphrodisiac. It is marketed in a number of products for body building and "enhanced male performance." Yohimbe is a prescription drug approved by the Food and Drug Administration (FDA) to dilate (widen) the pupils of eyes. The major identified alkaloid in yohimbe is yohimbine, a chemical that causes vasodilation, thereby lowering blood pressure. Since yohimbe can cause blood vessels to dilate and blood flow to increase, some physicians prescribe it for erectile dysfunction.

Yohimbe has been shown in several double blind studies to help treat men with impotence;<sup>34,35</sup> negative studies have also been reported.<sup>36,37</sup> In a 1997 meta-analysis that pooled the results of seven studies, 15 to 43 mg of yohimbine (a compound extracted from the yohimbe bark) every day for four to ten weeks was more effective than a placebo in helping men who were suffering from one or more sexual dysfunctions. Problem is that the meta-analysis couldn't determine which conditions were helped and which weren't. And two later studies found no benefit from yohimbe.

A tincture of yohimbe bark is often used in the amount of 5-10 drops three times per day. There are also standardized yohimbe products available for the treatment of impotence. A typical amount of yohimbe is 15-30 mg.<sup>38</sup>

Yohimbe is contraindicated in liver and kidney diseases. Side effects that can appear include, among other things, anxiety states, elevated blood pressure, exanthema, excitatory states, queasiness, sleeplessness, tachycardia, tremor, and vomiting. People with a history of heart disease, high blood pressure, or kidney diseases should be wary of yohimbe. Side effects are well recognized and may include central nervous system stimulation that causes anxiety attacks. At high doses, yohimbine is a monoamine oxidase (MAO) inhibitor. MAO inhibitors can cause serious adverse effects when taken concomitantly with tyramine-containing foods (e.g., liver, cheeses, red wine) or with over-the-counter (OTC) products containing phenylpropanolamine, such as nasal decongestants and diet aids. Individuals taking yohimbe should be warned to rigorously avoid these foods and OTC products because of the increased likelihood of adverse effects. Symptoms of over dosage include weakness and nervous stimulation followed by paralysis, fatigue, stomach disorders, and ultimately death. Serious adverse effects, including renal failure, seizures and death, have been reported to FDA with products containing yohimbe and are currently under investigation.

## Zinc

Zinc is an essential trace mineral, which, next to iron, is the second most abundant trace mineral in the body. We absorb 20 to 40% of the zinc that is in our food. Zinc from animal foods like red meat, fish, and poultry is the most prevalent. Zinc in vegetables, dairy products, and eggs are less available to our bodies.

Zinc is stored primarily in muscle but is also found in red and white blood cells, the retina of the eye, bones, skin, kidney, liver, and pancreas. In men, the prostate gland contains more zinc than any other organ.<sup>39</sup> Zinc is essential for normal sexual development during male adolescence and for producing healthy sperm. Zinc is necessary for the maturation of sperm, ovulation and fertilization. A lack of zinc can reduce testosterone levels.<sup>40</sup>

For men with low testosterone levels, zinc supplementation raises testosterone and also increases fertility.<sup>41</sup> For men with low semen zinc levels, zinc supplements may increase both sperm counts and fertility.<sup>42</sup> Most studies have infertile men take zinc supplements for at least several months. Unfortunately, only two good studies have tested zinc supplements on sexual function, and both involved a total of 17 men on dialysis for kidney disease. The men in one of the studies reported improved potency when zinc was added to their dialysis fluid.<sup>43</sup> The men in the other study reported no improvement.<sup>44</sup> Whether zinc helps healthy men is unknown.

The most common dosage level is 25mg daily. The dosage range for zinc is 2-50mg daily. Zinc is relatively non-toxic. Ingestion of high levels of zinc can induce copper deficiency. High doses of zinc (150mg/day) can cause diarrhea, dizziness, drowsiness, vomiting, loss of muscle coordination, and lethargy. One known negative side effect of too much zinc is that it lowers HDL (good) cholesterol and raises LDL (bad) cholesterol. Zinc decreases the absorption of oral quinolones, a class of antibiotics that includes ciprofloxacin, norfloxacin, ofloxacin, and levofloxacin, as well as tetracycline antibiotics.<sup>45-48</sup> Similarly, zinc interacts with nonsteroidal anti-inflammatory drugs (NSAIDs), and could reduce the absorption and effectiveness of these medications. If you take NSAIDs and are considering taking zinc supplements, talk with your healthcare provider first. Penicillamine, a medication used to treat Wilson's disease and rheumatoid arthritis, decreases zinc levels. Since zinc supports immune function, it should not be taken with corticosteroids, cyclosporine, or other medications intended to suppress the immune system. Hormone replacement therapy consisting of estrogen and progesterone derivatives may reduce loss of zinc in the urine, particularly in women with osteoporosis. There has been at least one report of an interaction between zinc and hydralazine, a medication used to treat high blood pressure, which resulted in a lupus-erythematosus-like syndrome (characterized by a facial butterfly rash, fever, leg and mouth ulcers, and abdominal distress). It would be wise to refrain from using zinc supplements with hydralazine.<sup>49</sup>

## Useful Resources

- \* <http://www.supplementinfo.org>
- \* Foster, S. and Tyler, V.E., (4<sup>th</sup> ed.). *Tyler's Honest Herbal: A Sensible Guide to the Use of Herbs and Related Remedies*, New York, the Haworth Herbal Press. 2000.

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# Supplements for Strength and Energy

Shafinaz Hussein

The demand for sports performance has led to an increase in consumption of ergogenic supplements, also called energy enhancing supplements. As a result of The Dietary Supplement Health and Education Act of 1994, manufacturers do not have to get FDA approval to market a product. This translates into freedom to choose but it also means vulnerability to unsafe substances and fraud. Creatine, choline, carnitine, coenzyme Q10, ephedrine, androstenedione, growth hormone and amino acids are among the many ingredients in energy supplements. Studies done on these supplements are few and focus on the short term, instead of the long term. Before consuming these aids, it is important to consider risks and effects associated with these supplements. Efficacy is also influenced by age, gender and level of physical activity.

With an increasing demand on sports performance, it is not uncommon these days to find an athlete loading up on supplements to give them that extra boost to extend their performance. Many non-athletes are also emulating their sports heroes in hopes of attaining more energy, strength and a healthier life. These supplements are more accurately referred to as ergogenic supplements or aids. Ergogenesis means the production of energy therefore an ergogenic supplement is defined as those substances that provide energy and increase physical performance beyond normal training.<sup>1</sup> The Dietary Supplement Health and Education Act of 1994 resulted in looser regulation of the supplement industry in contrast to the drug industry. The manufacturer of the supplement does not have to get approval from the FDA before placing the product on the market.<sup>2</sup> With this, consumers have more freedom with regards to supplements but are not protected from unsafe substances and fraud. This does not exclude ergogenic supplements. There are many such supplements promising to boost your strength and give you that extra edge. But before you start taking your supplements, there are many issues that need to be addressed, such as risks and effects. Among the many ingredients in supplements available, the most prevalent and well known are creatine, choline, carnitine, coenzyme Q10, ephedrine, androstenedione, growth hormone and amino acids.<sup>1</sup>

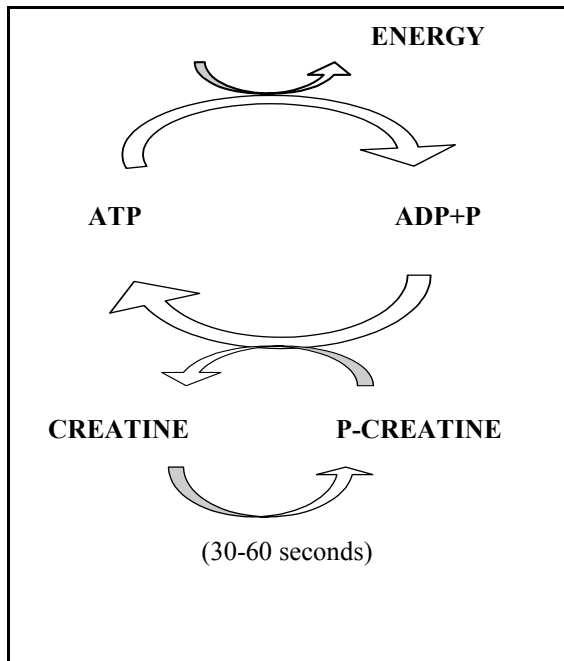
## Creatine

Creatine is naturally found in the body and composes about 0.2% of the body mass. It is acquired from the diet, in particular from eating meat, and is synthesized by the liver from the

amino acids, glycine, arginine and methionine, when creatine from the diet is insufficient. The body uses creatine to help generate energy when the supply of ATP has depleted. ATP is the fuel molecule of the body. Energy is harvested from these molecules when the phosphate group is released from the molecule generating ADP and free phosphate. Phosphocreatine, creatine with a phosphate group attached, then helps regenerate the ATP supply by donating the phosphate group to the ADP. This also produces creatine. Creatine can be converted back to phosphocreatine, but it takes about 30 to 60 seconds. (Fig. 1).<sup>3</sup>

Studies found that consumption of 20g of creatine per day increases total creatine by about 20% in the muscles and activity time by about 4x. With anymore supplementation, creatine gets excreted into the urine as creatinine. Since, the lifecycle of creatine involves the conversion to phosphocreatine, during which no energy can be generated, the activities best suited for it are brief, intermittent, high-intensity activities, such as sprints, where the activity involves an all out expansion of energy in a short period of time and a long period of time of non-activity during which creatine can be converted to phosphocreatine. Studies have shown that endurance activities, such as marathons, do not benefit from creatine supplementation.<sup>4</sup> This is because the creatine is not converted to phosphocreatine, which is essential for energy production. In addition to this, creatine supplementation may even have a negative effect on the runners due to increased muscle weight, which reduces running time. One particular study demonstrated that athletes, supplemented with creatine, running a distance of 6 km had a slower finishing time compared to the control group, which had no creatine.<sup>5</sup>

In addition to this, there are athletes who respond to the supplementation, while others who do not. Besides a boost in energy, creatine can produce significant gain in lean muscle mass, but this can only occur with weight training. Studies have shown that muscles that were not exercised did not experience increase in mass so creatine intake alone will not promote increase in muscle mass.<sup>6</sup>



**Figure 1.** The ATP-ADP energy cycle in the body. When ATP is hydrolyzed to ADP and P (free phosphate), energy is released. When the ATP supply is exhausted, no energy can be harvested and no work can be done. To regenerate the ATP supply, p-creatine (phosphocreatine), donates a phosphate group to ADP producing creatine and ATP. Creatine is converted to p-creatine after 30 to 60 seconds.

Risks associated with creatine have not been thoroughly studied especially the long term risks, but many physicians and anecdotal reports have mentioned of potential risks such as dehydration, heat related illnesses, nausea, reduced blood plasma volume, muscle cramping, muscle strain, gastrointestinal disturbances and increased liver transaminases.<sup>4,6</sup> A growing concern of doctors and scientists is the effect creatine has on the kidneys. Since excess creatine is excreted into the urine, supplementation results in urine concentration of creatine that is about 90x higher than normal. This is a risk factor for nephrotoxicity, where the kidneys are damaged in a variety of ways, such as renal tubule toxicity and kidney stone formation. A recent study published in the American Journal of Kidney Diseases demonstrated in an animal model with renal cystic disease that creatine

supplementation increased the progression of the disease. Though studies on humans have not been done, it is advised that those with or at risk for renal disease should avoid creatine supplementation.<sup>7</sup> Finally, the Agence Francaise de Securite Sanitaire des Aliments or AFSSA, which is the French equivalent of the FDA, has noted the potential for cancer from creatine supplementation. This is based on theories that state that creatine may be converted to carcinogenic molecules. No long term studies have actually been conducted to test this hypothesis but this is something to keep in mind.<sup>8</sup>

## Choline

Choline is a lipotropic B vitamin involved in the workings of the muscle. Choline is used by the body to synthesize acetylcholine, which is a neurotransmitter secreted by the nerve cells to stimulate contractions of the muscles.<sup>9,10</sup> Choline can be found circulating in the blood and the plasma membrane of the cells. The plasma membrane is an alternate source of choline for acetylcholine synthesis when the choline in the blood is low.

Choline supplementation helps to increase sports performance by maintaining high concentrations of the molecule in the skeletal and cardiac muscles. When concentrations are high, acetylcholine release is increased as well, which in turn increases muscle contractions and sports performance.<sup>11</sup> It was found that athletes, after exercising for more than two hours, had a decreased level of plasma choline. This is associated with the fatigue athletes experience at the end of marathons or other endurance exercises lasting for more than two hours. Choline in the blood, obtained from the diet, is normally sufficient for activities lasting a short period of time,<sup>9</sup> however for activities lasting two or more hours, choline supplementation seemed to help in maintaining high choline levels. This was demonstrated in several studies where choline administration prior to exercise helped to maintain choline levels above the baseline for up to two hours after exercising. Studies done on timed swimming and running exercises for more than two hours showed improved performance and decreased time. Besides increased muscle contractions, choline also helped to alleviate fatigue.<sup>10</sup>

The body can synthesize choline from the amino acid glycine. Choline may also be obtained from foods such as liver, cauliflower, soybeans, spinach, lettuce, nuts and eggs.<sup>9</sup> For athletes in endurance sports, a choline rich diet may not be enough. Additional choline supplementation is available in capsules, sports bars and drinks. Choline can also be found in the form of lecithin or phosphatidylcholine, ingredients commonly found in foods and supplements.<sup>13</sup>

No adverse effects have been observed with low levels of choline supplementation, but higher doses, about five-gram doses, may cause diarrhea, nausea and abdominal discomfort.<sup>13</sup> Also, because of its role in nerve stimulation, higher doses may worsen epileptic conditions.<sup>14</sup> Users have also complained about fishy

body odor as a result of high choline or lecithin consumption.<sup>13</sup>

## Coenzyme Q10

Coenzyme Q10 (coQ10) is a fat-soluble molecule and is found in the mitochondria, which are the energy producing organelles of the cell. CoQ10 belongs to a group of molecules called quinones. This molecule plays a role in energy production in most living things that utilize oxygen and thus have been called ubiquinones (ubiquitous-quinones). The body produces energy, in the form of ATP molecules, first by breaking down glucose or other sugars. The electrons released from the breakdown are then brought to the mitochondria, where they flow along the electron transport chain and end up in the formation of water. CoQ10 is specifically found in the complexes that make up the electron transport chain, which is in the inner mitochondria membrane. It is this chain that is responsible for the production of ATP molecules.<sup>15,21</sup> In addition to its role in energy production, coQ10 is also an anti-oxidant. Anti-oxidants are molecules involved in the neutralization of free-radicals or oxidants, such as oxygen oxidants, which are naturally produced by the body. These free-radicals, though naturally produced, may be harmful since they are able to combine with other substances to damage cell membranes. An excess of free-radicals in the body, called oxidative-stress, may eventually lead to mitochondrial abnormalities, neurodegenerative diseases<sup>15</sup> and various cancers, such as breast cancer and colorectal cancer.<sup>24</sup> CoQ10 functions as an anti-oxidant by donating electrons to those free-radicals thereby neutralizing it. This ability is derived from the oxidation-reduction reactions that coQ10 undergoes in the electron transport chain.<sup>22</sup>

Because of its role in energy-production, supplement manufacturers have included it in many ergogenic supplements, even though there is no substantial scientific proof. On the contrary, one study indicated that cyclists experienced no significant change in oxygen uptake, anaerobic and respiratory compensation thresholds, blood lactate, glucose and triglyceride kinetics, heart rate and blood pressure before and after coQ10 supplementation.<sup>25</sup> The body can manufacture coQ10, however it also relies on the diet from foods such as organ meats, muscle meats, fish, spinach, soy and nuts. Reports indicate that there are no known side-effects of coQ10 supplementation but there have been anecdotal reports that say otherwise. Some consumers complain of headache and nausea during exercise. Other side effects reported include heartburn, fatigue, mild diarrhea and skin reactions.<sup>23</sup>

## Ephedra

Ephedra, also known as Ma Huang, is a Chinese medicinal herb commonly used to alleviate colds, flus, asthmas, and allergies. The active constituent of it, ephedrine, is also found in other over-the-counter cold medicines, such as Sudafed, and func-

tions as an adrenergic bronchodilators. It stimulates the  $\beta_1$  and  $\beta_2$  receptors of the sympathetic nervous system and the release of norepinephrine, which triggers the fight-or-flight responses. This type of response increases blood glucose levels, which can be utilized for ATP production. In addition to this, the heartbeat increases, pupils dilate, blood vessels constrict and so forth so that the body is prepared to 'fight' or 'flight'.<sup>26</sup>

Side effects associated with ephedra include nervousness, insomnia, dizziness, heart palpitations, high blood pressure, and weakening of the digestion. It is advised that those with heart disease, diabetes, hypertension or hyperthyroidism should avoid ephedra. There have been cases where athletes have experienced severe side effects, even death. In August of 2001, a Northwestern football player, Rashidi Wheeler died after a pre-season conditioning drill. He is among 80 deaths that have been linked to ephedrine. Physicians indicate that ephedra may be dangerous in combination with rigorous exercise. Because of its ability to constrict blood vessels, the body has a much difficult time dispersing heat from the body. When an individual performs rigorous exercise, the excess heat produced by the body may build up, leading to hyperthermia, which is increased body temperature beyond normal.<sup>27</sup> Ephedra with monoamine oxidase inhibitor (MOA) should be avoided since it can increase the effects of ephedra. Physicians have also warned against the combination of ephedra with caffeine, which is a common ingredient in most supplements. This combination has its effects on the cardiovascular and nervous systems, such as increases in the blood pressure. In general, the combination with stimulants should be avoided.<sup>26,27</sup>

In 1997, the Food and Drug Administration proposed labeling regulations for substances containing ephedrine in response to the deaths that have been linked to ephedrine. The proposals prohibit the sales of substances containing 8mg or more of ephedrine and the inclusion of stimulants in the substances with ephedrine. Other proposals include mandatory labeling stating that consumers must not use the product for more than seven days. The FDA also warns the consumer about ephedrine containing substances that claim to have the effects of illegal drugs such as ecstasy since they can produce severe side effects.<sup>28</sup>

## Androstenedione

Androstenedione, or andro for short, is an anabolic steroid that is produced by the adrenal glands, ovaries, testicles and other organs and can be converted to testosterone or estrogen. Other molecules related to it include androstenediol and norandrostenedione. These supplements have increased in popularity after the baseball player McGwire admitted to consuming andro. They are used to increase growth hormone and testosterone levels to boost athletic performance and sex drive. Though some athletes report increased strength, many studies indicate that andro produces no significant effect on strength. One study

published in the Journal of the American Medical Association, showed no significant increase in strength between two groups of men, ages 19 to 29, where one was given andro and the other a placebo.<sup>29</sup> Another double blind study involving fifty men, who were given either a placebo, androstenedione or androstenediol, revealed significant increase in testosterone levels in those men given androstenedione. Both androstenediol and androstenedione decreased the levels of high-density lipoprotein cholesterol and increased the risk for coronary heart disease.<sup>30</sup>

Besides an increased risk for heart disease, other side effects associated with the increased testosterone levels include acne, scalp hair loss, aggressiveness, irritability and increased risk for cancer. Women may experience increased facial hair growth. Estrogen levels may also be increased with supplementation, which can induce development of breasts in men. Older men may experience prostate enlargement.<sup>29</sup>

The International Olympics Committee, the National Football League and the National Collegiate Athletics Association have banned the use of andro. Professional baseball however remains open to andro.<sup>29</sup>

## Growth Hormone

Human growth hormone (hGH) is a hormone that is produced by the anterior pituitary gland that stimulates the liver and other tissues to produce Insulin-like Growth Factor-1 (IGF-1). It is IGF-1 that exerts the effects associated with growth hormone at various target sites. When hGH was first discovered, its function was thought to be only for lengthening of bones. Children with hGH deficiency were given the hormone so that they will reach average height. But with more research, scientists have discovered that hGH functions in many other ways to maintain a youthful body. The hormone levels decrease as we age and the consequences of that are the signs of aging. Increasing the hormone in the blood has been shown to enhance skin thickness and elasticity, decrease wrinkles from sun damage, increase bone density, decrease LDL (low density lipoprotein, the bad cholesterol), increase HDL (high density lipoprotein, the good cholesterol) and improve blood flow to the kidney. For athletes, the benefits of increasing GH levels include decreased total body fat, increased lean muscle mass, exercise capacity and energy levels.<sup>39</sup>

There are several ways to increase GH levels in the blood and one way is through injection by prescription under the supervision of a physician. Any other method of administration such as sprays, pills and creams do not work for many reasons. First off, the size of the molecule is too large to penetrate the skin and membranes therefore oral sprays or creams simply do not work. When ingested, the molecule has to be broken down into smaller fragments such as amino acids to be

absorbed. For this reason pills do not work either and it would be equivalent to supplementing with amino acids. Furthermore, the amount of GH in those supplements is very minute. If there were a significant amount of GH in it, it would be regulated by the FDA. This is why GH injection from the doctor's office can only be obtained with a prescription. Besides this, it is very difficult to store the molecule at room temperature at suboptimal conditions without it losing its shape or breaking into smaller fragments. Only perfectly intact molecules are able to function and have effect. The source of the growth hormone is also crucial. The only form that works is the one obtained through recombinant DNA technology. The gene responsible for the hormone is inserted into the bacterial genome so that when the bacteria multiply, the gene for the hormone is expressed as well. Hormone obtained this way is free of microorganisms or any other impurities. GH from other animals does not work since the hormone is species specific. Plants do not produce GH so be skeptical of plant derived GH.<sup>39</sup>

Other ways to possibly raise GH levels in the body is by using secretagogues or hGH precursors. Secretagogues are substances that stimulate the pituitary gland to release GH. Such substances may increase the hormone but they also increase the levels of other hormones significantly that may be undesirable. Some of the other hormones such as cortisol may counteract the effects of GH and thereby reduce the efficacy. In general, secretagogues may increase the levels of GH but the amount raised is very small and is accompanied by the increase of unwanted hormones as well. HGH precursors are molecules that will eventually form the hormone hGH. By supplementing with these precursors, the body will more likely form the hormone. Research has indicated that generally, there are no changes in the hormone level and if there was an increase in the levels it is only limited to young athletes. Scientifically, this may not be proof for the efficacy of the substance since young adults naturally produce the hormone at high levels.<sup>39</sup>

## Amino Acids

Amino acids are abundant in nature but only twenty are found in our bodies. They are used to build other kinds of amino acids and various proteins that are used in building muscle and in metabolic reactions. There are also amino acids that are not involved in protein synthesis, which is the case for carnitine. Amino acids are categorized into two groups: non-essential and essential. Non-essential amino acids are those that can be produced by the body, while the essential amino acids are those that cannot be made by the body and must be obtained from the diet. It is important to consume amino acids several hours before or after meals since they can reduce absorption of other nutrients. Excess of any one kind of amino acid may interfere with the absorption of other amino acids so it is important to consume them in moderation.

*Carnitine* is not involved in protein synthesis like other amino acids but is involved in fat oxidation in the mitochondria, which is the powerhouse of the cell. The mitochondria breaks down fat-

ty acids to produce energy for work. Carnitine's specific role is to escort fatty acids into the matrix of the mitochondria. Without carnitine, fatty acids are impermeable to the inner membrane of the mitochondria. Fatty acid degradation, termed beta-oxidation, yields ATP molecules, which provides energy for the body to do work. Fatty acids are secondary sources of energy, which means that the body uses them when the glucose supply, the primary source of energy, is exhausted. Despite that, fatty acids are important sources of energy- they provide about 70% of the energy needed by the skeletal muscles. In addition to this, carnitine is also involved in the removal of metabolic by-products. They escort them out of the cells and out of the body into the urine.<sup>15</sup>

The major source of carnitine, making up about 75% of the requirement, comes from the diet from foods such as organ meats, fish, muscle meats and dairy products. The body may also produce the molecule from the amino acids, methionine and lysine.<sup>16</sup> Theoretically, carnitine may be able to improve athletic performance by providing more energy through beta-oxidation and reducing muscle soreness by decreasing the build up of metabolic wastes such as lactic acid, however research studies and anecdotal reports have been ambiguous. Some studies have shown that carnitine supplementation improves maximal oxygen consumption respiratory, which is a measurement of metabolism, while other studies have shown otherwise.<sup>17,18</sup> Some anecdotal reports mention that carnitine helped to decrease muscle soreness, while others report no effect.<sup>19</sup> The benefit of carnitine may also depend on the type of physical activity. Intense exercises such as sprints may benefit more than endurance activities, such as marathons.<sup>20</sup>

It should be noted that L-carnitine, also known as left-handed carnitine or acetyl-L-carnitine is the physiologically active isomer. The right-handed carnitine or D-carnitine is the inactive isomer and should be avoided because it may actually decrease metabolic reactions in the cell.<sup>18</sup> Products containing both isomers should also be avoided because it decreases carnitine stores.<sup>16</sup>

*Arginine* is a non-essential amino acid. It can be found in foods such as meats, nuts, milk, cheese, eggs, grains, vegetables (except celery and turnip) and chocolate. Its function include metabolism of nitrogen, which is a product of protein degradation. It also stimulates the production of growth hormone (GH) from the pituitary gland. However the amount of GH produced through arginine supplementation may be very small to have any significant effect at all. One may have to consume enormous amounts of arginine to stimulate the production of significant amounts of GH. A large amount of arginine supplementation or of any other amino acids is not advisable. Side effects that have been reported include diarrhea, nausea and ataxia. Arginine also works to stimulate the thymus and thus increase the immunity. There are several precautions that must be noted with arginine supplementation. Those infected with herpes should not consume arginine since it increases the flare-

ups. The virus responsible for herpes requires arginine for it to grow and multiply.<sup>38</sup> Arginine supplementation should also be avoided for those with schizophrenia and diabetes.<sup>31</sup>

*Glutamine* functions in increasing muscle mass by decreasing the breakdown of muscles. Though the liver may be able to produce it, which makes it a non-essential amino acid, it is conditionally essential. This means that under certain conditions, supplementation with glutamine may be needed since the body may not be able to produce enough. Such conditions include strenuous exercise, critical illness or trauma. One research study done on athletes, where the glutamine levels before and after exercise were measured, revealed that glutamine levels after exercising decreased significantly in contrast to pre-exercising levels. Some athletes even had lowered levels of glutamine several days after the activity. This shows that glutamine from the diet and manufactured by the body may not be enough and supplementation may be required for these athletes. Glutamine also helps to neutralize acids that build up during exercise. These acids cause muscle soreness and fatigue and are neutralized by the production of bicarbonate stimulated by glutamine. Glutamine's negative charge also helps to negate the positive charge of the acids. Besides increasing muscle mass, glutamine also stimulates the pituitary gland to release growth hormone (GH) however the amount of GH secreted by the stimulation of glutamine may be very low that there might not be significant effects of the hormone. Besides supplement pills, glutamine can be found in foods such as chicken, fish, meat and vegetables. Side effects have not been reported when taking low doses. High doses of about 20mg or more are not recommended.<sup>33, 34</sup>

*Leucine, isoleucine and valine* are essential amino acids and are categorized under branched chain amino acids (BCAA). They may be found in dairy products and red meat. These amino acids help to preserve muscle glycogen stores, prevent degradation of muscle protein and help to maintain muscle tissue,<sup>35</sup> all of which can help to increase energy levels, endurance, mental performance while at the same time preventing fatigue. According to the central fatigue theory, BCAA help in reducing the uptake of tryptophan in the brain. Tryptophan is the precursor of serotonin, which depresses the central nervous system and causes fatigue. Low levels of BCAA increase the uptake of tryptophan therefore supplementation with it is theorized to delay fatigue. Many research studies have been performed and the results are ambivalent.

Some studies showed that BCAA supplementation helped to improve endurance and mental performance while others showed no effects of BCAA.<sup>37</sup> The scientists in the University of Illinois revealed, through a series of experiments done on rats, that recovery time is decreased when leucine is ingested after intensive workouts.<sup>36</sup> Further research has to be done to resolve the role of BCAA in exercise. If the central fatigue theory is true, then endurance athletes will most likely benefit from BCAA supplementation by delaying fatigue. Power ath-

-letes, who are active in sports, have a short duration of intense energy expansion, will probably not benefit from BCAA.<sup>37</sup>

## Conclusion

These ingredients comprise a small fraction of the cornucopia of ingredients available. Since the FDA does not regulate these substances, the issue of safety should be of concern to consumers. The fact that supplements consist of natural products and/or substances that are naturally produced by our bodies does not mean that it is harmless. Impurities, improper dosing, misleading labels, dangerous concentrations and drug interactions are all ingredients for disastrous consequences. In choosing a supplement, it is highly recommended to seek the advice of a physician because of the potential for complications. Some energy supplements may conflict with prescription, illegal or over-the-counter drugs. They may also conflict with other supplements, such as weight loss supplements. In addition to this, energy supplements when consumed with alcohol or energy drinks may cause adverse effects. Many

studies that will be encountered will be ambivalent; some claiming that it is the best product available while others stating that it is useless. It is important to read those studies that have been conducted by the government or various educational institutions. Studies done by the supplement manufacturers will tend to be biased. In addition to this, most studies done are short-term studies and there are no substantial studies done on the long-term effects of these supplements.

Also, the studies done are on specific types of people, such as athletes, who have much different metabolism than the average person. Because of this, the studies and anecdotal reports from consumers may not be applicable to some people. People differing in the level of physical activity, gender and age will react differently to supplements. Perhaps this is one reason behind the multitude of results in the research conducted.

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# Anti-Depression Supplements

Michelle Biba

**Depression strikes about 17 million Americans adults each year. An estimated 15 percent of chronic depression cases end in suicide. Americans are inching themselves closer and closer to over the counter medicines. Most of the common symptoms of depression include tension, anger, irritability, mood swings, headache, bloating, and changes in appetite and sleep. There is a wide selection of over the counter medicines that include herbal supplements. The most common ingredients that are found in the anti-depression supplements include St. John's Wort, kava, serotonin, SAME, and Valerian.**

Millions of Americans suffer from Depression and Anxiety each day. Depression strikes about 17 million American adults each year--more than cancer, AIDS, or coronary heart disease--according to the National Institute of Mental Health (NIMH). An estimated 15 percent of chronic depression cases end in suicide. Women are twice as likely as men to be affected. Although seeking a counselor to help these people with depression may not be the readily accessible option, Americans are inching themselves closer and closer to over the counter medicines. Although some people think Depression is Depression, many don't realize that there are different types of depression and that some herbal medications may not be effective enough to remedy the depression. There is a wide selection of over the counter medicines that include herbal supplements.

Approximately 12% of the American population in 1997 have used herbal medications at some point in their time, a 380% jump from 1990<sup>1,2</sup>. The most common ingredients that are found in the Anti-Depression supplements include St. John's Wort (*Hypericum perforatum* L.). Along with a few other herbal supplements such as kava kava, serotonin, SAME and valerian, we find that anti-depressant supplements are not recommended for people who are suffering from major depression. Those who are suffering from major depression should seek help from a physician.

Most of the anti-depressants found on the market are targeted on helping the patient control the amount of serotonin levels in the brain. Several of these anti-depressants are targeted for controlling the chemical imbalances in the brain. Selective reuptake inhibitors (SSRIs) inhibit the reuptake of serotonin. These anti-depressants affect the uptake of norepinephrine, serotonin and dopamine to different degrees. The most common symptoms of depression include tension, anger, irritability, mood swings, headache, bloating and changes in appetite and sleep. Depres-

sion is a serious case that affects about 17% of our population today. Some of the most popular anti-depressants that are prescribed by a doctor are Paxil, Zoloft and Prozac. These anti-depressants inhibit the re-uptake of the serotonin levels in a given individual.

The use of herbal supplements after perioperative care has been considered rather detrimental to one's health. There are 8 herbs that are used on a considerable basis within the population. These herbs account for more than 50% of all single herb preparations among the 1500 to 1800 herbal medications sold in the United States.<sup>3</sup> Among the eight commonly used herbs, Echinacea, Ephedra, garlic, ginkgo, ginseng, kava, St. John's Wort and valerian, St. John's Wort, the one that is responsible for improving one's mood. It can significantly increase the metabolism of many concomitantly administered drugs, some of which are vital to the perioperative care of certain patients. The long half-life and alterations in the metabolism of many drugs make concomitant use of St. John's Wort a particular risk.<sup>3</sup> Pharmacokinetic data suggests that perioperative taking herbal medicines should discontinue their use of such herbs at least 5 days prior to surgery. It is also recommended for those who are awaiting an organ transplant to discontinue the use of herb medicines.

Several studies have been conducted in order to determine the effectiveness of treating depression with St. John's Wort. Randomized, controlled double blind trials were selected. The absolute increased response rate with the use of St. John's Wort ranged from 23% to 55% higher than with the placebo, but ranged from 6% to 18% lower compared with tricyclic antidepressants.<sup>4</sup> It has been found that hypericum extract has biological activity, such activity includes pseudohypericin, xanthones, monoterpenes, Beta-sitosterol, quercetin, and catechin. Many of these substances have been shown to bind to neuroreceptors in the brain and to inhibit the uptake of various neurotransmitters thought to be involved in depression.<sup>5-7</sup>

## Comparison of St. John's Wort with other antidepressants

In one study, the tricyclic antidepressants were compared with the effectiveness and the amount of doses that were used in the herbal medicines. The usual dosage of a tricyclic antidepressant is usually one dose, however with the herbal medication, the dosage was increased to 4-5 doses, which still didn't meet the minimum amount of doses that is required to treat the depression when using tricyclic antidepressants. The side effects are rare and appear to be well tolerated. They include nausea, rash, fatigue, restlessness, and photosensitivity.<sup>4</sup> Although these symptoms seem to be rare, there is no exclusive way to prevent them.

## St. John's Wort

This is an aromatic perennial herb that belongs to the family Hypericaceae. The name is derived from St. John's the Baptist, since the herb was found close to his birthday, June 24. It has been used and described as the most useful remedy in the Middle Ages. Recently, in Europe the herb has been administered as a tea to cure cases of anxiety, depression and unrest.<sup>8</sup> In a meta-analysis of 23 randomized trials of St John's Wort extract in 1757 outpatients with depressive disorders, Linde et al. concluded that St John's Wort was significantly superior to placebo, and effective comparably with standard antidepressant drugs. The daily dose of either hypericin, the reference substance for standardization or of total extract varied from 0.4 to 5.4 mg and 300 to 1800 mg, respectively. In 13 studies comparing a single St John's Wort extract dose with placebo, 55.1% of St John's Wort-treated depressed patients showed significant improvement vs. 22.3% with placebo.<sup>9</sup>

An increasing amount of support due to efficacy to help instigate the purpose of using St. John's Wort as a treatment for Depression. Since this herb seems to be distributed as the first line for drug for treating depression many can find this herb on the market. The market is out there for St. John's Wort however, not enough is known about the mechanisms of action nor the science behind the herb.

The three active ingredients to St. John's Wort are hypericin, pseudohypericin, and hyperforin. These are the three active ingredients in St. John's Wort, which are thought to be responsible for its antiviral and antidepressive properties.

In one study performed in Germany, it was found that St. John's Wort was effective towards combating depression in patients with mild depression and those who had suicidal tendencies (scored 18 or above on the Hamilton depression scale). The authors of the study agree that this herbal drug would be an effective first-line treatment in patients with mild to moderate de-

pression.<sup>10</sup>

## S-Adenosylmethione (SAME)

SAME was introduced into the U.S. market as a dietary supplement in 1999. In a number of other countries, SAME has been used for over 20 years to treat certain conditions such as depression, osteoarthritis, and liver disease.<sup>11</sup> It is naturally found in human cells. This potential anti-depressant plays a role in the methylation reactions of the body, which includes gene expression, cell membrane homeostasis, and hormone, and neurotransmitter synthesis.<sup>12</sup> Using SAME comes with the notion that serotonin, dopamine and melatonin are metabolized and that's how depression occurs. When the SAME is used, an increase of cerebrospinal fluid occurs which would indicate a crossover of the blood-brain barrier. Some depression patients may have low serotonin levels associated with low levels of SAME.<sup>13,14</sup> In a meta-analysis done in Italy, SAME was found to be more efficacious than placebo in the treatment of depression and is equally

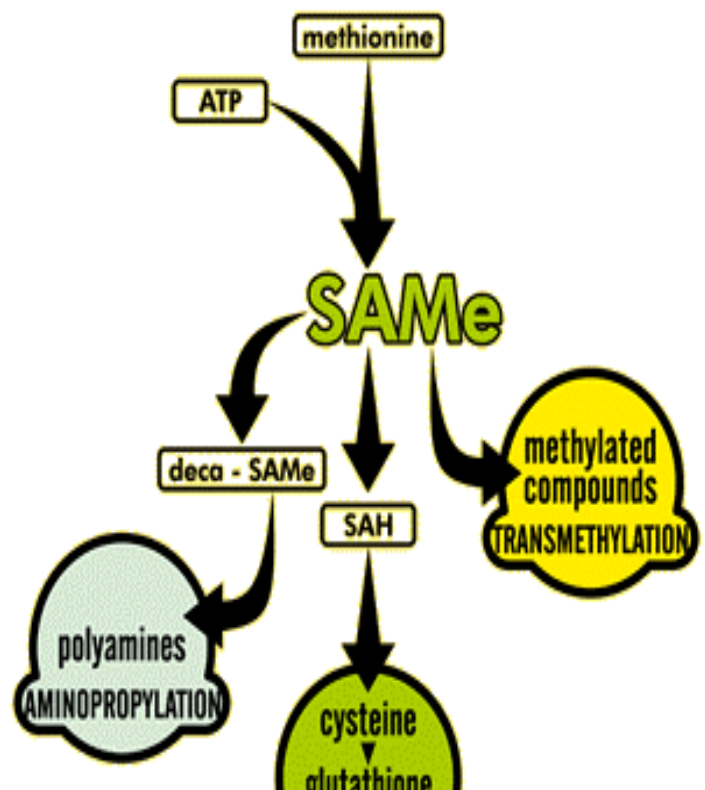


Figure 1: During transmethylation, S-adenosylmethionine (SAME) influences nerve-cell communication by increasing the activity of neurotransmitters, such as dopamine and serotonin.<sup>11</sup>

effective as tricyclic antidepressants, with a lower amount of side effects found.<sup>14</sup> Although SAME acts as an antidepressant, it warrants further research. After several studies have been made there are no validated long-term safety or efficacy of SAME, further studies should be made in order for this amino acid metabolite to be distributed.

For the past 20 years, S-adenosylmethionine (SAME) has been safely and successfully prescribed by European physicians to treat their patients with depression and osteoarthritis. Since SAME's recent introduction in the U.S., physicians have experienced similar successes.<sup>11</sup> The results of over 75 clinical trials confirm that SAME is safe and efficacious. Patients taking prescription antidepressant medications should consult their physician before beginning to take SAME. Individuals with bipolar depression should only use SAME under medical supervision.

A 1997 randomized, double-blind, multicenter study found no statistical difference in side effects between patients who received 1200 mg SAME per day (n = 62) and those who received placebo (n = 61).<sup>15</sup> A two-year study published in 1987 reported that SAME is well tolerated at 400 mg daily.<sup>16</sup> The tolerability was assessed as "very good" by over 80 percent of both patients and physicians, while no patients or physicians assessed tolerability as less than "medium." No patients discontinued the study due to side effects.

## Kava Kava

Kava refers to both the rootstock and to the traditional inebriating beverages derived from *Piper methysticum* Forst. f (family Piperaceae). The kava rootstocks come from the tropical Pacific Islands. They Pacific Islanders would normally consume these drinks at dusk or with an evening meal. By grinding the rootstock and soaking the pulp in cold water, the active constituents come into a thick brew.<sup>17</sup> The US Food and Drug Administration is looking into the possibility that kava-kava can damage the liver. An FDA spokesperson said that they heard reports from Europe, especially Germany and Switzerland, of possible links to liver complications.<sup>18</sup> Kava has found to be ineffective in treating mild depression and is still an unknown herb with respect to the side effects it may produce.<sup>19</sup>

A double-blind study conducted late last year investigated the effects of kava (*Piper methysticum*) on stress related to "daily hassles of life." The study involved 60 subjects between the ages of 18 and 60, of whom 29 took kava and 31 placebo. Subjects were assessed five times during the four-week study in five areas: interpersonal problems, personal competency, cognitive stressors, environmental stresses and varied stressors. In each of the four weeks after baseline, the group taking kava supplements showed statistically significant decreases in stress in every category, while the placebo group showed little varia-

tion.<sup>20</sup>

Over the past 110 years, kavalactones were deemed the active compounds in kava kava. Although the kavalactones are the primary active components, other components appear to possess activity as well. Relaxing and anti-anxiety effects of a crude kava preparation have been shown to be more pronounced than those of isolated kavalactones. Kavalactones have also been shown in studies to be more rapidly absorbed when given in the kava extract rather than the isolated kavalactones.<sup>21</sup>

We find that kava kava has some benefits since small doses produce a sense of well-being whereas large doses may produce relaxation, lethargy, and drowsiness. The herb may improve memory, vigilance, and reaction time. The anti-anxiety effect has been noted as being similar to oxazepam (a tranquilizer). It has been demonstrated to decrease anxiety, heart palpitations, chest pain, headaches, dizziness and gastric irritation. It also relaxes muscles and relieves spasms in both skeletal and smooth muscles.<sup>22</sup>

## Valerian

The valerian is a tall perennial herb whose hollow stem bears opposite leaves and white or reddish flowers.<sup>23</sup> German health authorities have indicated that valerian is an effective treatment for restlessness and for sleep disturbances resulting from nervous conditions.<sup>23</sup> It has been reviewed through a few studies that valerian is not an effective herbal supplement in treating depression. It may aid sleeplessness, however even that may be something that researchers are still questioning. Valerian is used as an anti-anxiety drug and has been reported to have sedative as well as anti-depressant qualities. Valerian has also been used to reduce headaches, chest tightness, mydriasis, abdominal pain, and the tremor of the hands and feet.<sup>24</sup>

A 58 year old man with a history of coronary artery disease, hypertension, and congestive heart failure was admitted to a hospital. He had a history of using 53mg to 2 g of valerian root daily to help him sleep and relax. Even though they had treated him for almost attaining cardiac arrest, during his extubation he had under went a psychotic mental state equivalent to delirium. His use of valerian indicated that perhaps, the herb has interfered with his GABA release transmission. Valerian extracts have been shown to influence synaposomal GABA release.<sup>25</sup> The use of benzodiazepines have been found to exert their anxiolytic and adverse effects by enhancing the  $\gamma$ -aminobutyric acid (GABA) neurotransmission. Physicians need to be warned using valerian root, since it may associated to serious withdrawal symptoms.<sup>26</sup>

**TABLE 1. Differential product effects to human**

Product	Use	Adverse Effect	Maximum Recommended Amount
<b>St. John's Wort</b>	Works well as TCAs for mild or moderate depression	Rare photo-sensitivity rash	300 mg 3 times daily
<b>SAMe</b>	Possibly efficacious in treatment of depression; poorly studied, cost prohibitive	None recorded	400 to 1,200 mg daily
<b>Kava Kava</b>	Improvement of mental function. Small doses promote a sense of well-being.	Safe if not consumed at excessive quantities (skin lesions would occur)	For anxiety relief: 50-70 mg 3 times daily For sedation: 180-210 mg nightly
<b>Valerian</b>	Treat sleep disorders and restlessness	Heart disturbance if taken after a surgery	200 mg to 1g a day

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