Caffeine: An Overview

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Caffeine is a psychoactive stimulant drug (Mahomed, 2014), found in plants like coffee beans, tea leaves, cacao seeds, and cola nuts (Tilling, 1997). Caffeine is widely available, in over 60 plants (Barone, 1984), which contributes its presence in a wide range of products like coffee, tea, energy drinks, soft drinks, and medicines, which modern people consume frequently (Preedy, 2013). People from all over the world, of all ages, socioeconomic statuses consume caffeine daily (Preedy, 2013). While consumption of caffeine is high, it is still a drug that can have an effect on multiple aspects of the human body. The popularity of caffeine consumption, around the world, creates the need for understanding the full effects of caffeine on the human body.

Caffeine occurs naturally in plants. A variety of leaves, beans, and fruit, like coffee beans and tea leaves (Mahomed, 2014), contain caffeine as a chemical defense mechanism against predators like insects and fungi (Frischknecht, 1985). Plants only need to produce a small amount of caffeine to have an effect on predators. Caffeine can cause infertility, paralysis and death in predators. For example, the larvae of the tobacco hornworm will be killed if they are feed a nutrient medium that has been supplemented with only 0.3% caffeine (Frischknecht, 1985). When the larvae consume a nutrient medium with added caffeine, the worm’s phosphodiesterase activity and intracellular cyclic AMP are both inhibited. The inhibition of phosphodiesterase and intracellular cyclic AMP in the worms, causes a reduction in weight gain and ultimately death (Frischknecht, 1985).

Plants produce caffeine, which accumulates on the plant tissue that is at risk of being consumed by predators, like young leaves, seeds, and buds (Frischknecht, 1985). Caffeine is produced during the plant’s most fragile stages. For example, when a leaf
first buds, a layer of resin protects it but when the resin dries the leaf becomes particularly fragile. This is when the production of caffeine is most useful, because the leaf will be protected by caffeine until the leaf is able to increase its rigidity (Frischknecht, 1985). This is also when the leaves are harvested to be used in products like tea, because this is when the leaf contains the highest amount of caffeine. As the plant increases with age, and is less susceptible to damage from predators, less caffeine is produced (Frischknecht, 1985).

Tea is the oldest form of a caffeine-containing beverage on record. The first written record of tea is from 2737 B.C., during the reign of Chinese emperor Shen Nung (Barone, 1984). Tea has been popular in Asia for a substantial amount of time. However, tea did not reach Europe until the 1600s when Dutch traders introduced it (Barone, 1984). The history of tea is proof that beverages containing caffeine have been popular for thousands of years.

Coffee consumption has been popular for a considerable length of time. The first written record of coffee consumption is from the 10th Century (Barone, 1984). However, it is thought that coffee may have been cultivated as early as 575 A.D., in Ethiopia (Barone, 1984). Coffee was first eaten as a food when the berries were eaten whole or added to food, and later a beverage similar to wine was made from coffee berries (Barone, 1984). Coffee consumed as a hot beverage was first developed around 1000 A.D. by the Arabians who called the hot wine ‘gahwah’ (Barone, 1984). The drink then spread through Turkey, and eventually reached Europe during the 1600’s (Barone, 1984). The popularity of coffee has yet to decrease, and is still popular around the world.
Consumption of caffeine in the form of cocoa and chocolate products has had popularity similar to that of coffee and tea. Cocoa consumption is relatively new, compared to the history of tea and coffee, as the first record of cocoa consumption comes from 1519 A.D. (Barone, 1984). During the first recorded incident of cocoa consumption the emperor of the Aztecs served a sweetened chocolate drink to the Spanish conquerors (Barone, 1984). The drink was brought back to Spain, and quickly became popular, especially among the upper class. Then a method of making chocolate bars was developed in Switzerland in 1876, and has been wildly popular ever since (Barone, 1984).

The most recent popular use of caffeine has been in soft drinks. Caffeine was used as a flavor component in soft drinks since the 1880s (Barone, 1984). The use of caffeine in soft drinks is different from tea, coffee and chocolate because caffeine does not occur naturally in soft drinks. Instead caffeine that has been isolated is added to the soft drinks during their production.

People have consumed caffeine for many centuries in its natural forms (Barone, 1984). Caffeine can be extracted and isolated from plants through the process of decaffeination (Mahomed, 2014). To decaffeinate plant material the plant material is roasted, soaked it in water, the plant matter is removed and the remaining water is passed through carbon filters (Mahomed, 2014). Once extracted caffeine is a white, bitter, crystalline xanthine alkaloid (Mahomed, 2014). The purified caffeine powder can then be added to products like drinks or medicines.

Caffeine can occur in products naturally or isolated caffeine can be added during production. Coffee and tea are examples of natural caffeine products. This means most
forms of coffee and tea contain caffeine only as a result of the plant products used to make the coffee or tea, and no additional isolated caffeine is added. Medications that contain caffeine often contain isolated caffeine that is added to the product during the manufacturing process. The ability to isolate caffeine is essential to modern products because it provides the opportunity to add caffeine to products that would not naturally contain caffeine.

In the United States, at least 80% of adults consume caffeinated products according to the Food and Drug Administration. This percentage is considered a large number for United States due to a population of roughly 320 million people. However, not every adult is knowledgeable about the side effects and limits of their caffeine intake. The FDA mentioned studies suggesting that there will be no adverse effects as long as caffeine is consumed in moderate amounts. These moderate amounts are limited to 300-400 mg daily for healthy adults with no medical conditions. As for pregnant women, this amount is reduced to 200 mg of caffeine intake daily.

From acknowledging these daily limits, one can proceed to safely explore the world of caffeinated products. Some of the familiar caffeinated products include coffee, tea, soft drinks, energy drinks, and dark chocolate bars. Other less popular caffeinated products are over-the-counter pills and caffeine powder. All of these products contain a variation of caffeine concentration which determines the serving size of each product. Most soft drinks are clear in labeling their caffeine content, but a few products can be unclear with their labeling which makes it hard for consumer to determine the safe amount. For example, caffeine powder can be the most dangerous caffeinated product to
consume because normal consumers do not have the knowledge to determine the safe limit of consumption.

Not only are some consumers oblivious to the caffeine concentration in products, but so are they to the ways coffee beans are processed to preserve their caffeine content. According to Spiller (1998), there are two ways to process green coffee beans: the dry method and the wet method. The dry method is less expensive and less controlled than the wet method (Spiller, 1998, p. 5). Through the dry method, the coffee berries are harvested all at once both from the tree and the ground to be evenly dried in the sun. As the berries dry out, the red skin, pulp, mucilage, and parchment fuse together to create a thick hull. Spiller (1998) also mentioned, “This hull is removed in a hulling machine that simultaneously polishes off most of the silverskin layer” (p. 5). In order to remove the silverskin layer completely, the coffee beans first needed to be soaked in water then the silverskin is removed mechanically before the beans can be packaged and shipped (Spiller, 1988, p. 5). On the other hand, the wet method is executed through handpicking the coffee berries. After they are picked, they get transported from a water-flotation system to a pulping machine to have the outermost skin and pulp removed while exposing the mucilage (Spiller, 1988, p. 5). The mucilage of these berries then get removed in concrete fermentation tanks with the help of lactobacilli and yeasts (Spiller, 1988, p. 5). After this process, the parchment layer gets exposed and the hulling process follows to complete the wet processing method of coffee beans (Spiller, 1988, p. 5).

One other caffeinated product with three distinct methods of processing is tea. Tea processing methods are more specific than coffee because each method is created for a specific end-product. Segall mentioned that most tea leaf are processed to yield Green
and Black teas, and some small amount is processed to yield Oolong tea (Segall, 2000, p.3). For Black teas, the leaves are picked from the plant before the withering process can initiate. This process is to reduce moisture exposure by drying the leaves under the sun from two to twenty-four hours. The process following withering is called the bruising step which is to gently break the leaves. Segall said the objective is to break the veins of the leaves to allow the juices to rise to the surface for further drying. The leaves then get rolled out to be dried as many as six times. This is when various fermentation periods occur with “oxidative enzymatic process” (Segall, 2000, p.3). The temperatures for the fermentation period must not exceed 80°F to prevent enzyme inactivation (Segall, 2000, p.3). When these leaves cool down, they are ready to be sold as Black tea.

The method to process Green tea is slightly different from Black tea because it does not have the oxidative enzymatic activity that Black tea has. The leaves that are picked are immediately followed with oxidative enzyme inactivation. This meant the objective is to avoid sun exposure to allow leaves to cool until they can be roasted. After the roasting process, the leaves are allowed to cool before they get rolled and roasted again until it obtains a dark greenish to blue-olive color. In the final step, the leaves are dried and can still retain moisture up to 10% (Segall, 2000, p.4).

As for Oolong tea, the leaves are semi-fermented which means the process is quite similar to black tea. After the leaves are withered, they get short period of sun exposure to stimulate oxidative enzyme activity to initiate fermentation. The process is followed by dry heating, and then rolling which is similar to the Black tea processing. The final step is to have the leaves rolled and killed until they reach the perfect level of dryness (Segall, 2000, p.4).
Some studies have shown that from these tea processing methods, some green tea catechins can have some health benefits. The catechins were tested to have antioxidative chemicals, antibacterial and antiviral activities (Hara, 2000, p.165). The catechins can play important roles in intestinal flora, antibacterial function, digestive tract (Hara, 2000, p.166). With these full benefits from green tea catechins, tea not only provides caffeine for alertness, but it also has many health benefits.

Caffeine metabolism is the process by which the psychoactive drug is absorbed into the bloodstream and broken down into metabolites. This pathway begins with caffeine absorption through small blood vessels that line the walls of the stomach and small intestine. The acidic environment of the stomach does not break down caffeine before absorption occurs. In the small intestine absorption takes place in a region called the duodenum. The duodenum is the first part of the small intestine that is attached to the stomach. It takes approximately 45 minutes for caffeine to reach maximum concentration in the bloodstream. Absorption would be slightly slower after a meal with a full stomach, or after a long period of fasting. Caffeine has a half-life of four to five hours, however this can be prolonged for pregnant women, infants, and patients with hepatic disease (Thorn, 2012, p. 2). The half-life of caffeine in newborns may be as long as 100 hours because of the slower rate of caffeine metabolism due to their undeveloped digestion system.

Once caffeine has been absorbed into the bloodstream, it is metabolized in the liver by an enzyme complex called cytochrome P450 oxidase. This process is slower than the absorption of caffeine from the small intestine. The enzyme complex splits the psychoactive drug into three metabolites known as Dimethylxanthenes which play
different roles in the body’s regulation. These metabolites are then further metabolized by enzymes and excreted in the urine. Only around 3% of the psychoactive drug is excreted in the urine, while the rest is completely metabolized.

The three metabolites are Paraxanthine, Theobromine and Theophylline, and have different effects on the human body. Paraxanthine increases lipolysis, leading to elevated levels of glycerol and free fatty acids in the blood plasma. Almost 84% of caffeine is broken down to Paraxanthine during metabolism. Unlike the other two metabolites, Paraxanthine cannot be found in natural products such as plants.

The second most abundant metabolite resulting from caffeine metabolism is Theobromine at 12%. It is highly fat soluble, and has a longer half-life than caffeine (Mitchell, 2011. 816). Theobromine is a bitter alkaloid that can be found in tea and chocolate. It dilates blood vessels, increasing the amount of blood that can flow through them. This metabolite is also a diuretic, which means it increases urine volume by increasing blood flow through the kidneys (Acheson, 1980, p. 989). Other effects include myocardial stimulation, and smooth muscle relaxation. Moreover, Theobromine can decrease calmness, which is one of the major effects of caffeine ingestion. If consumed in excess, Theobromine may cause nausea. Around 18% of Theobromine is excreted unchanged in the urine.

Theophylline, the third metabolite, only makes up 4% of the Dimethylxanthenes. It is active in coronary dilation, and cardiac stimulation. The metabolite relaxes smooth muscle of pulmonary blood vessels, and bronchial airways. For people suffering with asthma, this effect allows them to breathe more easily; however, the dose required for that effect is much higher than what is available in a caffeinated beverage or food. In high
doses, Theophylline has the potential to cause central nervous system seizures (Stavric, 1988, p. 727). Overall, Theophylline has greater toxicity than Paraxanthine and Theobromine, and the small traces of unchanged caffeine in the body before excretion.

After caffeine makes its way to the liver, it is carried to the heart, and is circulated throughout body. Caffeine is both water and fat soluble, which allows it to reach different parts of the body more easily. When caffeine reaches the brain it blocks certain neurotransmitters reducing the feeling of fatigue. Caffeine blocks gamma-aminobutyric acid (GABA) receptors in the central nervous system. GABA promotes relaxation so by blocking its receptor a person feels more awake and might even experience a rapid heart rate. The adenosine receptor is also blocked by caffeine preventing adenosine from stimulating the feeling of sleepiness. Caffeine is able to do this because it shares a similar structure with adenosine. Furthermore, blocking the A2A adenosine receptor causes vasoconstriction of blood vessels in the brain (Diukova, 2012). Consequently, there is a reduction in cerebral blood flow. This leads to an increase in neuron firing, and decreased level of fatigue. In addition, Caffeine affects other neurotransmitters such as serotonin and epinephrine further reducing the perceived level of exhaustion and promoting a false sense of alertness.

Furthermore, caffeine interacts with other parts of the central nervous system. Caffeine causes an increase in dopamine levels. High concentrations of dopamine improves sustained attention, and further reduces feelings of exhaustion. Another effect of caffeine interacting with the CNS results in the reduction of skeletal muscle pain. This reduces the perception of the amount of pain inflicted on the body, or the amount of effort exerted by the body.
In response to the excess activity in the brain, the pituitary glands stimulate the adrenal glands situated on top of the kidneys. The release of adrenaline which is also known as epinephrine has numerous effects on the body. It increases blood fatty acid and glucose levels, and mobilizes fat and carbohydrate energy stores. Adrenaline is responsible for the “fight or flight” response. It prepares the body for intense physical activity. Some of the effects of the increase in adrenaline release include dilation of pupils and breathing tubes, muscle tightening, and increase in heart rate.

As mentioned previously, caffeine is readily absorbed by the body. Because of its ability to be absorbed there are many effects of caffeine in various tissues of the body. It changes function of naturally occurring substances and interacts with chemicals in the body. With any substance that has this broad of a ability to move through the body, one can imagine the effects of said substance would be far reaching and difficult to identify or quantify.

There are many difficulties that arise when trying to identify the effects of a specific substance that is found naturally in many commonly consumed products (drinks). Many studies of the effects of caffeine use coffee as the source of caffeine, but coffee contains many other compounds that can be beneficial and influence the results of these studies. One could argue that tea and coffee should be the sources of caffeine for studies since these are some of the popular modes of caffeine consumption, but the effects observed would not be due to only caffeine. Now that pure caffeine powder is accessible the effects of pure caffeine and the limit of healthy consumption is of interest.

The effects of caffeine are particularly important for expectant mothers because their decisions about consumption can influence the lives of their children as well as
themselves. There are recommendations for caffeine intake for expectant mothers, but if there is any chance that the caffeine could cause adverse effects it would be better for these mothers to reconsider the consumption of any caffeine.

When a child is in the womb it is completely dependent on the mother for all nutrients and needs, including an ample oxygen supply. The developing fetus has a requirement for oxygen just like an adult, however it has no direct access to the air or any way to acquire this oxygen for some of its development. Instead of using its nascent lungs, the fetus receives oxygen from the mother’s blood stream. Thus any fluctuations in the oxygen content of the mother’s blood will impact the supply to the fetus, fortunately there are natural ways that the fetus can adjust to these changes.

Before describing the controls that allow the fetus to adapt, it is important to understand the range of circumstances that can cause a lowered level of oxygen in the blood (hypoxia). Unless pregnant women are in perfect conditions, they are constantly adjusting to their environment, as all humans must. Changes in altitude can decrease the oxygen available to the mother. Over time she may be able to increase her ability to absorb oxygen, but for a while she will simply have less at this higher altitude. Also smoking and anemia can cause hypoxia. One would hope that a mother would not be smoking, but the case of anemia for an expectant mother is rather common (Buscariollo, 2011).

To combat these oxygen fluctuations, the fetus relies on the adenosine/adenosine receptor interaction (Buscariollo, 2011). When oxygen is low the adenosine can bind and decrease the firing of the neurons which will in turn lead to bradycardia (slower heart
rate). A slower heart rate will mean that the infant requires less oxygen and can save its
tissues from a lack of energy and electron receptors.

It was found that, as in adults who drink coffee, the caffeine competed with the
adenosine for adenosine receptors and disrupted this protective pathway (Yamada, 1989).
Additionally hypoxia is a phenomenon that is an important part of the development of the
heart in combination with functioning adenosine receptors. Caffeine was also associated
with reduced birth weight and increased risk of miscarriage (Buscariollo, 2011).

Increased risk of miscarriage seems like a good reason to avoid caffeine
altogether, but studies have also uncovered some interesting benefits to healthy adults
consuming caffeine. These include possible weight loss, applications and memory
stability in association with a high fat diet.

Studies of rats fed varying levels of fat in their diet have been shown to have a
decrease in memory capacity with an increase in fat (Greenwood, 1990). Most notably
the increase in saturated fat had the largest detrimental effect on the rats memory and
cognitive ability. Another study using rats showed that this decrease in memory ability
was mitigated or even eliminated with the consumption of moderate amount of caffeine.
In addition, the administration of caffeine prevented the weight gain that accompanied
the increase in fat consumption in these rats (Moy, 2013). This type of study with
humans would take too much time and due to the belief that the knowledge that the high
fat diet is deleterious, would be unethical. Nonetheless, there is no unequivocal evidence
that these same benefits would be seen in humans.

Another impact of caffeine on the body is on the bone mineral density,
specifically with chronic caffeine consumption in women. In one epidemiological study,
it was found that postmenopausal women (who are at high risk for bone density loss) who consumed coffee with regularity (average of 2-3 serving/cups a day) had decreased bone density (Harris, 1994). In addition a study on rats indicated that caffeine consumption also decreased bone density. In both cases however the participants were consuming caffeine with daily regularity. The women had be consuming beverages with caffeine for most of their lives and the in the case of the rats the pregnant females were given caffeine and the bone density of the resulting offspring was measured (Lacerda, 2010).

This decrease in bone mineral density seems to be associated partly with an interaction between caffeine and the parathyroid gland, which regulates bone remodeling and calcium deposition (Lu, 2013). Rats who had been given caffeine had higher urine and blood calcium levels while exhibiting lower bone calcium levels (Lacerda, 2010).

Finally, caffeine has been identified as a way to increase athletic performance by encouraging the use of fat as an energy source (Jenkins, 1995). In this way the athlete can use up fat and save glycogen for when the fat is gone. Generally the muscle will attempt to use glycogen sooner and thus run out and cause the athlete to “hit the wall”. These effects have not been seen for short intense exercise performance, which possibly may be due to the way that caffeine improves performance. Using fat first is not a priority if the workout in question is short enough that glycogen stores would not be depleted by its completion. Caffeine also changes the athletes perception of exertion and well being, making the workout seem easier and less strenuous.

The main drive of most consumers would be discovering the balance of benefits and risks a product may provide. The common risks associated with caffeine such as irregular heart rate, dehydration, or restlessness would be small price for athletes to pay.
As mentioned before, caffeine as a stimulant can provide athletes the slight advantage boost by being more alert, feeling energetic, and depending on their sport the type of biological stores utilized for fueling their bodies. As a result, caffeine is considered a controlled substance by athletic committees and associations including the International Olympic Committee (IOC) and National Collegiate Athletic Association (NCAA). The regulation of caffeine consumption by Olympic athletes are regulated at 12 micrograms per milliliter of urine, while 15 micrograms per milliliter of urine is acceptable based on the NCAA regulations (Spriet, 2011).

Caffeine when metabolized has a half life of 6 hours within the human body; therefore, half of the amount of caffeine consumed will be metabolized in a 6 hour time frame (Student Life, 2011). For comparison, the consumption of caffeine on average by an adult in the United States ranges from 200 mg to 1000mg per day. Thus, for athletes' urine sample to reach the IOC regulation would require the consumption of 5 to 6, 8 ounce cups of coffee in one sitting, which is equivalent to 9 milligrams of caffeine per kilogram of body weight. The athlete would then have to exercise for one hour to let the body absorb and metabolize the caffeine (Spriet, 2011). Consequently, the IOC is capable of determining abuse of caffeine to increase the athlete's advantage as evident by the large quantities of regular sized coffees needed to exceed the regulation limits. In addition, the amount of caffeine ingested by athletes within the range of 5-9 milligrams per kilograms body weight provided athletes the best improvement in endurance sports such as running and cycling (Spriet, 2011).

The use of caffeine for alertness and endurance can provide athletes with performance enhancing advantages, while caffeine is commonly consumed by non-
athletes as well. The intake of caffeine by children, however, should be cautious due to hyperactivity and the source of caffeine such as from sugary beverage (Evert, 2013). The consumption of caffeine on a regular basis will develop dependence and tolerance, which if not consumed in adequate amount will result in withdrawal symptoms. Common withdrawal symptoms include drowsiness, irritability, or headaches (Evert, 2013). On the other hand, over consumption of caffeine and intolerance to caffeine produce effects that include lack of sleep, anxiety, tremors, or even death (Evert, 2013). The risk of irresponsible caffeine consumption increases as the general public regardless of drinking age is exposed to the marketing schemes of caffeinated alcoholic cocktail beverages.

The increasing popularity of caffeinated alcoholic cocktail beverages are putting consumers at risk when consumed irresponsibly. Alcohol consumed in excess volume or in high concentration will impair judgments or even raise blood alcohol to a lethal level of 0.30 percent. Caffeine as previously explained is a stimulant which will make consumers alert, while mixing the substance with a depressant such as alcohol will result in a fatal concoction (Dininny, 2010). Regardless if the cocktail is prepared by mixing energy drinks with alcohol or bought as a premade mix the widely recognized product, Four Loko, made by the Drink Four Brewing Company sparked attention of the FDA when consumers reported multiple hospitalization due to alcohol poisoning and death due to driving under the influence (FDA, 2013). The marketing of these caffeinated alcoholic beverages are appealing to adolescence and increases under age drinking because of the close resemblance of the packaging of the product to other non-alcoholic energy drinks and non-caffeinated beverages. According to the CDC, non-alcoholic energy drinks are consumed by 31% of 12 to 17 year olds and 34% of 18 -24 year olds ; thus, the exposure
to these products may lead to the marketing exposure of the alcoholic variants of the beverage (CDC, 2010).

The cocktail of caffeine and alcohol permits the consumer to develop false perception of their alcohol tolerance level believing they are awake and capable to intake more of the beverage or to operate machinery. As a result, in November of 2010, a 21 year old woman of Maryland died due to a traffic accident after consuming the product, Four Loko. In addition, a month earlier in 2010 there were reports of underage drinking of the product put ten students from Central Washington University at risk of alcohol poisoning. Therefore, by November of 2012, the FDA has issue a warning to prevent the manufacturing and sales of all pre-mixed caffeinated alcoholic drinks.

The consumption of any substance or product should be considered by the consumer independently, to determine if the benefits or advantages provided is worth the risks. Caffeine when consumed in small amount provide qualities that some consumers value as beneficial such as being alert and awake through sources such as coffee or teas. However, the same values can also be seen as disadvantages and prove to be deadly due to ill-considered consumption. As caffeine is one of most easily accessible drug, the regulation of caffeine can be improve through increasing awareness of consumer of potential risk. Consumer awareness will allow increased perspective of risk from caffeine intake to develop wiser judgments.
References


