Ever wonder what alluring image this logo is trying to portray? It is a siren, a creature that lives by the sea and lures sailors with its charm and a soothing melody. In essence, coffee is the siren. In the same way that sirens lure their sailor victims, caffeine mesmerizes its consumers. The consumer is lost in a world of anxious, nervous, heart-pounding, adrenalin-fueled, wakefulness. But how did this world come to be?

The first Starbucks store opened in Seattle, Washington in 1971 and there were 46 stores operating in the US by 1989. The first international store was opened in Tokyo, Japan in 1996. As of 2013, Starbucks has had more than 3 billion customer visits in over 19,000 stores in 62 countries. The average Starbucks customer visits the store six times a month while 20% of Starbucks regulars go 16 times a month. As much coffee (and caffeine) as that looks, those numbers don’t even cover non-Starbucks coffee drinkers. However, this considerable number of coffee and caffeine consumers do not encompass non-Starbucks coffee drinkers. In the US alone, there are about 100 million daily coffee drinkers. Of that number, 34% frequent higher-priced places (e.g., Starbucks, Coffeebean, etc.) while 29% go to lower-priced outlets (e.g., McDonald’s, Dunkin Donuts, etc). Every year, the US spends over $4 billion importing coffee, and another $18 billion is spent on specialty coffee. The average coffee drinker spends about $160 a year on coffee. The amount of money spent on coffee, whether by the individual or the country, illustrates what a big role coffee plays in our lives.

But caffeine isn’t isolated to coffee. It reaches consumers of all ages through a variety of sources such as tea, soft drinks, chocolate, some drugs, and a wider variety of plants. Caffeine was initially only accessible directly through its plant sources, such as the coffee plant, tea leaves, and the kola nut and so on. Despite the readily access to caffeine, the compound was able to be added to other products such as energy drinks only after its isolation and synthesis.

\[1,3,7\text{-trimethyl}-1H\text{-purine-2,6(3H,7H)\text{-dione}}, \text{known more commonly as caffeine, is a crystalline xanthine alkaloid.} \]

Alkaloids are compounds found in plants with nitrogen atoms that are basic and readily help form salts; when extracted and sublimated from tea leaves, caffeine is a base. Specifically, caffeine is a pseudo alkaloid for two reasons: first, presence of a heterocyclic ring with nitrogen embedded and second, the compound is not a derivative of an amino acid [1]. It is should be noted however, the structural resemblance of caffeine to the caffeine’s structure resembles that of adenosine, the purine nucleoside and sugar, which is used to examine caffeine’s effects on the body.

Though adenosine and caffeine have similar structures, they play completely different roles in the body. Adenosine has a similar structure to caffeine but its role in the body is entirely different. This neurotransmitter is a sugar that binds to its associated receptors around the body. When adenosine triphosphate (ATP) is broken down in neurons for energy usage during wakeful
hours, adenosine concentrations increase. The adenosine in the neurons is transported into the extracellular space where “A1 (adenosine) receptors of the basal nucleus neurons are particularly sensitive to the increased levels of adenosine” [7]. Due to their sensitivity, potassium ion concentrations increase inside the neuron, leading to its inhibition. GABA neuron activity also decreases, which in turn disinhibits neurons responsible for Slow-Wave Sleep (SWS) [7]. GABA, known as gamma-aminobutyric acid, decreases a neuron’s action potential, which at a certain level will not allow a neuron to generate action potentials [8]. When a neuron stops generating action potentials, other neurons nearby will not be excited. Thus, wakefulness decreases as a result when SWS neurons are disinhibited. However, caffeine has the opposite effect in which neuron action potentials increase and exciting other neurons, adding to the state of wakefulness.

Caffeine is a stimulant that interacts with the central nervous system by binding to adenosine receptors in the brain and around the body, effectively prevents adenosine from binding and inducing its associated effects. These include drowsiness, dilation of blood vessels, lowering of blood pressure and body temperature, lowering the rate of digestion, and the easing of stress [2]. The binding of caffeine causes neurons to fire more rapidly, causing a chain reaction involving the pituitary gland, which releases hormones that bind to adrenal glands that subsequently release “adrenaline (epinephrine)”, the “fight-or-flight” hormone [3]. Actions that arise from this cascade include increased blood flow and pressure, increased glycogen breakdown for the release of glucose into the bloodstream, and increased contraction of muscle cells.

Before caffeine can stimulate the body, the liver must first metabolize the compound. Three main products result from the breakdown, each with its own effects (Fig. 1). Paraxanthine increases the liver’s rate of lipid breakdown, leading to increased fatty acid concentrations in the blood stream. Theophylline, produced in a miniscule amount, relaxes the smooth muscle in the lung’s bronchi. Theobromine dilates or widens the blood vessels and decreases blood pressure. In addition, caffeine itself inhibits phosphodiesterase, an enzyme that catalyzes the degradation of cyclic AMP [4]. Protein kinases that depend on cAMP will not work properly as a result. For example, protein kinase A (PKA) is activated only in the presence of cAMP. These kinases (enzymes) specifically regulate “glycogen, sugars and lipid metabolism” [4]. In particular, activated PKA phosphorylates several kinds of proteins such as glycogen synthase, which aids in the packaging of glucose into glycogen when blood glucose levels are high. Caffeine inhibition of adenosine is not only tied to the three main products.

When caffeine is metabolized, the following urinary metabolites are synthesized: 1- methyl xanthine, AFMU, and 1-methyluric acid (Fig. 2) [5]. These compounds are excreted in excess urine, a consequence of caffeine ingestion. All of the metabolites produced from caffeine are purines and have some resemblance to adenosine. This explains why caffeine metabolites act
as competitive inhibitors with respect to adenosine: similar structures may bind to the same receptor but produce different reactions and symptoms in the body. Caffeine structure is not the only factor that affects how the human body responds to the stimulant.

The variations in certain genes and their respective DNA sequences account for the difference in the bodily response of individuals towards caffeine intake. CYP1A2 is the main cytochrome P450 enzyme that catalyzes reactions of caffeine metabolism. The differences in the DNA sequence of this enzyme affect how well or how fast caffeine is metabolized by a consumer. Known as single nucleotide polymorphisms (SNPs), these DNA sequences differ in one nucleotide which increases the amount of CYP1A2 enzymes in the liver, resulting in faster and more efficient breakdown of caffeine [6].

![Figure 3. Caffeine metabolism showing enzyme catalysis by CYP1A2 [7]](image)

SNPs in ADORA2A, a gene that codes for adenosine A2A receptors in the body, also affect the degree to which caffeine affects the body. Emma Childs, a Research Associate (Assistant Professor) in the Department of Psychiatry at the University of Chicago, and a group of participants conducted a study on caffeine’s anxiety-inducing effects based on the presence of SNPs in study participants’ ADORA2A gene. One group did not have SNPs in their ADORA2A gene while another group tested positive for the SNPs. After consumption of 150 mg of caffeine, participants with the SNPs began feeling anxious. In contrast, the group without SNPs in the gene was able to consume up to 450 mg of caffeine, at which the individuals had to cope with increasing anxiety [6]. Thus, even miniscule changes in one nucleotide of a gene can significantly affect how caffeine affects different individuals.

Caffeine is deemed good for several reasons: it induces alertness and a rush of adrenalin during periods of weariness and much-needed energy, it provides economies such as the U.S. and Japan a source of revenue, and in short, a great start to anyone’s day. Yet, there are also downsides to caffeine intake from coffee, tea, and other drinks that are comprised of this compound. Caffeine leads to effects such as anxiety and the lowering of blood pressure but most importantly, preventing the human body from sleeping and repairing tissues and cells. The compound is safe to take as long as the consumer does not become habitual to the point where caffeine becomes addictive.
Works Cited


