HEY ARE EVERYWHERE, FROM GAS STATIONS TO DRUG STORES TO BODEGAS TO VAPE SHOPS, and they come in a wide range of flavors: menthol, scotch, vanilla, and even cappuccino. Also, unlike regular cigarettes, people under the age of 18 are legally allowed to purchase e-cigarettes in many states. This helps explain why e-cigarette use by teens tripled between 2013 and 2014; in a recent survey, 17% of high school seniors reported using an e-cigarette in the previous month.

E-cigarettes are becoming more popular than regular cigarettes among high school students. Some teens say that vaping, or inhaling and exhaling the vapor produced by an e-cigarette, helps them relax; some like the flavors; some think they are a safe alternative to regular cigarettes; and others like performing smoke tricks for friends. But are e-cigarettes really safer than regular cigarettes—and, if so, what is the chemical basis for the difference between the two?

**E-cigarettes versus regular cigarettes**

The biggest difference between e-cigarettes and conventional cigarettes is that e-cigarettes don’t burn. Instead, a battery-operated cartridge inside an e-cigarette converts liquid nicotine into a vapor. This is an important distinction because the greatest danger associated with tobacco is the smoke, which contains a toxic mix of more than 7,000 chemicals, including more than 70 substances that can cause cancer.

Some of the toxic components of cigarette smoke include carbon monoxide, hydrogen cyanide, and formaldehyde (dangerous gases); benzene (a component of gasoline); and polyaromatic hydrocarbons and tobacco-specific nitrosamines (compounds that may cause mutations in our DNA). The absence of this harmful smoke does not mean that e-cigarettes are totally safe, though. They still contain nicotine, the compound that makes cigarettes addictive.

Nicotine is derived from the roots of plants in the nightshade family, which includes tobacco plants, and accumulates in their leaves. These plants use nicotine to keep away herbivores, the animals that eat them.

At some point during human history, people discovered that the small doses of nicotine in tobacco act as a stimulant, making people who smoke it feel more alert. Tobacco was smoked in the Americas long before Christopher Columbus arrived, and European settlers of the New World introduced the practice of tobacco smoking to Europe, from which it spread across the Old World.
Although nicotine in regular cigarettes is just one component of smoke from tobacco leaves, nicotine in e-cigarettes is typically extracted from tobacco leaves in the lab, which is how it can be delivered without many of the other harmful compounds found in regular cigarettes.

### Addictive nicotine

What makes nicotine so addictive? Within roughly 10 seconds, nicotine moves straight from a regular cigarette to the brain. There, it competes with a chemical called acetylcholine (Fig. 1). Acetylcholine is a neurotransmitter, a molecule that relays messages between nerve cells, called neurons. The brain uses neurotransmitters to tell your heart to beat, your lungs to breathe, and your stomach to digest. Neurotransmitters can also affect mood, sleep, concentration, and weight.

In the brain, acetylcholine binds to special molecules, called receptors, on the surface of a neuron. Once acetylcholine binds to a receptor, the receptor changes its shape and allows sodium ions to flow inside the neuron. This flow of ions is how neurons “talk” to each other. The flow of ions also causes the release of other neurotransmitters and hormones that affect your mood, your memory, and even your appetite.

Because the chemical structures of nicotine and acetylcholine are similar, nicotine can bind to the same receptors that acetylcholine does; in chemical terms, both molecules have an affinity for the same receptors. In fact, some acetylcholine receptors are called nicotinic receptors, for their ability to bind nicotine! In Fig. 2, the similar parts of the acetylcholine and nicotine structures are shown in red.

Acetylcholine binds to its receptor through its trimethylammonium group, which consists of a nitrogen atom bound to three methyl groups (−CH₃). The trimethylammonium group binds to two types of amino acids that are part of the receptor (Fig. 3). These amino acids each contain a benzene ring—a hexagonal arrangement of six carbon atoms—which has a partial negative charge in the center of the ring and a positive charge around the outside. So, the trimethylammonium group, which is positively charged, binds to the negatively charged center of the benzene rings in each type of amino acid. This type of bond is called a cation-π interaction.

Nicotine binds to the same receptor using a group of atoms similar to acetylcholine's trimethylammonium group. It is positively charged and contains a nitrogen atom bound to one methyl group and two −CH₂ groups (Fig. 2).

By binding to acetylcholine receptors, nicotine stimulates the adrenal glands to produce epinephrine, a hormone and neurotransmitter also known as adrenaline. This chemical increases heart rate and blood pressure while constricting blood vessels, which explains why smoking helps people feel energized and alert. It also stimulates the production of dopamine, a neurotransmitter that controls the brain’s pleasure center, which keeps smokers coming back for more.

### Nicotine’s effects on the body

Normally, your body carefully monitors the concentration of acetylcholine, to ensure that you are receiving the right amount of this chemical. Your cells can produce more acetylcholine, store it, release it, or break it down, depending on how much you need at a given time. For example, when you are concentrating hard on a test question, lifting weights, or facing off with a scary figure in a dark alley, the cells in your body will release more acetylcholine.

When you are relaxing with friends or watching your favorite TV show, your cells can work on breaking down unneeded acetylcholine molecules that are loose in the body and rebuilding stores for the next time the chemical is needed. When nicotine binds to nicotinic receptors, this system doesn’t work as well, because nicotine is not regulated by the body.

Although neurons typically release small amounts of acetylcholine in a regulated manner, nicotine activates neurons in many different regions of the brain simultaneously. All of this unregulated stimulation causes cells to release acetylcholine, leading to heightened activity throughout the brain—whether the situation requires it or not.
The health effects of nicotine

By essentially hijacking the acetylcholine system, nicotine can affect brain development. Teens’ brains are still developing—especially the prefrontal cortex, which is the area of the brain involved in decision-making and planning. The prefrontal cortex does not finish maturing until around age 25.

Researchers have studied what happens to the prefrontal cortex in adolescent mice and rats exposed to nicotine. By measuring currents inside their brains, they have found that nicotine can alter the connections that develop between neurons. These types of changes can affect learning and impulse control, which are important for success in school and life.

Nicotine also has effects on other parts of the body. For example, it constricts blood vessels by causing cells to release a chemical called norepinephrine. Norepinephrine helps keep you alert in difficult or dangerous situations, but too much of it for too long causes blood pressure to rise, which increases the risk for heart attack and stroke. More smoking leads to a higher concentration of nicotine in the body and more pronounced health effects.

Are e-cigarettes safe?

Whether e-cigarettes should be considered a healthier alternative to regular cigarettes is controversial. Research suggests that e-cigarettes are a better choice than regular cigarettes for someone who chooses to smoke, because they allow users to avoid the toxic slew of chemicals contained in cigarette smoke. So, e-cigarettes may be an alternative for people who are already used to smoking.

Findings from one recent study show that e-cigarettes can help people to quit smoking, presumably by allowing them to gradually decrease their exposure to nicotine (similar to how nicotine patches work). But this research is contentious, because other studies have found that e-cigarettes do not seem to help people who want to quit smoking. In fact, a recent study funded by the National Institutes of Health found that students who have used e-cigarettes by the time they start ninth grade are significantly more likely to start smoking regular cigarettes within the next year than students who have not tried e-cigarettes.

Many people are concerned that fun flavors, easy accessibility, and big advertising budgets may lure teens into trying e-cigarettes and potentially becoming addicted. Evidence from animals, paired with what we know about the development of the human brain, clearly indicates that nicotine is addictive, no matter the form in which it is delivered, and that it has health consequences.

SELECTED REFERENCES


Figure 3. Acetylcholine binds to two types of amino acids, tyrosine (left) and tryptophan (right), which are on a cellular receptor, through a type of molecular interaction called a cation-π interaction. These amino acids belong to the protein that makes up the receptor, shown here in a simplified way as a chain of amino acids. In reality, the chain of amino acids is folded in a complex three-dimensional structure.