One of the first medical plants referenced in the historical record is Ma Huang, a shrub indigenous to China. When the dried stems of Ma Huang are steeped in hot water, the resulting extract contains therapeutic levels of ephedrine (1). The early Chinese noted the ability of Ma Huang to alleviate cold symptoms. The effect of Ma Huang is attributable to ephedrine, which is a vasoconstrictor and stimulant.

Compounds that (1) are extracted from natural sources, (2) contain a basic nitrogen atom, and (3) have a degree of structural complexity are called **alkaloids**.

Ephedrine is a member of a large class of molecules called phenethylamines. The parent compound of this class, phenethylamine (2). All compounds in this class contain phenyl and amino groups linked by a two-carbon tether. In the case of phenethylamines, these three structural elements (phenyl, amino, and tether) define the **pharmacophore** of the class. A pharmacophore is the minimal functionality for the compounds to be biologically active. Understanding which parts of a molecule are crucial for activity is an important concept in medicinal chemistry.

Two other members of the phenethylamine class are pseudoephedrine (3) and methamphetamine (4). Pseudoephedrine is a diastereomer of ephedrine and is a common ingredient in over-the-counter cold medications. The popular cold medicine brand Sudafed partially derives its name from pseudoephedrine. The availability of pseudoephedrine in pharmacies makes it a favorite starting material for the illegal production of methamphetamine. Methamphetamine, often simply called "meth", is a powerful, addictive stimulant.

The stimulant properties of phenethylamines makes the molecules excellent candidates as diet drugs. Indeed, a number of diet drugs are built upon the phenethylamine scaffold. Two examples are phentermine (5) and fenfluramine (6). In the late 1990s some physicians began prescribing phentermine and fenfluramine together. The co-use of the two drugs was called "fen-phen". Fen-phen was a very potent diet medication and quickly rose in popularity in diet centers. Unfortunately, some patients taking fen-phen suffered heart valve damage, and a few patients even died from heart issues.
Undesirable effects of a drug are called **adverse effects** or **adverse events**. Examples of adverse effects can range in severity from severe, including major organ damage or death, to mild, such as drowsiness or dry mouth. Note that adverse effects and adverse events are not identical. An adverse event is *any* event observed during a clinical trial. An adverse effect is an effect that is statistically linked to usage of the drug. For example, if a patient experiences headaches during a clinical trial, that would be an adverse event. If headaches were observed in other test subjects at a rate that was statistically higher than the control group, then the headache would be classified as an adverse effect. A **side effect** is any extra effect of the drug. Side effects can include adverse effects but may also include beneficial effects as well.

*The video is incorrect in its use of the terms adverse effect, adverse event, and side effect.*

The co-administration of phentermine and fenfluramine was not an approved or tested use of the medications. The practice of prescribing medications in an unapproved fashion is called an **off-label use**. Off-label use is common and frequently very beneficial for patients, but the practice does carry increased risks. Early investigations into fen-phen focused on off-label use with the idea that the combination of drugs caused the adverse effect. Continued research revealed that some patients taking fenfluramine alone also develop heart valve problems. Even 15 years after the discovery of fen-phen's problems, lawsuits continue to be filed against fen-phen's manufacturer.

The phenethylamine drug class includes compounds with a number of potent effects. The history of the class can be traced by 5,000 years to ancient China and the Ma Huang plant.