

## **Ephedra** (*Ephedra sinica*)

### **History**

- Ephedra (also known as Ma Huang) has been used in Traditional Chinese Medicine for over 5,000 years, primarily as a stimulant and diuretic.
- The primary active ingredient (ephedrine) was isolated in 1887 and was introduced to the U.S. in 1924 as a decongestant and bronchodilator for asthma.
- In the U.S. today ephedra is used widely as a weight loss supplement, accounting for 4% of herbal sales in this country. Much of this consumption is in the form of combination therapies which may not necessarily draw attention the fact that they contain ephedra.
- Ephedra is banned for use as a performance enhancer in the Olympics and the NFL, although it is allowed by Major League Baseball. In February 2003 ephedra was implicated in the death of 23-year-old Baltimore Orioles pitcher Steve Bechler.
- The sale of ephedra was banned in Illinois in May 2003 following the death of a 16 year old football player there linked to the use of ephedra.

### **Most studied uses**

Weight loss, asthma, and nasal congestion due to URI's and allergic rhinitis.

### **Other common uses**

Athletic performance enhancer , recreational stimulant, "energy booster".

### **Summary of the evidence**

- The most active component of ephedra is ephedrine which has long been recognized as an effective sympathomimetic for use in the treatment of mild asthma and nasal congestion. Ephedrine is available over the counter as an FDA-regulated drug.
- In low doses ephedra can cause nervousness, tremor, insomnia, and palpitations.
- In high doses, ephedra is potentially dangerous, having been strongly linked to stroke, arrhythmia, MI, heat stroke, and sudden death. The FDA has taken the unusual step of requiring a warning to this effect on all ephedra product labels.
- There is scant data on ephedra's use for weight loss or athletic performance. For such uses, any small potential benefit appears to be outweighed by ephedra's potential harm.

## **Pharmacology**

- Most active components are ephedrine and pseudoephedrine which are found mostly in the stems of the plant. They are structurally related to amphetamines.
- Both ephedrine and pseudoephedrine are well-established sympathomimetics with potent non-selective agonist effects on alpha, beta-1, and beta-2 receptors.
- Long-term use results in the depletion of norepinephrine. As a result, the chronic use of ephedra often leads to a loss of efficacy (tachyphylaxis).

## **Mechanism of action**

- Ephedrine and pseudoephedrine are anorexiant, thermogenic and ergogenic, increasing metabolism and suppressing appetite.
- Bronchodilation occurs primarily through agonist effects on beta-2 receptors.
- Decongestant effects occur primarily through alpha mediated vasoconstriction.

## **Clinical studies**

- Asthma: studies have shown that ephedrine is effective in asthma, although it causes more severe cardiac side-effects than selective beta-2 agonists, e.g. albuterol.
- Weight loss: a recent meta-analysis found that ephedra may promote a slight amount of short-term weight loss (in the range of 2 pounds) compared to placebo. The durability of such loss is unknown, however, since no trial lasted longer than 6 months. (Shekelle 2003)
- Athletic performance: no trials have been done for this indication. (Shekelle 2003)

## **Adverse effects**

- An analysis of national data estimates that 69% of all adverse effects attributable to herbal supplements in the U.S. were due to ephedra (Bent 2003).
- Data pooled from more than 50 trials has estimated a 2-3 fold increase compared to placebo in the rate of psychiatric, gastrointestinal, and cardiac symptoms. (Shekelle 2003)
- The U.S. government has received more than 16,000 reports suggesting possible links between the use of ephedra and adverse events including strokes, heatstroke, heart arrhythmia and psychotic episodes. Reports have indicated that more than 100 people have died after using ephedra, although other factors were likely involved in some cases.
- Partly as a result of the wide publicity surrounding the death of a 23-year-old baseball player in February 2003, the FDA now requires that products containing ephedrine include a warning that heart attack, stroke, seizure and death have been reported after its use, a risk which increases with strenuous exercise.

### **Contraindications/cautions**

- Patients with the following conditions should not use ephedra: hypertension, heart disease, depression, anxiety, insomnia, anorexia/bulimia, hyperthyroidism, narrow-angle glaucoma, urinary retention, and benign prostatic hyperplasia (BPH).

### **Important drug/herb interactions**

- Use with great caution in patients taking CNS or cardiovascular stimulants because of the risk of severe hypertension.
- Ephedra increases steroid clearance and may decrease the effectiveness of steroids.
- Ephedra can increase the risk of cardiac arrhythmias in patients taking digoxin or receiving halothane anesthetic.
- The risk of heat stroke and other severe adverse events increases when used in combination with other sympathomimetics such as caffeine .

### **Formulation and dosage**

- Amounts in various products vary enormously, with a typical dose being about 10 mg of total ephedrine and pseudoephedrine daily although commercial products can contain up to 20 mg per dose.
- The most appropriate doses which can be considered both safe and effective are controversial.

### **References**

1. Haller CA, et al. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Eng J Med* 2000;1833-1838.
2. Bent S, et al. The relative safety of ephedra compared with other herbal products. *Ann Intern Med.* 2003;138:468-71.
3. Shekelle PG, et al. Efficacy and safety of ephedra and ephedrine for weight loss and athletic performance: a meta-analysis. *JAMA.* 2003 Mar 26;289(12):1537-45.

### **For Additional Information**

1. Natural Medicines Comprehensive Database. Available through UW Healthlinks.
2. About Herbs. <http://www.fammed.washington.edu/predoctoral/CAM/sites.html>.
3. Herbmed.org for more general background.
4. For information about the quality of specific brands, check Consumerlabs.com.

