ZIZYPHUS
A tonifying sedative

SOURCE
Zizyphus refers to the seed of Zizyphus jujuba, var. spinosa, often labeled simply as Zizyphus spinosa (see Figure 1). The Chinese name for the herb is suanzaoren [suan = sour; zao = date; ren = seed; hence, seed of the sour date], or just zaoren. This herb is related to the one commonly called jujube, which comes from the fruit of Zizyphus jujuba (see Figure 2); the Chinese name for jujube is dazao (da = large; a smaller, red variety is called hongzao; hong = red). Both zizyphus and jujube are said to have sedative properties, with zizyphus being the primary sedative derived from a plant in the practice of traditional Chinese medicine (the mineral cinnabar has long been relied upon as a sedative).

The Shennong Bencao Jing (ca. 100 A.D.) includes a description of zizyphus (1):
Zizyphus is sour and balanced [in nature; being neither too warming or cooling, but combining both warming and cooling effects]. It mainly treats heart and abdominal cold and heat and evil binding qi, aching, pain in the limbs, and damp impediment. Protracted taking may quiet the five viscera, make the body light, and prolong life. It grows in rivers and swamps.

The reference to “protracted taking” and the resulting beneficial effects refers to the practices of the Taoists seeking immortality, and is a formulaic presentation rather than providing any specific information about the herb. The main indications provided here are the herb’s balanced nature and its ability to treat problems of the heart, including cold, heat, and bound qi.

A typical modern presentation of the indications for zizyphus is this one from Chinese-English Manual of Commonly Used Herbs in Traditional Chinese Medicine (2): “1. Nourish the heart, benefit the liver, and tranquilize the mind; 2. Stop sweating.” The latter indication is relied on when treating insomnia accompanied by night sweating, as commonly occurs with menopausal insomnia and insomnia associated with prolonged feverish diseases (i.e., consumptive diseases).

Zizyphus seeds are usually stir-fried prior to use; the seeds are turned rapidly in a hot wok (Figure 3) and then allowed to cool in straw baskets (Figure 4). The fried herb is said to be especially useful for nourishing the liver blood, calming the spirit, and stopping sweating; the raw herb may be used to drain the liver and gallbladder; it also calms the spirit, but is less nourishing. Pharmacology evaluations indicate that both the raw and fried seed have similar sedative actions (16). The reference in the ancient literature to the sour taste of the herb depicts the fruit pulp; the seed itself is deemed sweet (15), in fact, the taste is relatively bland.

MEDICINAL USE
Zizyphus is probably best known in the system of ancient Chinese medicine for its key role in the formula Suanzaoren Tang (Zizyphus Combination) of the Jingui Yaolue (220 A.D.). In that text, the formula is described simply as follows (3): “Zizyphus Combination treats weakness fatigue, and distress due to weakness, which causes insomnia.” Zizyphus is the main ingredient of the formula both in terms of the quantity used and its central action for the treatment of deficiency and insomnia, which are the formula’s main indications.

Even today, if one discusses sedative formulas with prominent physicians in China, this formula is mentioned as being particularly effective; in books about using traditional formulas, Zizyphus Combination is among the first to be listed.
A modern presentation of the formula is (4):

- Zizyphus (suanzaoren) 18 g
- Anemarrhena (zhimu) 10 g
- Hoelen (fuling) 10 g
- Cnidium (chuanxiong) 5 g
- Licorice (gancao) 3 g

The actions of the formula, as described in the modern text, are to nourish the blood, clear heat, relieve restlessness, and treat insomnia. Anemarrhena is a cold-natured herb that contributes the action of clearing heat; as indicated in the Shennong Bencao Jing passage, zizyphus also contributes to clearing heat, even though it doesn’t have a cold nature. Zizyphus provides all the other actions attributed to the formula. Its blood nourishing effect is complemented by that of cnidium, while both licorice and hoelen provide additional sedative effects and contribute to the overall tonification therapy by improving the spleen functions.

In the context of analyzing Zizyphus Combination, one can mention the use of the related herb jujube in the well-known sedative formula Ganmai Dazao Tang (Wheat and Jujube Combination):

- Wheat (fuxiaomai) 15 g
- Jujube (dazao) 14 g
- Licorice (gancao) 9 g

The dosage of jujube is usually measured by the number of fruits, in this case 7; the seeds are removed and the remaining fruit is about 2 grams. The actions of this small formula are to nourish the heart, normalize the function of stomach and spleen, calm the mind, and treat insomnia and spasms. The role of wheat, which is normally consumed by many people in large quantities (as in the form of noodles or bread), may be to treat B-vitamin deficiencies that can arise in people who do not normally eat wheat or other sources rich in these vitamins (B-vitamins play an important role in nervous system functions). This type of deficiency has been a common problem in the Orient. For example, in Japan, until quite recently, beri beri (a Vitamin B1 deficiency that causes leg edema) was a common disorder because the diet lacked good sources of the vitamin, which is found in whole grains). The combination of jujube and licorice in this formula serves as a spleen tonic and sedative, which is a role similar to that of zizyphus and licorice in Zizyphus Combination.

TRADITIONAL THEORY OF INSOMNIA DUE TO FATIGUE

While there are many causes of insomnia, serious fatigue is seen as both a cause and result of insomnia. As relayed by the modern physician Jiao Shu De (10):

According to ancient teachings, the liver is the root of extreme fatigue. A high degree of exhaustion causes serious overnight insomnia, irascibility, dizziness of head and eyes: all indicating the extreme glowing of liver yang, imbalance of yin and yang, and an inability of yang to return to yin...Also, inability of blood to nourish the heart with exhaustion of the heart (mental fatigue) leads to wandering of the heart spirit from its shelter, causing insomnia with heart palpitations.

The liver- and heart-nourishing zizyphus seed, with its astringent quality that helps prevent the heart spirit from wandering too far, is an ideal remedy for this type of disorder. Another explanation of insomnia was provided by the physician Lu Yong Chang (11):

According to the ancient teachings: ‘The day is yang; the night is yin. The wei qi circulates in the yang [the body surface] during the day and circulates in the yin [the central visceral] at night. In other words, the yang enters the yin in the night. The meeting of yin and yang creates a peaceful serene state, which is sleep. If the yin is deficient and unable to receive the yang, or the yang is in excess...
and unable to enter the yin, this causes disconnection of yin and yang with resultant insomnia.'... As stressed by Zhang Jingyue [famous physician of the Ming Dynasty]: 'The insufficiency of genuine yin, essence, and blood will cause disconnection of yin and yang, thus disturbing the peace of the spirit and generating insomnia. The heart shelters the spirit and is the house of the yang...

Sleep occurs when the wei qi enters the yin and creates a quiet environment. In the words of the ancients, when the yang has a home to return to, the sleep will ensue. When the heart is disturbed by worry and shakes the spirit, restlessness occurs, which generates insomnia.'

Zizyphus is used to help assure that the yang has a home to return to by nourishing the yin and blood of the heart and liver (essentially, making them soft and comforting). According to Xu Da-chun, a Qing Dynasty physician (18): “Everyone knows that one employs zizyphus and fu-shen if one can not sleep.” Fu-shen is part of the herb known as hoelen, one of the ingredients of Zizyphus Combination. The herb is a fungus that grows on the roots of pine trees; fu-shen is the portion that includes the root, while hoelen is the portion that does not include the root.

While zizyphus is useful for the cases of yin and blood deficiency, it is not deemed suitable for all cases of insomnia. A modern Chinese physician, identified only as Liu (12), expressed some specific reservations, as relayed by translator C.S. Cheung:

Liu is reluctant to use zizyphus indiscriminately. Although it is a good agent for nurturing the heart and calming the spirit and is excellent for the treatment of restless heart insomnia with palpitations [due to anxiety and fright], yin deficiency, and profuse perspiration, it is not indicated for insomnia of wet phlegm evil heat or for liver stagnation and qi stagnation. This is because it possesses a sour, astringing property, which may prevent the dissipation of evil [phlegm accumulation and stagnated qi] and therefore delay the recovery from the illness.

To a certain extent, this concern is overstated, in that the fried seed that is actually used is not sour, though it does have a tonifying and astringent quality that can be considered a contraindication for the conditions described here. The concern about phlegm accumulation is often addressed by including polygala with zizyphus in formulas; polygala has both sedative and phlegm-resolving qualities. Qi stagnation may be addressed by inclusion of saussurea, which regulates qi and has secondary sedative effects. As one example, a widely used sedative preparation is Guipi Tang (Ginseng and Longan Combination), which is a spleen tonic formula (includes ginseng, astragalus, atractylodes, ginseng, and licorice to tonify spleen qi) that incorporates sedatives: zizyphus, polygala, saussurea, jujube, and longan (longan, like jujube, is a sweet fruit that is said to benefit the spleen and have a calming effect). Another example is provided by the modern physicians Wu Zimou and Li Hongjian (13), who described differentiation of complexes associated with insomnia and suggested a formula with for the type characterized as “stagnated obstruction of phlegm-heat.” The formula includes a high dose (20 grams) of zizyphus, indicating that they believe it can still be used, but it also is comprised of several phlegm-resolving herbs-pinellia, citrus, chih-shih, bamboo, trichosanthes fruit, and polygala. Citrus and chih-shih also disperse central qi stagnation.

By contrast, if a sedative formulation is made up of many rich tonifying herbs, then the concern expressed by Liu will apply. His hesitance to provide zizy-
phus in that context is reflected in the statement, from Commonly Used Chinese Herb Formulas with Illustrations (14), that the tonic prescription Tianwang Buxin Dan (Ginseng and Zizyphus Formula) should not be used by “those having gastrointestinal [spleen] weakness with moist tenacious sputum.” Although the formula contains herbs that benefit the spleen and others that resolve phlegm (sputum), its strong focus on nourishing yin and blood is considered sufficient to cause concern for those who have the problem of stagnated and accumulated fluids. Zizyphus is one of the ingredients at issue; others are the oily biota seed and the richly sweet herbs rehmannia and scrophularia.

SEDATIVE CONSTITUENTS OF ZIZYPHUS

Laboratory animal studies of zizyphus extract confirm a sedative effect, though the constituents that contribute this effect have not all been specifically identified. Some sedative effects were shown to be produced by several different components (5, 6). The only components of zizyphus that are present in quantities likely to be responsible for the observed clinical effects are triterpenes.

The unique triterpenes for this herb are known as jujubosides. Additionally, there are related triterpene compounds (such as betulinic acid and oleanolic acid) that are found in several other herbs. Structurally, the jujubosides are nearly identical to the active constituents found in ginseng, an herb that is traditionally used as a sedative and a tonic. According to one analysis, the triterpene level in zizyphus is 2.5% (8), so that an 18 gram dose, as used in Zizyphus Combination, would yield about 360 mg of triterpenes, a level typically relied upon for most triterpenes. The simple powder of zizyphus, consumed orally, appears to be effective in relatively low dosage. One report indicates that good effects were obtained using 0.8-1.2 grams of the powder before bed (9).

In one of the best known patent remedies for insomnia, Tianwang Buxin Dan (Ginseng and Zizyphus Formula), many herbs with triterpenes are combined together, including zizyphus, ginseng, platycodon, and polygala. The formula also provides herbs that contain steroidal saponins (e.g., ophiopogon and asparagus) that have a similar structure and that are likely to have similar effects. The indications and applications of this large formula are almost identical to that of the smaller and more ancient Zizyphus Combination. The famous tonic mushroom ganoderma contains triterpenes similar to those found in ginseng and zizyphus, and is classified, like zizyphus, as a tonic sedative. It is sometimes recommended as a single herb remedy for insomnia.

TOXICITY AND SIDE EFFECTS

Zizyphus is reported to have very low toxicity when taken orally (5). In laboratory animals (mice and rats), a huge single dose of 50 grams herb per kilogram of body weight produced no toxic symptoms, and a daily dose of 20 grams per kilogram for 30 days did not produce toxic reactions. Side effects are not reported. Modern pharmacology evaluation of zizyphus seed oil and zizyphus extract suggest that with prolonged feeding they can reduce serum triglycerides and cholesterol (mainly LDL), and reduce fatty degeneration of the liver (17). These properties have also been attributed to the triterpenes of ginseng and ganoderma.
ZIZYPHUS IN THE ITM FORMULARY

Formulas for calming the mind and alleviating insomnia are commonly administered in modern clinical practice. The ITM Formulary includes five formulas in which zizyphus is the key ingredient:

**SALVIA/AMBER TABLETS**
with zizyphus, ginseng, salvia, succinum, dragon tooth and bamboo sap
for agitation, anxiety, and insomnia caused by experience of disturbing events.

**BU NAO WAN (Pine Mountain)**
with zizyphus, schizandra, ginseng, biota, polygala, succinum, dragon tooth, and other herbs to nourish the brain, improve memory, and calm agitation.
for improving memory, concentration, and sleep, preventing deterioration of brain functions during stressful periods.

**ZIZYPHUS 18**
with zizyphus, ginseng, schizandra, ophiopogon, biota, albizzia, polygala, and several other herbs used to tonify the qi, nourish the blood, and calm the spirit.
for nervousness and insomnia due to chronic deficiency conditions.

**NARDOVA (White Tiger)**
with zizyphus extract, nardostachys extract, L-Theanine and albizzia and hops
for anxiety, depression, insomnia, premenstual symptom

**COMPOUND GL**
with zizyphus, ganoderma, ginseng, salvia, succinum, polygala, and several other herbs used to tonify the qi, calm the spirit, and improve digestive functions.
for chronic fatigue associated with anxiety and digestive disturbance.
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