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Kudzu–the Miracle Vine

Kathy Abascal, B.S., J.D., R.H. (AHG), and Eric Yarnell, N.D., R.H. (AHG)

Abstract

The clinical uses of, and research on, *Pueraria montana* var *lobata* (kudzu, kuzu, *ge gen*) and related species are reviewed in this article. Kudzu's applications in alcoholism and the herb's ability to lessen the negative effects of alcohol are covered as are the herb's applications for treating menopausal symptoms, osteoporosis, diabetes, stroke, and cardiovascular disease as well as how kudzu acts as a hepatoprotectant.

Introduction

Pueraria montana var *lobata* (formerly *P. lobata*), along with related species (kudzu), was one of first plants mentioned in Traditional Chinese Medicine (TCM). In TCM, the root and the flower were used to treat the ill effects of alcohol, fever, headache; to relieve stiffness in the back and neck; and to treat the early stages of measles. Today, in Asia, kudzu is commonly used to treat stroke, heart disease, and diabetes. Western use of kudzu is largely limited to treating drinking problems and menopausal symptoms.

Kudzu was first introduced to the United States in 1876 and rapidly became a popular garden plant owing to its large leaves and fragrant flowers. During the Depression, the government paid to have kudzu planted to stabilize the soil,[1] and it was then called "the miracle vine." Kudzu, however, under the right conditions, can grow a foot a day and, thus, soon became invasive. Its invasiveness gained it new common names such as "mile-a-minute vine," "foot-a-night-vine," and "the vine that ate the South."

Although clinical studies on kudzu are sparse, the plant has interesting properties that suggest that practitioners should be using kudzu to treat a greater variety of ailments. If its potential benefits are investigated and confirmed, the plant will once again be known as "the miracle vine."

Kudzu Species and Constituents

Many different species of kudzu are used in Asia. In China, *P. montana* (also known as *P. thunbergiana*) and *P. thomsonii* are used interchangeably. *P. mirifica* and *P. tuberosa* are also used frequently. There are subtle differences between the species but these are not well-defined. For instance, *P. montana* has shown a more potent antioxidant effect than *P. thomsonii* has and contains higher amounts of important isoflavones.[2] In a screening, *P. montana* flower had a higher estrogenic potency than its root did.[3]

Kudzu contains a number of strong phytoestrogenic compounds in both its roots (puerarin and daidzin) and flowers (kakkalide and tectoridin). Human intestinal bacteria hydrolyze these isoflavones, resulting in metabolites (daidzein, irisolidone, and tectorigenin) that have more potent estrogenic activity than their precursors.[4,5]

Alcoholism and After-Effects of Intoxication

Kudzu is used in Western botanical medicine to treat chronic drinking problems, and we have used the herb successfully for this. (See box entitled A Kudzu Case Study.) It is also used to prevent the negative aftereffects of intoxication. Unfortunately, there are only two clinical studies on kudzu and drinking. In the first clinical study, kudzu appeared to be ineffective.[6] This study, however, has been severely criticized because both the active and the control group were virtually completely abstinent and "under the conditions of this study, no drug would have been effective because the control group was so good."[7] In addition, the researchers ignored the fact that only 1 person withdrew from the kudzu group while 10 patients who were taking the placebo withdrew.

In the second clinical study, heavy drinkers (N = 14) were treated with placebo or kudzu (two 500-mg capsules 3 times per day*) for 7 days.[8] The patients were allowed to drink their preferred brands of beer, and their drinking behavior was monitored. Kudzu significantly reduced the number of beers consumed. It also significantly increased the time it took to consume each beer. Kudzu appeared to prolong the acute effects of the first drink, thereby reducing the desire for additional alcohol. Although there was a significant change in drinking patterns, the magnitude of the decrease in intake was modest.[8] This study supports the traditional use of kudzu to prevent intoxication and after-effects.[7]

In animals, kudzu and its constituents show a consistent ability to inhibit alcohol preference effectively, a preference that returns when the kudzu is discontinued.[9–12] Studies also sup-

*The capsules contained 19 percent puerarin, 4 percent daidzin, and 2 percent daidzein.

port the use of kudzu to thwart the negative effects of alcohol. Kudzu appears to alleviate the negative effects of alcohol intake by enhancing lipid metabolism and the hepatic antioxidant defense system.[13] Kudzu counteracts alcohol-induced decreases in Fos-positive cells in the brain, a measurement of alcohol's ability to cause a loss of neurons.[14]

Kudzu flowers increased the elimination of acetaldehyde, which may help prevent flushing, palpitation, headache, and other symptoms associated with excessive alcohol intake.[15,16] One study, however, showed that puerarin, daidzin, and daidzein had no effect on aldehyde dehydrogenase but they did shorten alcohol-induced sleep time and caused blood alcohol levels to peak later and lower.[10]

Kudzu crude extract and puerarin both produced neuroprotective effects against developmental ethanol exposure in vitro,[17] and kudzu flowers had an ameliorating effect on the ethanol-induced impairment of both memory registration and retrieval in mice.[18]

Menopause and Osteoporosis

Kudzu contains a number of strong phytoestrogenic compounds. While kudzu is often used by botanical practitioners to treat perimenopausal symptoms, good clinical studies are lacking. Kudzu is of particular interest in menopause because preliminary studies show that the plant protects the body against bone loss and appears to promote bone formation. If this is verified in clinical trials, kudzu may be a safe and effective treatment for osteoporosis.

Only three small clinical trials were located on kudzu in menopause. In the first, 25 menopausal women who had severe hot flashes and night sweats used isoflavones from kudzu and *Trifolium pratense* (red clover) along with other nutrients. The women's hot flashes decreased and their scores on a subjective assessment of quality of life improved, while the markers for cardiovascular disease improved somewhat, and markers of breast cancer risk improved significantly, suggesting that kudzu may help manage symptoms such as hot flashes and offer some protection against other diseases associated with menopause.[19]

In the second trial, 37 pre- and postmenopausal women with hot flashes, night sweats, and urogenital and psychologic symptoms took kudzu capsules (50 or 100 mg per capsule) once daily for 6 months. The patients' scores on a modified Greene climacteric scale decreased in both groups. However, while the treatment alleviated climacteric symptoms, the results were less positive in women who had anemia and abnormal liver profiles.[20]

In the third trial, 127 postmenopausal women took hormone replacement therapy (HRT), kudzu (containing 100 mg isoflavone), or no treatment for 3 months. Kudzu had no significant effect on follicular stimulating hormone (FSH) or luteinizing hormone (LH), but kudzu did improve flexible thinking in the Mini-Mental State examination.[21] This improvement was supported by an animal study in which puerarin (100 mg per kg) administered long term to ovariectomized mice ameliorated learning and memory deficits by normalizing levels of glutamate and gamma-aminobutyric acid (GABA).[22]

***Pueraria montana* var *lobata* (kudzu). Drawing © by Eric Yarnell, N.D., R.H. (A.H.G.).**

Animal studies suggest that kudzu can moderate menopausal hormone imbalances. In one study, naturally menopausal monkeys were given various doses of kudzu. The lowest dose (10 mg per day) reduced FSH beginning on day 15 in a third of the animals while the higher doses (100 and 1000 mg per day) decreased FSH levels throughout the experiment. After treatment, FSH levels continued to decrease for 5–20 days in these animals. The lowest dose decreased LH throughout treatment in a third of the animals while the higher doses prominently decreased LH beginning on day 10, and the effect persisted up to 30 days post-treatment.[23]

Bone Loss in Aging

Bone loss in menopausal women is a significant problem. Kudzu contains high amounts of isoflavones known to prevent bone loss induced by estrogen deficiency. In one study of menopausal monkeys, kudzu (1000 mg per day) decreased serum parathyroid and calcium levels, indicating an ability to ameliorate bone loss.[24]

In ovariectomized rats, kudzu significantly inhibited the induced total femoral bone mineral density (BMD) reduction at the low dose (5 percent of diet) and completely prevented it at the middle dose (10 percent of diet). Intake of the middle dose completely prevented a decrease in trabecular bone volume and thickness. Intake of the high dose (20 percent of diet) further increased bone volume and thickness. In this study, kudzu did not affect uterine weight, which declined.[25]

Kudzu had a similar effect in orchidectomized mice. The decrease in femur BMD in the control group was completely inhibited by kudzu as 10 percent of their diet. The high dose (20 percent of diet) significantly increased BMD with a potency sim-

A Kudzu Case Study

The patient was a 56-year-old man with cirrhosis secondary to hepatitis C and excessive alcohol ingestion, osteoarthritis, depression, and one episode 4 years ago of bleeding esophageal varices requiring hospitalization. He had struggled unsuccessfully to stop drinking. The following herbal formula was prescribed for him (at a dose of 1 tsp three times per day):

- *Schisandra chinensis* (schisandra)—fruit glycerite for cirrhosis and stress, 20%
- *Centella asiatica* (gotu kola)—whole plant glycerite for cirrhosis, 15%
- *Taraxacum officinale* (dandelion)—root glycerite for cirrhosis, 15%
- *Mahonia aquifolium* (Oregon grape)—root glycerite for cirrhosis, 9%
- *Picrorhiza kurroa* (kutki)—root fluid extract as an antiviral, 9%
- *Astragalus membranaceous* (astragalus)—root glycerite as an adaptogen, 9%
- *Glycyrrhiza glabra* (licorice)—root fluid extract for cirrhosis, stress, flavor, synergizing effects, and as an antiviral, 9%
- *Pueraria montana* (kudzu)—root glycerite for alcoholism, 5%
- *Hypericum perforatum* (St. John's wort)—herb glycerite for depression and as an antiviral, 5%
- *Ceanothus greggii* (red root)—tincture as an abdominal lymphatic, 4%
- *Aconitum carmichaelii* (Sichuan aconite)—prepared root tincture for pain, 1%

Although the kudzu component of the formula was relatively modest, the patient was able to stop drinking and stated he has had little desire for alcohol since he started the formula. He has only drunk on two occasions in the 8 months since he started the formula. Although his herbal formula does contain a small amount of alcohol, it does not seem to have caused him any ongoing liver problems or to have contributed to his drinking problem. His depression has improved dramatically, and his osteoarthritis and other pains have been reduced significantly. His serum liver enzymes have been improved and his cirrhotic symptoms have also been steadily reduced.

ilar to that of estradiol, suggesting the potential use of kudzu to prevent osteoporosis in elderly men with hypogonadism.[25]

In vitro experiments confirm that kudzu's isoflavones have a positive effect on bone. Puerarin stimulated cell proliferation, differentiation, maturation, and mineralization of rat osteoblasts,[26] and another study showed that kudzu enhanced many factors, including mineralization in bone cells, suggesting an ability to stimulate osteoblastic bone formation.[27]

Benefits for Patients with Stroke

In 1998, more than 11 million persons experienced stroke in the United States.[28] This is an enormous health issue that kudzu may help address.

In China, subarachnoid hemorrhages caused by aneurysms are treated with surgery after rupture and by calcium antagonists. Herbs are often included in treatment plans, and kudzu (as a crude extract, in formulas or as an isolated extract, usually puerarin) is said to have been proven to be beneficial both to prevent and treat this disorder.[29] In a study of vascular dementia, a Chinese formula containing kudzu was compared with the Western drug nimodipine at 2 mg per kg per day.† The formula improved learning ability and memory compared with controls and was more effective than nimodipine for improving spatial discrimination.[30]

Cerebral infarction is an ischemic condition that results in localized brain tissue death and usually a persistent focal neurologic deficit. Kudzu is commonly included as part of the treatment for this disorder in Asia, and 14 clinical trials (N = 1141) on the clinical use of kudzu for cerebral infarction were analyzed in a recent review. While the methodological quality of the trials was deemed to be poor, the review authors concluded that kudzu may improve the short-term neurologic deficit caused by cerebral infarction.[31]

The formula *Chungpesagantang* is used in Korea for patients who have stroke and for rats with inhibited platelet aggregation. Kudzu tested separately also inhibited adenosine phosphate (ADP)–induced platelet aggregation ex vivo, while neither the formula nor kudzu alone affected plasma clotting times. However, the formula did protect mice from death caused by pulmonary thrombosis.[32]

A Chinese decoction containing kudzu (*xuefu zhuyu*) promoted microcirculation and reperfusion in rabbits with acute spinal-cord damage. The formula also reduced edema, indicating a protective effect on damaged spinal cords.[33] Another Chinese formula (*wulong dan*, also containing kudzu) had a protective effect on neuronal injury and apoptosis caused by local cerebral ischemia in rats.[34]

Puerarin increased cerebral blood flow in dogs, and attenuated cerebral and spinal cord injuries resulting from ischemia in rats and rabbits. In a rat model of cerebral ischemia, puerarin (100 mg per kg intraperitoneally) decreased the infarct volume by 34 percent and improved neurologic functions. Puerarin also significantly reduced apoptosis and necrosis in the cortex.[35]

Poststroke depression is a common and severe complication. Kudzu (75, 150, or 300 mg per kg) administered orally to mice after cerebral ischemia reperfusion reversed the resulting low levels of a metabolite of dopamine and norepinephrine and alleviated the depressive-like behaviors in the mice.[36] Kudzu has also shown a potential benefit in dementia in animal studies.[18,37,38]

Cardiovascular Benefits

In China, puerarin injections are widely used to treat coronary heart disease and angina pectoris. A review of clinical trials on unstable angina (N = 1240) showed puerarin to be about as effective as conventional Western treatments, and a combination of puerarin and Western drugs was more effective than the drugs alone. The drugs included isosorbide dinitrate, beta-blockers, cal-

†The formula, a *shuanggen* cephalocathartic decoction, was dosed at 4 g per kg per day. Nimodipine is used to reduce the incidence and severity of ischemic deficits in subarachnoid hemorrhages.

cium-channel blockers, aspirin, nitroglycerine, and others. The researchers noted that these results should be interpreted with care owing to the very low methodological quality of the studies.[39] In another clinical trial, 500 mg of puerarin administered by venoclysis before anesthesia reduced increases in serum enzymes, indicating that puerarin may prevent myocardial injury caused by anesthesia in patients who have hypertension.[40]

Daidzein was remarkably effective for preventing ventricular fibrillation and arrhythmia in mice and rats. This substance antagonized induced arrhythmia in rabbits and prevented induced ventricular fibrillation and ensuing death in rats.[41]

Studies show that puerarin dilates coronary arteries, relieves spasm, increases coronary blood flow and blood supply to the ischemic area, slowly reduces heart rate, improves myocardial oxygen demand, improves coronary circulation and contractility of the ischemic heart, acts as a safe and potent beta-blocker, suppresses platelet aggregation, lowers blood viscosity, and improves microcirculation.[39,42]

Kudzu and puerarin also have reduced the atherogenic effect of dietary cholesterol in rats and improve cholesterol profiles significantly in vivo and in vitro.[43–46]

Finally, in a study of hospitalized patients with dyslipidemia (N = 120), a formula containing kudzu (*tiaozhi zengshou tang*) was compared with pravastatin (10 mg per day) and a combination of the formula and the drug. The formula and pravastatin had similar effects on total cholesterol, triglycerides, and high-density lipoprotein (HDL) blood levels (81 percent versus 80 percent improvement), while the combination reportedly achieved a 97 percent improvement.[47]

Potential for Diabetes Prevention and Treatment

Kudzu also shows potential both to treat diabetes and prevent its complications. Various kudzu formulas are used for this purpose in Asia, but kudzu is not widely used in diabetes in Western practice. No clinical trials were located on this use of kudzu, but both animal and in vitro studies suggest that practitioners should consider its potential benefits for people with diabetes.

Some kudzu-containing herbal formulas have been studied in animals. A compound known as *lian zhu* improved blood sugar, glycosylated hemoglobin, urinary protein, and various other parameters in rats with diabetes.[48] Another formula, *Shinomittel*, did not reduce elevated blood sugar levels in rats with diabetes but did have a synergistic effect on blood sugar levels when combined with insulin.[49]

In addition, isolated constituents of kudzu have shown positive effects in animals and in vitro. Puerarin dose-dependently decreased plasma glucose concentrations in rats with diabetes and also somewhat reduced glucose levels in normal rats. In isolated soleus muscle from rats with diabetes, puerarin enhanced the uptake of glucose dose-dependently, suggesting that puerarin may increase glucose utilization and lower plasma glucose in rats who are diabetic and lack insulin.[50]

In vitro studies show that puerarin may protect islet cells effectively from the toxic action of reactive oxygen species (ROS) in diabetes.[51] Puerarin has also decreased lens epithelium cell apoptosis in rats with diabetes, indicating a potential use in the prevention of diabetes-induced cataracts.[52] In diabetes, most patients have both atherogenic lipid abnormalities and insulin resistance.

Compounds that target the peroxisome proliferators-activated receptors (PPARs) can correct these problems and kudzu, in a bioassay, activated PPARs significantly.[53] Kaikasaponin III from kudzu flowers showed antithrombosis activity in rats with diabetes; there are also indications that the substance may have hypoglycemic and hypolipidemic effects by moderating phase I and II enzyme activities.[54] In another study, tectorigenin produced similar in vitro effects on phase I and II enzyme activities as did the drug glibenclamide.[55]

Kudzu Blossom Jelly

Ingredients
4 cups of kudzu[a] blossoms
4 cups of water
1 tablespoon of lemon juice
1 pectin package
5 cups of sugar

Preparation
Make kudzu blossom tea and allow it to sit overnight. Strain flowers. Bring the tea to a boil. Add sugar and pectin (while stirring constantly) and bring to a full rolling boil for 1 minute. Remove mixture from heat and skim off the foam. Pour hot jelly into clean jars and process in a hot water bath for 5 minutes.

[a]Latin binomial is *Pueraria montana.*

Hepatoprotective Effects

As mentioned above, kudzu has long been used to mitigate the damage alcohol can inflict on the body, particularly on the liver. Preliminary studies show that kudzu has a hepatoprotective action. Nine kudzu saponins have shown hepatoprotective activity.[56] Their ability to inhibit the elevation of alanine aminotransferase was stronger than that of glycyrrhizin, which was used as a positive control.[57] The crude saponins from kudzu flowers were also found to be effective for ameliorating experimentally induced liver injury.[58] Kakkalide (100 mg per kg) administered orally to mice with induced liver injury had a more potent hepatoprotective effect than did silybin, a compound found in *Silybum marianum* (milk thistle), a well-established hepatoprotectant.[59]

An extract of kudzu flowers provided significant protection against carbon tetrachloride–induced damage in rats,[60] and tectorigenin had a greater inhibitory effect on increases in liver enzymes than did dimethyl diphenyl bicarboxylate, which is used as a commercial hepatoprotective agent.[61]

Puerarin administered to rats with liver fibrosis significantly increased apoptosis of activated hepatic stellate cells, which indicates that puerarin may be able to reverse induced liver fibrosis in rats.[62] In a similar experiment, a formula containing kudzu (*quinggan huoxuefan*) obviously reduced liver fibrosis and

normalized all liver enzymes tested.[63] In rats with fatty livers, formulas containing kudzu significantly modified indicators of the onset of fatty liver disease in the animals.[64–66]

Other Potential Benefits

Kudzu and its constituents and metabolites (puerarin, tectorigenin) have shown cytotoxic activity against various cancer-cell lines.[67,68] The flavonoids of *P. Montana*, which showed significant antimutagenicity in the Ames test with kaikasaponin III, having the most potent action.[69]

In an asthmatic rat model, puerarin administered intragastrically improved a number of parameters involved in the onset of asthma.[70] Tectorigenin inhibited the passive cutaneous anaphylaxis reaction potently and inhibited the effects induced by immunoglobulin E (IgE).[71] Daidzein has inhibited potently the passive cutaneous anaphylaxis reaction in mice.[72]

One of kudzu's traditional uses is to reduce fever. Kudzu's glycosides (daidzin and genistin) had a significant antipyretic effect on lipopolysaccharide (LPS)–induced fever in mice.[73] In a screening of 170 plants used in Korean herbal medicine, kudzu had one of the strongest antioxidant actions in vitro.[74] Other studies have confirmed that the plant has significant antioxidant activity.[75–77] Kudzu also has an anti-inflammatory effect that may be useful for treating osteoarthritis.[78,79] Finally, the plant showed a potential benefit in a rat model of preeclampsia.[80]

Safety of Kudzu

Puerarin is the major isoflavone found in kudzu. Puerarin is rapidly absorbed and has reached peak levels at 2 hours with a half-life of approximately 4.3 hours in healthy volunteers. The elimination half-life was not significantly altered by repeated administration. As accumulation will not occur, and plasma levels remain at biologically active levels for even 8 hours after the last steady-state dose, three times per day dosing is recommended.[81]

Kudzu is used in cooking and generally is considered to be very safe.[82] However, both *P. montana* extract and puerarin show a complex effect on different cytochrome p450 isoforms. Puerarin induces CYP 2A1, 1A1/2, 3A1, and 2C11, while kudzu itself induces CYP 1A2, 3A1, and 2B1. Both have inactivated CYP 3A, 2E1, and 2B1, suggesting a potential for drug interactions.[76] In rats given a *P. montana* extract intragastrically, a loss of approximately 50 percent of both total p450 content and CYP-2E1-dependent p-nitrophenol hydroxylase activity was observed in purified hepatic microsomes. At the same time, a threefold increase in NADPH CYP-reductase activity was recorded.[75]

In rats, a kudzu decoction had a significant effect on the metabolism of the drug methotrexate and, when combined with the drug, resulted in surprisingly high mortality rates (14.3 percent and 57.1 percent, respectively). When methotrexate was given intravenously, its half-life was increased by 53.9 percent, and its clearance was decreased by 47.9 percent.[83] This shows that caution is needed when combining kudzu with other drugs. However, as mentioned above, kudzu and puerarin are commonly used in China in combination with a variety of drugs to treat stroke and heart conditions.

The information on the reproductive safety of kudzu is sparse, but there are indications that its estrogenic effect may be undesirable in premenopausal females and in male animals. In a study, *P. mirifica* increased menstrual-cycle length significantly in monkeys, and, at a high dose (1000 mg per day) the animals' cycle disappeared entirely and did not return to normal after discontinuation of the regimen. The researchers surmised that ovulation may have been suppressed by a lowering of gonadotropins.[84]

In another study using the same dose regimen, there was a significant increase in lengths of the follicular phase and total menstrual cycle in the high-dose group, but no change occurred when using the lower doses. Gonadotropin levels did not change during the first and second menstrual cycles of the post-treatment period. However, the highest dose disturbed ovarian function and menstrual cycle in the monkeys.[85]

P. tuberosa administered to rats postcoitally caused a hypertrophy of corpora lutea and the animals' uterine histoarchitecture appeared to be nonreceptive on the day of implantation.[86] However, common blood values were not affected by this treatment and kudzu was deemed to be safe in rats at these acute and subacute dosage regimens.[87]

In male rats, *P. tuberosa* root (100 mg per day) reduced the weights of testes, epididymis, seminal vesicle, and ventral prostate. Sperm motility was reduced significantly and the treatment reduced the fertility of male rats by 100 percent.[88] However, in gonadectomized rats, kudzu normalized gonadotropin levels after 1 week in males and after 2 weeks in females. In male rats on the highest dose, epididymis weight increased.[89]

In one study, daidzein and puerarin had no effect on LH levels but, at a high dose, increased uterine weights significantly. The researchers concluded that these compounds would be unlikely to alleviate vasomotor symptoms in postmenopausal women but, owing to the compounds' uterotropic effects, at high doses, might increase the risk of endometrial hyperplasia.[90] Other clinical studies discussed above, however, did show a benefit on such symptoms in women.

These studies combine to show that reproductive health should be monitored when kudzu is given to men and women in their reproductive years.

There are no reported adverse effects from the use of kudzu in humans. In China, puerarin is often administered by injection. There are reports of patients experiencing fever, allergy, skin reaction, hemolysis, and injury to kidney or liver after taking puerarin intramuscularly or intravenously.[39]

Kudzu has been shown to absorb heavy metals (copper, cadmium and zinc) effectively from the soil while growing.[91] Thus, a clean source for the herb is important.

Conclusions

Kudzu is a plant with remarkable properties that Western botanical medicine is just beginning to utilize. Its multitude of potential uses ranging from diabetes to stroke and cardiac ail-

ments deserves greater investigation both in research and in clinical use. □

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Kathy Abascal, B.S., J.D., R.H. (AHG), is executive director of the Botanical Medicine Academy, Vashon, Washington. **Eric Yarnell, N.D., R.H. (AHG),** is president of the Botanical Medicine Academy, a specialty board for using medicinal herbs, and is an adjunct faculty member at Bastyr University, Kenmore, Washington.

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