Herbal remedies for Alcohol dependency

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ABSTRACT
Alcohol dependency is a major health and socioeconomic dispute throughout the world. Medicinal plants have been used for the treatment of alcohol dependency in China for years, but have only recently attracted the attention of western scientists. Recently, extracts of St. John’s wort which have been traditionally used to treat mild to moderate depression, have drawn interest as potential antidipsotropic agents. Also experimental data shows that Pueraria lobata, Tabernanthe iboga, Panax ginseng, Salvia miltiorrhiza and Hypericum perforatum have also been proved to be effective in decreasing alcohol consumption. Recent experimental evidence and critical re-examination of empirical data from traditional medicines suggest that novel pharmacological approaches for treatment of alcoholism and alcohol abuse may stem from natural substances. These data suggest that medicinal plants may constitute novel and effective pharmacotherapies for alcoholism. The present review summarizes the findings of the effects of these promising plants in alcohol addiction.

Key Words: Alcohol, St. John’s wort, Traditional medicines, Pharmacotherapies, Addiction.

INTRODUCTION
Alcohol is foreign to the human system and is normally destroyed in the liver by oxidation, yielding acetaldehyde, which is in turn destroyed by aldehyde dehydrogenase. Alcohol abuse and dependence holds an important role in the public health because of both the medical consequences and economical costs. The pharmacological treatment of patients with the alcohol dependence plays a key role in achieving alcohol abstinence and prevent relapse, especially if it is the conceived together with the psychosocial interventions already used for many years. Within pharmacological approaches, some recent preliminary data suggest the possible utility of complementary medicines (CMs) in the treatment of alcohol dependence. CM is defined as “diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine.” In spite of the utility of the CM being described in different diseases, the data concerning its possible use in alcohol-dependent patients are controversial and do not permit the drafting of final conclusions. Recent lines of experimental evidence suggest that noval pharmacological approaches for the treatment of alcohol dependence could stem from some natural substances. A recent study by a group highlighted that 16.50% of the Italian Alcohol and Drug Addiction Services us CMs for alcohol dependence treatment, and in these services 10.08% are treated with phytotherapy.
METABOLISM (Fig. 1):
When alcohol is consumed, it passes from the stomach and intestines into the blood, a process referred to as absorption. Alcohol is then metabolized by enzymes, which are body chemicals that break down other chemicals. In the liver, an enzyme called alcohol dehydrogenase (ADH) mediates the conversion of alcohol to acetaldehyde. Acetaldehyde is rapidly converted to acetate by other enzymes and is eventually metabolized to carbon dioxide and water. Alcohol also is metabolized in the liver by the enzyme cytochrome P450IIE1 (CYP2E1), which may be increased after chronic drinking. Most of the alcohol consumed is metabolized in the liver, but the small quantity that remains unmetabolized permits alcohol concentration to be measured in breath and urine. The liver can metabolize only a certain amount of alcohol per hour, regardless of the amount that has been consumed. The rate of alcohol metabolism depends, in part, on the amount of metabolizing enzymes in the liver, which varies among individuals and appears to have genetic determinants. In general, after the consumption of one standard drink, the amount of alcohol in the drinker's blood (blood alcohol concentration, or BAC) peaks within 30 to 45 minutes. (A standard drink is defined as 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits, all of which contain the same amount of alcohol.) The BAC curve, shown on the previous page, provides an estimate of the time needed to absorb and metabolize different amounts of alcohol.

SYNTHETIC DRUGS USED FOR THE TREATMENT
Many synthetic drugs including Disulfiram works as a deterrent against drinking by making the person sick if they consume any alcohol. Naltrexone (Revia) blocks the effects of alcohol in the brain and reduces alcohol craving. Acamprosate (Campral) relieves the distress and discomfort alcoholics experience when they stop drinking. Disulfiram interferes with this metabolic process, stops the process with the production of acetaldehyde and prevents the oxidation of acetaldehyde into acetic acid. Because of this, antabuse will cause a build up of acetaldehyde five or 10 times greater than normally occurs when someone drinks alcohol. Naltrexone is used along with counseling and social support to help people who have stopped drinking alcohol and using street drugs continue to avoid drinking or using drugs. Naltrexone should not be used to treat people who are still using street drugs or drinking large amounts of alcohol. Naltrexone is in a class of medications called opiate antagonists. It
works by decreasing the craving for alcohol and blocking the effects of opioid medications and opioid street drugs.

Acamprosate is used along with counseling and social support to help people who have stopped drinking large amounts of alcohol (alcoholism) to avoid drinking alcohol again. Drinking alcohol for a long time changes the way the brain works. Acamprosate works by helping the brains of people who have drunk large amounts of alcohol to work normally again. Acamprosate does not prevent the withdrawal symptoms that people may experience when they stop drinking alcohol. Acamprosate has not been shown to work in people who have not stopped drinking alcohol or in people who drink large amounts of alcohol and also overuse or abuse other substances such as street drugs or prescription medications.

But these synthetic drugs included many side effects such as, Flushing, Nausea, Copious, Vomiting, Sweating, Thirst, Throbbing, Headache, Respiratory Difficulty, Chest Pain, Palpitations, Dyspnea, Hyperventilation, Tachycardia, Hypotension, Syncope, Marked Uneasiness, Weakness, Vertigo, Blurred Vision, Confusion.

HERBAL DRUGS USED IN THE TREATMENT

Medical interventions in the field of alcoholism are primarily aimed at:

a. relieving the consequences of alcohol withdrawal syndrome;

b. arresting alcohol drinking, maintaining sobriety for as long as possible.

Pharmacotherapy is conceived to provide a substantial contribution to these goals, facilitating the psychological support and social rehabilitation of alcoholic patients. Recent experimental evidence and critical re-examination of empirical data from traditional medicines suggest that novel pharmacological approaches for treatment of alcoholism and alcohol abuse.

Pueraria lobata

The anticraving and ‘antidrunkeness’ effects of extracts of *Pueraria lobata* Owhi, Fabaceae., also known as kudzu, have been known to traditional Chinese physicians for centuries. A recent experimental study demonstrated that the daily intraperitoneal administration of a crude extract of *P. lobata* roots halved alcohol intake in alcohol-prefering Syrian Golden hamsters.

In this study, two putative active principles have been identified; indeed, administration of two major isoflavones present in *P. lobata* extracts, daidzin (Fig. 2) and daidzein, induced ethanol intake even a choice between alcohol solution and water.

Confirmation of the ability of *P. lobata* to reduce alcohol consumption in laboratory animals comes from a recent study testing the anti-alcohol effect of a herbal mixture comprising *P. lobata* this mixture is commonly used in China to prepare the so-called ‘tea of sobriety’. Administration of this mixture reduced alcohol consumption in alcohol-prefering rats.

A further study showed that intraperitoneally administered daidzin lessened intoxication induced by anaesthetic doses of alcohol in rats. However, daidzin effectiveness in shortening alcohol-induced sleep time, a reliable measure of alcohol intoxication was observed after the intragastric infusion of alcohol, but not when alcohol was administered intraperitoneally. Consistently, blood alcohol levels (BALs) elicited by oral administration of alcohol reached a lower peak and declined slower in daidzin-treated rats than in vehicle-treated ones. The ‘sobering-up’ effect of daidzin appears to be due to a slowdown of gastric emptying, which would expose alcohol for a longer time to first-pass metabolism in the stomach.

![Fig 2. Chemical structure of Daidzin](https://www.ijrpp.com)
Tabernanthe iboga
The reducing effect of ibogaine on alcohol intake was observed only when ibogaine was injected intraperitoneally or intragastrically but not subcutaneously, suggesting that the active principle of ibogaine could be a metabolite produced by the liver, since drugs administered intraperitoneally or intragastrically usually undergo first pass metabolism. Recent preclinical evidence indicates that ibogaine may significantly affect morphine and cocaine self-administration in rodents. Lately, ibogaine has been reported to markedly reduce voluntary alcohol intake in alcohol-prefering rats. This effect was not due to any interaction of ibogaine with alcohol metabolism, as indicated by virtually equal BALs between ibogaine and placebo-treated rats. The reducing effect of ibogaine on alcohol intake was observed only when ibogaine was injected intraperitoneally or intragastrically but not subcutaneously, suggesting that the active principle of ibogaine could be a metabolite produced by the liver, since drugs administered intraperitoneally or intragastrically usually undergo first pass metabolism. Accordingly, a subsequent study demonstrated that both the intraperitoneal and subcutaneous administration of noribogaine, a primary metabolite of ibogaine, significantly suppressed alcohol intake in alcohol preferring rats.

It has been hypothesized that ibogaine may exert its attenuating effects on voluntary ethanolic intake by interacting with the brain systems involved in the mediation of the reinforcing effects of alcohol.\[15, 16\]

Panax ginseng
It was proposed that ginseng accelerated alcohol metabolism and lowered BALs by increasing ADH activity and plasma clearance. However, a more recent study demonstrated that administration of red ginseng extract altered alcohol absorption from the gastrointestinal tract. Early works recorded that ginseng saponines (Fig. 3) increased the rate of oxidation of ethanol in alcohol-fed rats\[17\] and red ginseng extract prevented memory failure and excitation in alcohol-intoxicated mice.\[18\] Later, using healthy human volunteers\[19\] demonstrated that in 10 out of 14 cases ginseng extract accelerated alcohol clearance by 31–51%. Ginseng saponines apparently stimulate the microsomal ethanol-oxidising system and the aldehyde dehydrogenase (ADH) enzyme action and therefore there is a faster removal of acetaldehyde with rapid shunting of excess hydrogen into lipid biosynthesis.\[20\] It has been also shown that rats plasma levels are lower (20%) when alcohol is administered orally with red ginseng extract than when alcohol is given alone. However, further studies\[21\] support the idea that ginseng may promote faster disposal and elimination of alcohol from blood after drinking.

Fig 3. General structure of the Ginsenosides [14]
Salvia miltiorrhiza

Reducing effect of *S. miltiorrhiza* extract on BALs occurred only when alcohol was administered intragastrically and not intraperitoneally, suggesting that *S. miltiorrhiza* extract may alter alcohol absorption from the gut.

A recent study from this laboratory demonstrated the ability of a *S. miltiorrhiza* extract, standardized to contain 13% tanshinone IIa and administered orally, to significantly decrease by approximately 50% in comparison to placebo-treated subjects voluntary alcohol intake in selectively bred Sardinian alcohol-preferring sP rats. A compensatory increase in water intake left total fluid consumption virtually unchanged. A subsequent experiment showed that the dose of *S. miltiorrhiza* extract capable of reducing voluntary alcohol intake in sP rats decreased BALs by approximately 60%; the reducing effect of *S. miltiorrhiza* extract on BALs occurred only when alcohol was administered intragastrically and not intraperitoneally, suggesting that *S. miltiorrhiza* extract may alter alcohol absorption from the gut. The hampered absorption likely leads to a reduced perception of the reinforcing properties of alcohol; this phenomenon may explain, at least in part, the decreased intake of the alcohol solution observed in the rats treated with the *S. miltiorrhiza* extract.[22]

Hypericum perforatum

The antidepressant and mood-elevating effects of St. John’s wort - *Hypericum perforatum* L. Hypericaceae, have been known since the time of Hippocrates. Recent clinical studies have demonstrated that *H. perforatum* is as effective as major synthetic antidepressants in the treatment of mild to moderately severe depressive disorders. The high degree of comorbidity existing between certain depressive states and alcohol abuse led to evaluate *H. perforatum* efficacy in controlling alcohol consumption. Recent studies demonstrated the ability of *H. perforatum* extracts to halve voluntary alcohol intake in different lines of selectively bred alcohol-preferring rats, including sP rats. Interestingly, sP rats possess a genetically determined, high tendency to depression; voluntarily consumed alcohol exerts an antidepressant-like effect in this rat line. Thus, it can be hypothesized that the antidepressant-like effect of the H. perforatum extract may substitute for those of alcohol contributing to reduce its intake.[23]

HPE contains a variety of biologically active compounds, including naphthodianthrones (hypericin and pseudohypericin), fluoroglucynol derivatives (hyperforin, adhyperforin), several flavonol glycosides (quercetin, hyperoside or hyperin, rutin, isoquercitrin), biflavones (amentoflavone), phenylpropanes (chlorogenic acid, caffeic acid), proanthocyanidins, tannins, xanthones and certain amino acids, such as GABA.[23, 24, 25]

Hypericin and hyperforin have been proposed to mediate several effects of HPE. A large body of evidence suggests that hyperforin may represent the major component responsible for the antidepressant effect of HPE.[26, 27, 28, 29, 30, 31, 32, 33, 34]

Hyperforin is known to inhibit the uptake of aminergic transmitters such as serotonin and noradrenaline into synaptic nerve endings.[35] It also increases the extracellular levels of other transmitters including acetylcholine, glutamate, and GABA. These effects may be secondary to an increase of the intracellular sodium concentration mediated by openings of non-selective cation channels in the synaptosomal membrane.[36] Hyperforin also interacts with a variety of receptors and ion channels including glutamatergic and calcium channels.[37, 38] However, the inhibitory effects of HPE on ethanol intake are not mediated by GABA agonist actions.[39]

**CONCLUSION**

Alcoholism is a chronic disease for which there is no cure, but there is hope. Alcoholism is treatable. Alcoholics can learn to live without alcohol. With proper treatment, alcoholics can live a happy, satisfying and productive life. Contacting an alcoholic rehabilitation treatment center is the first step toward recovery.

Treatment for alcoholism begins with an evaluation by the addiction team. They will first determine whether alcohol abuse has become addiction. If the individual hasn’t lost control over their drinking, treatment may focus on reducing alcohol consumption. But if the person has become dependent on alcohol, total abstinence is the only effective treatment goal.

Recent experimental evidence and re-examination of empirical data from traditional medicines suggest that novel pharmacological approaches for the treatment
of alcoholism and alcohol abuse may stem from natural substances. Several plant derived compounds have been shown to significantly reduce alcohol intake, mostly in animal studies. Although several neurotransmitter systems seem to be involved in their effects on alcohol seeking behaviour, the exact mechanism of action of these compounds remain to be clarified. Until extensive clinical studies are carried out, it will be difficult to extrapolate the findings on animal models of alcohol dependence to a human cohort. The role these compounds in the treatment of alcoholism will ultimately depend on the outcome of carefully conducted clinical trails. Nevertheless, the extensive positive findings in animal model suggest the outcome of clinical trails is likely to be positive as well especially when pharmacological treatment is combined with psychological support counselling. Herbal therapy can bring a new hope in the treatment of alcohol addiction.

REFERENCES


