

UNLOCKING NATURE'S POTENTIAL: A COMPREHENSIVE REVIEW OF CNS-STIMULANT ACTIVITY IN NATURAL HERBS

Abstract

Stimulants of the central nervous system (CNS) are psychoactive medications that temporarily improve mental and physical function by increasing CNS activity. Despite their considerable benefits for a variety of illnesses, they are nonetheless frequently used as illegal narcotics of abuse. Children with Attention Deficit Hyperactivity Disorder (ADHD) are prescribed methamphetamine and amphetamine; nevertheless, according to the National Department of Health, 2-3.5% of adults in the USA use these medications. At greater doses, it causes a widespread action that can result in convulsions. Several plant species with central nervous system (CNS) stimulant action are highlighted in this review study. Based on their pharmacological activity, CNS stimulants are categorized into three groups: cognitive enhancers, psychostimulants, and psychoanaleptics. Tea, coffee, and cocoa are examples of psychostimulants that temporarily improve mental and physical function by raising the (CNS). Cognitive enhancers, like ginkgo and gotu kola, are used to treat vertigo, short-term memory loss, and inattention in addition to improving memory. The article covers the cutting-edge methods being used in research to develop herbal CNS stimulants and botanicals.

Keywords: Natural Products, CNS Stimulants, Attention Deficit Hyperactivity Disorder, Psychostimulants and Psychoanaleptics

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I. INTRODUCTION

CNS-stimulants are the hallucinatory pills that cause brief upgrades in intellectual and bodily feature through bettering the pastime of central anxious mechanism. They allow superb advantages for a vary of issues but however they are extensively used as illicit resources of abuse. In children with Attention Deficit Hyperactivity Disorder (ADHD), amphetamine and methylphenidate are given medications. According to the National Department of Health, between 2.5% and 3.5% of individuals in the USA utilize these capsules. It produces generalized motion which on greater doses may additionally produce convulsions. Ephedra vulgaris (Ma huang), Catha edulis (Khat), and Erythroxylum coca (Coca) are a few examples of tablets that have been used historically and are known to have CNS stimulating properties. The Chinese herb ma huang, which is having central stimulating activity, has been used as a circulatory stimulant, diaphoretic, antipyretic, and antitussive agent for some over 5100 years. After ephedrine is remoted from plant which was once used in remedy of allergies and comparable prerequisites. CNS stimulants have a range of unique effects, including improved alertness, awareness, wakefulness, endurance, productivity, motivation, increased arousal, motility, coronary heart rate, and blood pressure. These drugs are commonly used in weight loss therapy due to their ability to suppress appetite and reduce food intake. They are also effective in treating medical depression and bipolar disorder, particularly cases of atypical or treatment-resistant depression. Additionally, CNS stimulants provide relief from orthostatic hypotension, postural orthostatic tachycardia syndrome, and nasal congestion. The specific effects of these drugs depend on the substance used as well as its potency and dosage. At moderate doses commonly prescribed in medical practice, CNS stimulants effectively reduce hyperactivity without causing serious side effects. The pharmacological mechanisms underlying the effects of stimulants involve acting as nicotine acetylcholine receptor agonists, adenosine receptor antagonists, and increasing norepinephrine (noradrenaline) and/or dopamine activity through inhibition of monoamine transporters.

II. CLASSIFICATION OF CNS STIMULANTS

Different categories are used to classify CNS stimulants based on their pharmacological action including psychostimulants, psychoanaleptics, and substances that enhance brain function. In the United States alone, more than 15 million people consume high-dose vitamins or natural remedies regularly. In terms of weight loss products expenditure in 2001, a significant portion amounting to \$17.7 billion out of a total of \$37.1 billion was attributed to natural supplements aimed at shedding pounds. These figures have shown a consistent annual increase ranging between 6% and 7%. The usage of natural products for medicinal purposes as well as disease prevention has witnessed substantial growth. Stemming from negative impacts on the cardiovascular system are other natural remedies like St. John's wort and ginkgo biloba which deserve attention in the United States. St. John's wort is a highly favored herb among the masses. However, it is important to note that its consumption leads to the activation of hepatic cytochrome P450 enzyme system responsible for drug metabolism, resulting in potential adverse effects such as arrhythmia recurrence and hypertension. Therefore, it is likely that major adverse responses may arise from using this herb. Ginseng, on the other hand, has been linked to both hypertensive and hypotensive effects.

2.1 Herbal CNS Psychostimulants

2.1.1. Cocaine

Cocaine, an alkaloid derived from the *Erythroxylum coca* plant, is typically extracted as a paste due to the instability of its free base form. This paste is then converted into a salt form, such as hydrochloride or sulfate. The specific salt form depends on the method of consumption, whether it be IV injection or snorting. Despite its long history of use in Central and South America for its milder stimulant effects, cocaine's medical use is only approved in the United States. Dopamine is released from nerve terminals and binds to dopamine receptors, exerting its pharmacological effects before being taken up by dopamine reuptake transporters and metabolized by monoamine oxidase enzyme (MAO). However, cocaine acts differently in the periphery by blocking the uptake of NA, adrenaline, and dopamine into adrenergic nerve endings. This leads to higher concentrations of these transmitters around the receptors and results in CNS stimulation. Additionally, cocaine functions as a local anesthetic by inhibiting Na channels. Only in the United States is it approved for medical use. Recent research suggests that cocaine's convulsigenic effects may be caused by blockage of NMDA receptors. The addictive nature of cocaine and its ability to reinforce behavior have been directly linked to its blockade of dopamine reuptake. Prolonged use of cocaine can lead to cardiovascular and neurovascular issues depending on the dosage used for therapy purposes. While rarely used in medicine today, some individuals claim that 4 mg/kg is required for ophthalmic purposes.

2.1.2. Caffeine

Caffeine actively inhibits adenosine receptors and phosphodiesterase, leading to increased levels of dopamine, adrenaline, and serotonin. This stimulation of the central nervous system results in heightened mental alertness, reduced fatigue, and improved attention. Additionally, caffeine has shown potential benefits in managing symptoms of Parkinson's disease and metabolic disorders like obesity. Regular consumption of caffeine within recommended limits (less than 400 mg per day for adults weighing 70 kg) generally does not have significant negative effects. Caffeine toxicity is rare, with a lethal dose estimated at 150-200 mg per kg or 10-20 grams per day. Various plants containing caffeine have been utilized as central nervous system stimulants.

2.1.3. Tea (*Camellia Sinensis*)

Tea is a popular beverage that has numerous health benefits such as reducing glucose levels, lipids, weight, and blood pressure. It also improves metabolic profiles and reduces the risk of depression and stroke. The caffeine content in tea leaves can range from 3 mg to 30 mg, making a cup of tea with 7.5 mg to 75 mg of tea leaves caffeine-rich. The level of caffeine varies depending on the components of the tea plant, with higher levels found in leaf buds and younger leaves compared to mature and older leaves. However, excessive consumption of tea may lead to sleeplessness, anxiety, restlessness, and tachycardia due to its high caffeine content.

2.1.4. Coffee (Coffea Robusta/Arabica)

In western nations, coffee is the third most consumed beverage and a primary source of caffeine. The amount of caffeine in coffee varies depending on the species, with *C. arabica* containing 1.45 and *C. robusta* (*C. canephora*) containing 2.38. However, it is important for patients to avoid consuming high doses of caffeine as it can cause insomnia and anxiety.

Aside from its stimulating effects on the central nervous system, high caffeine intake has been found to increase the excretion of calcium and magnesium in urine, potentially affecting the bone health of women, according to Giulia Runti's research. Additionally, arabica coffee extract exhibits antibacterial properties against *Staphylococcus epidermidis* and *Enterococcus faecalis* bacteria.

2.1.5. Cocoa (Theobroma Cacao)

Cocoa, also known as cacao, is derived from a plant. It contains minerals, methylxanthines (theobromine 1 to 4 and caffeine 0.07 to 0.36), polyphenols, and cocoa butter. The flavonoid content of cocoa has neuroprotective and neuromodulatory effects. Flavanols in cocoa work in two ways: directly on cells and through cell cascades, resulting in the expression of proteins that promote neuroprotection and neuromodulation, improve neuronal function, and stimulate neurogenesis; as well as by increasing blood flow in brain and sensory tissues. This makes cocoa beneficial for cognition improvement, protection against insulin resistance, and anti-inflammatory properties. Cocoa consumption has been found to prevent melancholy by converting tryptophan into serotonin in animals. However, it can occasionally cause constipation, prolonged heart rate, prolonged urine output, and adverse skin reactions.

2.1.6. Cola Nut ((Cola Nitida/Acuminata)

The cola plant comes from West Africa. Kola nuts need theobromine and caffeine. *Cola acuminata* and *Cola nitida* seeds grow cola nuts. 1.5 to 3.8 of the natural cola nut extract has caffeine. It can treat migraines, depression, exhaustion, and help with weight loss. The food industry uses it for flavoring. Pregnant women should avoid it because it can cause stomach infections.

2.1.7. Guarana(Paullinia)

The Guarana plant comes from the central Amazonian Basin and is often used in Brazilian smooth drinks. Guarana contains caffeine, which makes up 2.5-5% of the extract's dry weight. This caffeine gives guarana its stimulating effects on the central nervous system. There are also small amounts of other substances called theophylline and theobromine in guarana. Guarana also contains saponins and tannins, which are believed to contribute to its psychoactive effects. People usually consume guarana with ginseng to help reduce physical or psychological stress. However, it's important to note that guarana-infused energy drinks may have negative effects on mental health, such as anxiety, restlessness, and irritation.

2.1.8 Yerba Mate (Ilex Paraguariensis)

Yerba mate is made from dried leaves of the *Ilex paraguariensis* plant. It is used for caffeine and medical purposes in southern Latin American countries like Brazil, Argentina, Paraguay, and Uruguay. In the United States, it is sold as tea bags, pills, and in food and nutritional supplements. Yerba mate contains a high amount of caffeine (1 to 2 percent of its weight) which stimulates the central nervous system. It may also be used to treat kidney, bladder, lung, esophagus, and oral cancers.

2.2 Psychoanaleptics

2.2.1 Ephedra

MA huang, also known as ephedra, has been recognized in China since ancient times. The most common form of ephedra is *ephedra sinica*. It contains ephedrine and pseudoephedrine, which act as CNS stimulants similar to amphetamines. Ephedrine increases the release of noradrenaline and adrenaline, reducing appetite and promoting fullness through the hypothalamic centers that control food demand. Ephedrine also boosts metabolic rate, aiding in weight loss by activating receptors. In 2004, the FDA banned the sale of dietary supplements with ephedra in the US due to the unjustified risk of harm or illness they pose.

2.2.2 Khat Khat

Catha edulis leaves or young shoots are used to stimulate the central nervous system. The plant is commonly grown in East Africa and the Arabian Peninsula. Khat contains unique chemicals that have psychedelic effects. The main chemical, cathinone, is similar to amphetamine and is responsible for most of khat's effects. Cathinone and amphetamine may have similar effects on metabolism and appetite suppression. Although ghrelin or Peptide YY secretion is not affected, regular consumers feel more hungry or full.

2.2.3 St. John's wort

St. John's wort is a plant that has yellow flowers and is found in North America, West Asia, and Europe. Recent research shows that this plant can help treat many different conditions, like cancer, inflammation, and bacterial and viral diseases. It can also act as an antioxidant and protect the brain. St. John's wort has a substance called hypericin that works as an antidepressant. Studies have found that hypericin can stop the breakdown of certain chemicals in the brain and increase their levels.

2.3 Cognition Enhancers

2.3.1 Ginkgo

Ginkgo biloba is a type of tree that has been grown in China for a long time because it has medicinal properties. It is used to treat vertigo, temporary memory loss, and attention deficit disorder. It can also help with cerebral vascular issues. Research by Bryn Williams shows that ginkgo extract can improve cognition in people with dementia by interacting with

the glutamatergic system. Ginkgo biloba also acts as a neuroprotective by preventing damage to the brain and protecting against stress. It can also help remove harmful substances from the body.

2.3.2 Gotu Kola

Centella asiatica is a herb with active components called triterpenoid glycosides, asiaticoside, madecassoside, Asiatic acid, and madecassic acid. According to Nora E. Grey et al., the plant extract can boost mitochondrial respiratory and antioxidant genes, which is important for conditions like Alzheimer's disease. Glutamate can cause neuronal degeneration, but asiatic acid can reduce this damage by limiting free radicals and preventing cell death. In studies, Centella extract has shown protective effects against cognitive impairment.

2.3.3 Ginseng

Ginseng extract is made from dried Panax ginseng roots and has been used in Asia for over 2000 years. Studies suggest that it can improve cognitive function in Alzheimer's disease. The active ingredients in ginseng prevent the buildup of amyloid and protect rats' spatial memory. It also stops the production of advanced glycation end product (AGE). In rat cortical cells, ginseng extract prevents the development of reactive oxygen species (ROS) and neuronal death caused by glutamate, N-methyl-D-aspartate, or beta-amyloid.

III. HERBAL CNS STIMULANTS IN RESEARCH:

Alpinia Galangal

Dried rhizomes of Alpinia galanga L. (Zingiberaceae) are the main components of this substance. Its exclusive use is in cooking. This herb is found in various regions of Southeast Asia and India. Researchers conducted different pharmacological experiments on the crude methanolic extract and ethyl acetate fraction of A. galanga to determine its CNS stimulating activity. The remarkable effects were observed in mice through actophotometry and the rotarod test, using both methanolic and ethyl acetate extracts of A. galanga. Mice treated with dosages of 250 and 500 mg/kg showed increased locomotor activity when given the methanolic extract or ethyl acetate fraction of A. galanga's rhizome. CNS stimulants enhance motor coordination, leading to an increase in performance time.

Cucurbita Maxima

The Cucurbitaceae family consists of the short-lived shrub Cucurbita maxima. The seeds' oil is employed for addressing anxiety issues and weakness, while the seeds themselves have traditionally served as a bitter tonic. In this study, Swiss albino mice were utilized to examine the recreational effects of CNS stimulants. Historically, caffeine has been used as a reference drug. The crude extract exhibited significant CNS stimulant activity compared to the control group, and its results were in line with those demonstrated by the reference medication.

Researchers have examined how *Rhinacanthus nasutus* (*R. nasutus*) leaf extract affects the impaired lipid and glucose metabolism in obese mice. Blocking the release of glucose from the liver as well as its uptake by fat and muscle cells can exacerbate weight problems caused by a high-fat diet (HFD) along with typical lipid metabolism. In this study, obesity was induced in mice through a 12-week high-fat diet consisting of 60 kcal fat. Following an initial six-week weight loss program, obese mice were administered water extracts of *R. nasutus* leaves at doses of 250 and 500 mg kg per day for the subsequent six weeks. To conduct a histological study and analyze protein expression, the liver and adipose tissues were removed. Various parameters such as blood glucose levels, lipid profiles, insulin, leptin, and adiponectin levels were measured. The results revealed that after six weeks of treatment, the water extract of *R. nasutus* effectively reduced elevated lipid concentrations in both serum and liver tissues of obese mice. This study highlights the potential of *R. nasutus* extract in improving impaired glucose and lipid metabolism associated with high-fat diet-induced obesity by enhancing insulin sensitivity in liver and adipose tissues. The use of natural products for disease prevention and treatment is increasing since herbal CNS stimulants are much safer than synthetic pills.

IV. CONCLUSION

In comparison to natural CNS stimulants, which are affordable, have minimal side effects and a wide safety margin, artificial drugs are more expensive, and have a narrower safety margin, thus the focus of study for CNS disorders. Except for addictive substances like cocaine and khat, all other medications such as caffeine and ephedra have a wider safety margin and fewer adverse effects than amphetamine and methylphenidate. Research is being conducted extensively on innovative techniques that prioritize natural CNS stimulants. Solutions are being sought for various issues related to research, production, and software. It is necessary to develop a suitable delivery system that enhances the drug's pharmacological activity while reducing its toxicity. The therapeutic potential of herbal pills is promising but requires investigation using costly medication delivery technologies.