STUDY ON HERBAL DRUGS THAT STIMULATE THE CENTRAL NERVOUS SYSTEM

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Abstract
This review highlights various CNS-stimulating plant species. Pharmacological classifications include psychostimulants, psychoanaleptics, and cognition enhancers. Psychostimulants like Tea, Coffee, and Cocoa temporarily increase mental and physical function (CNS). Ephedra, Khat, and St. John's wort are used to lose weight. Ginkgo and Gotu kola increase memory and alleviate vertigo, short-term memory loss, and attention deficit. Novel formulation creation methods for herbal CNS stimulants and botanicals in research are also discussed.

Keywords: *Herbal CNS stimulants, psychostimulants, psychoanaleptics, cognition enhancers*

Introduction
Psychoactive central nervous system stimulants temporarily increase mental and physical function (CNS). They are extensively abused despite their many therapeutic advantages. The National Department of Health estimated that 2-3.5% of US adults take amphetamines and methylphenidate, which are given for ADHD in children. Generalized action may cause seizures at larger dosages.

Ma huang (Ephedra vulgaris) in China, khat in Africa, and coca in South America are examples of ancient CNS stimulants. For over 5100 years, the Chinese herb ma huang has been used as a circulatory stimulant, diaphoretic, antipyretic, and antitussive. After isolating ephedrine from plant used to treat asthma and related disorders.

CNS stimulants improve alertness, wakefulness, endurance, productivity, motivation, arousal, locomotion, heart rate, and blood pressure. Catecholamine or serotonergic medications suppress appetite and reduce food intake, making them popular weight loss treatments. They treat clinical depression and bipolar illness, especially atypical and treatment-resistant depression. It reduces nasal congestion, orthostatic hypotension, and POTS. Stimulants decrease hyperactivity and are typically safe at therapeutic levels.

CNS stimulants boost norepinephrine and dopamine activity through monoamine transporter inhibition, adenosine receptor antagonism, and nicotine acetylcholine receptor agonism.

Pharmacologically, CNS stimulants are psychostimulants, psychoanaleptics, and cognition enhancers. Almost 15 million Americans use herbal treatments or high-dose vitamins.

In 2001, $37.1 billion was spent on weight-loss goods, $17.7 billion on herbal supplements. Herbal products are increasingly used for illness prevention and treatment. St. John's wort and gingko biloba are cardiovascular-harming herbs. The US's best-selling herb is St. John's wort. St. John's wort activates the hepatic cytochrome P450 system, which

metabolisms drugs, and may cause arrhythmia, hypertension, and other side effects. Ginseng causes hypertension and hypotension. Yet, Chinese medicine uses ginseng for myocardial infarction, congestive heart failure (CHF), and angina pectoris. Ginseng misuse may induce hypertension, behavioral problems, and diarrhea. Current research does not support its usage for cardiovascular diseases.

This article discusses popular herbal CNS stimulants and innovative formulation development methods.

Herbal CNS stimulants

Psychostimulants

Cocaine

Cocaine, an alkaloid isolated from the coca plant (Erythroxylum coca), is pasted and turned into a salt like hydrochloride or sulphate since free base is unstable. This salt may be made by snorting or injecting cocaine. However, it has been used from thousands of years in Central and South America for its more modest stimulant effects.

Dopamine is released from nerve terminals into synaptic cleft, bound to dopamine receptors, and processed by monoaminooxidase enzyme (MAO).

Cocaine in the periphery prevents NA, adrenaline, and dopamine absorption into adrenergic nerve terminals, increasing transmitter concentrations surrounding the receptor and stimulating the Brain.

Cocaine blocks Na+ channels to anesthetize locally. Only the US allows medicinal usage. Recent data shows that inhibiting NMDA receptors may cause cocaine's convulsigenic effects. Cocaine reinforces and addicts by blocking dopamine reuptake.

Cocaine abuse may produce cardiotoxic and neurovascular problems. Treatment dosage determines severity. Cocaine may be used in ocular and ear procedures to decrease bleeding and edema and as a local anesthetic.

Caffeine

Caffeine stimulates the CNS. More than 60 plant species contain caffeine, including coffee, tea, cocoa, guarana, yerba mate, and kola nut.

Adult Americans use 4mg/kg of caffeine daily. Caffeine increases dopamine, norepinephrine, and serotonin and stimulates the CNS by nonselectively inhibiting adenosine receptors and phosphodiesterase. Caffeine boosts mental alertness, lowers weariness, and may lessen metabolic disorders including obesity and Parkinson's disease. Daily caffeine use (less than 400 mg/day or 6.5 mg/kg/day for a 70 kg adult) seldom causes serious side effects. Caffeine toxicity is uncommon; the deadly dosage is 150–200mg/kg or 10–20gm/day.

Following plants are used as CNS Stimulants due to its caffeine content:

Tea (Camellia sinensis)

Tea follows water in popularity. Tea lowers glucose, cholesterol, weight, blood pressure, and stroke risk and improves metabolic profiles. A cup of tea with 7.5 mg to 75 mg of tea leaves has 3 mg to 30 mg of caffeine. Caffeine levels vary per tea plant section. Caffeine is concentrated in leaf buds and younger leaves. Caffeine in tea may induce sleeplessness, anxiety, restlessness, and tachycardia.

Coffee (Coffea robusta/arabica)

Westerners use coffee as a caffeine source third most often. C. arabica has 1.45% caffeine and C. robusta 2.38%. (C. canephora). Caffeine may promote anxiety and sleeplessness. Giulia Runti also found that Arabica coffee extract has antibacterial activity against Staphylococcus epidermidis and

Enterococcus faecalis and that excessive caffeine consumption may increase calcium and magnesium urine excretion, which might influence bone health in women.

Cocoa (Theobroma cacao)

Cocoa, often known as cocoa, is made from the seeds of the Theobroma cacao L. tree and used in chocolate. Cacao contains cocoa butter, minerals, methylxanthines (theobromine 1%–4% and caffeine 0.07%–0.36%), and polyphenols. Its flavonoid neuromodulates and protects. Flavanols work through direct interactions and cellular cascades to express neuroprotective and neuromodulatory proteins, stimulate neurogenesis, and enhance neuronal function, and increase brain and sensory system blood flow. Hence, it improves cognition, prevents insulin resistance, and reduces inflammation. In one animal investigation, cocoa-derived tryptophan converted into serotonin prevented sadness. Chocolate is well-tolerated but may produce allergic skin reactions, increased urine, heart rate, and constipation.

Cola Nut (Cola nitida/acuminata)

Western African cola species. Kola nuts contain theobromine and caffeine. Cola nitida and acuminata seeds produce cola nuts. Cola nut herbal extract contains 1.5%–3.8% caffeine. It treats depression, migraines, weight loss, and exhaustion. It flavors meals too. Due to gastrointestinal discomfort, it should not be taken during pregnancy.

Guarana (Paullinia cupana)

Brazilian soft beverages use the center Amazonian Basin's Guarana plant. Caffeine, which makes up 2.5–5% of the extract's dry weight, is the CNS stimulant in Guarana. Other purine alkaloids including theophylline and theobromine are found in lower amounts. Saponins and tannins in guarana contribute to its psychoactivity. Guarana is usually used alongside Ginseng to ease stress. Guarana-containing energy beverages may cause anxiety, restlessness, and irritation.

Yerba Mate (Ilex paraguariensis)

Aquifoliaceae Ilex paraguariensis leaves make yerba mate. Southern Brazil, Argentina, Paraguay, and Uruguay utilize it for caffeine and therapeutic purposes. It is sold in the US as tea bags, pills, and food and nutritional supplements. High caffeine concentrations (1% to 2% dry weight) stimulate the CNS. Persistent intake may cause oral, esophagus, lung, bladder, and kidney cancer.

Psychoanaleptics

Ephedra

China has long used Ephedra, or MA huang. Most ephedra comes from Ephedra sinica. Ephedrine and pseudoephedrine give it amphetamine-like CNS stimulant properties. Centrally, ephedrine increases the release and inhibits the reuptake of noradrenaline and adrenaline, decreasing food intake and promoting satiety via hypothalamic appetite centers. Ephedrine boosts energy expenditure, reducing weight. β receptor activation causes thermogenesis. The FDA prohibited ephedra-containing products in 2004. The FDA deemed these supplements unsafe.

Khat

Khat is CNS stimulant Catha edulis leaves or young shoots. East Africa and the Arabian Peninsula grow it. Khat has numerous chemicals. Khat's main psychotropic alkaloid, cathinone, is a structural counterpart of amphetamine. Cathinone with amphetamine may reduce metabolism and appetite. Habitual users reduce appetite and promote fullness without changing ghrelin or Peptide YY.

St. John's wort

St. John's wort, Hypericum perforatum, is a perennial plant from Europe, West Asia, and North America with yellow flowers. This plant may cure cancer, inflammation, bacterial, and viral infections, and function as an antioxidant and neuroprotectant, according to recent studies. St. John's wort's antidepressant hypericin. Monoamine oxidase degrades neurotransmitters. Hypericin inhibits MAO and boosts neurotransmitters, according to research.

Cognition Enhancers

Ginkgo

The Chinese tree Ginkgo biloba's dried leaves have been used medicinally for millennia. It treats vertigo, short-term memory loss, and inattention. It treats cerebral vascular diseases. Bryn Williams found that ginkgo extract directly affects the glutamatergic system and improves cognition in dementia patients. Ginkgo biloba inhibits amyloid-β neurotoxicity, protects against hypoxic stress, and scavenges radicals.

Gotu Kola

Psychoactive Centella asiatica herb. Triterpenoid glycosides such asiaticoside, madecassoside, Asiatic acid, and madecassic acid make Centella asiatica active. Nora E. Gray et al. found that plant extract boosts mitochondrial respiration and antioxidant genes regardless of amyloid β exposure. Mitochondrial malfunction and oxidative stress are linked to Alzheimer's disease and other disorders. NMDA receptor overstimulation causes glutamate-induced neuronal degeneration. Asiatic acid lowers intracellular free radicals and H2O2-induced cell death. Triterpene asiatic acid and its derivatives protect cortical neurons against glutamate-induced excitotoxicity in vitro. Centella extract at 100, 200, and 300 mg/kg protected rats against cognitive impairments, oxidative stress, and memory loss.

Ginseng

Since 2000 years ago, China, Korea, and Japan have utilized dried Panax ginseng roots. Ginseng extract improves cognition in Alzheimer's disease. Ginseng prevents amyloid beta and spatial memory impairment in rats. Reduces AGE formation. Red ginseng water extract (0.3–3 mg/mL) prevents glutamate, N-methyl-D-aspartate, and β-amyloid-induced neuronal death and neurodegenerative disorders in rat cortical cells.

Clinical trials

Sr. No.	Herbal Plant	Participants	Intervention	Co
1	Caffeine	Volunteers(10females and 9 males aged61-79; 66 ± 2 years)	Pre and 60 minutes post ingestion	Enh perf mar dex read effo hea
2	Ephedra	One hundred and twenty-five otherwise healthy obese women (body mass index >=25 kg/m2) were recruited and randomly assigned to three groups: ephedra group (n = 41), evodia group (n = 45) and placebo group (n = 39).	ephedra extract in capsules (pseudo-ephedrine 31.52 mg) or evodia extract in capsules (evodiamine 6.75 mg, rutaecarpine 0.66 mg) or placebo capsules as well as participating in a low-calorie diet for 8 weeks	Eph wer safe sho the eph witl diet redu

3	Khat	Six habitual khat chewers	For a period of 3h,chewed either khat leaves or lettuce	Chewing khat significantly decreased subjective feelings of hunger and increased fullness, anorexigenic effect of khat is due to ethinone	Murray CD et al., 2008		scor but 200 Imp repo leve
4	Hyperic um	one hundred thirty-five patients (57% women; mean age, 37.3 +/- 11.0) were randomized to double- blind treatment and were included in the intent-to-treat analyses.	12 weeks double-blind treatment with LI-160 St John's wort extract (900 mg/d), fluoxetine (20 mg/d), placebo.	St John's wort was significantly more than placebo and fluoxetine and showed a trend toward superiority over placebo for antidepressant efficacy.	Fava M et al., 2006		
5	Ginkgo	a randomized, double-blind, placebo-controlled trial	daily doses of 480 mg EGb 761, 240 mg EGb 761 or placebo for weeks	It was safe and well tolerated, and may have particular value in elderly patients with anxiety related to cognitive decline	Woelk H et al., 2007		
6	Gotukol a	Thirty-three participants (18 male and 15 female; average age 33 yrs)	Centella asiatica (CA) in a fixed dose regime (500 mg/capsule, twice daily, after meal)	CA further significantly improved theal willingness for adjustment and cognition, and may be used as a promising anxiolytic agent	Jana U et al., 2010		
7	Ginseng	30 participants	200 and 400 mg	Reduced reaction time on 3-back reaction time at 400 mg but increase in reaction time with 200 mg. Increased 3-back sensitivity index	Reay et al. (2009)		

Novel Approaches for Herbal CNS Stimulants

Sl No.	Active Constituent	Formulation	Route Administrat
1	Ginkgoflavon Glycosides	Phytosome	subcutaneous
2	Ginsenosides	Phytosome	oral
3	Ginkgo flavonoids	Nanoparticle	oral
4	Theasinesis	Phytosome	oral
5	Ginseng, Guarana	Fast Dissolving Oral Films	oral
6	Ginseng	Nanoparticle	oral

Herbal CNS stimulants in research

Alpinia galanga

Alpinia galanga L. rhizomes are dried (Zingiberaceae). Cooking uses it most. The plant grows in India and Southeast Asia. Crude methanolic extract and ethyl acetate fraction of A. galanga stimulate the Brain in pharmacological testing. Actophotometry and rotarod tests showed substantial activity in mice from A. galanga methanolic and ethyl acetate extracts. A galanga rhizome methanolic extract and ethyl acetate fraction increased locomotor activity in mice at 250 and 500 mg/kg. CNS stimulants improve motor coordination and mouse rotarod time. At 500 mg/kg, A. galanga methanolic extract and ethyl acetate fraction improve gripping time.

Cucurbita Maxima

Short-lived Cucurbitaceae shrub Cucurbita maximum . Seeds are bitter tonics, and the oil from them helps heal sadness and nerve problems. This CNS stimulant investigation used Swiss albino mice. Reference drug: caffeine. Compared to control group, crude extract demonstrated strong CNS stimulant action equivalent to reference medication.

Rhinacanthus nasutus

Rhinacanthus nasutus leaf extract was tested on obese mice with impaired glucose and lipid metabolism. Obesity caused by HFD and improper lipid metabolism may disrupt insulin signalling by decreasing hepatic glucose release and fat and muscle cell glucose absorption. Mice fed a 60 kcal% fat diet for 12 weeks became obese. After six weeks of diet, obese mice received 250 and 500 mg/kg of R. nasutus leaf water extract daily for six weeks. Histopathology and protein expression studies need liver and adipose tissue removal. Glucose, lipids, insulin, leptin, and adiponectin were measured. R. nasutus water extract reduced serum and hepatic lipid contents in obese mice after 6 weeks. R. nasutus extract increases liver and adipose tissue insulin sensitivity to improve glucose and lipid metabolism in mice with high-fat diet-induced obesity. Herbal CNS stimulants are safer than synthetic drugs and are being used more for disease prevention and treatment.

Conclusion

Herbal CNS stimulants are cheaper, safer, and have less adverse effects than synthetic ones, hence they are being studied increasingly for CNS problems. Except for cocaine and khat (abusive substances), caffeine and ephedra are safer and have fewer negative effects than amphetamine and methylphenidate.

Novel herbal CNS stimulant targeted methods are being studied. Numerous research, manufacturing, and application issues must be resolved. A suitable carrier should decrease medication toxicity and boost pharmacological activity. With value-added medication delivery technologies, herbal pharmaceuticals offer great therapeutic potential.

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