

THE ETHNOPHARMACOLOGY OF *CENTELLA ASIATICA* (L.) URBAN (APIACEAE)

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ABSTRACT.—*Centella asiatica* is a creeping, prostrate, perennial herb of both the Old World and the New World tropics. It is marketed as a medicinal herb in China, Java, India, Madagascar, Sri Lanka and recently in the United States. The oldest traditions surrounding this herb derive from the earliest Chinese pharmacopoeias and associate it with the qualities of restorative, detoxification prolongation of life and a general energizer. These qualities as well as other attributes are common to the belief systems of other regions where the herb is used. An analysis is presented in which the known chemistry and pharmacology is related to efficacy of both herbal preparations and chemical isolates. The implications of *in vivo* and *in vitro* assays are discussed. Much of the ancient and contemporary lore surrounding this plant is justified on the basis of experimental evidence. When consumed in large amounts it has been found to cause vertigo, act as a narcotic and induce comatose states.

Several plant species and genera have been confused with *Centella asiatica* (L.) Urban. The reasons are twofold: Chinese characters have been variously deciphered and transliterated into Roman text and these derive from diverse provinces where the genus has been used. Secondly botanists have attempted to use Chinese transliterations to elucidate the plant in question and have implicated *Conocephalus*, *Nepeta* and *Hydrocotyle*. Beyond the issues of correct botanical nomenclature, marketing of *Centella asiatica* under a variety of names that are registered or indicated as a trademark introduces further complications. Some suppliers of herbal pharmaceuticals have used corruptions of a Chinese name for *Centella asiatica* to introduce a combination of plant products. The Chinese **Fo-ti-ts'ien** which translates as "ground coin" is often presented as **Fo-ti-tieng** which, according to Dr. Charles Tseng (pers. comm.), translates as "that which creeps" implicating any number of prostrate herbs.

One of the earliest encounters with *Centella asiatica*, found under the entry **Chi-hsueh-ts'ao**, is the *Pen Ts'ao* of the Chinese herbalist Li Shih-Chen dating to 1578. The volume reportedly involved twenty-six years of scholarly investigation and as much pragmatic experimentation. In addition, it relied heavily upon an oral tradition extending to the Emperor Shen-Nung who lived around 2737 B.C., long before the appearance of a written language in China. Li Shih-Chen's publication did not appear in English until the recent translation and additional research added by Stuart and Porter-Smith (1973). These investigators included their own observations and annotations to the herbal remedies already included in this giant compendium. Commercial sources of "registered **Fo-ti-tieng**" often contain additives such as kola nut (*Cola nitida* or *Cola acuminata*) and meadowsweet. *Centella asiatica* is also marketed in the United States under the trade name *Gotu Kola* and the ingredient is indicated as *Hydrocotyle asiatica*. *Hydrocotyle* is a different genus in the family Apiaceae and it has an upright habit.

Some other synonyms in China are: **P'o't'ung-chien** "broken copper coin" and **Kang-kuo lung**, for which I have no translation. These are but a few names from the diverse areas of one country where the herb has found considerable popularity.

There is every reason to be suspicious of many of the eight thousand prescriptions that appear in the *Pen Ts 'ao*; on the other hand, we have reason to be cautious in approaching the ever proliferating number of prescription and patent medicines that flood our drug stores and supermarkets. Many of these are the same materials sold under a variety of names. When a preparation is of herbal origin, it is unlikely that the buyer will be able to find an indication of the genera and species involved. A case in point is a popular laxative (one of America's favorite medicants) that is composed of the seed husk of *Plantago psyllium* that absorbs water, swells and releases mucilage. This simple herbal seed husk is sold under a great number of patented names and without generic or specific identification.

There is clarification needed with regard to the entry *Chi-hsueh-ts'ao* in the *Pen-ts'ao*. While this entry in a reference to *Centella asiatica*, there is also a discussion in the same place of *ti-ch'ien-ts'ao*, which is the mint *Nepeta glechoma*. A misunderstanding of Bretschneider (1850) led to the subsequent popular belief that *Chi-hsueh-ts'ao* (*Centella asiatica*) was *Nepeta Glechoma* which has no significant pharmacological action. As a result, the herb *Centella asiatica* was ignored in the West for a considerable period of time, and a serious consideration of it did not appear until the studies of Bontemps (1942). In the interim it remained a popular folk remedy in China, Ceylon, Java, India and elsewhere. As such, the entire leafy structure of the plant was eaten or an extract of the plant juices was used both externally for dermatitis, wounds and sores, and internally for a number of specific and non-specific diseases. Most commonly it was thought to be a cure for leprosy, tuberculosis, mental retardation and general debilitation of health (Table 1).

Centella asiatica is so inconspicuous that it is scarcely noticed unless searched out. It creeps along the ground by means of numerous stolons that establish new plants in moist soil adjacent to the progenitor forming dense mats in marshy or boggy areas. Copious stands are found in tropical areas of India, Ceylon, and parts of China. It seems to have few natural predators (excepting mealy bug) and requires no real cultivation. The leaves, about the size of a quarter when well grown, are covered with a combination of glandular and sterile hairs. The flowers are barely visible to the naked eye as are the two-parted fruits (schizocarps) that follow. The fruits are traversed with oil tubes that carry an oil with fragrance characteristic of the leaf oils. Being a member of the family *Apiaceae* (formerly *Umbelliferae*) it is related to parsley, celery, carrots and dill.

In China it was historically known as "snow plant" for reason of its cooling properties. It is also classified in Western herbal medicine as a refrigerant, that is to say a botanical agent that has cooling effects and may be used to allay fevers. More importantly the Chinese regarded the plant *Centella asiatica* (also known under *Chi-hsueh-t-ao*) as able to prevent both disease and senescence.

The term "adaptogen" is coming into prominence in the terminology of eastern Europe and especially the Soviet Union and Asia. An adaptogen (Brekhman and Daroymov, 1969) is a naturally derived compound or plant that is non-toxic, has the ability to increase resistance to stress, and is effective against some bacterial agents, viruses and toxins. Adaptogens have a normalizing effect by stabilizing blood pressure and endocrine imbalance. The question put before us is this: Is *Centella asiatica* an adaptogen? If so, what actual chemical properties does it exhibit, and what diseases is it effective against?

According to Leyel (1970) the Chinese referred to *Centella asiatica* as "elixir of life". She lists the constituents as "vellarine, having the odor and bitter persistent taste of the fresh plant, resin, some fatty aromatic body, gum, sugar, albuminous matter, salts, mostly alkaline sulphates and tannin." She indicates the action to be that of an alternative (changing a morbid state of being into one of health), diuretic and tonic. Collectively these suggest an adaptogen or in her terms, elixir of life. It is unfortunate that

she does not provide bibliographic references, for her suggestions regarding the plant as a tonic and as a narcotic in large doses are most intriguing. Accounts of longevity and virility are derived from Leyel's treatment of the herb. She asserts that the Chinese herbalist Chang-li-yun lived to the age of 256 years and married 24 times, attributing this to his having drunk an infusion of *Centella* every day. Likewise the Indian sage, Nanddo Narian, is alleged by Leyel to have lived to the age of 107, using the plant to ward off disease.

Leyel's account of Professor Menier of Paris discovering in the leaves an energizing property which influences the brain, as well as vitamin G, operative on the endocrine system, is most intriguing. It corresponds to the work of Jules Lepine, a biochemist who had previously described these properties from his studies of the plant.

By 1933 the French government had established an agricultural and medical experimental station in Algeria to study this herb. The English founded the Ayurvedic College of Research in Colombo, Ceylon where similar studies have been conducted. Leyel states that Dr. Menier of the Academie Scientifique in Paris reported vitamins G and X as stimulators of the endocrine system (without any specific structural formulas presented), and as detoxifiers of the body and stimulants of the central nervous system. All are alleged to generally enhance metabolism.

Oliver-Bever (1983) has classified *Centella asiatica* as a plant having a stimulant action on the autonomic nervous system. He notes also that the leaves and stems in infusion have been used in India for the treatment of leprosy and other dermal diseases (as recorded in the *Indian Pharmaceutical codex.*), while larger doses are said to have a narcotic effect.

Reports on the effects of *Centella* as a tonic or stimulant differ with habitat. This can be attributed to saponin content which is variable and is habitat dependent. The most common condition is to find asiaticoside and medacanoside present. When arabinose is present in the saponins, a less usual condition, brahmoside and brahminoside (triglycoside and tetraglycoside of brahmic acid) are formed (Appa Rao et al., 1969). These workers also found betulinic acid and stigmasterol in the arabinose-containing variants. Apart from habitat dependent variation there would appear to be genetically based variation accounting for the consistency of reports within, but not between, continents.

Asiaticoside (a genin glycoside of a pentacyclic triterpenic acid) was isolated from plants of Madagascar by Bontemps (1942), but was not able to be extracted from Ceylonese plants (Bhattacharya and Lythgoe, 1949). However, the plants from Ceylon contained the related compound centelloside as well as centoic acid and centellic acid. This was subsequently confirmed by Boiteau et al., 1949, 1956, and by Oliver-Bever, 1960. Dutta and Basu (1967) identified asiatic acid, asiaticoside, mesoinositol and an oligosaccharide of centellose. Rao and Seshadri (1969) confirmed that saponin and flavonoids were in both the arabinose containing a variety of *Centella* and those without arabinose.

The presence of asiaticoside is significant in that it has been found to dissolve the wax capsule of *Mycobacterium leprae*, the causal agent of leprosy. Further, when asiaticoside is oxidized to oxyasiaticoside, which takes place *in vivo*, tubercle bacilli are inhibited (Boiteau et al., 1949). Studies by Appa Rao et al. (1969, 1973) on 30 mentally retarded children free from neurological disfunctions, and 43 "presumed normal" adults revealed significantly improved ability and behavior among the children after feeding the whole plant as a dietary supplement for 12 weeks. In the adult "control group" there was an increase in mean levels of serum cholesterol, blood sugar, and total protein. Among these same adults, there was a decrease in mean levels of blood urea, serum acid and phosphatase. The suggestion (not advanced by these researchers) is that this plant may be especially useful in cases of gout and perhaps in some kinds of diabetes. Reports on narcoses from the ingestion of large amounts of *Centella asiatica* are sporadic and are in need of substantiation via controlled experimentation.

Rock (1920) believed the plant to be poisonous and suggested that it not be eaten, at least not those growing in the Hawaiian Islands where it is known as "wild swamp violet" for reasons unknown. The allegations that it causes gastritis and dermal irritation seem to be unfounded as regards the the general populace.

Arnold (1968) in writing on *Poisonous Plants of Hawaii* suggests that Rock is incorrect in his assertions of "dangerously poisonous." Arnold cites de Grand Pre (1888) in suggesting the plant is a stimulant and energetic (sic) in small doses, but produces vertigo and a tendency to coma in large doses. He concludes, ". . . It is obviously not especially dangerous."

Stigmasterol is an interesting isolate in that it is usually obtained from *Glycine maximum* (soy bean) or *Physostigma venenosum* as starting materials for hormone synthesis. Most hormones obtained in a pure state and on a large scale must be synthesized by combining chemical and microbiological processes. Starting with a preformed steroidal nucleus is far more feasible than any attempt at total synthesis.

The finding of mesoinosital (Inositol) by Dutta and Basu (1967) is intriguing. This hydroxycyclohexane is widely distributed in both plants and animals and is a growth factor for animals and for microorganisms. As such some have considered it a vitamin and at least two patents exist covering it. The chemical is classified also as a lipotropic agent enhancing fat metabolism (Sebrell-Harris, 1954). The previously mentioned compounds are summarized in Fig. 1.

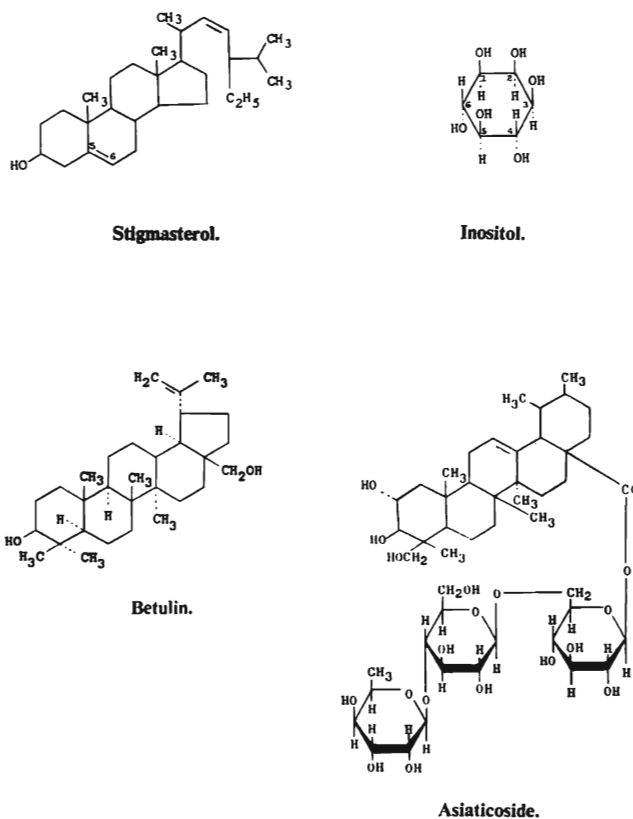


FIG. 1.—Structural formulae of four compounds isolated from *Centella asiatica*.

Dwayne Ogzewalla, Professor of Pharmacognosy at the University of Cincinnati and his student Prakongsiri Boonkong (pers. comm. 1984) have convincing data that skin damage from podophyllin (*Podophyllum peltatum* resin) is ameliorated and healed by applications of *Centella* in a neutral cream base as a carrier. The same did not hold true when the *Centella* cream was applied to lesions caused by *Toxicodendron*. Mice fed for three months with 10% dry weight of *Centella* added to their diet showed no difference in weight or activity from the control group. This study continues and was at the time of communication hampered by the inability of the researchers to get relatively pure asiaticoside or asiatic acid.

TABLE 1.—*Centella*: Crude plant material.

Region of Derivation	Author-Researcher	Utilization or Properties
India, Ceylon & Madagascar	Indian Pharmaceutical Codex	Leprosy Diuretic Narcotic
India, Ceylon, Madagascar & Tropical West Africa	Oliver-Bever, 1983	ANS Stimulant Bitter Tonic Analeptic
India	Jain, 1981	
Khasi & Jaintia		Dysentery Boils Tumors
Orissa		Cough Syrup Dysentery
China	(Fide Leyel, 1970) Chang-li-yun Narian Menier	Diuretic Tonic/Narcotic Alternative "Adaptogen" "Adaptogen" Endocrine Tonic Vitamins G and X Detoxification
India	Appa Rao et al., 1973	Rehabilitation of Mental Retardation in Children: Decrease in blood urea, serum acid and phosphatase
Hawaii	De Grand Pre, 1888	Stimulant, Nerve Tonic Energetic

In summation it may be stated that *Centella asiatica* is a plant with potential in medicine. It has been ignored in the United States and is seldom seen in cultivation. As the uses outlined in Tables 1 and 2 suggest, there are a number of known diseases for which it may be a remedy or cure and in addition it may serve as an adaptogen allaying stress and retarding or eliminating the development of diseased states.

TABLE 2.—*Effects of isolates of Centella Asiatica (L.) Urb.*

Regional Source	Researcher(s)	Isolate(s)	Uses
Madagascar	Bontemps, 1942	Asiaticoside (Madecassol)	Anti-Leprosy Drug (<i>Mycobacterium leprae</i> capsule dissolved)
Madagascar	Boiteau et al., 1949	Oxyasiaticoside	Tubercule Bacilli Inhibited <i>in vivo</i>
Sri Lanka (Ceylon)	Bhattacharya & Lythgoe, 1949	Centelloside Centoic acid Centellic acid (Asiaticoside absent)	Not indicated, but Centelloside is related to Asiaticoside
India	Appa Rao et al., 1969	Arabinose Brahmic acid Brahmoside Brahminoside Isobrahmic acid Betulic acid Stigmasterol	Ascites and Rheumatism Hormonal Nucleus
India	Dutta and Basu, 1967	Asiatic acid Asiaticoside Centellose Medacanoside Mesoinosital (Inosital)	Growth Factor Lipotrophic Agent
India	Rao and Seshadri, 1969	Flavonoids Sapogenins	Chemical Confirmation: Presence of these in all chemical variants

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