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Pharmacological Activities of *Cassytha Filiformis*: A Review

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ABSTRACT

Cassytha filiformis L. (Lauraceae), a medicinal plant is traditionally used for the treatment of cancer, African trypanosomiasis and many other related diseases. This plant has a wider distribution throughout India and used medicinally in China, Indochina, Madagascar and South Africa. Thus, *Cassytha filiformis* is medicinally used as an antiplatelet, vasorelaxant, alpha-adrenoreceptor antagonist and also as a antitrypanosomal agents. Some of the isolated compounds from the extracts of this plant are aporphine alkaloid, oxo-aporphine alkaloid, cassyformine, filiformine, cathaformine, lignan, actinodophine, and octenine. In modern medical research, *C. filiformis* has been investigated to possess a number of biologically active chemical compounds with the therapeutic potential in human health applications. In this review, we have explored the various dimensions of the plant *Cassytha filiformis* and compiled its few pharmacological applications to reveal its medicinal properties and its application in the pharmaceutical industries.

Key words: *Cassytha filiformis*, Trypanosomiasis, Aporphine alkaloid, Octenine.

INTRODUCTION

A sprawling parasitic vine *Cassytha filiformis*, is widely distributed throughout the regions of tropics much along the seashores up to the extent of 300m. It is found to be parasiting on many other host plants like *Acacia*, *Azadirachta*, and *Mangifera*. Stem were threadlike, leaves were reduced to minute scales and spirally arranged, glabrous or pubescent. Inflorescence seems to be reduced to one flower being sessile or shortly seen as pedicellate, green or white coloured. Fruits were round black berries. Flowering and fructification is found all over whole the year[13]. The "woevine" is usually found as a cosmopolitan in the region of tropics but sometimes becomes a

pest of economic importance because of its attachment to the valuable orchard trees and other ornamental plants by means of its tough threadlike extensive branchlets. This plant is considered to be unique in the family of Lauraceae as it is a parasite. Because of the nature of its particular characteristics, it is taxonomically classified in a separate tribe.

Cassytheae comes within the family Lauraceae and it is represented by the single genus *Cassytha* which further describes 18 different species under it. The genus derived its name, *Cassytha*, from the Greek name of *Cuscuta*. The vine has several common names in the regions of the tropics. For example, South Sea Islanders called this vine as "*tentanini*" which has the meaning "to go round and round," and this seems to be a true descriptive adjective for the plants entwining habit[1].

Taxonomical classification:

Kingdom	: <i>Plantae</i>
Subkingdom	: <i>Tracheobionta</i>
Superdivision	: <i>Spermatophyta</i>
Division	: <i>Magnoliophyta</i>
Class	: <i>Magnoliopsida</i>
Subclass	: <i>Magnoliidae</i>
Order	: <i>Laurales</i>
Family	: <i>Lauraceae</i>
Genus	: <i>Cassytha L.</i>
Species	: <i>Cassytha filiformis L.</i>

Botanical description:

C. filiformis is a leafless and perennial vine with small scales as a replacement of the leaves and adheres to the host by the haustoria that penetrates the epidermis of the other plants, and hence helps to spread through the tops of the trees and bushes, thus ultimately forming a long festoons of colourful greenish yellow vines. The individual stems that are copiously branched has a range of 1 to 3 millimeters in the diameter and finally attain a maximum length of 10 to 20 feet. The flowers were borne all over the year with a bisexual nature with a stamen and perianth arrangement that looks similar to the ordinary avocado. The ovary is the one first getting exposed and later on becomes enveloped by the enlargement and then the over growth of the calyx tube occurs. The fruit is about the size of the large pea and gets closely enclosed by means of the succulent calyx. The single seed possess a membranous testa and the separation between cotyledons is not properly defined[1].

Synonyms:

English: Love vine, greek kasytas

Spanish: Alambrillo, bejuco dorado, bejuco fideo, fideos, tente en el air

Chinese (Taiwan): Kume, wu-kentaso

Japanese: Sunazuru

French: Liane parasite, liane d'amité, liane ficelle, liane sans fin, mouttaré, fausse cuscute, cord a violon, vermicelli

German: Schlingfaden[13].

Plant parts used:

The aerial parts and the leaves were usually used to extract the active components of the plant that has a potential application in the medicine[13].

Traditional uses:

In Taiwan, *Cassytha filiformis* was reported as a beneficial medicine against the gonorrhoea, kidney ailments and as the diuretic. In Africa it was used to treat the cancer, African trypanosomiasis and other diseases[13]. Apart from the above, some unusual uses were made of the plant by the natives in the Gilbert Islands in which the vine was worn on the body by the dancers. The smooth orange yellow strands were designed as the beautiful necklaces and as the head wreaths or might be used as the cloth by crossing over the chest and then wrapping around the arms. Men were also reported to use it in the love magic while women used the extracts of the vine as a colouring agent or as a dye to provide a black color for the fabrics[1].

It was a plant treasured by the Hawaiians as a light-hearted or as a ceremonial human ornament and also in the decorative garlands and in the lei. It is a valued plant in the traditional societies with much diverse healing applications and hence provides a promise for the modern medicine. It was used as a food plant to humans and animals. The vine was used in the thatched roof construction. It was considered as a potential biological control agent for the invasive plants. It is also a pestiferous and pathogenic weed which is a major threat to the agriculture and other endangered plants as they are capable of transmitting the pathogens between the plants[2].

They possess several aporphine alkaloids that was often used in the African folk medicine to treat certain diseases such as a cancer, African trypanosomiasis and other diseases as mentioned above[6]. In the traditional ayurveda, *Cassytha filiformis* is used as the major substitute for *Cuscuta*[9].The brown colour of the stem is used as the colouring agent and hence possess a major application in the dyeing industries [11].

Phyto chemical constituents:

The plant genus *Cassytha* (Lauraceae) provides a rich source of the phytochemical constituent such as aporphine alkaloids . The total alkaloid content in the plant, *Cassytha filiformis* showed a variation with respect to the material is estimated to be around the value of 0.11-0.43 % .In the Brazilian species of *C. filiformis* totally thirteen alkaloids were found . In Taiwan, the methanolic extraction of *Cassytha filiformis* were analyzed for a group of aporphine alkaloids and was found to be cathafiline, cathaformine, actinodaphnine, Nmethylactinodaphnine, predicentrine and ocoteine.

In Japan, the earlier work showed that the cassyfiline was described as a light orange-brown microgranules and possess a chemical structure C₁₉H₁₉O₅ N .The crude alkaloid extract of *C. filiformis* gave four aporphine alkaloids neolitsine, dicentrine, cassythine (=cassyfiline) and actinodaphnine . Their chemical structure was also determined by the spectroscopic data. They all are found to be cytotoxic[13]. They have apparently the same flavonoid composition, i.e., quercetin 3-O-robinobioside, quercetin 3-O-rutinoside, quercetin 3-O-galactoside, kaempferol 3-O-robinobioside, isorhamnetin 3-O-rutinoside and isorhamnetin 3-O-robinobioside [4].

Several aporphinoid alkaloids isolated from the samples originating from Taiwan, Brazil, Australia and New Guinea but compositions were found to be quite variable among the different origins. Samples of *C. filiformis* from Benin were also studied and six aporphines were identified, which were then analysed for the *in vitro* cytotoxic properties. The major alkaloids (actinodaphnine, cassythine, and dicentrine) were also found to have the anti-trypanosomal properties in the *in vitro* condition against the tested organism *Trypanosoma brucei brucei*.

A methanolic extract of a Chinese sample was identified to possess a remarkable vasorelaxing activity and also the inhibitory effect on the platelet aggregation. A bio-guided fractionation of the above extract were allowed to isolate cathafiline, cathaformine, predicentrine, ocoteine, actinodaphnine and *N*-methylactinodaphnine in which all of the compounds showed the potent anti-platelet actions. Ocoteine was identified as a selective α 1-adrenoceptor antagonist in the isolated rat thoracic aorta [6].

MATERIALS AND METHODS

Anti-platelet and vasorelaxant activity:

Six compounds were extracted out of the methanolic extract taken from the fresh plants of *Cassythia filiformis* and was found that they had exhibited a significant vasorelaxant and inhibitory effects on the platelet aggregation. All the six alkaloids isolated has showed the anti-platelet effects with the variable extent [13].

Cytotoxicity activity:

The alkaloid extract of *Cassythia filiformis* plants was found to show a cytotoxic property in the invitro condition with IC50 value of 2.2 μ g/ml. Three alkaloids, particularly actinodaphnine, cassythine, dicentrine were found to be very active in vitro on the trypanosomes with IC50 values of 3-15 μ M tested by using the optical methods. The mechanism is that the alkaloids have the ability to bind effectively to the DNA molecule and hence behaves as a typical intercalating agents. Actinodaphnine, cassythine, dicentrine also interferes with the catalytic activity of the enzyme topoisomerases. Four alkaloids isolated from a crude extract of *C. filiformis* (neolitsine, dicentrine, cassythine, actinodaphnine) were also tested on the cancer and non-cancer cells in the in vitro condition in which neolitsine was found to be the most active agent against the HeLa and 3T3 cells. Cassythine and actinodaphnine has showed the highest activity against Mel-5 cells and HL60 cells respectively [13].

Pharmacological activity:

Ocoteine isolated from the *Cassythia filiformis* was found to be acting as a alpha 1-adrenoceptor blocking agent which was tested in rat thoracic aorta. The study revealed that the mechanism of action is due to its competitive antagonism of the phenylephrine induced vasoconstriction. At the higher concentrations, it was found to block the 5-HT receptor and alter the Na⁺ and steady state outward currents in the tested rat ventricular myocytes [13].

Antioxidant activity:

The antioxidant activity of *Cassythia filiformis* extracts such as hexane, ethyl acetate and methanol were used for the assessment based on their radical scavenging activity (RSA) using

the DPPH assay. The methanolic extract was found to show potent antioxidant activity on comparison with the standard Butylated hydroxytoluene (BHT). The methanolic extracts were further evaluated by the other methods such as Ferric thiocyanate (FTC) method, Thiobarbituric acid (TBA) test and Superoxide anion radical scavenging assay. The results obtained from the above experiment suggested that the methanolic extract of *Cassytha filiformis* have provided a promising therapeutic potential and could be further applied as a potential source for the drug development by the pharmaceutical industries [5].

Anti-trypanosomal activity:

Trypanosomiasis is a potent fatal disease affecting both the human and the other domestic animals in the regions of tropical Africa and South America. Approximately, it was found that around 50 million people in 36 African countries were at the risk of getting infection and there were about 300,000 to 500,000, people currently infected and there were 100 deaths every year due to the above diseases [10]. *In vitro* effect of the crude alkaloid extract and the isolated compounds such as Actinodaphnine, Cassythine, Dicentrine on the infecting organism *Trypanosoma brucei brucei* was tested and was found that the compounds showed the maximum inhibitory effect against the organism [6].

Diuretic activity:

Aqueous and alcoholic extract of *Cassytha filiformis* was tested for its diuretic activity in Wistar rats. Total urine output volume and the concentration of Na⁺, K⁺ and Cl⁻ ions excretion in the urine were finally estimated. Aqueous and alcoholic extract of *Cassytha filiformis* was found to exhibit a significant diuretic activity by causing the marked increase in the Na⁺ and K⁺ excretion [12].

Other studies:

Parasite-host interaction study:

Parasite-host interaction of *Cassytha filiformis* and *Zizyphus jujube* through the histochemical studies showed the occurrence of the specialized glandular cells that helps in facilitating the adhesion of the parasite to the host plant and further in the specialization to obtain the nutrients from the phloem tissue of the host plant. Histoenzymological studies indicated the occurrence of the high acid phosphatase enzyme activity of the parasite, which helps in the digestion of macromolecules and in the intercellular transport of parasite. Partial photosynthesis activity of parasite was also noticed by means of the acceptance of the hydrogen ion that was released from the photolysis of water through the Hill reaction. Biochemical studies revealed that there was a reduction in the chlorophyll *a*, *b* and also the total chlorophyll pigments of the host mainly due to host-parasite interactions, even though the parasite (*Cassytha*) is found to be autotrophic in the nature [7].

Sub-chronic toxicity study:

The sub-chronic toxicity of the aqueous herbal extract of the *Cassytha filiformis* was tested in male wistar albino rats. The LD₅₀ of the aqueous extract was also determined. The effects on body and organ weights, and also certain other haematological and plasma biochemical parameters were considered as the indices of organ toxicity. The aqueous extract did not show any affect on the plasma glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate

transaminase(GPT). However, there was a significant reduction in the alkaline phosphatase (ALP) level. There were no affect noticed on the electrolytes, total and direct bilirubin, creatinine, and also in the glucose level. The aqueous extract was found to elicit the hypercholesterolaemic effects, but it did not show any affect in the Hb, WBC, RBC, PVC, platelets, MCH, MCHC, MCV levels and in the differential counts. It also reduces the body weight gain and the absolute weight of the kidneys. This study finally suggested that the aqueous extract of *C. filiformis* when administered at the normal therapeutic doses was not likely to produce any severe toxic effects on some of the organs or on the haematological and biochemical indices in the rats [8].

Anatomical studies:

In *Cassytha filiformis*, the epidermis was found to be composed of a single layer of the paranchymatous cells with the stomata. The paranchymatous cork tissue was found to be located immediately under the epidermis, which is of 4-7 layered. Stellar region was found to be started with the starch sheath. Conjoint, collateral and open type vascular bundles were arranged in a ring, and consists of about 13-15 in numbers. Pith was relatively small and hence made up of paranchymatous tissue [9].

Preliminary phytochemical evaluation:

TLC analysis was done to both the aqueous and the ethanolic extracts of the plant *Cassytha filiformis* and for the evaluation, various solvent systems were tried. Among them, the solvent system, Toluene: ethylacetate: glacial acetic acid (5:7:0.1) showed the maximum separation in the TLC plate [9].

CONCLUSION

We conclude from the literature study and experimental results analysis that *Cassytha filiformis* is a traditional remedy for cancer, which is a major threat in the present world. The plant is also used to treat various human birthing issues, gonorrhoea, kidney ailments, African trypanosomiasis, acts as a diuretic and against many other diseases. They possess the pharmacological activities such as anti-oxidant, anti-trypanosomal, anti-platelet, vasorelaxant activities. Though, there are few disadvantages in the parasitic nature of the plant, the traditional uses of the plant listed in the above paper was marvelous. The alkaloids of the plant possess various application in the field of medicine but has to be explored further. The research work has to be carried out much in the above plant to extract the potential elements out of it. The plant is still used in their native places without knowing their actual mechanism of its effect. Hence, this review would be useful to the researchers and other clinical persons to understand its basic mechanism of action.

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