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Therapeutic efficacy of *Centella asiatica* (L.) and *Momordica charantia:* As traditional medicinal plant

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Abstract: India is called the botanical garden of the world for its rich natural resources. Over 6000 plants in India are in used in traditional, folklore and herbal medicine. The Indian system of medicine has identified 1500 medicinal plants of which 500 are commonly used. Plants have a long therapeutic history over thousands of years and still considered to be promising source of medicine in the traditional health care system. The efficacy and safety of herbal medicine have turned the major pharmaceutical population towards medicinal plant's research. In view of the widespread interest on using medicinal plants the present review on *Centella asiatica* and *Momordica charantia* is to provide information, in references to botanical, commercial, ethnopharmacological, phytochemical and pharmacological studies.

Keywords: Ethnopharmacological, Phytochemical, Pharmacological

1. Introduction

Plants are integral part of human civilization. Medicinal plants are also been relied upon by over 80% of the world population for their basic health care needs. Drugs based on the plants are of prime importance for several remedies in traditional and conventional medicine throughout the world and serves as a substitute for drug supply in modern medicine.

Medicinal plants with therapeutic properties are used for the treatment of many infectious diseases of humans as they contain many bioactive phytochemical constituents which are of curative effects. The medicinal properties of the plants are mainly due to the presence of secondary metabolites like alkaloids, cardiac glycosides, tannins, flavonoids, saponins, reducing compounds, minerals and vitamins[1]. Reactive oxygen species which create oxidative stress cause human diseases and disorders such as heart disease, inflammation, atherosclerosis, stroke, cancer, diabetes mellitus, malaria, HIV/ AIDS, etc.[2]. Antioxidants derived from plants contain the phenolics have many biological activities such as anti-inflammatory, anti-cancer and antimicrobial[3,4]. Plants also have the capability to safeguard the body from oxidative damage by scavenging the free radicals and inhibiting peroxidation and other radical mediated process[5]. Due to the profitable efficiency of medicinal plants on biological activities, there is a need for isolation of newer biological compounds from plants which can serve as novel drugs.

1.1. Centella Asiatica

Figure 1. *Centella asiatica*

Centella asiatica (L.) is a tropical medicinal plant from Apiaceae family native to Southeast Asian countries such as India, Sri Lanka, China, Indonesia, and Malaysia as well as South Africa and Madagascar [6]. *C. asiatica*, commonly known as "Gotu kola, Asiatic pennywort, Indian pennywort, Indian water navelwort, wild violet, and tiger herb" in English, is a tropical plant, cultivated successfully due to its

medical importance in some countries including Turkey, and it has a utilization in ayurvedic and Chinese traditional medicines since centuries[7]. The leaves, which are edible, are in yellowish-green color, thin, alternate with long petioles, and quite characteristic reniform, orbicular, or oblong-elliptic shapes with seven veins[8].

The plant grows horizontally through its green to red stolones which combine to each other and roots in underground. *C. asiatica*, wide range of biological activities desired for human health such as wound healing [9-11], anti-inflammatory [12,13], antipsoriatic [14], antiulcer [15, 16], hepatoprotective [17], anticonvulsant [18], sedative [19], immunostimulant [20], cardioprotective [21, 22], antidiabetic [23], cytotoxic and antitumor [24, 25], antiviral [26], antibacterial [27], insecticidal [28], antifungal [29], antioxidant [30–32], and for lepra [33] and venous deficiency treatments [34, 35].

Centella asiatica is one of the chief herbs for treating skin problems, to heal wounds, for revitalizing the nerves and brain cells, hence primarily known as a "Brain food" in India.

1.2. Phytochemical Content of Centella Asiatica

1.2.1. Triterpenoids

Include asiatcoside, centelloside, madecossoside, thankuniside, isothankunic acid, centellose, asiatic, centellic and madecassic acids [36,37] and brahmoside, brahminoside, brahmic acid, the structure of their genin, brahmic acid (m.p. 293°) has been established as 2,6-hydroxy, 23-hydroxy-methyl ursolic acid. Asiaticoside and madecossoside predominated in the leaves with less in roots [38].

1.2.2. Volatile and Fatty Acids

The fatty oil consists of glycerides of palmitic, stearic, lignoceric, oleic, linoleic and linolenic acids [39].

1.2.3. Alkaloids

An alkaloid, hydrocotylin (C22 H33 NO8) has been isolated from the dried plants [39].

1.2.4. Glycosides

Asiaticoside, madecossoside and centelloside have been isolated from the plant parts. On hydrolysis, these glycosides yield the triterpene acids, asiatic acid, madegascaric acid[40-42] and centellic acid.

1.2.5. Flavanoid

Flavanoids, 3-glucosylquercetin, 3- glucosylkaemferol and 7-glucosylkaemferol have been isolated from the leaves[41].The plant is reported to contain tannins, sugars, inorganic acids[43] and resin[39], amino-acids, viz. aspartic acid, glycine, glutamic acid, α-alanine and phenylalanine[44]. The total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium and potassium. The leaves are rich in vitamins such as vit.B, vit.C[45] and vit.G[46].

1.3. Pharmacological Uses of Centella Asiatica

1.3.1. Antioxidant Capacity

Antioxidant is used by aerobic organism to protect the cells from oxidative damage by oxidants during oxygen metabolism. The main antioxidant agents such as superoxidase dismutase (SOD), catalase, glutathione peroxidase (GSH-Px), glutathione, ascorbic acid and tocopherol are important to protect the cells due to their ability in eliminating free radicals such as reactive oxygen species (ROS)[47]. The consumption of *Centella* is useful for the antioxidant effect as it offer an effective and safe way of increasing body immune system against free radicals[48].

1.3.2. Neuroprotection Effect

Centella extract has been used in Ayurvedic medicine as a nerve tonic. The micronutrients in the extract is reported to be responsible in retarding brain aging and assist in renewal of neural tissue, hence it is effective in enhance memory and revitalize the brain as well as increase attention span and concentration[49]. In Ayurvedic medicine and traditional Chinese medicine, *Centella* has been used for centuries to control anxiety, helps in relaxation and mental calmness[50]. Studies in human and animal models have reported that *Centella* possesses anxiolytic activity potential.

1.3.3. Safety

Centella has been widely used in pharmaceutical industries and has shown good efficacy, performance and safety[51]. With a very low toxicity, the fresh *Centella* plants have been used in salads, vegetable and drink as juice[52]. It has been use for traditional Indian Ayurvedic and Chinese medicines for decades [53]

In Chinese medicine, *C. asiatica* is used for treatment of vomiting, epistaxis, urinary calculi, scabies and jaundice. In homeopathic medicine, it is used for treating ascariasis, elephantiasis and in granular cervicites. Clinical tests have formulated several benefits of *C. asiatica* extracts in terms of wound healing, burns and in skin diseases in gastrointestinal disorders and in treatment of leprosy, lupus, scleroderma, eczema, veins diseases and for treatment of psoriasis. It gives protection against diseases by enhancing immunity of the body.

1.3.4. Wound Healing

Madecassol, an extract of this plant containing madecassic acid, asiatic acid and Asiaticoside accelerates cicatrisation and grafting of wounds[54]. Asiaticoside promotes fibroblasts proliferation and extracellular matrix synthesis in wound healing [55].

1.3.5. Cytotoxic and Antitumour

Oral administration of the crude extract of *C. asiatica* and its partially purified fractions induced apoptosis in solid and Ehrlich Ascites tumour and increased the life span of these tumours bearing mice [56,57]. Asiatic acid was found to have anticancer effect on skin cancer [58].

1.3.6. Memory Enhancing

Aqueous extract of the herb showed significant effects on learning and memory and decreased the levels of norepinephrine, dopamine and 5-HT and their metabolites in the brain[59]. *Centella asiatica* contains brahmicacid,

isobrahmic acid, brahminoside and brahmoside. It has psychotropic, sedative and anticonvulsant properties. It is also useful in dementia, mental disorders and anxiety[60].

1.3.7. Cardioprotective

The alcoholic extract of the whole plant showed strong cardioprotective activity in limiting ischemia-reperfusion induced myocardial infraction in rats[61].

1.3.8. Radioprotective

Centella asiatica could be useful in preventing radiation induced behavioral changes during clinical radiotherapy[62].

1.3.9. Antidepressant

The total triterpenes had antidepressant activity and caused significant reduction of the corticosterone level in serum[63,64].

1.3.10. Immunomodulating

Pectin isolated from *C. asiatica* showed immunostimulating activities[65]and triterpenoid saponins[66] and methanol extracts showed preliminary immunomodulatory effect[67].

1.3.11. Antiprotozoal

Alcoholic extract of the entire plant showed antiprotozoal activity against *Entamoeba histolytica*[68].

1.3.12. Mental-Retardation

Centella asiatica tablets administered orally to mentally retarded children showed significant increase in general ability and behaviour patterns[69,70].

1.3.13. Antitubercular and Antileprotic

Asiaticosid is useful in the treatmen.t of leprosy[71] and certain types of tuberculosis[54]. Clinical trials conducted on normal adults showed that the drug increased the level of RBC, blood sugar, serum cholesterol and total protein. It has a calming effect on the body and supports the central nervous system.

1.3.14. Immunomodulatory

C. asiatica, contains triterpenoid, saponins in it possesses immunomodualtory activity[72,73].

1.3.15. Venous Insufficiency

The triterpenoid saponins present in *C. asiatica* strenghthen weakened veins by improving wall alterations in chronic venous hypertension and thereby protecting venous endothelium[74]. It also plays important role in stabilizing connective tissue growth by stimulating the production of hylauronidase and chondriotin sulfate and also imparts balancing effect on connective tissue[75]**.**

1.3.16. Autoimmune

Madecassol, component isolated from *C. asiatica* found to be efficacious in the treatment of chronic or subchronic systemic scleroderma and advanced focal scleroderma[76].

1.3.17. Anticancer

Preclinical studies have shown that methanolic extract of *C. asiatica* causes inhibition in breast cancer cells by inducing apoptosis in different cancer cell lines HeLa, HepG2 and SW48 and MCF-7.

1.3.18. Antidiabetic

Clinical studies have revealed that the two glycosides present in *Centella asiatica* (L.) viz. bhramoside and brahminoside exert sedative and hypoglyacemic effect[77] .

2. Momordica Charantia

The plant *Momordica charantia* Linn (family-Cucurbitaceae) is also known as bitter gourds, karela, bitter melon and balsam pear. These species include *M. angustisepala, M. balsamina* (Linn), *M. cochinchinensis* (Spreng), *M. cabrei, M. dioica* (Roxb), *M. elaterium, M. foetida, M. grosveroni, M. tuberosa or cymbalaria*[78]. It is a tropical vegetable common food in India. A monoecious climber or scrambling harbaceous vine found throughout India in the family curcubitaceae. Stem slender, more or less pubescent, leaves suborbicular, alternate, the blade with 5-7 deep palmate lobes and quite variable in their size[79]. Fruits are 5.0-25.0 c.m.long, ovoid, ellipsoid or spindle shaped usually ridged or warty, dehiscent irregularly as a 3 valved fleshy capsule or indehiscent. Flower monoecious, unisexual, tubular 5 lobed, moderate sized, pale yellow to orangish in colour. Male flower solitary and female flowers bracteate at the base with a fusiform and muricate ovary[80].

Figure 2. *Momordica charantia*

Seeds are brownish 13.0-16.0 mm long. The fruit of the plant posses tonic, stomachic, antibilious, stimulant, emetic, laxative, fruit pulp, leaf juice, and seed shows anthelmintic activity (in lumbrici)[81]. The fruits and leaves are useful in piles, jaundice, diabetes, leprosy, snake bite and it is found to have vermifuge and antioxidant property. Fruit is also useful in gout, rheumatism and sub acute cases of spleen and liver[82]. Popularity of *Momordica charantia* in various systems of traditional medicine for several ailments (antidiabetic, abortifacient, anthelmintic, contraceptive, eczema, emmenagogue, antimalarial, galactagogue, gout, jaundice, abdominal pain, kidney (stone), laxative, leprosy, leucorrhea, piles, pneumonia, psoriasis, purgative,

rheumatism, fever and scabies) focused the investigator's attention on this plant.

2.1. Phytochemical Content of Momordica Charantia

2.1.1. Terpenoids

The cucurbitane triterpenoids I, II and III isolated from leaves along with the momordicine I and II[83]. A series of cucurbitane type- triterpene glycosides called Goyaglycosides have been isolated along with momordicosides. The pyrimidine, arabinopyanosides, charine, vicine and others along with the triterpene momordicin, momordicinin reported. Charantin is cucurbitane type triterenoids in *M. charantia* and potential substances which have antidiabetic properties. Charantin is mix of two compound sitosteryl glucoside and stigmasteryl gluciside[84].

2.1.2. Proteins

α, β and γ momorcharins with N – glycosides activity and momordins a and b were identified alongwith ribosome − inactivating proteins and lectins[85].

2.1.3. Sterols and Fatty Acids

Mainly palmitic acid and oleic acid are major components with trace constitued such as steric acid, lauric acid, linoleic acid, arachidic acid, myristic acid and capric acids. β − sitosterol, compesterol ,daucosrerol and momordenol identified in seed oil as the sterol. The four mono methylsterols are also present known as obtusifoliol, cycloeucalenol, 4 – α methylzymosterol, lophenol and the desmethylsterols spinasterol[86].

2.1.4. Volatile Constituents

Voleris acid, aldehydes mainly pentanal, 2 hexenal, 2 heptenal and nonadienal. 2 butylfusan, menthol, nerolidol, pentadecanol , hexadecanal , mystenol , 3 hexanol are present as volatile constituent in *Momordica charantia* Linn. Fruit.[87]

2.2. Pharmacological Uses of Momordica Charantia

2.2.1. Antidiabetic Activity

Leung *et al.* (2009) elucidated the *M. charantia* is choice of fruit used for the complementary and alternative medicine[88]. Raman *et al.* (1996) studied that the oral administration of fresh Fruit juice (dose 6 c.c. /kg. body wt.) lowered the blood sugar level in normal and alloxan-diabetic Rabbits. Karela preparations have been shown to significantly improve glucose tolerance without increasing blood insulin levels and to improve fasting blood glucose levels. Blood and urine sugar levels and postprandial (after eating) blood glucose levels also fell[89].

2.2.2. Anti Cancer Activity

Semiz *et al.* (2007) elucidated the aqueous extract killed human leukaemia lymphocytes in dose-dependent manner. Bitter Melon and Bitter Melon Extracts inhibit cancer and tumor. An inhibitory action on both viral and host cell RNA and protein synthesis. Cytotoxic activity are a group of ribosome inactivating proteins named alpha- and beta-momorcharins, momordins, and cucurbitacin B[90].

2.2.3. Antiobesity Activity

Kumar *et al.* (2010) reported that the *Momordica charantia* increase the activity of adenosine 5 monophosphate kinase (AMPK), an enzyme that facilitates cellular glucose uptake and fatty acid oxidation. Compounds in bitter melon improve lipid profiles. They reduce liver secretion of apolipoprotein B (Apo B) – the primary lipoprotein of low-density "bad" cholesterol reduce apolipoprotein C- III expression, the protein found in very-low density cholesterol which turns into LDL/Bad Cholesterol and increases the expression of apolipoprotein A-1 (ApoA1) the major protein component of high density "good" cholesterol[91].

2.2.4. Anxiolytic Activity

Ganesan *et al.* (2008) studied that the oral Administration of 5 ml kg-1 of propylene glycol (vehicle control) Methanol extract of dried leaves of *Momordica charantia* Linn (Cucurbitaceae) was investigated for anxiolytic activities in animal models. Anxiolytic activity of methanol extract of dried leaves of *Momordica charantia* Linn was tested by elevated plus maze test[81].

2.2.5. Antidepressant Activity

Ganesan *et al.* (2008) elucidated the propylene glycol as vehicle control (5 ml kg-1); 100, 200 and 300 mg kg-1 of methanol extract of *M. charantia* Linn leaves were administered orally to the groups I to IV respectively and 5 mg kg-1 of imipramine (drug control) was administered intraperitonealy[81].

2.2.6. Anti Inflammatory Activity

Ganesan *et al.* (2008) reported further that the anti inflammatory activity was studied by Carrageenin-induced edema in rats and 60 % oedema inhibitions was observed with 300 mg/kg methanol extract of dried leaves of *Momordica charantia* Linn, which was nearly equivalent to that of 10 mg/kg of indomethacin[81].

2.2.7. Anti Viral Activity

Puri *et al.* (2009) studied that in vitro antiviral activity against numerous viruses including Epstein-Barr, herpes, and HIV viruses. An in vivo study a leaf extract have the ability to increase resistance to viral infections as well as to provide an immunostimulant effect in humans and animals (increasing interferon production and natural killer cell activity). MAP30 (Momordica Anti-HIV Protein), α- and β-momorcharins inhibit HIV replication in acutely and chronically infected cells and thus are considered potential therapeutic agent in HIV infection and AIDS[92].

2.2.8. Mosquito Larvicidal Activity

Singh *et al.* (2006) studied that the *Momordica charantia* was shown good larvicidal activity. The mosquito larvicidal property of *Momordica charantia* against three mosquito species— anopheles stephensi, Culex quinquefasciatus and Aedes aegypti (Diptera: Culicidae)[93].

2.2.9. Antifeedent and Antioviposition Activity

Lee *et al.* (2009) reported that the methanol extract of bitter melon leaves exhibited strong oviposition deterrent activity against *Liriomyza trifolii* females on the host plant leaf when it was dipped in the methanol extract at a concentration of 1 gm of fresh leaf equivalent/ml[94].

2.2.10. Anti-Genotoxic Activity

Paul *et al.* (2010) studied that the *Momordica charantia* decrease the genotoxic activity of methylnitrosamine, methanesulfonate and tetracycline, as shown by the decrease in chromosome breakage[95].

2.2.11. Wound Healing Activity

Sharma *et al.* (2009) reported that *Momordica charantia Linn*. fruit powder, in the form of an ointment (10% w/w dried powder in simple ointment base) showed a statically significant response ($P < 0.01$) in terms of wound contracting ability, wound closure time, period of epithelisation, tensile strength of the wound and regeneration of tissues at wound site[96].

2.2.12. Antioxidant Effect

M. charantia extracts possess potent antioxidant and free radical scavenging activities and this may be due to the presence of phenolic and flavonoid compounds like, galic acid, tannic acid, (+)-catechin, caffeic acid, p-coumaric, gentisic acid, chlorogenic acid and epicatechin[97,98].

2.2.13. Hepatoprotective Effect

The extract of *Momordica charantia* significantly reduces serum glutamic pyruvate ransaminase (SGPT), and serum glutamic oxaloacetate transaminase (SGOT) in rats. The hepatoprotective activity of *M. charantia* leaves may be attributed to the presence of flavonoids and ascorbic acid[99].

2.2.14. Antibacterial and Antifungal Activity

Clinically and experimentally, leaf extracts (Methanol, Ethanol and aqueous) of *M. charantia* have demonstrated a broad spectrum antimicrobial activity[100]. Meanwhile, essential oil of the seed of *M. charantia* showed antibacterial and antifungal activities may due to the presence of *trans*-nerolidol (61.6% of the total oil)[101].

2.2.15. Abortifacient and Antifertility Activity

The experimental documentation of abortifacient properties of *Momordica* proteins and momorcharins produced abortifacient activity in early and midterm pregnancy[102-104].

2.2.16. Anti-Ulcer Activity

The traditional use of *M. charantia* in the treatment of ulcers is supported by research, suggesting the dried-powdered fruits in filtered honey have significant and dose-dependent anti-ulcerogenic activity against ethanol-induced ulcerogenesis in rats. Matsuda *et al.,* demonstrated momordin Ic (10 mg/kg, b.wt. p.o.) potentially inhibited ethanol induced gastric mucosal lesions[105].

2.2.17. Immunomodulatory Activity

M. charantia extracts and its isolated constituents have a variable effect on the immune system. It has been shown to be immune stimulating in some studies and immunosuppressive in some conditions (allograpft rejection). α- and β-momorcharin showed immunosuppressive activity *via* lymphocytotoxicity or to a shift in the kinetic parameters of the immune response. However, its immunostimulant activity has been attributed to increase the interferon production and natural killer cell activity[106].

2.2.18. Hypotensive and Anti Prothrombin Activity

Wang and Ng observed mild hypotensive response with Momordin. *M. charantia* prolonged prothrombin time by inhibiting activation of factor X by factor VIIa-tissue factor complex or factor IXa[107].

2.2.19. Toxicity and Drug Interaction

The seed contains vicine and therefore can trigger symptoms of favism in susceptible individuals. In addition, the red arils of the seeds are reported to be toxic to children. Many *in vivo* clinical studies have demonstrated the relatively low toxicity of all parts of the *M. charantia* plant when ingested orally. Pregnant women should not eat bitter melon as it stimulates the uterus and may cause premature birth[108].

Table 1. *Photochemical estimation of Centella asiatica and Momordica charantia*

S.No.	Phytochemical	*Centella asiatica*	*Momordica charantia*
1	Alkaloids	+	+
2	Flavonoids	-	+
3	Tannins	-	+
4	Saponins	+	+
5	Terpenoids	+	+
6	Sterols	-	+
7	Antraquinones	-	+
8	Phenols	-	+
9	Quinones	-	-
10	Carbohydrates	+	+
11	Proteins	+	+
12	Glycosides	+	+
13	Reducing sugar	+	+
14	Steroids	+	-

3. Conclusion

In recent years, ethno-botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. The therapeutic potential of these plants in terms of its efficacy and versatility is such that further detailed research appears crucial. The elaboration of a wide variety of phytochemicals have significant pharmacological activity, and the large scale harvesting for other utilities render the plant of potential importance. Phytochemicals present in the plant indicates relevance to large scale harvesting, chemical modification, and utilization.

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