IJBPAS, November, 2021, 10(11): 3830-3842

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

TRADITIONAL MEDICINAL PLANT *MELOTHRIA PERPUSILLA* L. (*CUCURBITACEAE*): THEIR BOTANICAL, PHYTOCHEMICAL AND PHARMACOLOGICAL OVERVIEW

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Received 14th Jan. 2021; Revised 13th Feb. 2021; Accepted 13th March 2021; Available online 1st Nov. 2021

https://doi.org/10.31032/IJBPAS/2021/10.11.5696

ABSTRACT

Medicinal plants are used for treating different ailments and disorders in our daily life. The people in hilly and forest areas practice ancient medicine to protect their health and related problems primarily from their plant sources located within the surrounding environment. For treatment purposes, different modes of extraction from plant parts is considered due to the presence of secondary metabolites. Further considering the importance of medicinal plantsused by local peoples, *Melothria perpusilla* (*Cucurbitaceae*) is one plant used in traditional medicine due to their applications towards various ailments. The phytochemical compounds present in the plant is known to contribute to the growth and development of newer drugs in clinical research with greater efficiency and minimal side effects. On the basis of different pharmacological activities and huge therapeutic potential this plant provides the base for its selection. Finally, this review documents current knowledge on various phytoconstituents and pharmacological activities of *Melothria perpusilla* L and targets to contribute to arouse interest in the scientific communal of this promising plant.

Keywords: Ailments, Extraction, *Melothria perpusilla*, Phytoconstituents and Pharmacological

INTRODUCTION

The medicinal value of the drug plants are due to the presence of certain phytochemical constituents namely, alkaloids, resins, gums, glucosides, tannins,

essential and fatty oils, etc **[1]**. According to WHO (World Health Organization), 80% of the world's population primarily those of developing countries rely on plant derived medicines for their health and improvement **[2]**. Moreover, increasing demand of plants and exploitation by humans has become a great menace in their native habitat. The herbal medicine has been a step of universal developments in knowledge, innovations and current practices **[3]**. In India, medicinal plants listed in various indigenous systems such as Siddha (1121), Ayurveda (2000), Unani (751), Amchi (600), Allopathy (30) and Tibetan (337) plant species for different ailments and disorders **[4, 5]**. However, continuous supply of source material often become difficult due to labour cost, cultural practices, environmental changes, diverse geographical distribution, selection of plant and over exploitation by pharmaceutical industry **[6]**. Various technologies have been adopted for increasing the bioactive molecules of the plant **[7]**. The advantage of these technologies leads to high volume production of pharmaceuticals, neutraceuticals and other beneficial substances in today's world. Though a very good number of research works on traditional medicinal plants have been reported extensively, certain pharmaceutical drugs from plants need to be still authenticated for human benefits. Especially, in India scientific interest in traditional medicine has continuously been increasing till date. The local healers claim to offer drugs for diseases like cancer, asthma, hypertension, tuberculosis, rheumatism, leprosy, jaundice, etc have been clinically examined by number of researches in pilot trials **[8]**.

Cucurbitaceae, commonly called as cucurbits or gourds, a family of 95 genera in 15 tribes comprising 940 to 980 species which are essentially distributed in the tropical and subtropical areas of the globe, with hotspots of diversity in Southeast Asia, West Africa, Madagascar and Mexico **[9]**. In the economically significant plant family *Cucurbitaceae*, many difficulties have led to the geography of the closest relatives of water melon (*Citrullus lanatus*), cucumber (*Cucumis sativus*), loofah (*Luffa acutangula*), bitter gourd (*Momordica charantia*), chayote (*Sechium edule*), ivy gourd (*Coccinia grandis*), snake gourd (*Trichosanthes cucumerina*) and creeping cucumber (*Melothria pendula*) that remain ambiguous **[10]**. The secondary metabolite compound belonging to the class of Cucurbitacins, the most characteristic chemical of the group are bitter triterpenes that are toxic to organism but at the same time can also attract some specific herbivorous insects **[11, 12]**. Thoenissen *et al*. (2009) and Lee *et al*. (2010) reported that Cucurbitacins can be effective in slowing or stopping division of cells and

are therefore the subject of much research for applications in medicine, especially in cancer treatment **[13, 14]**. In Manipur, India the traditional medicine practitioners use specific plants for treatment of different disorders in the form of fresh preparation, decoction and powder of the whole or parts of the plant **[15]**.

The genus *Melothria* L. includes 12-15 species, confined to arid plains, clear and forest margins, grass- or woodlands from the southern part of United States through Central and South America down to northern Argentina **[9, 16]**. One species, *Melothria sphaerocarpa* L., is found in West Africa **[17]** and another species *Melothria pendula* L., is locally invasive to Asia **[18]**. These species are monoecious, small to medium sized, herbaceous climbers with simple leaves, small yellow or white flowers, a smooth fruit and often fleshy berry to 20 cm in *M. sphaerocarpa* **[19]**. Apart from the above mentioned species, some other species belonging to the genus *Melothria* are, *M. domingensis*, *M. perpusilla, M. scabra, M. charantia* and *M. heterophylla* etc. *Melothria mannii* is a minor crop cultivated due to it's nutritious seeds as so called 'egusi crop' (for making stews) in both west Africa and Central and South America **[20]**. It's essential to have a proper documentation of such plants to know the potential and values of medicinal plants for the progress of health and hygiene through eco-friendly system **[21]**. Attempts are in progress to prepare different remedies from all over the globe against various ailments as treatment in the form of drugs.

Melothria perpusilla L. belongs to *Cucurbitaceae* family andis a non-aromatic plant **[22]** and is most commonly found in the north eastern part of India and Nilgiri hills of Tamil Nadu **[23]**. Phytochemical compounds of an underexplored plant, *M. perpusilla* indicated the presence of flavonoids, cardiac glycosides, triterpenes, steroids and tannins from the extracts **[24]**. It is an attempt to appraise the valuable knowledge on the reports of *M. perpusilla* and its associated compounds but whereas this review summons the traditional uses, chemical compounds and their therapeutic activities of the plant.

***MELOTHRIA PERPUSILLA* L**

Melothria perpusilla L **(Figure 1)** is found in the wild habitat, usually at the grazing grounds and on the road sides **[25]**. It's popularly known as 'Lamthabi' in Manipuri and 'Bankundri' in Hindi and has been used in traditional medicine from ages **[26]**.

TAXONOMICAL CLASSIFICATION

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Eudicots

Order: Cucurbitales

Family: Cucurbitaceae

Genus: Melothria

Species: *M. perpusilla*

Figure 1: ***Melothria perpusilla*** **L– Plant**

MORPHOLOGY

M. perpusilla L. is a slender, hispid which has deeply striated, glabrous stem with cordate leaves. The fruits are globose and finely reticulate. The roots are oblong flattened and tuberous **[22]**. The plant is a monoecious, perennial climber with tendrils. Leaves are heart shaped and lobed with distant spiny teeth on the margin of the leaves. Colour of the flowers are yellow and look small. The fruits look similar to that of miniature watermelons and taste like cucumber **[15]**.

TRADITIONAL USES

The vegetative part of the plant are boiled with sugar candy in water and used for treatment of jaundice **[27]**. Singh *et al*. (2017 a) reported that local population of Manipur have used this plant against kidney diseases. The roots of *M. perpusilla* have curative action in fever and diarrhea **[22]**. Fruits possess anti-helmentic property and demulcent action **[28]**. The decoction of the whole plant mixed with mishri (rock sugar) is administered orally for jaundice **[29]**. Leaf shoot is boiled in water with equal proportion of *Mimosa pudica* and mixed with molasses for extract preparation **[25]**. Shailendra *et al*. (2017) reported that ethyl acetate extract significantly reduced blood glucose level. It's used in the treatment of hyperglycemia, probably inhibiting gluconeogenesis **[30]**.

CHEMICAL COMPOUNDS

Singh *et al*. (2017 a) reported that sterols and flavonol glycosides have been isolated from the chloroform extract **[22]**. Phytochemical investigation of *M. perpusilla* extracts revealed the presence of tannins, flavonoids and steroids that play a role in ameliorating hepatic damage by anti-oxidant mechanisms **[15]**. Singh and Singh (2012) reported that two sterols egosta-7, 22-dien-3b, 5a, 6b-triol and 3-0-b-Dglucopyranosyl-ergosta-7, 22-dien-5a, 6b-diol **[31]**. The active secondary metabolites isolated from *M. perpusilla* plant used for the treatment of jaundice in Manipur are sterols and glycosides **[32]**.

Basumatary and Narzary (2017) reported that methanolic extract of *M. perpusilla* plant revealed the presence of alkaloids, saponins, cardiac glycosides, steroids, anthraquinones, coumarins, phenols, tannins, flavonoids, anthocyanin, carbohydrates and lignin **[33]**.

CUCURBITACINS

The cucurbitacins **(Figure 2a)** are a group of bitter taste, highly oxygenated mainly tetracyclic, triterpenic plant substance derived from cucurbitane skeleton [19-(10→9β)-abeo-10α-lanost-5-en]. They are considered as non-steroidal since the methyl group from carbon 10 has moved to carbon 9 **[34]**. Cucurbitacin consists of tetracyclic cucurbitane nucleus skeleton with a variety of oxygenation functionalities at different positions with diverse chemical categories **[35]**. They are present as non-glycosylated or glycosylated triterpenoids and divided into 12 types, incorporating cucurbitacins A-T **[36]**. In specific, cucurbitacin E **(Figure 2b)** are the most widely distributed chemical constituents and possess anti-inflammatory **[37]**, anti-angiogenic, cytotoxic, immunomodulatory **[38]**, cytostatic and hepatoprotective activities **[39]**.

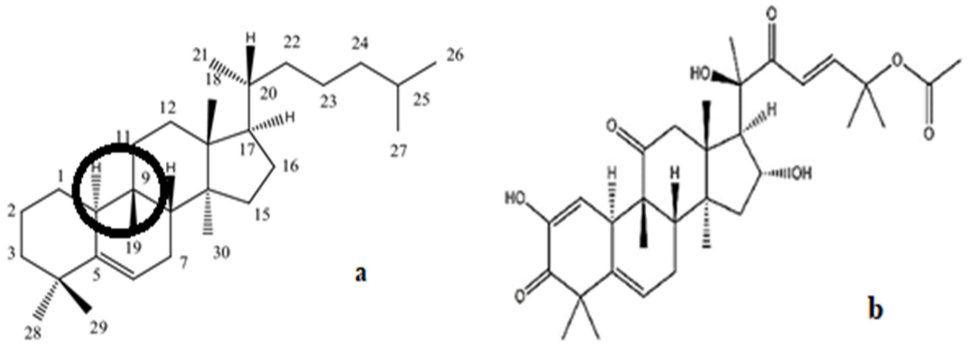

Figure 2: a) Basic skeleton structure of cucurbitacins; b) General structure of cucurbitacin E

CUCURBITACINS FOUND IN VARIOUS PLANTS

Many researchers have paid attention towards the *cucurbitaceae* family due to the presence of compounds in fruits, seeds and vegetables used in various ayurvedic preparations **[40]**. The cucurbitacins are also found in other families of the plant kingdom. They are usually found in the plant as β-glucosides **[34]**. Pandey (1969) reported that plants belonging to *cucurbitaceae* family are *Trichosanthes, Lagenaria, Luffa, Benincasa, Cucumis, Citrullus, Momordica, cucurbita, Bryonopsis and Corallocarpus* **[41]**. They are of great interest because of the wide range of biological activities.

A number of compounds of this group have been investigated for their cytotoxic, hepatoprotective, anti-inflammatory and cardiovascular effects **[34]**. Some of the previous research works have proved that cucurbitacins showed anti-inflammatory activity by the inhibition of cyclooxygenase (COX) enzymes **[42, 43]**. A lot of plants contain different forms of cucurbitacin compounds as found in **Table 1**. The list of plants is as follows:

Table 1: List of plants containing cucurbitacins

S. No	Plant species	Family	Compounds	References
1.	*Ecballium elaterium*	*Cucurbitaceae*	elaterin (cucurbitacin E)	[34]
2.	*Helicteres isora*	*Malvaceae*	cucurbitacin B and iso-cucurbitacin B	[44]
3.	*Ipomopsis aggregata*	*Polemoniaceae*	cucurbitacin B	[45]
4.	*Anagallis arvensis*	*Primulaceae*	cucurbitacin B, D, E, I, L and R	[46]
5.	*Gurania subumbellata*	*Cucurbitaceae*	cucurbitacin B, D and F	[47]
6.	*Picrorhiza kurrooa*	*Plantaginaceae*	cucurbitacin Q	[48]
7.	*Datisca glomerata*	*Datiscaceae*	cucurbitacin D and F	[49, 50]
8.	*Desfontainia spinosa*	*Columelliaceae*	cucurbitacin	[51]
9.	*Bryonia dioica*	*Cucurbitaceae*	cucurbitacin S	[52]
10.	*Wilbrandia species*	*Cucurbitaceae*	cucurbitacin P and Q	[53]
11.	*Elaeocarpus dolichostylus*	*Elaeocarpaceae*	cucurbitacin F	[54]
12.	*Crinodendron hookerianum*	*Elaeocarpaceae*	cucurbitacin F	[55]
13.	*Citrullus colocynthis*	*Cucurbitaceae*	cucurbitacin I, E and L	[56]

PHARMACOLOGICAL ACTIVITIES

Different studies were conducted to explore the therapeutic activities of *M. perpusilla* plant which revealed to be anti-helmentic, anti-diabetic and possesses other medicinal properties. A significant opportunity exists to identify new, natural plant derived compounds for the treatment of diseases or ailments. Further, studies are recommended for isolation of active constituents of the plant and define it's mechanism.

ANTI-DIABETIC PROPERTY

Ethyl acetate (EA) extract of *Melothria perpusilla* revealed 250 mg/kg and 500 mg/kg caused significant reduction in the blood glucose level ($p<0.05$) when compared to control and standard compound glibenclamide (standard) compound. Glibenclamide (0.5 mg/kg p.o) too caused significant reduction than the control ($p<0.05$) level **[22]**. Singh *et al*. (2017b) reported that EAEMP on dexamethasone induced hyperglycemia were studied in albino rat models **[23]**. Blood glucose level in the overnight fasted albino rats of different groups were 71.00±0.58 (control), 70.83±1.40 (test I 250 mg/kg), 69.50±0.89 (test II 500 mg/kg) and 68.17±3.06 (glibenclamide) respectively **[23]**.

HEPATOPROTECTIVE PROPERTY

There was significant increase ($p<0.001$) in the effect of hepatic enzymes (ALT, AST and ALP) in the CCl_4 treated group II when compared to normal or untreated group I. Standard drug, silymarin (100 mg/kg) and aqueous extract (AE) of *Melothia perpusilla* (200 mg/kg and 400 mg/kg) co-treatment groups (III to V) the hepatic enzymes were significantly reduced ($p<0.001$) when compared with CCl_4 alone treated group II. However, AEMP at the dose of 400 mg/kg was more effective ($p<0.001$) to bring down AST and ALT levels when compared with 200 mg/kg dosage **[15]**.

ANTIOXIDANT ACTIVITY

DPPH free radical scavenging activity of methanolic extract of *M. perpusilla* revealed screening of antioxidant activity

of plant extract using different concentrations 2, 5, 10, 50, 100, 200, 500 µg/mL. The results showed that *M. perpusilla* (97.54±0.15%) had the highest DPPH activity with an IC_{50} value of 134.96±0.35 µg/mL while the standard ascorbic acid showed 98.84±0.10% inhibition with an IC_{50} value of 25.01±0.52 µg/mL. Methanol extract of the plant exhibited good antioxidant properties with the strongest activity **[33]**. ABTS radical scavenging activity of methanolic extract of *M perpusilla* (90.29±0.23%) with IC50 value of 115.99±0.12 µg/mL. Ferric reducing antioxidant power (FRAP) scavenging activity revealed high antioxidant activity of *M perpusilla* that ranged from 38.57±7.14 to 855.23±10.91 µM TE/g DE **[33]**.

***IN VITRO* STUDIES**

In vitro regeneration from shoot and meristem of *Melothria perpusilla* L plant has been reported through tissue culture **[6]**. The explants were inoculated in MS medium with different concentrations of PGRs. Different colors of callus (light green, white with green spots and green) were observed in MS with BAP, kinetin and IBA. The best callus formation was observed with combination of 1 mg/L BAP + 1 mg/L IBA and 1 mg/L IBA + 1 mg/L kinetin within 1-3 weeks **[6]**. Till now there are no reports on callus induction and *in vitro* studies of *M. perpusilla* plant.

A lot of research is still needed to explore the compounds from this plant. High volume production of phytocompounds can be produced from *M. perpusilla* using different biotechnological applications. For this reason, different elicitors or precursors can be applied to cell cultures and their effects on the accumulation of phytochemicals were studied and can be attempted. In elicitation studies, the differences in cell cultures may cause different response to precursors and the synthesis of specific compounds in different amounts can be estimated.

FUTURE SCOPE AND RESEARCH

The most active constituents of the plant are present in the aerial parts like shoot and leaves. The review study depicts the importance of the whole plant which is used for various ailments. Preliminary phytochemical analysis of the plant extracts are performed and can be quantitatively estimated to find the unknown concentrations of the extract. Biosynthetic pathway of specific active chemical compounds are elucidated and large scale production of the compound can be planned. *In vitro* tissue culture provides the base for endemic plants through micro propagation technique.

Due to the chemical composition, the plant emerges as a useful resource for production of important pharmaceuticals.

This research is one of the promising field for the future development of drugs and production at industrial scale. Further research about the mechanism and interaction of drug molecules are essential in order to develop effective therapeutic protocols. In addition, research on different pharmacological activities through *in vivo* rat models can be demonstrated.

CONCLUSION

From the above study, the importance of *Melothria perpusilla* plant has been discussed and the chemical constituents present in them shows the potential therapeutic activities. This plant continues to play a key role in contribution to rural people livelihood. Many research efforts are underway and concentrated towards the beneficial effects on humans. Numerous studies have investigated the phytochemical compounds and different pharmacological activities. Cucurbitacins are the compounds of specific interest which can be produced in laboratory scale that can be formed into a drug that can be active against treatment of cancer in near future. These compounds from the plant are extracted from *in vitro* and quantitatively estimated. During the review, it has been found that little information regarding *in vitro* studies, are available. So, attempts can be made more and more to work on *M. perpusilla* plant. Finally, it can be concluded that this review might provide an additional incentive for the evaluation of traditional knowledge of this plant towards the people from across the globe and will be useful in the protection of patent rights too.

LIST OF SYMBOLS AND ABBREVIATIONS

ALT: Alanine Aminotransferase

AST: Aspartate Aminotransferase

ALP: Alkaline Phosphatase

MS: Murashige and Skoog

IBA: Indole Butyric Acid

BAP: Benzyl Amino Purine

ACKNOWLEDGEMENT

The author would like to thank the students of Department of Biotechnology, Muthayammal Engineering College, Rasipuram, Namakkal which could benefit the people and the community for solving the problems through current research.

CONFLICTS OF INTEREST

No conflicts of interest

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