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PHYTOCHEMICAL ANALYSIS AND PHARMACOLOGICAL STUDIES OF MOMORDICA CYMBALARIA (ATHALAKKAI): A SYSTEMATIC REVIEW

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ABSTRACT

This systematic review offers a thorough analysis of the phytochemical profile and various pharmacological evaluations of *Momordica cymbalaria*, a nutritionally rich but underutilized medicinal plant of the Cucurbitaceae family that is native to tropical India and Southeast Asia. Phytochemical investigations, mostly using gas chromatography-mass spectrometry (GC-MS), have identified 75 bioactive compounds across the leaves, roots, and callus, including triterpenoids and flavonoids. Pharmacological research demonstrates the plant's strong antidiabetic, antihyperlipidemic, and cardioprotective properties, highlighting its considerable therapeutic adaptability. Additionally, it has exceptional hepatoprotective, neuroprotective, and nephroprotective properties, especially when it comes to reducing oxidative stress and chemically induced toxicity. Additionally, studies highlight its promise in wound healing, anti-inflammatory responses through the NF-κB pathway, anti-cancer therapy (particularly against breast cancer), and the treatment of depression and anaemia. Interestingly, the plant has been shown to have abortifacient and anti-fertility qualities. Due to poor seed viability and habitat degradation, *M. cymbalaria* is in danger of going extinct despite its enormous therapeutic usefulness. This study highlights its function as a sustained "unconventional gem" for contemporary drug discovery and compiles recent data supporting its traditional use. However, to fully realize its medicinal potential and guarantee its ecological existence, more clinical research and immediate conservation initiatives are required.

KEYWORDS: *Momordica cymbalaria*, Phytochemical analysis, Pharmacological studies.

INTRODUCTION

The underappreciated vegetable *Momordica cymbalaria*, sometimes called Athalakkai or Karchikai, is a member of the Cucurbitaceae family and is indigenous to tropical parts of Southeast Asia and India. This climbing herb stands out for its nutritional profile, which is exceptionally high in potassium (500 mg/100g) and vitamin C (290 mg/100g), as well as its pyriform-shaped fruits with eight sharp ridges. In addition to its culinary use, it has long been a mainstay of traditional medicine, used to treat ailments like diarrhoea, rheumatism, and skin disorders. Its strong hypoglycemic and hypolipidemic properties are highlighted by contemporary pharmacological research, which makes it a promising natural option for the treatment of diabetes mellitus and cardiovascular health. Diverse pharmacological activities of *M. cymbalaria*, including analgesic, anti-inflammatory, antioxidant, hepatoprotective, nephroprotective, antidiabetic, cardioprotective, antidepressant, anticonvulsant, anticancer, antiangiogenic, antifertility, antiulcer, antimicrobial, antidiarrheal, and anthelmintic effects, have been reported by many investigators, and its methanolic extract is safe up to 2,000 mg/kg with no symptoms of toxicity observed.[1]

The plant also has strong nephroprotective and hepatoprotective qualities, which help the kidneys and

liver fight off different kinds of stress. Its significant antioxidant activity and possible anti-cancer properties are attributed to its abundance of bioactive components, such as cucurbitane triterpenoids, flavonoids, and phenolic acids. Additionally, *M. cymbalaria* is used for its ability to heal wounds and in conventional therapies for ulcers and infertility. The plant is in danger of going extinct because of habitat destruction and low seed viability, despite its enormous therapeutic potential and adaptability to different climates. To use this "unconventional gem" as a sustainable substitute for manufactured medications for modern health issues, more research and conservation initiatives are desperately needed.[2]

PLANT PROFILE

Taxonomic classification

- Kingdom: Plantae
- Super division: Spermatophyta- Seed plants
- Division: Magnoliophyta- Flowering plants
- Class: Magnoliopsida - Dicotyledons
- Order: Cucurbitales
- Family: Cucurbitaceae - Cucumber family
- Subfamily: Cucurbitoideae
- Tribe: Jolifficae
- Subtribe: Thladianthinae
- Genus: Momordica
- Species: Cymbalaria Hook. F.

Morphology of M. *M. cymbalaria*

- **Habit:** Climbing annual/perennial herb.
- **Stem:** Slender, scandent, branched, striate.
- **Root:** Woody, with perennial tubers.
- **Leaf:** Orbicular-reniform, deeply cordate base, 5–7 obtuse lobes.
- **Male flower:** Peduncle 5–30 mm, filiform, puberulous, ebracteate; 2–5 flowers/raceme; pale yellow corolla; 2 stamens.
- **Female flower:** Solitary; peduncle 28 mm.
- **Fruit:** 20–25 mm long (~24×15 mm), pyriform, 8 sharp ridges, attenuated apex, curved fleshy dark-green ribbed peduncle.
- **Seed:** 4.6 mm, ovoid, smooth, shiny.[3]

PHYTOCHEMICAL ANALYSIS

Momordica cymbalaria, a plant of the Cucurbitaceae family indigenous to South Tamil Nadu, has been used in traditional medicine for a long time. Recently scientists were working to identify the variety of compounds present in the whole plant by using advanced analytical methods such as GC-MS (gas chromatography-mass spectroscopy). The plant's pharmacological action is based on the secondary metabolites; here, GC-MS plays an important role by analyzing and isolating the small amount of phytoconstituents present in the plant. In the analysis of the plant, the following secondary metabolites have been identified:

The scale of the findings is striking across the three tissue types; the researchers identified seventy-five distinct bioactive compounds in total.

Table 1: Identified 75 distinct bioactive compounds.

Tissue Source	No. of Compounds	Dominant/Notable Compounds
Leaf	37	n-Hexadecanoic acid, Vitamin E, Cholesterol, Stigmasterol, β-sitosterol, Lupeol, Octacosanoic acid methyl ester
Leaf callus	20	5-(7a-Isopropenyl...) pent-2-enal, Spirost-8-en-11-one derivatives, Propanoic acid androstene ester, Diethyl phthalate
Root	18	Diethyl phthalate, stigmasterol (15.1%), d-mannose, n-hexadecanoic acid, β-sitosterol

Table 2: Key Bioactive Compounds and Reported Activities.

Compound	Found In	Reported Biological Activity
n-Hexadecanoic acid	Leaf, root, callus	Anti-inflammatory, antioxidant, pesticide, nematicide
Vitamin E	Leaf	Antiaging, antitumor, antidiabetic, anticancer, anti-inflammatory
Cholesterol / Cholestanol	Leaf	Cell-membrane constituent; antitumor, antioxidant
Stigmasterol	Leaf, root, callus	Antiviral, cancer-preventive, anti-inflammatory, anti-osteoarthritic
β-Sitosterol	Leaf, root	Anticancer, antimicrobial, antidiabetic, antifertility, antioxidant
Lupeol	Leaf	Antitumor, antioxidant, chemopreventive, antiarthritic, anti-inflammatory
Diethyl phthalate	Root, callus	Anti-carcinogenic; used in skin treatments and cosmetics
d-Mannose	Root	Urinary tract infection prevention
Ethyl iso-allocholate	Leaf, root, callus	Antimicrobial
Spirost-8-en-11-one derivatives	Leaf, root, callus	Anti-inflammatory, estrogenic, and progesterogenic. (4)

PHARMACOLOGICAL STUDIES

1. HEPATOPROTECTIVE ACTION

Momordica cymbalaria has a strong hepatoprotective property because it plays an important role in reducing the harm caused by sodium fluoride (NaF). When we are exposed to sodium fluoride, it causes hepatotoxicity by increasing the production of free radicals, which results in lipid peroxidation and then weakens the antioxidant defense mechanism of the liver. Experiments were conducted with Wistar male albino rats; the poisoning of NaF results in high levels of bilirubin and blood liver indicators such as alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). By using hydroalcoholic extract of *Momordica cymbalaria* (HAEMC), these blood indicators are successfully returned to normal levels and cause a dose-dependent increase in protein and albumin levels. This extract showed potent antioxidant properties by lowering lipid peroxidation and restoring reduced glutathione (GSH) and catalase levels.

By histopathological investigation, these results are validated, which demonstrated that the extract lessened fluoride-induced cellular degeneration, edema, and liver necrosis. Flavonoids and phenolic compounds, bioactive secondary metabolites, provide protective effects by stabilizing hepatic cell membranes and scavenging free radicals. *Momordica cymbalaria* is therefore regarded as a possible natural medication choice for the treatment of oxidative stress and liver damage brought on by fluoride.[5]

2. ANTI-HYPERLIPIDEMIC ACTIVITY

In streptozotocin-induced diabetic mice, studies on Mcy protein, which is a new anti-hyperlipidemic protein extracted from *Momordica cymbalaria,* were conducted. It reveals the strong antihyperlipidemic action. The risk of atherosclerosis and coronary artery disease is highly raised in the condition of diabetes, which further causes secondary problems such as hyperlipidemia. It is defined as high levels of serum triglycerides, total cholesterol, LDL cholesterol, and VLDL cholesterol. These triglycerides, total cholesterol, LDL cholesterol, and VLDL cholesterol are significantly decreased after 30 days of treatment with Mcy protein at a dose of 2.5 mg/kg body weight. HDL cholesterol, also known as “good cholesterol," is increased during this treatment.

The atherogenic index, which is an important indicator for determining cardiovascular risk, returned to normal because of these modifications. This mechanism of action is related to glycemic control and protein’s capacity to promote insulin secretion and pancreatic β-cell regeneration. In addition to this, the Mcy protein is successfully used as a common medication, glibenclamide, in restoring normal lipid profiles in kidney, liver, and skeletal muscle.

Treatment with *M. cymbalaria* fruit powder for 15 days in alloxan-induced diabetic rats produced a significant reduction in fasting blood glucose, serum cholesterol, and triglycerides, along with a significant improvement in hepatic glycogen levels close to normal, without any hypoglycemic effect in non-diabetic control animals. As a result, it shows that it provides natural treatment for diabetes-related dyslipidemia with negligible harm to the essential organs.[6]

3. NEUROPROTECTIVE ACTIVITY

The neuroprotective effect of a terpenoid saponin isolated from *Momordica cymbalaria* Fenzl in diabetic peripheral neuropathy assesses the neuroprotective potential of steroidal saponin (SMC). In this study the rats were divided into test and control groups by giving 45 mg/kg STZ to cause diabetes. Insulin (4 U/kg subcutaneously) and SMC (100 mg/kg orally) were given, and outcomes are noted. Another study was conducted, such as the tail flick and hot plate technique. By this technique, neuropathic pain was evaluated by inspecting the sciatic nerves and dorsal root ganglia (DRG). And oxidative stress was evaluated by measuring the activity of antioxidant enzymes, including lipid peroxidation, catalase, and superoxide dismutase (SOD). When comparing to diabetic controls, the results show that SMC increased hot plate response times, decreased tail flick latency, and increased pain sensitivity. In the groups that had SMC treatment, the blood glucose, cholesterol, triglycerides, and glycated hemoglobin (HbA1C) are normalized.

As a result, the histopathological studies show that SMC therapy increased myelination, decreased axon degeneration, and improved neuronal morphology in the sciatic and DRG nerves.[7]

4. CARDIOPROTECTIVE ACTIVITY

The cardioprotective activity of *Momordica cymbalaria* can protect the heart against injury induced by isoproterenol. The study shows that the extract of *Momordica cymbalaria* prevents the increase of cardiac marker enzymes, such as creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH), and serum glutamate oxaloacetate transaminase (SGOT), which are released into blood during myocardial damage. This extract of *Momordica cymbalaria* works by maintaining the structural integrity of the myocardium. And it prevents the depletion of antioxidants in the tissues of the heart. Histopathological studies proved that the extract of *Momordica cymbalaria* reduces muscle fiber necrosis, edema, and inflammatory cell infiltration in the heart. This plant extract also helps in hypolipidemic activity by lowering the “bad” LDL cholesterol and prevents the formation of atherosclerotic plaques in the coronary arteries.[8]

5. ANTI-ULCER ACTIVITY

The aqueous extract of *Momordica cymbalaria* fruit can prevent ulcers in Wistar rats caused by ethanol. Gastric ulcers are mainly caused by the imbalance between the protective factors like mucus and antioxidants and

aggressive factors like acid and pepsin. A dose of 500 mg/kg was found to be safe and effective by the research study acute oral toxicity study carried out in accordance with OECD criteria. By comparing the control group and treated group, it shows that pre-treatment with aqueous group generally decreased the stomach lesions. This extract shows a protective effect by preserving the level of non-protein sulfhydryl's (NP-SH) and by boosting gastric wall mucus, which is essential for protecting the stomach from chemical damage. It also causes reduction in both the volume of stomach content and overall acidity, indicating an inhibitory effect on aggressive gastric secretions. These results were corroborated by histopathological analyses, which show that the extract avoided the serious congestion, edema, and cellular damage caused by ethanol. The phytochemicals flavonoids and polyphenols have antioxidant properties that act against free radicals responsible for anti-ulcer effects. *Momordica cymbalaria* is used as a treatment for peptic ulcer illness, which is validated by the study's conclusion that it has strong antiulcer activity.[9]

6. HYPERGLYCEMIC ACTIVITY

The result of this study is that fruit extraction of *Momordica cymbalaria* gives the effect on diabetic rats to reduce the blood glucose level using chemicals-induced diabetes. But it has no activity/effect on the blood glucose level in animals without diabetes. The alloxan was used to induce in male Wistar rat for the effect if higher glucose level. And then the researchers gave the various doses of *Momordica cymbalaria* of meso-to-micro fractions like aqueous, ethanolic, and hexane orally. After the dose, then monitored the rat's fasting blood glucose level for up to 7 hours. In diabetic mice, the aqueous fraction of dose at 0.5 g/kg gives action to decrease blood glucose level (-4.58% in 3 hours), but it has no effect on control animals. The anti-hyperglycemic principle is a polar constituent (primarily) in *Momordica cymbalaria*, and this is evidenced by the ethanolic extract. It shows the moderate reductions of blood glucose level in fasting (-23.2%) at a dose of 0.5 g/kg. And the hexane extracts are minimal in overall reductions in fasting blood glucose levels. The aqueous extract produces a higher maximal reduction in glycemia and a quicker commencement of action when compared to the conventional oral hypoglycemic medication glibenclamide (0.2 g/kg). By considering these results, *Momordica cymbalaria* appears to have a great deal of promise as a diabetes treatment.[10]

7. ANTIFERTILITY / ANTI-OVULATORY ACTIVITY

The article explains that *Momordica cymbalaria* is a medicinal plant that may affect female fertility. In the study, researchers tested the root extract on rats and found that it disturbed the normal reproductive cycle, slowed down the growth of eggs in the ovaries, and reduced ovulation. The treated rats also showed changes in the ovaries under the microscope, which showed that the plant was affecting the reproductive organs in a real and visible way. When the extract was given to pregnant rats, the higher dose caused abortion, while the lower dose reduced the number of healthy babies. This means the plant has strong anti-fertility and abortifacient properties. The study is important because it gives scientific support to the traditional use of the plant, but it also shows that such herbal medicines must be used carefully because they can have powerful effects on the body.[11]

8. WOUND HEALING

Scientists investigated how *Momordica cymbalaria*, especially the extract from its tubers, could help heal wounds in diabetic patients. They found that a hexane extract of the tubers had strong antioxidant properties, effectively neutralizing free radicals. When this extract was tested on human skin cells using a scratch test (which mimics a wound), it helped the cells move and close the gap much faster than untreated cells, with the 50 µg/ml dose performing almost as well as EGF, a growth factor commonly used to promote healing. Safety tests on brine shrimp and zebrafish embryos showed that the extract was non-toxic at lower doses. Using these results, the team created an herbal transdermal patch containing the tuber extract along with pectin and other natural ingredients. The patch turned out to be flexible, smooth, and stable, pointing to its potential as a low-cost, eco-friendly option for treating diabetic wounds.[12]

9. ANTI-ANEMIC

Studies have also explored the anti-anemic potential of *Momordica cymbalaria*, particularly through its methanolic fruit extract tested in rats with phenylhydrazine-induced anemia. In this model, phenylhydrazine caused a sharp drop in red blood cell count, hemoglobin levels, hematocrit, and mean corpuscular volume, while also raising reticulocyte counts and reducing blood iron levels—classic signs of hemolytic anemia. When the rats were given the fruit extract at different doses, these values began moving back toward normal, with red blood cells, hemoglobin, and hematocrit improving and iron levels in the blood rising again. The extract also helped bring reticulocyte counts down, suggesting better maturation of new blood cells. Interestingly, the treatment normalized bleeding and clotting times as well and reduced the enlarged heart, liver, and spleen weights that typically occur during this type of anemia. The researchers attributed these protective effects to the plant's natural phytochemicals—flavonoids, alkaloids, steroids, and saponins, along with its iron and vitamin C content—working together through antioxidant activity to support healthier blood parameters. Overall, this study suggests that *M. cymbalaria* fruit extract could serve as a useful natural option for managing anemia.[13]

10. ANTI-CANCER ACTIVITY

Breast cancer is the leading type of cancer in females around the world, which causes morbidity. Along with that, the estrogen-negative tumor, which poorly responds

to hormonal therapy, is also a challenge. Since *M. cymbalaria* is traditionally used for cancer. Scientists now isolated a saponin compound that, when compared with tamoxifen, produces similar activity by boosting protective antioxidants such as superoxide dismutase, catalase, and glutathione. It also reduced the cancer biomarkers and restored the hormonal imbalance caused by the cancer.[14]

The extract reversed much of the cellular damage caused by the DMBA carcinogen, as confirmed by histopathological analysis and whole-mount tissue preparations. Treatment with the saponin extract decreased the total tumor cell count and decreased cell viability, thereby causing cancer cell death. In the MTT assay, the extract also showed unmistakable cytotoxic activity against MCF-7 breast cancer cells, with treated cells exhibiting statistically significant decreases in viability coupled with obvious microscopic indications of apoptosis-like alterations.[15]

11. ANTI-DEPRESSANT ACTIVITY

Depression, which is a common problem faced by humans all over the world by people of all age groups, is caused by various factors, and every year the morbidity rate increases due to patients committing suicide. *M. cymbalaria* is traditionally used for stress, insomnia, and hysteria due to its flavonoid and alkaloid content. Now scientists have developed a hydroalcoholic extract from the fruit of the plant, which has been compared with imipramine. The result shows dependent activity in mice when subjected to locomotor activity in an actophotometer and forced swim test; a higher dose shows reduced movement and calmness, while lower doses show slight improvement compared to the control group.[16]

12. ANTI-INFLAMMATORY ACTIVITY

Inflammation is a natural trigger response to the cell damage by injury to protect the surrounding cells; inflammation is produced by different enzymes such as COX-2, cytokines, and prostaglandin E_2. Scientists isolated a saponin compound from the plant that produces action against these inflammatory enzymes by interfering in the key regulatory pathway of NF-kappa-B that controls the genes behind inflammatory markers. It is not toxic at doses relevant to the anti-inflammatory effect.[17]

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