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Ethnomedicinal Insights and Pharmacological Potential of *Merremia tridentata*: A Systematic Review

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KEYWORDS

Merremia tridentata, phytocompounds, ethnomedicine, Pharmacological activities

ABSTRACT:

Introduction: Merremia is a genus of flowering plants in the morning glory family, Convolvulaceae. Members of the genus are commonly known as wood roses. M. tridentata commonly known as “Mudiarkunthal” or “Savulikodi” or “Thrippan Pullu” in Tamil and “Prasarini" in Sanskrit is reported to possess several medicinal values. It grows in all plain districts of Tamilnadu, the Western peninsula, and Bengal. Prasarini, is commonly known as the Chinese moon creeper seen in south Indian states. The name Prasarni means that it spreads in all directions.

Objectives: To explore the literature available about Merremia tridentata ethnomedicinal and pharmacological properties so that it provides information about its medicinal potential.

Methods: The information was collected from Science direct, PubMed, Google Scholar, Web of Science, Scopus and other literature sources.

Results: Merremia tridentata has various therapeutic activities for helminths, analgesic, constipation, tooth ache, hepatotoxicity, inflammation, dysuria, diabetes, etc. Prasarini is also used to treat allergic conditions.

Conclusion: Merremia tridentata is a rich source of phytochemicals such as carbohydrates, glycosides, proteins, alkaloids, flavonoids, tannins, phenols, and saponins. Phytocompounds such as diosmetin, luteolin, 7-O-β-D-glucosides and dissmetin – 7-O-β-D-glucoside, dodecanoic acid, tridecanoic acid, 12methyl-methyl ester, undecanoic acid, 10-methyl-methyl ester, tetra decanoic acid and cynaroside also present.

1. Introduction

The World Health Organization (WHO) reports that 80% of the world population relies on traditional medicine rooted in cultural practices for healthcare. While modern medicine has led to disease eradication and increased lifespan Indian and Chinese Traditional Medicine have developed over 3,000 years [1]. Many natural products are used in traditional medical systems for disease prevention and treatment. Currently, 25% of modern drugs and 60% of anti-infectives have natural origin [2].

The impact of Ayurveda on the medical field has been so profound that it is often called 'the mother of healing.' [3]. Natural products used in Traditional Chinese Medicine (TCM) and Ayurveda offer valuable insights into prevention and treatment. Integrating traditional systems with modern medicine holds potential for comprehensive treatments, but the lack of accessible literature on these practices limits their integration into modern healthcare, hindering global health advancement [4]. Herbal therapy, using plant parts, treats various ailments and supports the body’s healing processes [5].

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Folk medicine also plays a vital role, encompassing not only herbal remedies but also pharmaceuticals derived from minerals and metals [6,7]. Ayurveda, India's oldest traditional medicine system dating back to 6000 BC, emphasizes preventive and therapeutic health. Charak and Sushrut Samhitas, provide detailed classifications and pharmacological properties of 700 plants, laying the foundation for herbal medicine.

Herbal medicine has seen a resurgence in popularity in recent years, due to the adverse effects of synthetic drugs, the absence of curative treatments for various chronic diseases, the growing challenge of microbial resistance, and significant investments in pharmaceutical research and development. [4,8]

In the southern part of India, another traditional medical system called Siddha emerged, which is believed to date back to approximately 3000–2000 BC. Siddha medicine emphasizes holistic healing practices, incorporating physical and spiritual elements into its approach [9]. Meanwhile, in the West, the Unani system of medicine was pioneered by Hippocrates, often regarded as the "Father of Medicine," and further developed by the physician Galen. The integration of these diverse medicinal traditions highlights the global significance and timeless relevance of natural remedies in healthcare [10].

There are over 1900 species and 60 genera in the Convolvulaceae family [11]. The family Convolvulaceae is typically characterized by its vibrant, funnel-shaped flowers. Chemotaxonomic markers associated with this family include resin glycosides, calystegines, and tropane alkaloids.

The genus *Merremia* comprises approximately 182 species, including infraspecific taxa. Among them, *Merremia tridentata* and *Merremia emarginata* are the most frequently documented species. The genus *Merremia* includes several species, such as *Merremia emarginata, Merremia hederacea, Merremia tomentosa, Merremia yunnanensis, Merremia umbellata, Merremia kentrocaulos, Merremia mammosa, Merremia cissoides, Merremia quinquefolia, Merremia dissecta, Merremia guerichii, Merremia quinata, Merremia tuberosa, Merremia mammosa, Merremia aegyptia, Merremia palmata, Merremia pterygocaulos, Merremia platylphylla, Merremia peltata, and Merremia gemella*. Notably, the highest number of research articles reporting the ethnomedicinal uses of *Merremia* species found in India [12]. The majority of species are herbaceous climbers and lianas that are found in both temperate and tropical climates worldwide, however the tropics have a far greater diversity.

2. Methodology

A thorough literature search was conducted utilizing the databases such as Pubmed, Semantic Scholar and Google Scholar to collect pertinent information for this review. The primary keywords employed in the search included "Convolvulaceae," "*Merremia tridentata*," "*Xenostegia tridentata*," "genus *Merremia*," "formulation," "geographical distribution," "ethnobotanical uses," "phytochemical constituents," "ethnopharmacology," and "pharmacological activities." Additionally, other databases like ScienceDirect, SciFinder, Google Patents, Web of Science and Scopus were also used to gather further data. This comprehensive search resulted in 1,080 articles, books, and patents related to *Merremia tridentata.* By the PRISMA guidelines, the articles identified were systematically reviewed and summarized (Fig. 1).

3. Geographical distribution

Merremia tridentata is found in Nigeria, Central Africa, Asia, Malaysia, and Australia and also widely distributed throughout India, Sri Lanka, Angola, Mauritius, and Madagascar. In India, it occurs in the Indian Ocean islands, West Bengal, Bihar, upper Gangetic plain, South India, Orissa, Gujarat [13,14], Bhandara district of Maharashtra [15], five northern districts of Telangana [16], the Kalasamudram-Nigidi forest range, the Amagondapalem hills, the Kikati forest, the Errmalais and Nallamalai hills of Kurnool district, the Seshachalam hills of Chittoor district, the Palakondas, Lankamalias of Kadapa District and some of the isolated hill ranges in Ananthapur District, the Malnad region of the Western Ghats and the Maidan region of Andhra Pradesh. In Tamilnadu, it is found in the Anantha Victoria Marthandavarma canal of Kanyakumari district, South Vagaikulam region in Tirunelveli, Ponmalai hillock of Kanniyakumari District, Pavalamalai, Gobi, Erode district, Palamalai Salem district, Madukkarai hill, in the southern western ghats of Coimbatore district, Sivagangai district in Tamilnadu, Molamalai hill, Karur district [17-25]. The synonyms of *Merremia tridentata* are

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Evolulus tridentatus (L.).; *I. filicaulis* Vahl.; *Convolvulus tridentatus L.*; and C. hastatus *Desr.*; *Ipomoea angustifolia Jacq.*; *I. tridentata* (L.) Roth; *Merremia hastata* (Desr.) Hall.

4. Morphology of *M. tridentata*

M. tridentata is a perennial herb and has a small woody rootstock. The stem is prostrate-shaped and slender. The leaves are oblong-ovate and the flowers are pale yellow [26]. The epidermal cells have robust cuticles and walls. The hypodermis is chlorenchymatous and has only one layer. The cortex is parenchymatous and has four to six layers. One to two layers of sclerenchyma encircle the continuous ring of vascular tissue. There are two sides to the vascular ring. Large and composed of parenchymatous cells, the pith has a little depression in the middle. The pith contains the latex cells. The cortex and pith contain the secretory cavities [27]. To ascertain the macromorphological, micromorphological, and chemo-micromorphological profiles of *Merremia tridentata* (L.) Hallier f., the pharmacognostic analysis of leaf, root and stem was conducted. According to the leaf's architecture, collateral vascular bundles, paracytic stomata, peltate stomata and the lamina's epidermis has glandular trichomes and calcium oxalate druses. A bicollateral vascular cylinder, made up of xylem fibers and a few large, round or angular vessels, is found in the stem. In the root the secondary phloem is not separated from cortex. The rays of phloem are thin and straight. Vessels, fibers, and xylem rays are examples of secondary xylem [28]. The various names of *Merremia tridentata* in different languages is given in Table 1 [29].

5. Phytocompounds

The diosmetin, flavonoids, luteolin-7-O-β-D-glucosides, luteolin and dissmetin – 7-O-β-D-glucoside are found in the aerial portions of *M. tridentata* [30,31]. The seeds have yielded ergosine alkaloids. The root and aerial sections have yielded other chemicals, including pyrolidine alkaloids like hygrine and nicotine [32].

The GC-MS analysis of the *Merremia tridentata* root methanolic extract showed the presence of compounds such as dodecanoic acid, tridecanoic acid, undecanoic acid, 12 methyl-methyl ester, 10-methyl-methyl ester, and tetra decanoic acid as the main phytoconstituents. The other compounds such as heneicosanoic acid, 20-oxo methyl ester, hexadecanoic acid, methyl ester, 10-octa undecanoic acid, nona decanoic acid, methyl ester, hexa decanoic acid, 14-methyl methyl ester, 16-methyl methyl ester, and hepta decanoic acid were also found. The flavonoid-rich fraction showed the presence of cynaroside, quercitrin, cosmosiin, luteolin, and apigenin. FTIR-ATR methods were used to confirm the structure of the isolated chemical compounds such as alkene, aldehydes, alkynes, alkanes, alcohol, ester, ether, carboxylic acid aliphatic amines [33]. (Fig. 2)

6. Phytochemical constituents

Phytochemical analysis of *M. tridentata* revealed the presence of carbohydrates, glycosides, proteins, alkaloids, saponins, tannins, flavonoids and phenols. Petroleum ether extract showed the presence of steroids, chloroform extract showed carbohydrates, while acetone and methanol extracts confirmed the presence of alkaloids, flavonoids, phenols, tannins, polysaccharides, glycosides, phytosterols, polyphenol [34-36].

7. Supplementary Food

7.1. Food for Humans

In sub-Saharan Africa, rural tribes frequently include Wild Edible Plants (WEP) in their diets. Wild plant resources are widely used as food in Guinea-Bissau, West Africa. WEP, which includes a variety of plant parts from both native and introduced species, including fruits, roots, flowers, and leaves, are extensively consumed all over tropical Africa as nutritious food sources. Local inhabitants in West Africa actively or potentially consume a substantial percentage of the valuable plants that have been documented. They consume *Merremia tridentata* as edible food by cooking it [37]. A study about the Dalit food system in, Zaheerabad, Andhra Pradesh showed *Merremia tridentata* (Thadaka Dobbudu) consumed as a curry with pulses during monsoon and winter. Nutritional analysis revealed that these traditional foods are rich in essential nutrients, supporting their inclusion in school nutrition programs to improve dietary habits. Based on the nutritional assessment made Thadaka dobbudu has protein, fat, carbohydrates, fiber, calcium, phosphorus, iron, copper, magnesium, zinc, vitamin C, carotene etc., [38].

7.2. Food for animals

Merremia tridentata is used as a supplementary feed for young West African dwarf sheep in Benin, replacing

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Panicum maximum. *M. tridentata* offered higher protein and tannin levels, leading to greater weight gain over a six-week trial. Its abundance along roads and fallow lands reduced feed costs, improving household ruminant productivity. Despite its tannin content, *M. tridentata* enhanced sheep performance without affecting palatability, making it a valuable addition to conventional sheep feed [39].

8. Ethnomedicinal and Traditional Remedies

Merremia tridentata has various medicinal properties that are used over a long period by the peoples in various regions of the country (Table 2) (Fig. 3).

Merremia tridentata which is used in Tanzania, Senegal, and Zaire for treating snakebites [40]. The Nigerian people used the whole plant *Merremia tridentata* for the treatment of gonorrhoea [41]. *Merremia tridentata* utilized to relieve headaches by inhaling the steam produced from boiling the whole plant in water [42]. Hemiplegia is a neurological disorder impairs motor control, balance, and coordination, leading to difficulty in movement [43]. The people of Tamil Nadu, Madhya Pradesh and Chhattisgarh reveal *Merremia tridentata* as a treatment for hemiplegia, hemorrhoids, and urinary system disorders [44]. The whole plant is used for alleviating symptoms of gripe and malarial fever [45]. It is recognized as antiseptic agents for treating sores [46]. *Merremia tridentata* is traditionally used, especially for treating leprosy, based on insights from local practitioners [20]. *Merremia tridentata* root bark, is used to treat intestinal worms and constipation [17].

Merremia tridentata (Sitha Savaram) treats rheumatism and piles, while its subspecies *hastata* alleviates toothaches [16]. The whole plant extract addresses rheumatism, piles, and urinary disorders [47]. Mt leaves are used to treat cough and fever, while its roots possess anti-inflammatory properties and are used for toothache relief [25]. Along with being an effective laxative and astringent, it also helps with joint stiffness, hemiplegia, urinary tract infections, and overall debility.

M. tridentata is traditionally used to treat hemiplegia, haemorrhoids, urinary system diseases, inflammation, relieving toothaches and as a dentifrice [48]. Between 2000 and 2004, a survey in Tamil Nadu documented 114 medicinal plant species from 97 genera and 51 families for dental care in which *M. tridentata* is also included [49].MT decoction is traditionally used for ophthalmic conditions [50]. *Merremia tridentata* is traditionally valued for its astringent properties, treating swelling and urinary infections [51,47]. *M.tridentata* is used for the treatment of inflammation caused by Herpes. Herpes is a recurring inflammatory skin condition caused by a group of viruses [52].

Merremia tridentata root decoction is traditionally consumed to alleviate rheumatism and diabetes [53,19,47,54]. Skin eruptions refer to abnormal skin changes, including rashes, blisters, or lesions, caused by infections, allergic reactions, autoimmune disorders, or irritants [55]. *M. tridentata* with its stem and root is used to treat skin eruptions [56].

9. Pharmacognosy of *Merremia tridentata*

Merremia tridentata exhibits a wide range of pharmacological properties that support its traditional use in various healing systems. It possesses significant anti-inflammatory, analgesic, antioxidant, antidiabetic, anticancer, and antiarthritic activities, along with notable hepatoprotective and wound healing properties. These diverse therapeutic effects are attributed to the presence of various bioactive constituents, which contribute to its multifaceted medicinal potential. (Fig .4)

9.1. Anti-diabetic and Anti-hyperlipidemic

The stem ethanol extract (SE) of *M. tridentata* significantly lowered blood glucose in alloxan-induced diabetic mice after 15 days. A flavonoid-rich fraction (FF) from SE exhibited strong anti-diabetic effects. Diabetic mice had elevated TC, TG, LDL, and VLDL, with reduced HDL. Treatment with SE and FF improved lipid profiles, with FF showing superior effects, including reduced TG and increased HDL after 20 days [33].

The study conducted in albino male rats to assess the anti-diabetic activity of *M. tridentata* leaf ethanol extract (MTLE) showed that the glucose level was decreased and excess weight obtained due to hypoglycemic condition was also restored [56]. Another study which was conducted in albino male rats to assess the anti-diabetic activity using an aqueous extract of *M. tridentata* root also exhibited glucose lowering effect in diabetic rats [57]

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9.2. Anti-inflammatory

Carrageenan-induced paw edema in the acute inflammatory model was considerably decreased by the 50% methanolic extract of *M. tridentata*, in comparison with petroleum ether and benzene showing effectiveness comparable to standard Ibuprofen. These findings suggest that *M. tridentata* roots have strong anti-inflammatory properties against paw edema brought on by carrageenan [58]

The ethanol extract of *M. tridentata* has significantly reduced chronic inflammation in the knee joints of rats induced by complete Freund's adjuvant (CFA), compared to the standard drug. Additionally, key signs of chronic inflammation, such as redness, swelling, arthralgia, and joint immobility, were markedly lower in drug-treated animals than in control rats [59]

9.3 Anti-Oxidant

The yield percentage, total phenolics, and tannins extracted from *M. tridentata* roots and aerial portions using different solvent systems for *Merremia tridentata* Aerial Chloroform (MTAC), *Merremia tridentata* Aerial Aqueous (MTAA), *Merremia tridentata* Aerial Methanol (MTAM), *Merremia tridentata* Aerial Hexane (MTAH), *Merremia tridentata* Root Chloroform (MTRC), *Merremia tridentata* Root Aqueous (MTRA), *Merremia tridentata* Root Methanol (MTRM), and *Merremia tridentata* Root Hexane (MTRH) is calculated. Hot water extraction resulted in the highest yield followed by methanol extraction. However, the acetone extracts showed the highest levels of total phenols and tannins, and the methanol extracts showed mid-levels of total phenols and tannins. The lowest levels of total phenolics, and tannins were found in chloroform extract. Various *in-vitro* antioxidant assay such as the Ferric reducing antioxidant power (FRAP) assay, phosphomolybdenum reduction assay, free radical scavenging activity on DPPH, and ABTS assay was done to identify the type of extract with greater antioxidant activity. As a result, higher antioxidant properties and free radical scavenging properties were found in the ethyl acetate fraction of *M. tridentata*.

The aerial portions and roots of *M. tridentata* exhibit strong antioxidant and free radical scavenging properties in a variety of solvent extracts [60].

Merremia tridentata ethanol leaf extract was used to investigate the anti-hyperglycemic and antioxidant effects of (MTELE) on liver and kidney tissues in streptozotocin-induced diabetic rats. At the end of the study, liver and kidney tissues were analyzed for antioxidant activity. The diabetic control group showed a notable decrease in the activity of the enzymes such as superoxide dismutase (SOD) and catalase (CAT) in the liver and kidney tissues. These results suggest that MTELE has potential antioxidant effects and may help mitigate oxidative stress in diabetic conditions [56].

9.4 Ulcer

The anti-ulcerogenic property of the *Merremia tridentata* ethanolic fraction was studied against ethanol-induced ulcers in rats was compared with omeprazole, a proton pump inhibitor known for its anti-secretory and protective effects. The findings demonstrated that animals pretreated with *M. tridentata* ethanolic fraction exhibited dose-dependent protection of the mucosal layer [60].

9.5 Hepatotoxicity

Administration of ethanolic and aqueous extracts of *M. tridentata* has shown significant hepatoprotective effects, surpassing the efficacy of the standard drug silymarin. CCl_4-induced hepatotoxicity resulted in a significant, dose-dependent increase in liver enzyme levels (ALT, AST, ALP) and bilirubin. However, the administration of *M. tridentata* aqueous extract led to notable improvements across all parameters compared to the control groups. Co-administration of *Merremia tridentata* extract with CCl_4 significantly healed liver damage, with a decrease in ALT and AST levels, indicating stabilization of the plasma membrane and repair of liver tissue. The 30-day treatment with *Merremia tridentata* extract led to a reduction in ALP and ACP enzyme levels. Post-treatment showed better results than pre-treatment, suggesting that *Merremia tridentata* has bioactive compounds that stabilize biliary dysfunction and protect against lysosomal rupture, thereby restoring cellular integrity [61].

9.6 Wound Healing

Incision, excision, and dead space wound models in albino mice are used to assess the wound-healing capabilities of *Merremia tridentata*. A wound that was 6 cm long and 1.5 cm thick was made for the

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sutured incision model. In A 500 mm² wound area was created for the excision wound model. The mice were treated with various solvent fractions of *M. tridentata*, including petroleum ether, solvent ether, butanol, butanone, and ethyl acetate fractions. The study concluded that the ethyl acetate extract of *M. tridentata* exhibits significant wound-healing potential by enhancing tensile strength and promoting granulation tissue formation. [13]

9.7 Cardioprotective

Reduced cellular necrosis and vascular degeneration in cardiac myocytes by diosmin by reducing oxidative stress and inflammation [62]. Diosmin also raises myocardial glutathione content, plasma insulin, c-peptide levels and also improves the activities of glutathione S-transferase, catalase, and superoxide dismutase thus significantly reduce the levels of tumor necrosis factor-alpha (TNF-α), interleukin-6, interleukin-1β (IL-1β), downregulated cardiac Bcl-2-associated X protein and caspases 3 and 9, while upregulating the expression of B-cell lymphoma 2 (Bcl-2) mRNA [63].

Apigenin treatment in doxorubicin-intoxicated rats decreased oxidative stress and apoptosis in cardiomyocytes, which greatly decreased cardiac fibrosis, enhanced myocardial function, cytoplasmic vacuolization, myofibrillar loss, and cardiomyocyte degeneration, preventing the progression of myocardial damage. It inhibits the elevation of LDH, CK-MB, and cTnI, preserving the structural integrity of myocardial tissue.it also increases SOD activity and decreased malondialdehyde levels in the myocardium. Apigenin appears to preserve myocardial integrity by increasing Bcl-2 expression and reduction in Caspase-3 and Bax expression [64].

In isoproterenol-induced cardiac injury, luteolin helps to improve ECG abnormalities, minimize histological damage, preserve antioxidant enzyme levels, and lessen intracellular enzyme leakage by encouraging the increase of HO-1 expression through Nrf2 activation through the upstream signalling pathways PI3K-Akt and ERK1/2. Luteolin can shield H9c2 cells from H2O2-induced apoptotic cell death [65]. Luteolin effectively inhibits cardiac fibrosis and lipid deposition by suppressing the expression of markers associated with fibrosis, such as MMP2, MMP9, collagen I, collagen III, TGF-β and reduced lipid deposition by downregulating LOX-1 and CD36 [66].

M1 macrophages promote inflammation and cardiomyocyte apoptosis during myocardial infarction, while M2 macrophages support tissue repair, immune tolerance, and cardiac recovery. Quercetin increases M2 macrophage percentage and promotes their polarization, reducing ventricular remodelling and improving heart function. M2 macrophages have a higher α-ketoglutaric acid to succinic acid ratio than M1 macrophages. Quercetin lowers citric and succinic acid levels, shifting macrophage energy metabolism toward the M2 phenotype, enhancing tissue repair, and reducing inflammation post-infarction [67]. Quercetin supplementation in rats with aortic constriction led to reduced aortic medial thickness, arterial blood pressure, and cardiac hypertrophy, while restoring normal cardiac PKCβII translocation shows preventing structural and functional changes linked to heart disease [68].

The expression of the proteins Bcl-2, Bax, and Caspase-3 in the hearts of treated with diosmetin and control rats must be measured to better understand the molecular mechanisms underlying this effect [69]. Diosmetin reduced LVESV while increasing serum biomarkers LVWT, LVEF, FS, and HR, improving systolic and diastolic function [70].

The therapeutic potential of cynaroside in alleviating Doxorubicin-induced cardiotoxicity (DIC) through the activation of the AMPK/Nrf2/SIRT3 signalling pathway. By altering the energy metabolism of heart cells and strengthening antioxidant defenses, cynaroside significantly reduces oxidative stress, inflammatory cell death, and NLRP3-mediated cardiomyocyte pyroptosis induced by doxorubicin [71].

Cynaroside efficiently shields H9c2 cells from H2O2-induced apoptosis by lowering the production of reactive oxygen species (ROS) and preventing caspase activation via the death receptor and mitochondrial pathways. Cynaroside preserves mitochondrial function by regulating Bcl-2 proteins and modulating JNK and P53 expression, helping to prevent oxidative stress-induced cell death [72]. *Merremia tridentata* and found in other species has a protective property against cardiovascular disease. The cardioprotective properties evaluated are based on *in vitro*, preclinical, and clinical studies associated with atherosclerosis and several

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cardiovascular risk factors, including hypertension, diabetes, dyslipidemia, obesity, heart injury, and metabolic syndrome (MS) [73] (Fig. 5)

9.8 Cancer

Cancer was initially identified as a growing mass of tissue, or tumor. Observations focused on its appearance, rate of growth, and the way it seemed to "bite" into the body. Tumors were often seen spreading to other areas, and they were recognized as potentially fatal. At this stage, two key points were clear: First, cancer was understood as a disease involving abnormal and uncontrolled growth, with the ability to spread. Second, there was no distinction made between tumors and cancer, a distinction that is still often overlooked today. The "cellular theory" of disease, proposed by Rudolf Virchow in the mid-19th century, suggests that all diseases, including cancer, originate from changes in cells. This concept paved the way for understanding cancer as a disease characterized by abnormal cell growth [74].

DNA methylation research, especially about cancer, has primarily focused on CpG island promoter methylation. However, it is important to note that about 40% of human genes lack true CpG islands in their promoters. Cytosine methylation may also be involved in both cancer and normal development in these CpG-poor genes [75]. Age-related changes in tissue quality, such as fibrosis and alterations in the extracellular matrix (ECM), along with local and systemic and impaired immunosurveillance, promote tumor progression. Thus, as a secondary consequence of aging, cancer is facilitated in its clinical appearance and progression by aging itself rather than its underlying causes [76]. Various compounds such as apigenin, cynaroside, luteolin, quercetin, and cosmosin present in *Merremia tridentata* have anti-cancer properties. (Fig. 6)

9.8.1 Apigenin

The growth-suppressive activity of apigenin in gastric cancer cells seems to be partially linked to the induction of apoptosis [77]. GC cell line SGC-7901 and examined different levels of apigenin over 7 days, showing that apigenin inhibited cell growth in a time-dependent and dose-dependent manner [78], decreases the clonogenic efficiency of SGC-7901 cells [79] exhibited anti-proliferative effects on SGC-7901 cells [80]. Apigenin exhibits anti-proliferative effects on GC cells with both dose- and time-dependent inhibition observed in undifferentiated (HGC-27) cells compared to the semi-differentiated (SGC-7901) cell line [81].

The proportion of cells in the G1 phase increased and the proportion of cells in the S phase decreased as a result of apigenin's considerable inhibition of Huh7 cells [82]. The addition of apigenin in non-small cell lung cancer (NSCLC) A549 causes an increase in p53 expression, however, p53 siRNA can inhibit the apoptotic enhancement caused by apigenin in CDDP-resistant NSCLC [83]. Apigenin, reduces tumor volume and prevents metastasis in TRAMP models by inhibiting the PI3K/Akt/FoxO pathway in prostate cancer [84]. HeLa and C33A cells were treated with different concentrations of apigenin (0–100 μM) and the viability of human cervical cancer cells using the Presto Blue test. Apigenin significantly halted the G0/G1 and S stages of the HeLa cell cycle and also boosted the number of cells in the sub-G1 and G2/M phases and decreased the percentage of cells in the S phase in C33A cells. These findings show that apigenin causes cell cycle arrest, which kills cervical cancer cells [85].

9.8.2 Cynaroside

Cynaroside has potential effects on invasion, migration, apoptosis and cell proliferation in gastric cancer cell lines including HGC27, MKN45, SGC7901, and HK-2 cells [86] through the AKT/MET/mTOR pathway reduces the protein levels of p-mTOR, p-P70S6K, and p-AKT, significantly inhibiting gastric cancer cell growth and migration in vitro and in vivo[87].Cynaroside against cisplatin-induced nephrotoxicity in BALB/c mice by Tunel staining showed increased DNA fragmentation through the NF-κB pathway and suppresses the caspase-3/MST-1 signalling pathway, mitigating kidney damage and lowering blood levels of neutrophils, BUN, and creatinine [88].

In doxorubicin-induced necrosis, HK-2 cells (a human proximal tubule epithelial cell line) were treated with cynaroside showed mitigating DNA fragmentation, caspase-3 activation, and mitochondrial hyperactivation [89].

9.8.3 Luteolin

It inhibits oesophageal cancer stemness by downregulating SOX2 via PI3K/AKT pathway

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suppression and reversing EMT in vitro and in vivo. It reduces tumorigenicity and stemness in drug-resistant cells, likely through UBR5-mediated SOX2 regulation [90]. Luteolin reduced oral SCC-4 cell viability in a time and dose-dependent manner by inducing G1 phase cell cycle arrest by downregulating CDK2, 4, and 6, lowering pRb levels, and promoting apoptosis via increased Bax and cleaved caspase activation [91].

Luteolin induces apoptosis in HT-29 colon cancer cells via a caspase-dependent, mitochondria-mediated pathway exhibits strong antioxidant activity, reducing ROS levels and influencing redox balance and GSH levels and involved JNK and p38 MAPK pathways in apoptosis [92].

Luteolin treatment of MDA-MB-231 cells caused the cell cycle to be arrested at the S phase in a dose-dependent manner, lowers telomerase levels and preventing NF-kB inhibitor α and its target gene, c-Myc, from being phosphorylated [93].

Luteolin-induced cell cycle arrest in MCF-7 breast cancer cells at the sub-G1 and G1 phases, causing nuclear changes and disrupts mitochondrial membrane potential, releasing cytochrome c, increasing Bax, and reducing Bcl-2. It upregulated death receptors like DR5 and activated caspase-3, -8, and -9 while inactivating PARP [94].

Luteolin exhibited dose and time-dependent cytotoxicity in HeLa cells, inducing sub-G1 cell cycle arrest and mitochondrial membrane depolarization. It upregulated pro-apoptotic genes (BAD, BOK, FAS, TRADD, BAX) while downregulating anti-apoptotic genes (BCL-2, MCL-1, NAIP). Additionally, luteolin reduced the expression of cell cycle regulatory genes (CDK4, CDK2, CCNE2, CDKN1A, CDKN2B), highlighting its potential as an anti-cancer agent [95] for prostate cancer, glioblastoma, lung cancer, kidney cancer, liver cancer, etc [96].

9.8.4 Quercetin

The effects of quercitrin on the DLD-1 colorectal carcinoma cell line were assessed by incubating the cells with increasing concentrations of quercitrin followed by a WST-1 cell proliferation assay. The results demonstrated a time- and dose-dependent increase in cytotoxicity, caspase-3 activity and loss of MMP. The changes in nucleosomal enrichment factor (EF) were analyzed [97].

Quercetin on the proliferation of MCF-7 cells lowered cell growth and suppressed proliferation [98]. It regulates miR-146a, which, through mechanisms such as altering the expression of cleaved caspase-3 and EGFR, induces apoptosis and prevents invasion in breast cancer cells [99].

The cytotoxic effects of quercitrin on A549 and NCI-H358 NSCLC cell lines, were MRC-5 as controls, the changes in nucleosomal enrichment factor (EF) were assessed. These results showed a dose-dependent manner may be related to caspase-3 activity. There is no change in mitochondrial membrane potential (MMP), in A549 and MRC-5 cells [100]. It increases the expression level of miR-16, which inhibits claudin-2 expression in a promoter-independent manner by reducing the stability of claudin-2 mRNA. Since claudin-2 is a driver of proliferation, this regulation contributes to cancer inhibition [101].

Quercetin treatment altered 105 miRNAs in pancreatic cancer, including miR-194, miR-106, miR-29, miR-103, miR-29 and let-7. These miRNAs inhibit proliferation, invasion, and metastasis while promoting cell death. Let-7c regulates Numbl, antagonizing Notch signalling to prevent cancer progression [102].

In oral cancer, quercetin enhances the expression levels of miR-16, which targets MMP-9, MMP-2, and HOXA10 [103]. It has been shown to reduce cell viability and induce apoptosis by upregulating miR-22, thereby regulating the miR-22/Wnt1/β-catenin pathway in OSCC [104]. In quercetin-treated osteosarcoma 143B cells, there is reduced resistance to cisplatin, attributed to the quercitrin-induced. This decreases the levels of KRAS and upregulates miR-217, both at the mRNA and protein levels, inhibiting the PI3K/AKT oncogenic pathway and ultimately reducing cisplatin resistance [105].

9.8.5 Cosmosiin

The cosmosiin has various effects on the proliferation, migration, and adhesion of breast cancer cells, specifically MDA-MB-231, MCF-7 and 4T1 cell lines. Cosmosiin's ability to inhibit tumor growth in mice implanted with MCF-7 or 4T1 breast cancer cells by regulating the AMPK/mTOR signalling pathway,

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inducing both autophagy and mitophagy in MCF-7 and MDA-MB-231 cells. Additionally, cosmosiin was found to bind directly to the aryl hydrocarbon receptor (AhR), inhibiting its activity. This, in turn, affected the CYP1A1/AMPK/mTOR and PPARγ signalling pathways, contributing to the suppression of breast cancer progression [106].

10. Ayurvedic Formulation

10.1 Balarishta

Arishta is a fermented Ayurvedic preparation made from herbal extracts and sugar, traditionally brewed in earthen pots coated with ghee and smoked with pippali and used to balance doshas, it aids digestion, metabolism, and overall health. The Yogaratnavali recommends filling pots three-fourths full and fermenting for a month [107]. Ayurveda includes Fermented Traditional Medicines (FTM) like arishta. Balarishta, a fermented Ayurvedic formulation, is used for gastric issues, paralysis, nervous disorders, diuretics, autoimmune diseases, rheumatism and overall health. It contains *Merremia tridentata* root as a key ingredient in its herbal composition, enhancing its therapeutic benefits [108].

Arishta is prepared by boiling herbs into a decoction, and fermenting with jaggery, honey, and *W. fruticosa* flowers in a ghee-coated mud vessel. The mixture ferments for 6–10 days, then up to a month. After filtration, the clear upper layer (Prasanna) is used as a medicine [109].

10.2 As a natural polymer

Merremia tridentata root mucilage is used as a tablet binder, in comparison to starch. The results showed that *Merremia tridentata* root mucilage exhibited strong binding properties with ibuprofen. Thus, it is a cost-effective, natural alternative to synthetic binders in pharmaceutical formulations due to its biocompatibility, affordability and effectiveness [110].

10.3 Angiotensin-converting enzyme

The renin-angiotensin system (RAS) is now recognized as a local system in most organs. Angiotensin II primarily acts through AT1 receptors, while novel metabolites like Ang III–AT2 and Ang (1–7)–Mas pathways have opposing effects. RAS activation or inhibition influences hypertension in a tissue- and disease-specific manner [111]. *Merremia tridentata* extracts for antihypertensive potential by inhibiting ACE. Using HPLC, aqueous, ethanol, and acetone extracts effectively reduced ACE activity, highlighting their therapeutic potential [112].

Ang II-induced TGF-β production plays a key role in vascular disease and fibrosis by regulating cellular processes like proliferation, differentiation, and apoptosis. Increased TGF-β signalling enhances pSmad2/3 activity via the canonical pathway and pERK1/2 via the non-canonical pathway, impacting cell adhesion, migration and extracellular matrix regulation. Prolonged activation leads to fibrosis and vascular diseases, including aortic aneurysms. Abdominal aneurysms are linked to environmental factors, while thoracic aneurysms often have a genetic basis, such as Marfan syndrome. Ang II-triggered TGF-β signalling contributes to aneurysm formation, with RAS inhibition reducing pSmad2/3 and pERK1/2 signalling, revealing a potential therapeutic pathway [113].

11. Conclusion and Future Perspectives

Merremia tridentata is a widely distributed plant with significant ethnomedicinal value across various cultures globally. It has been utilized in traditional medicine for centuries due to its broad range of therapeutic properties for treating a variety of ailments, including diabetes, inflammation, cardiovascular diseases, ulcers, leprosy, piles, and rheumatism. Additionally, it has been employed in the treatment of urinary disorders, wound healing, hemiplegia, hemorrhoids, and constipation. The chemical composition has revealed the presence of various bioactive compounds, such as flavonoids, alkaloids, phenolics, steroids, and terpenoids, which are responsible for its wide array of medicinal effects and treat diverse health issues highlighting its therapeutic versatility. With further research, *Merremia tridentata* could lead to the identification of specific compounds that are particularly effective against certain diseases, paving the way for the development of targeted, natural treatments. *Merremia tridentata* could play a crucial role in modern medicine by providing safer alternatives to synthetic drugs, and offering treatments with fewer side effects while still maintaining therapeutic efficacy. The potential benefits of this plant make it an exciting subject for ongoing research and exploration.

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Table 1 Common names of *Merremia tridentata* [29]

Language	Regional /common name
Hindi	Prasarani
Kannada	Ilikivi soppu
Tamil	Mutiyar-kunthal
Malayalam	Prasarani, Thalaneeli
Marathi	Kali vel
Telugu	Lanja savaram, Seethamma jada
Gujarati	Bhintagariyo
Sanskrit	Prasarini
English	Arrow-leaf Morning Glory
Hausa	Gadon machiji
Vietnamese	Bìm Bìm ba rang
Igorot	Karadkad
Javanese	Rangitan
Malagasy	Antsarake, Atarikolo, Lelatandraka
Malay	Andor na loemat
Palauan	Kebeas
Tagalog	Maragta, Talanuk
Dutch	Drietandige Kruip-Winde
Oriya	Paniloi, Prasaruni
Konkani	Semdar kalaudi, Kalivel

Table 2: Ethno-medicinal property of *Merremia tridentata*

S.no	**Ethno-medicinal uses**	**Part Used**	**Location**	**Reference**
1.	Anti-venom	Whole plant	Zarie,Sengal and Tanzania	[40]
2.	Gonorrhoea	Whole plant	Nigeria	[41]
3.	Headache	Whole plant	Northern Nambia	[42]
4.	Hemiplegia	Whole plant	Tamilnadu, Chhattisgarh	[43-45]
5.	Helminths	Whole plant	-	[46]
6.	Leprosy	Whole plant	Tamilnadu	[20]

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7.	Intestinal worms	Root	Rayalaseema, Andra Pradesh	[17]
8.	Piles	Root	Tamilnadu	[16,47,25]
9.	Tooth ache	Root	Tamilnadu	[48,49]
10.	Urinary Tract Infection	Whole plant	Chhattisgarh	[51]
11.	Ophthalmias	Whole plant	Odisha	[50]
12.	Rheumatoid	Root	Aurangabad	[53,19]
		Whole Plant	Andhra Pradesh	[47]
13.	Asthma, Diabetes, Dysentry, cough, fever, skin disease		Tamilnadu	[51]
14.	Skin eruption	Stem & Root	Tamilnadu	[55,21]

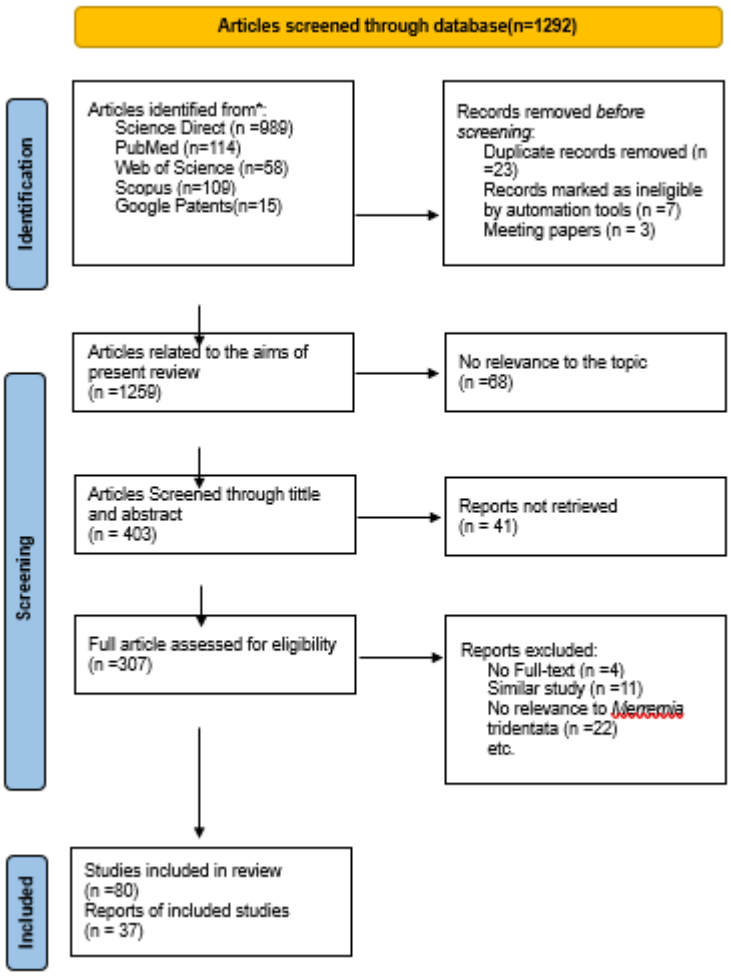

Fig. 1. PRISMA flow diagram illustrating the literature search, screening, and selection process

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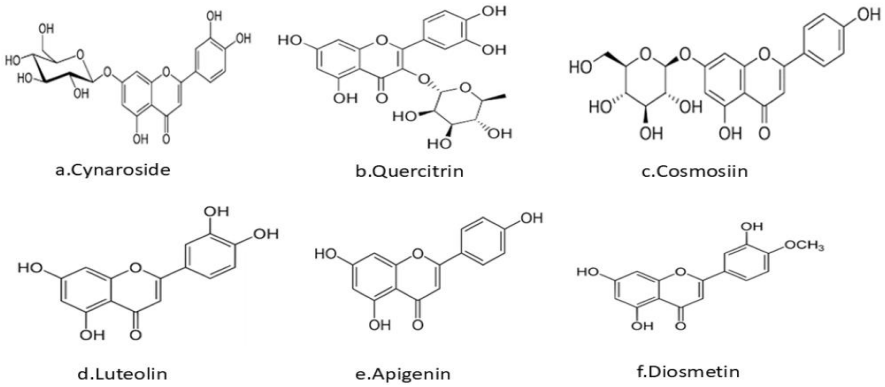

Fig. 2. Phytochemicals in *Merremia tridentata*

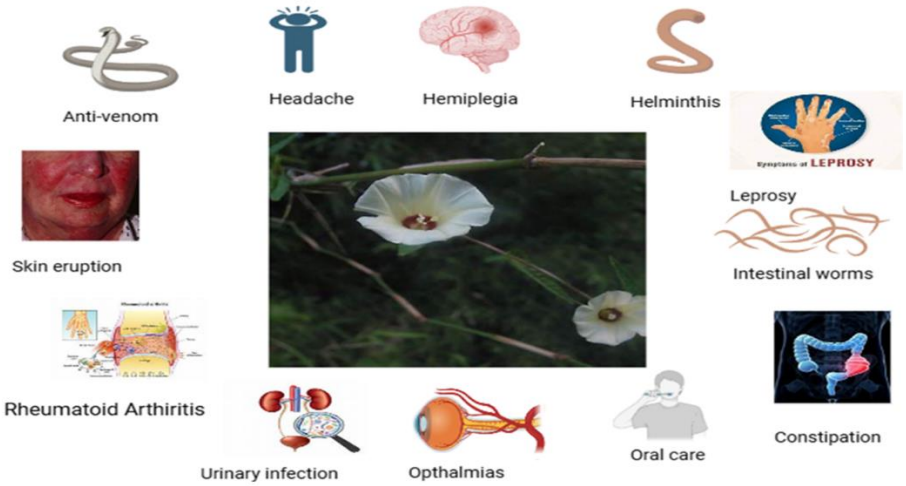

Fig. 3. Traditional medicinal applications of *Merremia tridentata*

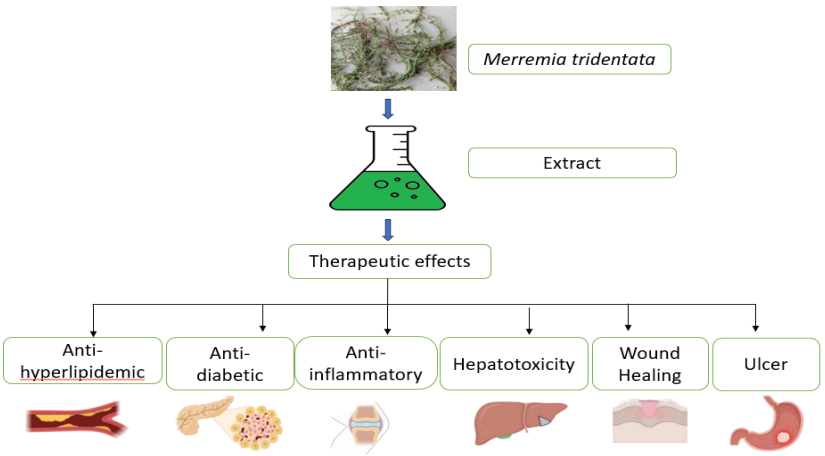

Fig.4. Pharamacological profile of *Merremia tridentata*

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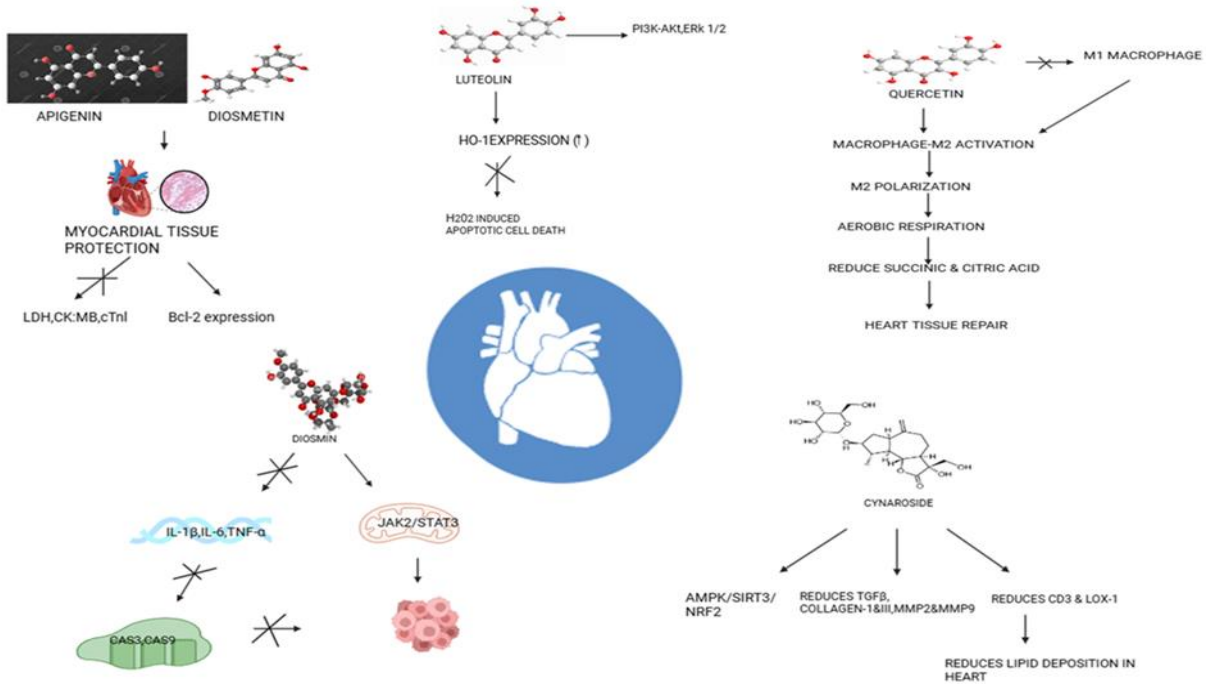

Fig.5. Cardioprotective effects of phytocompounds from *Merremia tridentata* through modulation of key molecular pathways.

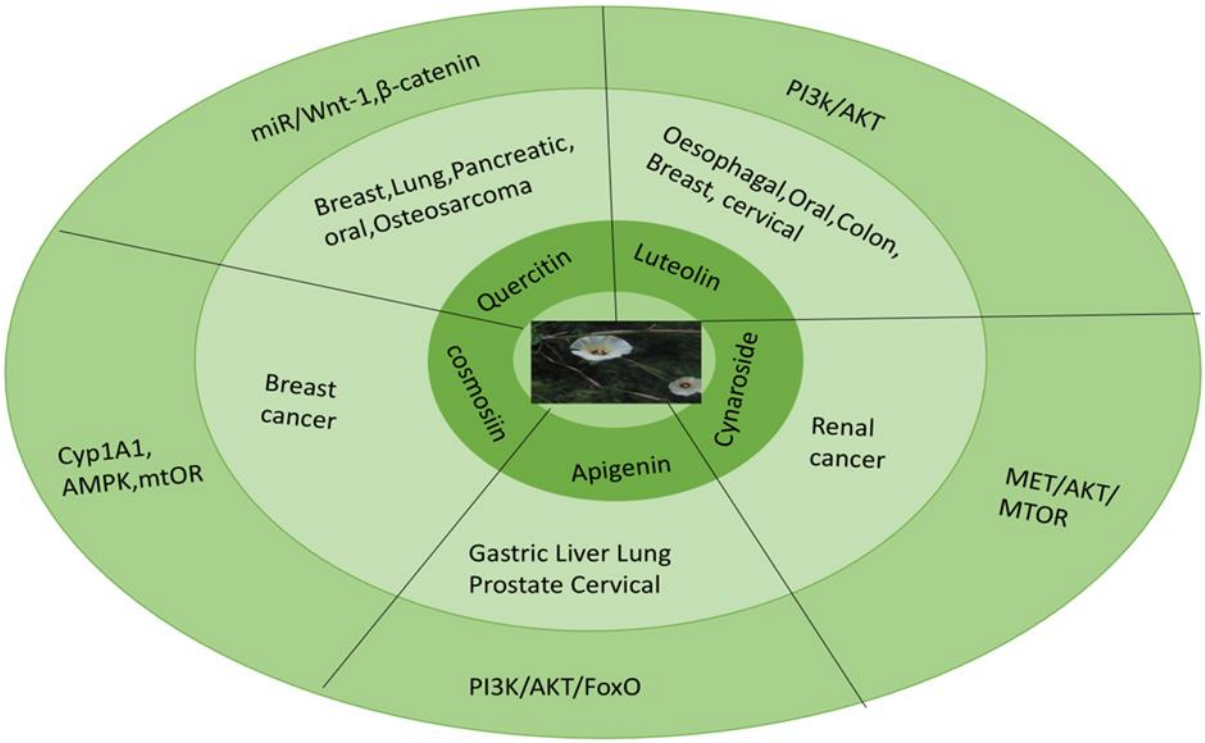

Fig. 6. Schematic representation of the anticancer activities of phytocompounds derived from *Merremia tridentata*, illustrating their molecular targets and signaling pathways