INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230 – 8407

Review Article

A REVIEW ON PHYTOPHARMACOLOGY OF MEDICINAL PLANT: *EUPHORBIA MILII* DES MOUL

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Article Received on: 13/05/21 Approved for publication: 28/06/21

DOI: 10.7897/2230-8407.1206146

ABSTRACT

Euphorbia milii Des Moul is a Madagascar-native deciduous shrub that is frequently planted for decorative purposes. Allied with family Euphorbiaceae. It is frequently referred to as a "Christ-plant" in English and "Kontok Mukut" in local language. It has been widely used as folk medicine from ancient times. Historically, the plant has been utilised as an anti-inflammatory, antioxidant, antispasmodic, anticancer, and antitussive agent, as well as a parasite and wart treatment. The major chemical elements identified in *Euphorbia milii* Des Moul are flavonoids, triterpenes, β-sitosterol, lupeol, cycloartenol, β-amyrin acetate and euphol. This study summarises the last two decades worth of scientific articles and books on this plant, highlighting its pharmacological action and health advantages against a variety of disorders.

Keywords: *Euphorbia milii* Des Moul, Folk medicines, Crown of thorns, Phytopharmacology, Medicinal plant, Milin.

INTRODUCTION

Importance of herbal medicines

Humanity has often been fascinated by naturally occurring compounds derived from prebiotic, microbial, plant, and animal sources[1]. Primitive man, in search of food and to cope effectively with human sufferings, started to differentiate between plants with conclusive pharmacological action and those that were unsuitable for medicinal purposes. This relationship between man and plants has developed, and numerous plants have been used as medicines [2]. Herbal medicine, also referred to as herbalism, is the science of determining the medicinal or therapeutic characteristics of herbs or herbal products. They can be manufactured from any part of the plant, but most frequently they constitute of roots, leaves, flowers bark seeds. They can be consumed orally, ingested, inhaled, or topically applied to the skin. Herbal products frequently contain a range of phytochemicals that exist naturally, many of which contribute to the therapeutic properties of the plant[3].

Herbal medicine is grouped broadly into few fundamental assemblages:

- Herbal medicine in Ayurveda (originated from the Sanskrit term Ayurveda, which translates as "the science of life"), began around 5000 years ago in India and extended to neighbouring countries like Sri Lanka.
- Herbalism in China, a subset of oriental traditional medicine.
- Herbal medicine from Africa.
- Herbalism in Western World, which originated in ancient Greece and Rome and eventually extended to North America, Europe and South America [4].

Because there was insufficient information at the time about the causes of illnesses or about which plant and how it may be used as a cure, everything was based on experience. With time, the rationale for the therapeutic use of a variety of medicinal herbs in the treatment of specific ailments became clear; hence, the application of therapeutic herbs gradually shifted away from the empiric and toward explicatory facts. Until sixteenth century, when iatrochemistry was invented, plants were used for therapy and prophylaxis[5]. At the moment, modernised traditional health care is burdened by significant problems of hazardous medications, chronic disease, resistant infections, age-related degenerative illnesses, and autoimmune disorders, despite significant scientific achievements[6].

As a result of the widespread usage of herbal therapeutic items on a global scale, public health concerns and questions about their protection are being progressively recognised. While a few herbal treatments have demonstrated promise and are extensively utilised, a large number of them remain untested and their usage is also unmonitored [7]. India has a diverse plant flora and a long history of using plants medicinally [8]. India has a long, safe, and ongoing history of using a variety of herbal medicines in officially recognised alternative health systems, including Ayurveda, Yoga, Unani, Siddha, Homeopathy, and Naturopathy[9]. Gujarat, Rajasthan, Haryana, Tamil Nadu, Andhra Pradesh, and Uttarakhand are the Indian states that generate the most therapeutic herbal plants. China is the second greatest manufacturer of medicinal plants after India, accounting for more than 40% of worldwide diversity[10]. The World Health Organization, reports that over 80% of the inhabitants in poorer nations cannot attain medicinal treatment so relying conventional medicines, predominantly based on plants, to meet their fundamental health care requirements[11]. India officially lists 45,000 plant species, while other estimates place the total number of medicinal plants found in the country's 16 agroclimatic zones at 7500, encompassing 63.7 million hectares of forest[12].

Future role of Indian Medicinal Plant Industry

There is a bright future for medicinal plants, as there are approximately half a million species worldwide, the majority of which have not been investigated for their medicinal properties, and whose hidden potential for medical activity may be decisive in the treatment of current and future studies[13]. With the growing use of traditional medicine (TM), include herbal medicines (HMs), it is critical to consider the safety and efficacy of TM use. The origins of TM are believed to have occurred in China about 3000 years ago. It had been transferred to South Korea in the tenth century, resulting in the formation of traditional Korean medicine (TKM), which has its own distinct characteristics. At the moment, a resurgence of naturalist's enthusiasm products in developed countries, which has created enormous opportunity for exports of a variety of items derived from natural herbs and plants. India's herbal sector, which exports medicinal plants and their products, has a bright future. To significantly improve exports, however, cultivation of high-quality plants must be undertaken[14].
Organic elements of plants can be classified as primary or secondary metabolites, the former of which plays a role in fundamental cellular metabolism and vice versa having a more restricted taxonomic range and no evident metabolic function. Secondary metabolites, biosynthesized from primary metabolites such as carbohydrates and amino acids, look to possess ecological functions, for instance protecting animals and plants from predators or attracting insect pollinators[15]. The underlying source of information is the Samhitas about therapeutic herbs chronologically. Amid these, the *Charaka Samhita* (1000 BCE–200 CE) and *Susruta Samhita* (1500 BCE–1000 BCE) are the first to characterise several plant species and their medical properties [16]. The *Charaka Samhita*, a backbone of Ayurveda, lists an unpleasant reaction to medications that occur whenever they are improperly made or utilised. Additionally, *Charaka* elegantly describes various elements relating to the host in an exquisite manner that should be proposed while choosing medications to minimise adverse effects, including the Patient's constitution (*Prakriti*), Age (*Vayam*), Disease (*Vikruti*), Tolerance (previous exposure) (*Satmya*), Psychological state (*Satwa*), and Digestive capacity (*Ahara-shakti*) [17]. According to World Health Organization about 4 billion people, or 80% of the global population, rely on traditional herbal remedy for basic health care[18].

Euphorbia is a vast genus with about 2000 species worldwide, around 195 of which are found in India. The genus included herbs, shrubs, and trees that grow in a variety of habitats[19]. The Euphorbia is named after *Euphorbus*, a Greek surgeon. He was the physician of Juba II, the Romanized ruler of a North African kingdom, and is said to have infused his remedies with their milky latex[20]. Medicinal plants are critical in human and medication development because they include a variety of compounds such as alkaloids, phenolic acids, flavonoids, and tannins. Over 3.3 billion people use therapeutic plants; they are the bedrock of folk medicine.

Euphorbiaceae contains numerous plants with medicinal properties, including *Acalypha indica* L. for the treatment of bronchitis, asthma, and pneumonia, *Euphorbia hirta* L. for inflamed glands, worms, and cough, *E. thymifolia* L. for eye and breast pain and *E. tiruclli* L. for enlarged spleen, jaundice, bladder stone, and tumours[21]. Euphorbiaceae is a family of angiosperm that is one of the largest, comprising over 300 genus, 49 tribes, and 8,000 species of plants ranging in size from enormous woody trees to climbing lianas to prostrate weeds. The family's members are cosmopolitan in distribution, appearing in both the New and Old World's tropical and subtropical zones, and encompassing a vast array of vegetative forms, some of which have great ethnomedicinal value[22].

PLANT DESCRIPTION

Euphorbia milii Des Moul is a scrambling, many-branched evergreen shrub reaching to a height of 60-90 cm. It thrives on dry to moderately moist, in full sun on well-drained soil. It is sensitive to temperatures below 35^0F in the winter. In hot summer regions, appreciates some noon shade. Although *Euphorbia milii* Des Moul is tolerant of poor soils, especially rocky-sandy soils, and even of drought, regular applications of moderate hydration may result in improved bloom with less leaf drop. Wet soils, especially during the winter, can be lethal. It performs best in locations with adequate air movement. Indoor plants require intense light and thrive in a coarse soil-based potting mix. Propagate from cuttings of the tip. The popular name *Euphorbia milii* Des Moul relates to the notion held by some that the crown of thorns worn by Jesus Christ during his crucifixion was fashioned from this plant stems[23].

GEOGRAPHICAL DISTRIBUTION

Euphorbia milii Des Moul is a flowering plant that is indigenous to the Inselberg region of Madagascar's Central Plateau, Africa. It has gained widespread popularity as an ornamental in a variety of tropical and subtropical regions, and is cultivated and naturalised throughout Europe, Africa, Asia, South America, North America, and the Caribbean. *Euphorbia milii* Des Moul is an imported, ornamental plant with a worldwide circulation[24]. It is primarily grown in Assam, Gujarat, Kerala, Maharashtra, Manipur, and Tamil Nadu in India.

SYNONYMS

Euphorbia splendens var. bojer (Hook.) Costantin and Gallaud
Euphorbia splendens subsp. bojer (Hook.) Denis
Euphorbia bojeri Klotzsch
Euphorbia bojeri Hook
Euphorbia breonii var. mucronulata Ram. Goyena
Euphorbia milii var. *milii*

PHARMACOGNOSY

Scientific classification
Domain: Eukaryota
Kingdom: Plantae
Phylum: Spermatophyta
Subphylum: Angiospermae
Class: Dicotyledonae
Order: Euphorbiales
Family: Euphorbiaceae
Genus: Euphorbia
Species: Euphorbia milii[25]

Vernacular names
International (English): Siamese Lucky Plant, Christ's plant, Christ plant, Crown-of-thorns, Christ's thorn.
India: Ainkona kalli (Tamil), Kanta Mukut (Bangla)
Chinese: Wàn nián cì, Tiě hăi táng, Fān zĭ cì,
Italian: Corona di spine, Spina di Cristo
Spanish: Corona de Cristo, Gracia de Dios, Tu-y-yo, Espinas de Cristo
Swedish: Kristi tornekrona
Indonesia: Mahkota duri[25]

Morphological characters

It is a succulent climbing shrub that reaches a height of 1.8 metres (5 feet 11 inches) and has densely spiky stems having cylinder-shaped or irregularly angled branches with spines that are hard, thin, and diverse. Leaves are pale green in colour and grow to a maximum length of 5 cm. They are alternate, oblong obviate, or short acuminate. The straight, slender spines, which can reach a length of 3 cm, aid it in scrambling over other plants. Fig 1: The leaves are up to 3.5 cm in length and 1.5 cm in width, and are mostly seen on fresh growth. Old leaves are not replaced, and only one new terminal growth will produce new leaves. Fig 2: Inflorescences emerge from the upper leaf axils and are characterised by a peduncle with two to four involucres, each of which has 2 spreading red kidney-shaped lobes. The flowers are small and unisexual (male or female only). They are surrounded by a pair of noticeable petal-like bracts that range in colour from red to pink to white and reach a width of up to 12 mm. The blossoms of Euphorbia are further diminished and then aggregated into an inflorescence or cluster of blooms called a "cyathium" (plural cyathia). This characteristic is shared by all species in the genus but not found elsewhere in the plant kingdom[26,23].

Figure 1: *Euphorbia milli* Des Moul plant

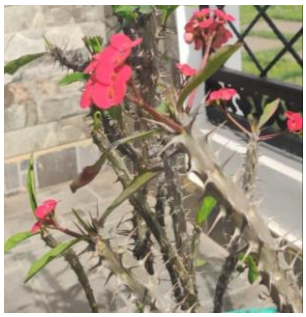

Figure 2: *Euphorbia milli* Des Moul aerial part

TRADITIONAL USES

Recent research indicates that over 5% of Euphorbia species are utilised medicinally[27]. *Euphorbia milii* Des Moul is frequently used in folk medicine to treat warts (in southern Brazil), cancer, hepatitis (in China), and trichiasis[28]. The whole plant paste is applied to dislocated animal bones, the leaves are used to treat snake bites and ringworm, and the seeds are used as a laxative for children. *Euphorbia milii* Des Moul flower powder and whole plant ash are used orally to treat asthma at doses of 500 mg three times a day and 250-500 mg twice a day, respectively[26]. Other medical uses for Euphorbia species are numerous and include the treatment of digestive problems, blood syndromes, genitourinary syndromes, microbial infection, scorpion stings, pregnancies/ puerperium, as well as sensory difficulties. The formulations are used as skin remedies to alleviate warts, itching, hair loss, dermatitis, acne, sunburn, boils, rashes and irritation, as well as for their disinfecting, antiseptic and emollient characteristics[29]. *Euphorbia milii* Des Moul undiluted latex was discovered to irritate the eyes and skin of mammals. While several diterpene esters of ingenol are powerful skin irritants, they lack tumour-promoting potential when compared to other intently linked ingenol and phorbol derivatives. Milli amines obtained from *Euphorbia milii* Des Moul latex were found to be highly molluscicidal[30].

PHYTOCHEMISTRY

Chemical constituents

Numerous researches on the chemical composition of Euphorbia species have been done. The results indicated the presence of several chemical compounds [27]. The most frequently encountered phytochemicals in *Euphorbia milii* Des Moul are β-amyrin acetate, β-sitosterol, cycloartenol, lupeol, euphol, alkaloids, phenolic compounds, carbohydrates, anthocyanin, β-cyanin, proteins, amino acid, cardiac glycosides, steroids, anthraquinone, tannins, phlobatannins, reducing sugar, saponins, coumarin, triterpenes, and flavonoids (name which terpenes and flavonoids)[31,32].

Qualitative phytochemical analyses definitely demonstrated the presence of alkaloids in the ethanolic extract of *Euphorbia milii* Des Moul thorn part and amino acids, proteins and cardiac glycosides in the ethanolic extract of *Euphorbia milii* Des Moul stem part[33].

Hye Sook Yum-Choi *et al.* examined *Euphorbia milii* Des Moul methanolic extract, which resulted in the extraction of two chemicals from the plant. The GC MS analysis Fig (3-5) identified (1) as a combination of 72% 1-octacosanol (1a) and 28% 1-triacontanol (1b) and (2) was recognized as β-sitosterol[34].

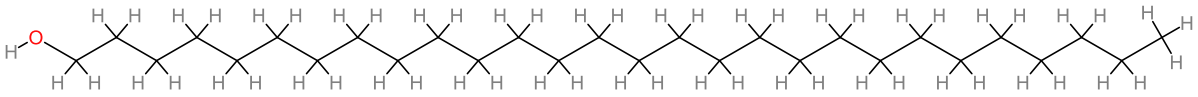

Figure 3: 1-octacosanol (1a)[35]

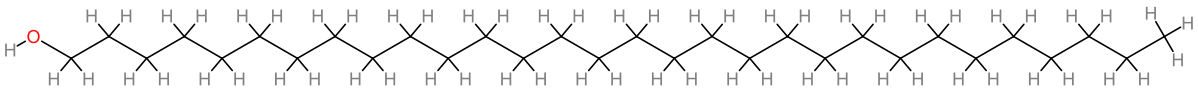

Figure 4: 1-triacontanol (1b)[36]

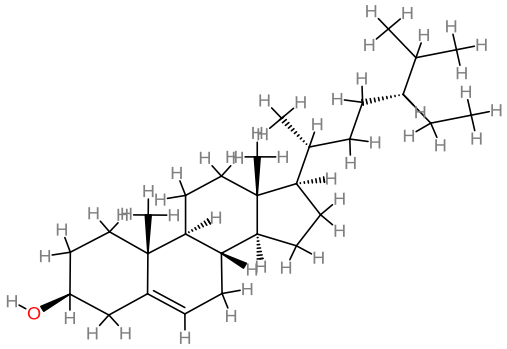

Figure 5: β-sitosterol (2)[37]

Shao-Nan Liu *et al*. examined *Euphorbia milii* Des Moul isolated three new ent-rosane diterpenoids **Fig (6-8)** with a novel 7/5/6 fused-ring system Euphomilone A **(1)** a 5/7/6 tricyclic system Euphomilone B **(2)**, and a 10,19-oxygen bridge Euphomianol A **(3)**. Compound **1** is the first naturally occurring diterpenoid with a tricyclic system of 7/5/6. Compound **2** is the first rosane-type diterpenoid with a fused ring structure of 5/7/6. The ether connection between C-10 and C-19 of **3** is the first discovered in diterpenoids of the rosane type[38].

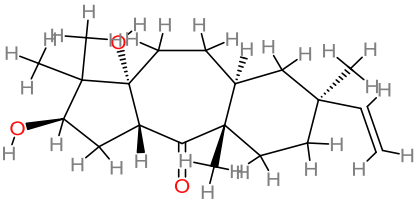

Figure 6: Euphomilone A (1)[39]

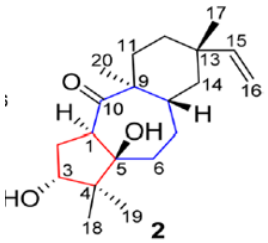

Figure 7: Euphomilone B (2)[40]

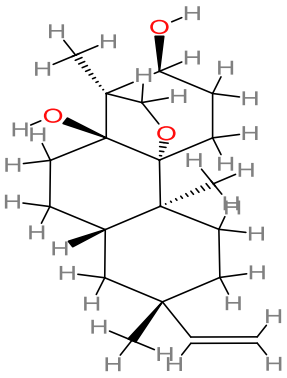

Figure 8: Euphomianol A (3)[41]

K.C. Fonseca *et al*. isolated Eumiliin, a monomeric protein, from *Euphorbia milii* Des Moul latex using a combination of ion-exchange chromatography with DEAE-Sephacel and gel filtering with Sephadex G-75[24].

Talha Ali Chohan *et al*. identified *Euphorbia milii* Des Moul and found as a new source of benzodioxole and barbital compounds. The presence of cyclobarbital and benzodioxole derivatives as important components of the *Euphorbia milii* Des Moul Chloroform fraction of the *Euphorbia milii* Des Moul methanolic extract. According to GC–MS research, the MeOH extract may have contributed to the *Euphorbia milii* Des Moul extraordinary ability to stop HepG2 cancer cells from spreading [42].

Kamurthy H. *et al.* reported Two triterpenoids, Taraxerol (Fig 9) and 28-hydroxyfriedelan-1,3-dione-29-oic acid, one flavone, Quercetin 3-O-(2"-O-galloyl)-a-L arabinofuranoside, and two phenolic compounds, For the first time, 7 7'-dihydroxy, 8, 6'-bicoumarin, and 9-acetyl-3'4' dimethoxy dehydroconiferyl-3-alcohol were identified from *Euphorbia milii* Des Moul flowers. On the basis of the spectrum data, the isolated compound structure was determined (IR, 1H 13C and NMR and mass)[43].

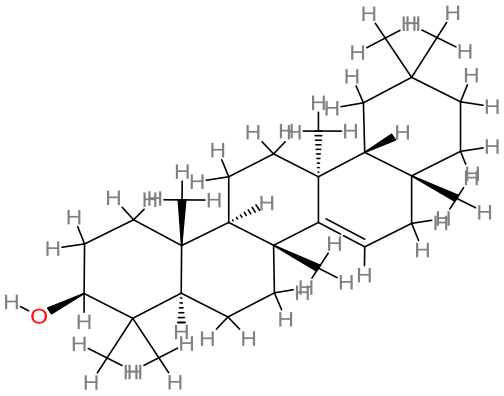

Figure 9: Taraxerol[44]

Saleem H. *et al*. compared the biological activity and chemical composition of dichloromethane (DCM) and methanol (MeOH) solvent extracts of *Euphorbia milii* Des Moul aerial and root portions were compared, and the aerial part's different components were separated. Sesquiterpene was found as a secondary metabolite in *Euphorbia milii Des Moul* aerial methanol extract, as molecule: Eremopetasitenin along with Phenolic (Lusitanicoside), Coumarin (Fraxetin), Alkaloid (Megastachine), and Glycoside (Peruvoside) metabolites. Coumarin was found as a secondary metabolite in the methanol extract of *Euphorbia milii* Des Moul root, and the compound was identified as:(7,8-Dihydroxycoumarin) along with Glycoside (Isopetasoside), Sesquiterpenes (Eremopetasitenin), Flavonoid (Dichotosinin, Abruquinone B, Kaempferol3-(6''-acetylglucoside)-7-glucoside, Kaempferide 5-glucoside-7-glucuronide, Herbacetin 8-acetate), Phenol (Ellagic acid, Licochalcone A)[45].

Subhash C. Yadav *et al.* isolated a new serine protease named 'milin' from the latex of the medicinal plant *Euphorbia milii* Des Moul using a single step of cation exchange chromatography on SP Sepharose fast flow[46].

Salvador Pancorbo *et al.* extracted cycloartenol and β-amyrin acetate were from *Euphorbia milii* Des Moul petroleum ether preparation Fig: (10-13). GC analysis revealed the presence of

lupeol and euphol as minor ingredients, as well as the presence of flavonoids in the methanol extract [47].

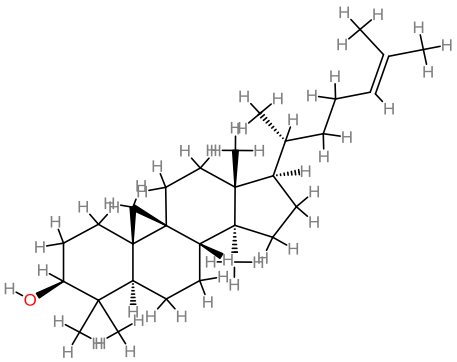

Figure 10: Cycloartenol[48]

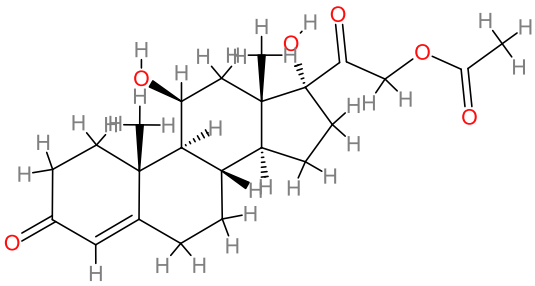

Figure 11: β-amyrin acetate[49]

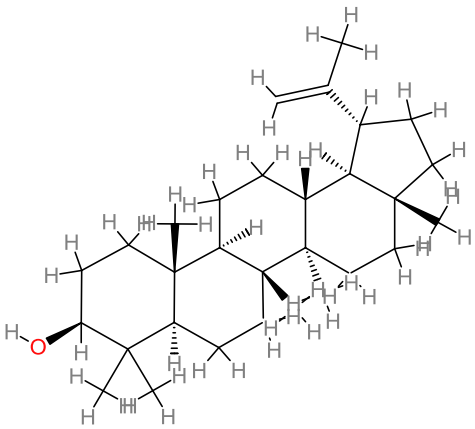

Figure 12: Lupeol[50]

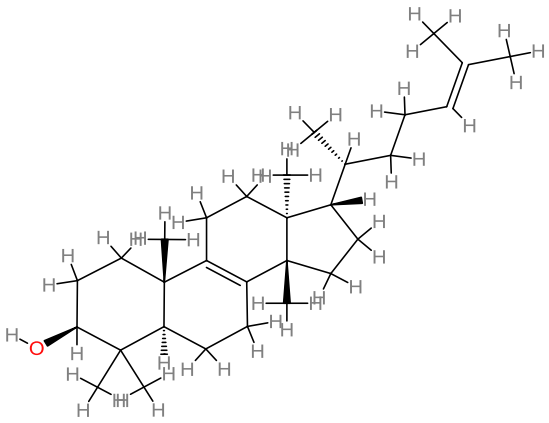

Figure 13: Euphol[51]

PHARMACOLOGICAL ASPECTS

Muscle relaxant, Antinociceptive and Sedative Activity

Tong Shen *et al*. investigated the sedative, muscle relaxing, and antinociceptive properties of zinc oxide nanoparticles (ZnO NPs) produced from *Euphorbia milii* Des Moul aqueous extract. The ZnO NPs increased the efficacy of *Euphorbia milii* Des Moul aqueous sample and exhibited significant sedative, muscle relexant and analgesic properties[52].

Abdur Rauf *et al*. investigated the antinociceptive properties of a crude methanolic extract of *Euphorbia milii* Des Moul aerial parts. The antinociceptive effect was evaluated using a chemically produced pain paradigm (acetic acid)[31].

Antibacterial activity

A.ch. Pradyutha *et al.* reported that the plant extracts were screened for phytochemicals including carbohydrates, tannins, steroids, terpenoids, saponins, flavonoids, alkaloids, and soluble starch, as well as for antibacterial activity against Micrococcus luteus MTCC 106, Arthrobacter protophormiae MTCC 2682, Rhodococcus rhodochrous MTCC 265, Salmonella enterica MTCC 3858, Staphylococcus aureus MTCC 737, and Bacillus subtilis MTCC 441 and suggested that extracts of *Euphorbia milii* Des Moul in ethyl alcohol and ethyl acetate were optimised and had very strong antibacterial action against Gram positive and Gram negative bacteria[53].

Jayalakshmi Basavegowda *et al.* studied *Euphorbia milii* Des Moul against human infections and demonstrated a zone of inhibition higher than 10mm against all bacterial strains[54].

Antioxidant and Antitumor activity

Sreenika. G. *et al.* discovered *Euphorbia milii* Des Moul exhibited antioxidant and anticancer characteristics by triggering apoptosis and lowering reactive oxygen species levels, demonstrating the chemopreventive character of natural products[55].

Marie Cris D. *et al.* identified the phytochemical contents of *Euphorbia milii* Des Moul leaf extracts and quantified their total phenolics, total flavonoids and free radical scavenging activity. The maximum DPPH radical scavenging activity (74.37 percent) was discovered in *Euphorbia milii* Des Moul methanolic leaf extract, indicating that the plant is an abundant source of antioxidants and a potential source of treatments for a variety of chronic and degenerative disorders induced by oxidative stress[56].

Antimicrobial activity

Devanaboyina Narendra *et al.* used the cup plate method to investigate the antimicrobial activity of hexane, methanol, ethyl acetate and water extract of *Euphorbia milii* Des Moul flowers against gramme positive Bacillus subtilis, Proteus vulgaris, Staphylococcus aureus, and gramme negative Escherichia coli. These findings demonstrate that the plant *Euphorbia milii* Des Moul (Euphorbia) has phenolic compounds that provide antimicrobial activity against gramme positive and gramme negative bacteria[57].

Abdur Rauf *et al.* conducted phytochemical analyses and discovered the occurance of cardiac glycosides, steroids/phytosterols, anthocyanin, proteins, terpenoids, flavonoids and tannins in the leaves. Susceptibility tests of its chloroform and methanol fractions using a well diffusion experiment demonstrated significant antibacterial efficacy against Klebsiella pneumoniae and Staph epidermis. Additionally, the ethyl acetate portion of the roots displayed significant antibacterial efficacy against the majority of pathogens tested[58].

Diuretic activity

R. Haleshappa *et al.* discovered the presence of phlobatannins in ethanolic extract of the thorn and stem part of *Euphorbia milii* Des Moul, indicating that the plant possesses diuretic properties [33].

Mild Hypersensitive activity

R. Haleshappa *et al.* discovered flavonoids in *Euphorbia milii* Des Moul ethanolic extract. Flavonoids are water-soluble antioxidants that protect cells from oxidative damage, implying antimicrobial, anticancer, anti-inflammatory, and mild hypersensitivity capabilities[33].

Cytotoxic and antiviral potentials

Sadia Chaman *et al.* investigate *Euphorbia milii* Des Moul leaf is cytotoxic and virucidal to PPRV. These actions could be a result of the leaf's flavonoid content, but additional isolation and characterisation of the virucidal chemicals is necessary to have a better understanding of their underlying mechanism of action[59].

CONCLUSION

To be sure, *Euphorbia milii* Des Moul is a versatile plant with a wealth of medical properties. This plant is an unmatched source of a varied array of chemicals with a variety of therapeutic effects. Zinc oxide nanoparticles (ZnO NPs) from *Euphorbia milii* Des Moul aqueous extract examined their sedative, muscle relaxing, and antinociceptive properties. The present literature survey demonstrates unequivocally that *Euphorbia milii* Des Moul is a significant source of numerous therapeutically effective compounds.

This plant is beneficial in following: antioxidant, antitumor, antimicrobial, antibacterial, diuretic, cytotoxic, antiviral, and mild diuretic. Due to the presence of many natural products such as euphol, triterpenes, flavonoids, saponins, sugar, tannins, alkaloids, β-amyrin acetate, β-sitosterol, cycloartenol, lupel, proteins, glycosides, and phenolics these activities occur. This plant has been successfully utilised for a long length of time to cure a wide variety of health problems. *Euphorbia milii* Des Moul is toxic, and contact with the sap can result in blistering. The current research effort demonstrates a compelling case for the use of *Euphorbia milii* Des Moul in the treatment of a variety of pharmaceutical disorders. Our current examination indicates that additional research is necessary to separate the chemicals responsible for *Euphorbia milii* Des Moul impact.

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Cite this article as:

Shivali Sagar and Monika Bisht. A review on phytopharmacology of medicinal plant: *Euphorbia milii* Des Moul. Int. Res. J. Pharm. 2021;12(6):67-74.
http://dx.doi.org/10.7897/2230-8407.1206146

Source of support: Nil, Conflict of interest: None Declared