



Therapeutic Role of Euphorbia Nerifolia their Active Constituents and Pharmacological Activity in Disease prevention and Treatment

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ABSTRACT

One of the best and most common plant types is the genus Euphorbia (spurges). A member of the family Euphorbiaceae, Euphorbia nerifolia Linn is a plant that grows frequently in the dry, mountainous, and rocky regions of North and Central India. In Ayurveda, the entire plant, including the leaf and root, is used to cure conditions such as ulcers, fever, extorting piles, bronchitis, tumours, leucoderma, piles, inflammation, increase of spleen, blood insufficiency, ulcers, and cough and cold. A study on the pharmacological effects of E. nerifolia showed that its latex was cytotoxic, anti-arthritis, and anti-inflammatory, and that its leaf extract was an in-vitro antioxidant and wound healer. Thuhar (Euphorbia nerifolia) is a herbal medicine that has been used as a part of conventional medicine throughout the majority of the world for thousands of years. Thuhar is a medication of herbaceous origin that has a milky or latex consistency (sheerdar nabat). There are numerous different types of thuhar that can be found in simple Unani literature, including danda thuhar, nadhara thuhar, chauthara thuhar, unglia thuhar, and naghani thuhar. The scientific term nerifolia literally translates to "Leaves resembling an oleander." Over 1500 different classes of Euphorbia exist around the world, ranging from weeds that grow annually to forests. Euphorbia nerifolia, sometimes known as "Sehund" or "Thuhar," is a robust herb. Also known as milk restrict English. Euphorbia nerifolia has a long history of use as a potent remedy for a variety of illnesses, including rheumatism, sciatica, niqrous (the ability to taste), bronchitis, waja-ul-uzn (otalgia), inflammatory environments, asthma, leucoderma, and others. In this essay, an effort has been made to compile the immunomodulatory effects of thuhar (Euphorbia nerifolia) and their therapeutic applications.

Keywords: Euphorbia Nerifolia , Phytoconstituents , Therapeutic uses, Infectious diseases , Molecular Mechanisms , COVID-19, Pharmacological activity.

Introduction

Medicinal plant usage is as old as humankind in the therapeutics. There are about,45,000 medicinal shops species in India. The officially proved shops with medicinal eventuality are 3000 but traditional interpreters use further than 6000. Bioactive composites in shops have also been employed for fresh purposes, videlicet as arrow and outrage venoms for stalking(several Aconitum species), venoms for murder, hallucinogens used for ritualistic purposes, instigations for abidance, and hunger repression, as well as inebriants and drugs. The factory chemicals(bioactive composites) used for pharmacological or toxicological goods are largely the secondary metabolites. These secondary metabolites called bioactive composites can be classified into several groups according to their chemical classes, similar alkaloids, terpenoids, cardiac glycosides, saponins, steroids, limonoid, tannins, flavonoids, and phenolics [1].



Figure 1. Euphorbia nerifolia plant.

Euphorbiaceae, the spurge kin, comprises five type, 49 tribes, some 7300 variety and 283 genera of blooming plants distributed generally in the tropical domains [2,3]. The largest genus of classification Euphorbiaceae is Euphorbia with about 1600 class. They range from annual weeds, vines, succulents, herbs (*Phyllanthus amarus*), bushes (*Ricinus communis*) and trees (*Phyllanthus emblica*). In several variety of Euphorbia, the stem is modified to act photosynthesis. There are more than 35 class are found in steamy, subtropical and warm temperate regions of South-East Asia; Vietnam has in addition to 24 species, Thailand has 25, Sumatra has 6, Java has 5, Borneo has 5, Philippines has 6, Sulawesi has 5, Lesser Sunda Islands has 11, Moluccas has 7 and New Guinea 15, Australia has 45 class [4].

The Euphorbia is named afterwards a Greek surgeon called Euphorbus. He was specialist of Juba II who was the Romanised ruler of a North African kingdom, and is assumed to have used their white latex as an ingredient for welcome potions. The tinted covering of these species has various medicinal application in addition to some harmful effect. Euphorbia neriifolia Linn (Indian Spurge tree, Hedge Euphorbia usually known as Snuhi) concern the family Euphorbiaceae, is one of the various species of Euphorbia type plants, with expansive range of local medicinal uses during the whole of the areas in which it is developed. This is one of the herbs widely used in the Indian whole of medicine. They all have latex and a singular flower structure. Euphorbia neriifolia plant is stated to contain carbohydrate, tannins, flavonoids, alkaloids, 24-methylene cycloartenol, triterpenoidal saponins, etc. As Euphorbia neriifolia plant is selected for the review by way of wide variety uses in the traditional cures such as for the situation of abdominal troubles, bronchitis, tumors, leucoderma, piles, inflammation, expansion of spleen, chlorosis, ulcers, fever and in never-ending respiratory troubles. It secondhand as analgesic, hepatoprotective, immunostimulant, antagonistic-inflammatory, temperate CNS depressant, wound restorative, radioprotective agent [5,8]. Influenza, Severe Acute Respiratory Syndrome (SARS), West Nile Fever, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and new outbreak of fervid pneumonia began by a novel coronavirus, SARS-CoV-2 (COVID-19), are just a few instances [5,6]

❖ Taxonomical classification [13]

| | |
|---------------|---------------|
| Kingdom | Plantae |
| Subkingdom | Tracheobionta |
| Division | Magnoliophyta |
| Superdivision | Spermatophyta |
| Class | Magnoliopsida |
| Subclass | Rosidae |
| Order | Euphorbiales |
| Family | Euphorbiaceae |

❖ Distribution

Euphorbia neriifolia evolves widely around the dry, rugged and hilly fields of north, main and South India mostly in Deccan Peninsula and Orissa. It is inborn plant of South Asia, but now regionally cultivated and naturalizing in Sri Lanka, India, Burma (Myanmar), Bangladesh, Thailand and during the whole of the Malaysian region except that Borneo; also infrequently cultivated in added topical domains. It is also in the direction of E. Asia - S. China, Vietnam, and New Guinea [6]. Euphorbia is an herb and temporary. The parts of the plant that grow above the ground are used to form medicine [7].

❖ Morphological Description

Euphorbia neriifolia is refined in gardens, and is seemingly spontaneous. Small erect overweight glabrous shrub, erect, arms $\frac{3}{4}$ in diameter slay and prepare animal for meat cylindrical or dimly 5-angled accompanying sharp stipular thorns arising from dense subconfluent tubercles in 5 irregular rows like cactus. The branches are 2-4 meters extreme, the trunk and earlier branches are grayish and tubular; medium branches are being lightly twisted, stoud, fleshy, and 4 or 5 angled or feathered; younger one are usually 3-feathered, wings labulate accompanying a pair of stout, sharp, 2- to 4- mm long spines climbing from the thickened bases at each leaf of petioles-scar. Leaves are succulent, deciduous, 6-12 fingerbreadth long, terminal on the branches, gestured narrowed into a very short stalk of plant. The leaves are arise from the parts of wings towards completely of the branches, are fleshy, ovoid-obovate, 5-15cm long, or in young plants rather longer, portrayed or blunt at the tip [8]

❖ Synonyms[9]

| | |
|-----------|-----------------------------------|
| Hindi | Sehund.Canda thukar |
| English | Common milk hedge,Holy milk hedge |
| Arabic | Jakum |
| Kannada | Male kalli |
| Marathi | Thor,Tridhara Nivdunga |
| Malayalam | Illa kalli |
| Punjab | Thor |
| Telugu | Akujemuddu |
| Tamil | Ilaikalli |
| Sanskrit | Snuhi |
| Ayurveda | Sthavara vishay varga,upavisha |
| Latin | Euphorbia Nerifolia |

❖ Botanical Description

Euphorbia neriifolia, is a sharp, xerophytic, irritable, delicious shrubby, fleshy, big, erect much separate bush, that constantly grows into a limited seedling of 2-8 meters climax or supporting curved branches cactus like plant. The forest looks pretty like a cactus but accompanying abundant, determined leaves on younger parts of the plant, and mature to 8 meters [10,11].



Figure 2. Different parts (leaves, latex, fruits, and flowers) of the *Euphorbia neriifolia* plant

➤ Flowers

Male and female flowers happen concurrently inside the unchanging bunch. On slender, stiff, and forked peduncles, three to seven flourished cymes or panicles develop alongside in the axils of the top leaves. Globose are 1.5–2 mm × 4–5 mm in size, flushed and flattened, conspicuous in groups of timbers, the center individual is subsessile, the lateral one have a 6–7 mm peduncle, 5 mm ovoid, 1–3 mm broad cyathial glands. Although the corolla is lacking, the involucre is trimmed with two about round to oval, brilliant crimson bracts about 3–7 mm in time. The inflorescence, or cluster of flowers on the plant, is of the cyathium type (individual female flower and numerous male flowers are present in the alike bunch) [11,12].

➤ Fruits

Fruits resemble capsules. Three-fid style, stigmas kind of dilated, smooth, ten to twelve millimeters in width, and minutely jagged. They appear in a type of climates and are only visible in February and March [12].

➤ Seeds

Seeds are flat and concealed with fine hairs [13].

➤ Branch

The saccular arms are from a pair of robust stipular spines on the tubercles of limb, which are meeting in five vertical sleep-inducer lines or ribs. Branches enhance increasingly stupidly 5-gonous in segmentation. Throughout the plasto-never-ending stages, the central meristem is conspicuous. The central and minor meristems have a tight histogenic network. Reticulate bark covers the trunk [24].

➤ Stem

Green and tubular stem and large arms also being round and terete, spiral rim portion, Sharp stipular thorns, with hollow room in centre holding white twist mass. The more immature branchlets are somewhat verticillate, accompanying two or more whorls without articulations, overweight, cactus-like, swirled, light-green, having no covering, 8-30 (-40) mm thick, frequently leafless, and backbone shield in 5 distinct rows on approximately distinct angles (not feathered) which are apparent for a long time [15]. The container and older arms are being grayish and cylinder. Bunches of delicious dense leaves happens on the arms [10]. Central meristem is famous during the whole of plastrochronic chapters. There is close histogenic friendship 'tween main and minor meristem [15].

➤ Leaves

The young leaves are dark green in color and have a durable feel (Figure 1). Periclinal portions at the after second and divide into four equal parts tiers of the minor meristem initiate the leaves [16].

➤ Latex

Latex is a cloudy sap-like fluid present in containers and channels that is to say frequently introduced following fabric damage that happen all along the laticiferous system's composition [17].

➤ **Stipular Thorns**

The spines are narrow, about 4–12 mm long, grayish dark to evil in color, penetrating, and continuous, arising from short cylindrical shorten faraway, and spirally systematized tubercles 2–5 mm length and 2–3 cm divided [12].

➤ **Glands**

Glands are across ovoid and yellow [18]

❖ **Therapeutic uses**

E. neriifolia is famous in India for allure curative properties, that involve antidiabetic, antiarthritic, anticonvulsant, antimicrobial, and antioxidant features [19]. It is still secondhand for wound-healing, radioprotective, immunomodulatory, twitching, anticancer, seductive, and cathartic characteristics [20,21]. It is repeatedly utilized in Unani cure as a sole or linked cure for arthritis and a range of added conditions, containing sleep-inducer, completely clean, respiring stimulus, antiviral, paronychia, and interferolick, [22]. Flavonoids, which are contained in the plant's working diet, have happened explained to decrease the risk of chronic disease [23]. This plant is secondhand in Ayurveda to treat bronchitis, tumors, misfortune of knowledge, leukoderma, piles, swelling, delirium, hate increase, ulcers, blood deficiency, and delirium [13,24]. The leaves are secondhand for carminative, stomachic, and syrup for soothing cough purposes [19,47]. Flavonoids private from *E. neriifolia* leaf are further exploited to treat differing chronic afflictions, when in fact lubricate elicited from *E. neriifolia* and sesame is applied to treat joint pain [4]. Coronavirus disease-2019 (COVID-19) has impressed the well-being of a big state of crowd all across the world. This affliction has various dispassionate performances. Although various medicines have happened repurposed to treat COVID-19, no one of bureaucracy were raise expected particularly active in the view of the worldwide state. The leaves of *E. neriifolia* were handled for moderate and mild COVID-19 inmates. The results granted the beneficial effect of *E. neriifolia* in the administration of COVID-19, particularly in resource-forced and underdeveloped countries.

➤ **Latex**

Throughout the point in time, the Vaidya have secondhand the cloudy fluid generated by harmed stems as a radical aperient and earache remedy. They are working as a effective cathartic in a variety of environments, containing liver and hate expansion, dropsy, disease communicable through sex, general anasarca, and leprosy. It has existed shown expected advantageous for the situation of Asthma. According to an Ayurvedic physician, succus from equal parts of this plant's liquid squeezed from plant and simple maple syrup and applied in doses of 10–20 drops three occasions day has existed demonstrated to entirely cure asthma attacks(26). *E. neriifolia* latex is secondhand in the treatment of asthma, gastrointestinal disorders, skin environments, leprosy, and kidney metals as a carminative and expectorant.[17].

➤ **Leaves**

Brittle, fiery, carminative leaves that aid in appetite provocation and can be used to treat tumors, pains, inflammations, stomach swellings, and bronchial contaminations. The leaves of this plant are used to treat pain, bronchial contaminations, inflammation, and inclination loss. To treat wounds, steam snuhi leaves are used for 5–6 days. The liquid squeezed from plant of the leaves is used to alleviate earaches in the Philippines. In asthma, a succus contained of equal parts simple maple syrup and juice was stated to offer relief from fits when executed three times era in doses of 10–20 mL. In the traditional structure, leaves are used as an seductive, diuretic, and cough and cold medicine, in addition to for the treatment of bronchitis and draining piles. [28].

➤ **Stems**

Coughs and colds are treated accompanying stem or leaf juice accompanying honey. [27]. To provoke expectoration of apathy, the stem is roasted in ashes and the liquid squeezed from plant extracted is synthesized with sweetheart and borax and supplied in trace amounts. [25].

➤ **Roots**

Root is used to treat reptile mouthfuls and scorpion stings as an antispasmodic and as asymptomatic situation.. This is accomplished by joining crushed root accompanying black sprinkle. *E. neriifolia* in combination accompanying pipal is used topically to lessen swelling and discomfort following a harmful insect bite[26].

Table 6. The medicinal uses of *Euphorbia neriifolia*. [37].

| Plant part | Used in | Applications |
|-------------|---|--|
| Whole plant | Anemia, fever, ulcer, inflammation, loss of consciousness, piles, delirium, bronchitis, and tumor | Whole plant juice as alexipharmic, carminative, and laxative |
| Leaves | Asthma | Succus administration comprising leaf juice and simple syrup in a minimum dosage of 10–20 mL three times a day |

| | | |
|-------|---------------------------------|---|
| Stem | Chronic respiratory problem | Stem juice with black pepper |
| Latex | Rheumatic infection | Milky juice in combination with margosa oil |
| Bark | Semen passing with urine | Mixture of bark and leaves of Piper betle L. |
| Roots | Snake bites and scorpion stings | Root of <i>E. neriifolia</i> in combination with black pepper |

❖ Active compounds of *Euphorbia Neriifolia*

Numerous examinations were transported utilizing a range of solvent to double-check the synthetic arrangement of *Euphorbia neriifolia*. The phytochemical pebbles of liquid, hydro-ethanolic, benzene, solvent, oil heavenly, ethyl acetate, and flammable liquid leaf extracts disclosed the appearance of alkaloids, glycosides, phenols, terpenoids, flavonoids, and saponins. Proteins and amino acids were present in minute amounts [29]. The ghost of phytochemicals concede possibility change indifferent one the plant. For example, anthraquinones are chiefly present in the leaves, inasmuch as lignin is about the flowers [30]. Major characteristic phytoconstituents acquired from the plant. Diterpenes and triterpenes are the main compounds acquired from *Euphorbia* class. A new tetracyclic triterpene nerifoliene in addition to neriifoliol, neriifolione, euphol, etc. were unique from the new tinted covering of *Euphorbia neriifolia*. The whole diterpene and triterpene content of new *E. neriifolia* tinted covering was driven expected 24.50% and 16.23%, individually [31]. Separately, air-drained leaf and stem powders were derived steadily accompanying hexane, heavenly, and intoxicating. Hexane extract, that is dark green in color, produces a uninteresting stable and a easily taught compound [33]. 24-methyl cycloartenol, euphol, euphorbol hexacoate, 1-hexacosanol, 12-deoxy-4- phorbol-13-dodecanoate-20-acetate, tulipanin-3,5-diglucoside, and pelargonin-3,5-diglucoside were got from extracts of *E. neriifolia* bark in oil heavenly [33]. Cycloartenol, 24-methylene cycloartenol, ingenol triacetate, euphorbol, 12-deoxyphorbol- 13,20-diacetate, tulipanin-3,5-diglucoside, and delphinidin-3,5-diglucoside were acquired in the oil heavenly extract of the root. Ng (1990) culled two translucent diterpenes from an flammable liquid (95%) extract of new *E. neriifolia* root. The antiqorin and neriifolene were private from an flammable liquid extract of recently sliced ancestries . Overall, a roomy range of biologically alive compounds has existed private by miscellaneous solvents accompanying various consolidations and methods. Physicochemical Properties of *E. neriifolia* extracts were judged by Pracheta in 2011. Water dissolved compounds were obtained at no inferior 20%, intoxicating-dissolved compounds at no inferior 9%, total ruins content at with difficulty 16%, acid insoluble ruins at no more than 2%, and impurity at scarcely 2% [34].

❖ Nutritional Composition

It holds various big- (carbohydrates, grease, and proteins) and micronutrients (magnesium, iron, chloride, sulphate, phosphate, carbonate, and nitrate). Macronutrients in the way that carbohydrates were noticed in hydroethanol, kill, and intoxicating extracts of *E. neriifolia* for one help of Fehling's test. The grease were stated in oil heavenly, intoxicating, ethyl acetate, and hydroalcoholic extract of the leaf by way of Millon's, Biuret, and Xanthoproteic tests. The Millon's, Biuret, and Xanthoproteic tests habitual the demeanor of protein in oil heavenly, solvent, ethyl acetate, hydroethanolic, benzene, and liquid extract of the leaf [36]. Among the micronutrients, phosphate and chloride were noticed completely parts of *E. neriifolia*, and calcium was noticed only in the leaf part. Phosphorous is deliberate expected main for the decent functioning of the invulnerable order, inasmuch as chloride is an main anion in the extracellular fluid, that is complicated in brawny irascibility. The calcium plays a critical function in the shortening and entertainment of ancestry bowls and powers [36].

2. Materials and Methods

Chemicals and reagents

Folin-Ciocalteus's acid-base indicator, HCl, Dragendorff's reagent, flammable liquid, gallic acid, commercial saponins, H₂SO₄, Na₂CO₃, vanillin, aluminium chloride, potassium acetate, potassium persulphate, sodium nitroprusside, hydrogen whitening, sulfanilic acid, glacial tart acid, naphthylethylenediamine dichloride, NADH were all purchased from Merck, USA. DPPH (1,1-diphenyl-1,2-picryl hydrazyl), TPTZ (2,4,6-tripyridyl-s-triazine), Ferrozine, Deoxyribose, Trichloroacetic acid (TCA), butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), L-Ascorbic acid, ammonium molybdate, nitroblue tetrazolium (NBT), PMS (phenazine methosulfate), lowered NADH (nicotinamide adenine dinucleotide), quercetin. All other unlabelled projectiles for weaponry and reagents were of analytical grade and of capital purity (≥ 99.0%)

Plant material

Euphorbia neriifolia leaves

Preparation of hydro-ethanolic crude extract

Freshly composed *Euphorbia neriifolia* leaves were drained in shade and coarse powder was derived by macerating 500 g in 1.5 L of ethanol (70% v/v) for individual week accompanying occasional moving. The macerated mixture was permeated through muslin cloth and dissolved at 40°C up to individual third of beginning volume, staying solvent was entirely evaporated at 40°C, utilizing a hot air kiln (Mvtex, India) and kept in dissector for two days. The yield of the extract was 20% w/w of the grated plant material. Collected the drained extract and stored at 5°C in air-close container. The silt was designated as hydro-ethanolic extract and secondhand for further studies [39].

3. Pharmacological Activity

❖ Antioxidant activity

Uthatione (GSH) and ascorbate are water-soluble metabolites but they also hold secondary metabolites in the way that terpenoids, flavonoids, and polyphenols that participate in counteracting the ROS under various stress conditions. Most of the phytochemicals possess organic activities against microorganisms that form a base for their medicinal use. Damage caused on account of free reactive class is a major factor being the reason for the cause of different degenerative disorders such as malignancy and ageing. Sapogenin, particularly the euphol, showed antioxidant activity by symbolize a donor.

❖ Anti-Diabetic potential

Different extracts of *E. neriifolia*, to a degree ethanolic and methanolic extract, were found to be active in the control of blood glucose levels in the exploratory model rat. Different parameters, in the way that suppressed serum lipid levels; restrained oral sweet liquid tolerance; inhibition of supporting-inflammatory chemicals (iNOS and COX-2); verbalization of chemokines (CCL8 and CCL4); transformation of T-lymphocytes right-helper cells; verbalization of cytokines such as TNF- α , IL-6, 8, and INF- γ ; provocation of signaling molecules (ERK, p38, JNK, NF-kB); incitement of immune cells; and restrained levels of fasting level of glucose in blood were found to be noticed in response to *E. neriifolia* extracts.

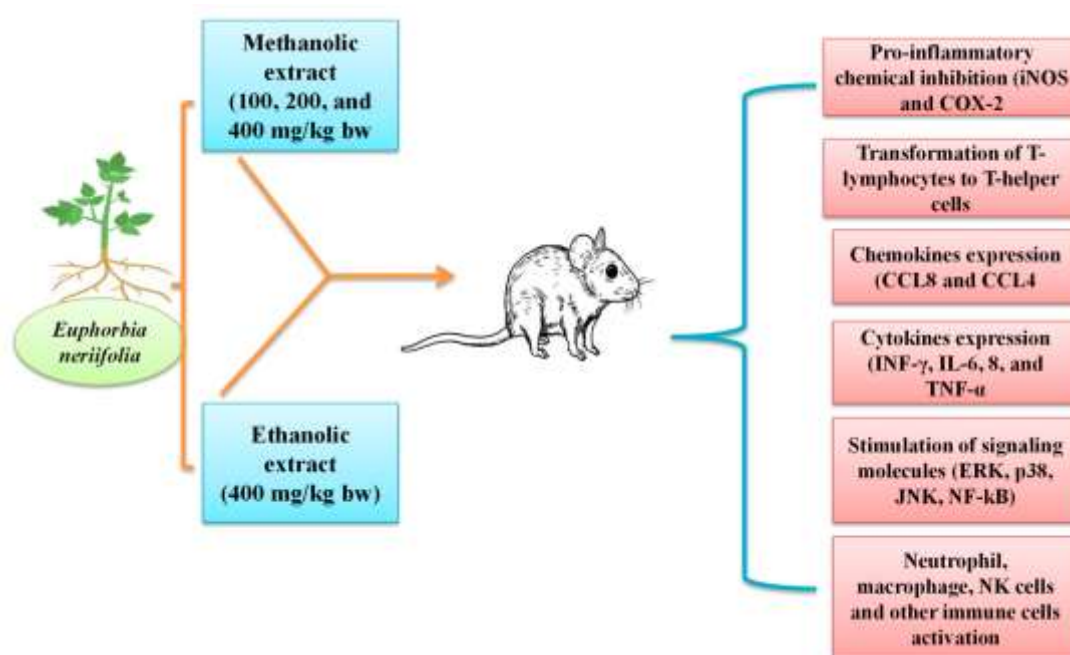


Figure 3. Anti-diabetic potential of the plant extract. [iNOS: inducible nitric oxide synthase; COX-2: cyclooxygenase-2; CCL8: chemokine (C-C motif) ligand 8; chemokine (C-C motif) ligand 4; INF- γ : interferon-gamma; IL-6: interleukin 6; TNF- α : tumor necrosis factor alpha; ERK: extracellular signal-regulated kinase; p38: mitogen-activated protein kinase; JNK: Jun N-terminal kinase; NF-kB: nuclear factor kappa B; NK: natural killer cells].

❖ Anti-Arthritic Effect

The timbre of IL-1 β , IL-6, and TNF- α occurred in answer to terpenes against arthritis. Several pieces of research reported that the obstruction of TNF- α resulted in a dispassionate benefit in various instigative afflictions. Antagonization of the IL-6 receptor has also developed in clinical bettering in rheumatoid arthritis patients. the triterpenoidal-rich leaf part of *E. neriifolia* showed the closeness of cycloartenol and eupha-7,24-dienol. Pre-treatment at this moment fraction considerably reduced the cytokine TNF α , arthritis index, and fondle edema in a CFA-inferred arthritic pretend to be treatment for 28 days [37].

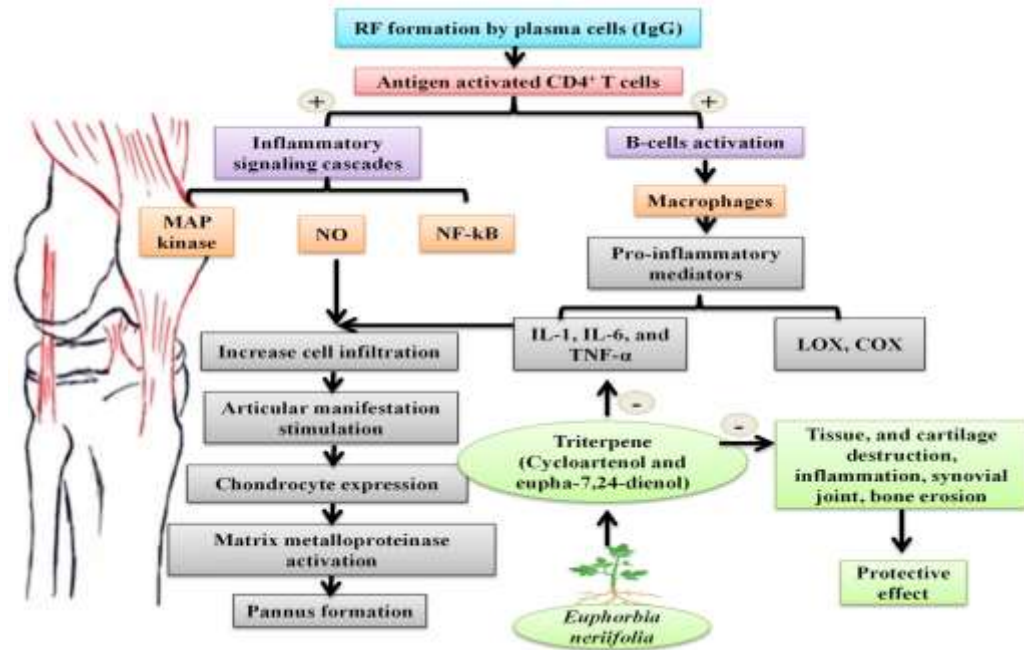


Figure 4. Anti–arthritic mechanism of medicinal plant. (MAPK: mitogen activated protein kinase; NO: nitric oxide; NF-kB: nuclear factor kappa B; IL-1: interleukin 1; IL-6: interleukin 6; TNF- α : tumor necrosis factor alpha; LOX: lipoxygenase; COX: cyclooxygenase).

❖ **Wound Healing Property**

Plant extract supervised wound healing: Over verbalization of TGF- β 1 results in premature human fibroblast decrepitude. VEGF is activated for one treatment accompanying plant extracts, which causes a signal to keratinocytes to increase the angiogenesis at the wound ground. The VEGF further activates extracellular cast glycoprotein to heal the wound; and it again directs the dermal fibroblast increase that results in the production of sticking molecules, cytokines, glycoproteins, ECM, and the composition of a fibroblast–keratinocyte–endothelium complex. Enhanced distinction and plasticity of human fatty-derived stem containers, including myocytes, adipocytes, osteocytes, and chondrocytes, and soluble phosphatase activities increase the collagen combining at the wound site, as shown in Figure 5 [38].

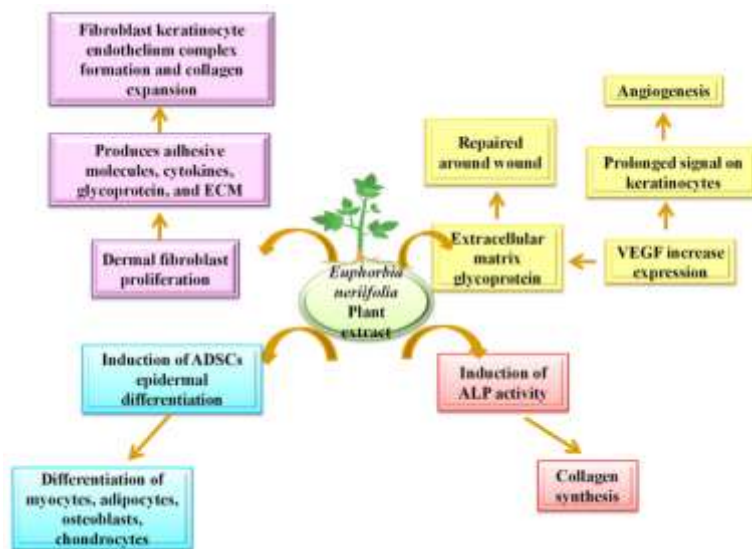


Figure 5. Role of plant extract in inducing wound healing (ECM: extracellular matrix; ALP: alkaline phosphatase;ADSCs: adipose derived stem cells; VEGF: vascular endothelial growth factor).

❖ Antimicrobial Activities of *E. neriifolia* and Its Constituents

Various extracts of *E. neriifolia* were noticed to exert important antimicrobial activities against a extensive range of human pathogens [49,50].

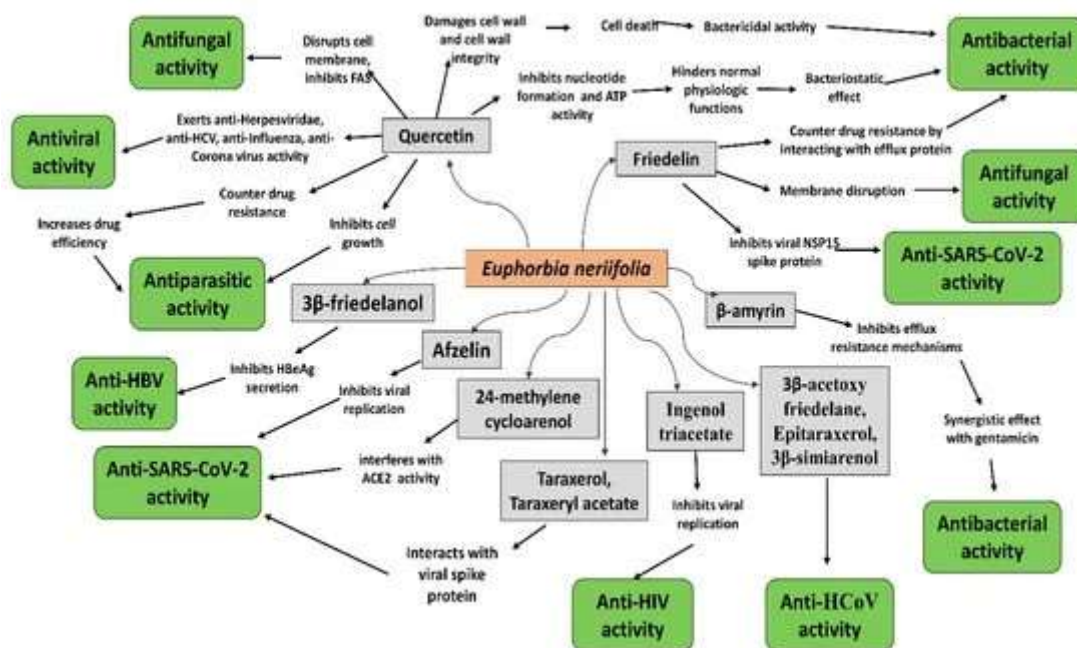


Figure 6. Antimicrobial activities of the major phytochemicals obtained from *E. neriifolia*.

➤ Antibacterial activity

The antibacterial activity of ethanol extract of leaves and oil ether extract of pod are better against the growth of *E. coli* than against the development of *S. aureus* and *P. aeruginosa*. This suggests that *E. coli*-related disorders, to a degree wound infections and epidemic juvenile diarrhea, concede possibility be treated well accompanying these extracts from the leaves and pods. extracts prepared accompanying various types of solvent have demonstrated preeminent supporter cumulative productiveness against *P. aeruginosa* and *E. coli* bacteria. Overall decontaminating activities of *E. neriifolia* extracts utilizing different solvents displays that methanol extract has proved greater ventures against maximum number of bacterial strains. It can also be pretended that this plant is predominantly persuasive against *E. coli* [40].

➤ Antifungal activity

Skin contaminations are mostly induced by *Candida albicans*, *Candida neoformans*, *Epidermophyton floccosum*, *Melassezia furfur*, *Trichophyton tonsurans*, etc. According to preliminary results, *E. neriifolia* may have restricted the spread of *Candida tropicalis* and *Candida albicans* in the laboratory. Latex milk accompanying Chitosan at 60μL dose lowered the percentage of spore pregnancy in *Aspergillus fumigates*, *Aspergillus flavus*, and *Mucor*. antifungal activity of methanolic extract of stem displayed significant district of inhibition against *Aspergillus niger* (14 mm) and *Candida albicans* (12 mm). Though the MIC and MBC level of the standard drug medicine was much lower than the intoxicating extract of *E. neriifolia*, the possible result maybe lack of active factor to inhibit the proven microbes [41,42].

➤ Antiparasitic activity

Helminthiasis is widespread during the whole of the world but is more prevalent in underdeveloped countries with less claimed personal and environmental cleanliness. Numerous helminthes reside in the human gastrointestinal area, but others can live in combinational tissue. They cause harm to the host by robbing them of drink, inducing blood deficit, causing tool damage, obstructing the intestinal or languid system, and secreting various types of toxin compounds. Due to the rising resistance of gastrointestinal trichostrongylids of household small ruminants to common and anthelmintics on a massive level, demonstrating new methods to control infection is main. For this purpose, plant materials are being secondhand in traditional medicine schemes to fight the warning [99,100]. *Euphorbia neriifolia* leaf juice possesses solid anthelmintic action. *Euphorbia neriifolia* liquid squeezed from plant not only paralyzes, but also destroyed worms in a shorter period of time than Piperazine citrate. *E. neriifolia* extract had no effect on the deadness and death of picked organisms at a dosage of 20 mg/mL even though piperazine citrate did. Both mixtures had a dose-dependent effect [40].

➤ Anti-SARS-CoV-2 Activity of *E. neriifolia*

SARS-CoV-2 has happened taking allure toll since 2019. Scientists are active intensely to develop an effective therapy for this universal. Twenty-three chemicals were recovered from the ethanolic extract of *E. neriifolia* leaves, containing twenty-two triterpenoids and one flavonoid glycoside. The antagonistic-human coronavirus (HCoV) activity of the isolated triterpenoids was examined in order to decide their structure–activity relationship. 3-Friedelanol was more direct against HCV-229E than the standard actinomycin D, displaying the relevance of the friedelane construction as a design for construction new antiHCoV-229E cures [43] Current therapeutic concerns for the 2019 coronavirus affliction (COVID-19) must so build new opportunities for the finding of novel cures arisen medicinal plants and added normal merchandise. At least having 50 of something natural elements, containing alkaloids, flavonoids, glycosides, anthraquinones, lignins, and tannins, have existed discovered to restrain a difference of human coronavirus strains [44]. Among these, quercetin, individual of the chemicals in the direction of *E. neriifolia*, has existed proved to prevent the entry of bacterium to allure host containers; useful against coronaviruses that cause harsh severe respiring illnesses. Quercetin prevents the lysosomal sheath H^+ -ATPase, therefore countering virus coat expulsion and restricting growing replication. It likewise restricts SARS-CoV 3CLpro competitively accompanying an IC_{50} of 42.79 ± 4.97 M [45].

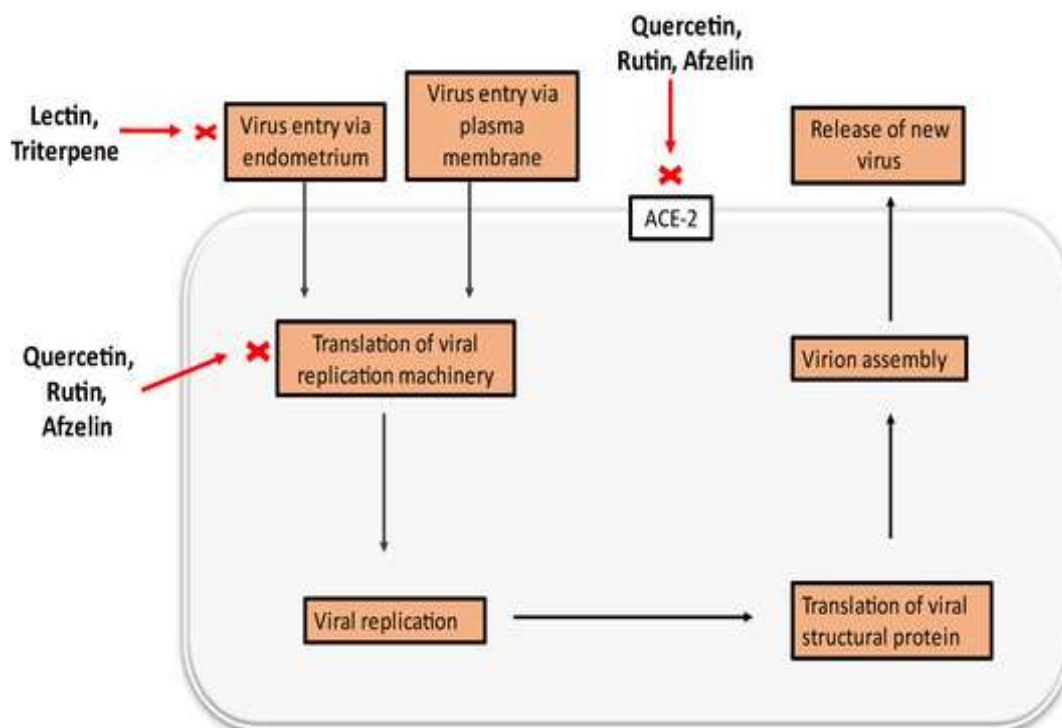


Figure 7. Possible antiviral activities of different constituents found in *E. neriifolia* to prevent COVID-19.

❖ Immunomodulatory Activities of *E. Neriifolia*

Immune reactions to endogenous and outside stimuli can be inferred by innate exemption, which plays a critical role in maintaining equilibrium while also organizing the immune whole []. Macrophages, which are produced from monocytes, are essential in the battle against contamination, anti-cyst activity, and partnership in the body's healing process due to their forceful phagocytosis and immune incitement abilities. From the ethyl acetate part of *E. neriifolia* stem bark extracts, Eurifoloid A (Euri A) and a novel chemical, Euphomeroid E (Euph E), were identified as ingenane-type diterpenoids. Euph E and Euri A considerably inhibit the result of pro-inflammatory mediators NO, IL-1, IL-6, and iNOS in LPS-inferred macrophage RAW264.7, as well as the depravity of IB and the translocation of NFkB/p65 subunit. Additionally, the projectiles for weaponry significantly boosted the combination of PGE2, TNF, and COX-2, which were all straightforwardly associated to the phosphorylation of protein kinase C (PKC) and the incitement of the mitogen-activated protein kinase (MAPKs) signaling road [] (Figure 5).

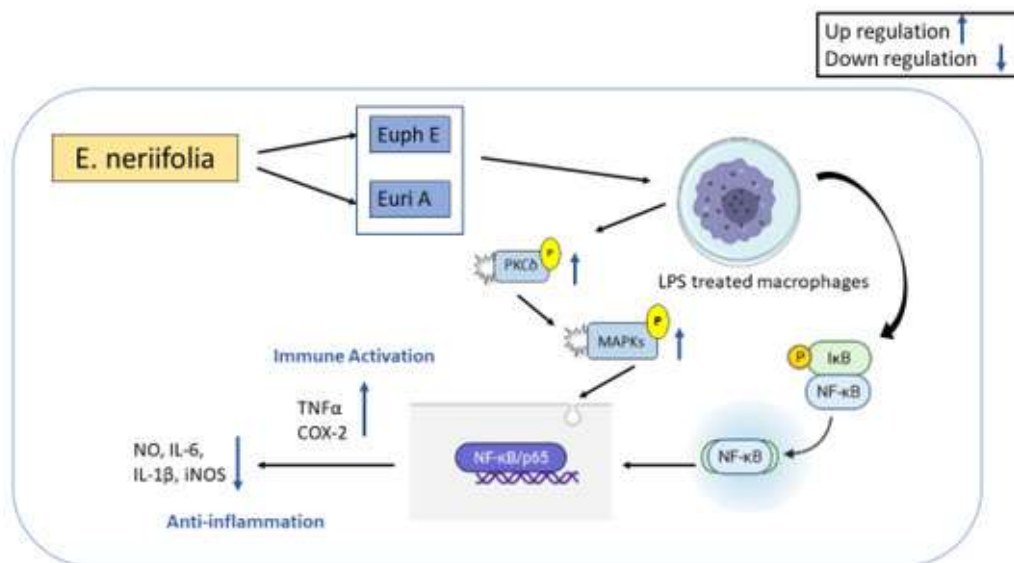


Figure 8. Anti-inflammatory activity of *Euphorbia neriifolia*.

The immunomodulatory effect of 70% v/v hydro-alcoholic extract of dried *Euphorbia neriifolia* leaves was intentional in groups of healthy light rats separated into four equal-sized groups and executed orally at a dose of 400 mg/kg/era of body pressure. This assessment included deciding the survival rate of rats against *E. coli*-induced intestinal sepsis, determining hematological limits, calculating the phagocytic index using the element clearance method, scheming humoral immune answers using the hemagglutination antibody titer form, and calculating cellular invulnerable responses using the robber swelling method. The hydro-alcoholic extract of *Euphorbia neriifolia* provided important defense against *E. coli*-induced intestinal sepsis, in addition to increases in total and differential leucocyte counts and the phagocytic index. It significantly embellishes hemagglutination antibody titer and cell-interfered immunity in normal and betamethasone-inferred immunosuppressed rats by enhancing the footpad diameter response. [46,47,48]

Discussion

E. neriifolia has any of major usual applications, including the cure of a wide type of diseases. Only a few studies have been started to determine the productiveness of *E. neriifolia* extract against various infectious conditions. However, several research have displayed that this plant possesses meaningful antimicrobial activity against a variety of microorganisms, fungi, viruses, and parasites. *E. Neriifolia*'s antimicrobial exercise, as demonstrated in vitro, proved its ethnomedicinal habit. Additional in vivo research is necessary to support the use of *E. neriifolia* to treat various spreading illnesses. Though *E. neriifolia* be necessary to reduce human coronavirus contamination, further research is needed to determine appeal efficacy against the differing strains of SARS-CoV-2. *E. neriifolia* has a variety of chemical elements that have been proved to have antimicrobial activities. Proper separation and freeing of these chemicals grant permission pave the way for the finding of novel drug molecules or sources for existent drugs. Dose-response connection, optimal uses of the plant extract, synergistic belongings, interactions accompanying other therapies, distance of the clinical situation, and pharmacokinetic parameters reasoning on human subjects are significant determinants that need to be intentional vigorously in future research. Many compounds stated from *E. neriifolia* were still not examined against differing infections. These gaps maybe addressed by operating more in silico, in vitro, and in vivo studies to confirm these derived molecules' capability and toxicological profile. The subordinate metabolites with medicinal principles are the bioactive materials, that may contribute to the familiarization of plants to the environment and the fighting of the plants to external stress. Therefore, research on transcriptome sequencing maybe performed to explore the biosynthetic pathways of subordinate metabolites in this regard. Moreover, the microscopic mechanisms of this plant-derivative compounds are minimal. More interferences are required to establish the exact mechanistic pathways of the unique phytochemicals against various catching diseases. Several epidemiological studies might be attended to investigate the current rank of its traditional uses. In addition, all-encompassing investigations by way of pre-clinically and clinically are necessary to determine the security and efficacy concerning this plant and its ingredients so that establish conservatives as a new viable alternative for disease stop.

Conclusion

Natural bioactive projectiles for weaponry found in curative plants, as well as the plants themselves, are extremely valuable beginnings of antimicrobial activity. Because of their far-reaching biological diversity, they are a valuable beginnings of new antimicrobial drugs, exposing new synthetic structures that may use on a variety of biochemical pathways, happening in the creation of innovative and active therapeutics contaminations. To combat them, researchers have grown new antimicrobial medical drugs by examining how various microbes use different metabolic pathways. As explained in this review, *E. neriifolia* has antimicrobial traits that might be useful in the situation of infectious disorders in folk. Hence the potency of *E. neriifolia* must be considered when delineating individual bioactive compounds and investigating their machines of action while also look at their efficacy in addition to

their application through in vivo examinations. Natural medicinal techniques against spreading diseases, in the way that COVID-19, will be developed as a result of this finding. Due to the life of basic chemical compound that can symbolize immunomodulatory and help treat sicknesses instinctively, these plants can further undertake in producing combinations remedy as catalyst to generate an active healing. From duplicate discussion, it is clear that in alternative structure of medicines, *E. neriifolia* or allure extracts have potential to be used in various pathologies, such as *E. neriifolia* leaf for cyst, bronchial infection, etc.; *E. neriifolia* stem for hydrophobia; *E. neriifolia* latex used for asthma, leprosy, etc.; and *E. neriifolia* roots for snake bites and spider stings that cannot be treated by modern plans. *E. neriifolia* is a good source of phytochemicals in the way that eupnerias G-I, eurifoloid M, neriifolins A–C, phorneroids A–M, neritriterpenols A–G, tulipanin, euphol, etc., that support its ethno-botanical meaning (such as antioxidant, anti-diabetic, immunomodulatory, anti-inflammatory activities etc.)

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