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Open Access REVIEW

Botanical Description and Pharmacological Properties of *Clitoria ternatea*, *Piper nigrum*, *Glycyrrhiza glabra*, and *Ocimum tenuiflorum*: A Review

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ABSTRACT

Clitoria ternatea had nootropic, anticonvulsant, and anti-inflammatory effects. It improves memory and raises rat acetylcholine levels. The flower is generally bilateral; nevertheless, petal mutations exist in nature, resulting in a radial appearance of the bloom. The leaves have pinnate venation with seven leaflets. The terminal leaflet is larger, while the base leaflet is smaller. The pods are flat, linear, and exhibit olive, brown, and black hues, measuring around 5-7 cm in length and holding 6-10 seeds per pod. It contains the alkaloids, glycosides, flavonoids, resin, saponins, phenols, triterpenes, proteins, and carbohydrates. In reality, black pepper, green pepper, and white peppercorns are all the same fruit (Piper nigrum); the color differences are due to different phases of maturation and processing techniques. When the pepper berries are half-ripe and on the verge of turning red, they are picked to make black peppercorns. Pepper contains the alkaloids i.e., piperine (5-9%). In northern India, Glycyrrhiza glabra is known as mulethi. *G. glabra* is native to the Mediterranean and certain regions of Asia. Sweet wood, licorice, madhuk, and kalitak are some names for it. Cough, cold, pain, edoema, and other conditions have historically been treated with G. glabra. The plant is a herbaceous perennial that reaches a height of one to two meters and has a long, robust main taproot. The taproot is 15 cm long and has three to five offshoot taproots. New stems are produced every year. The leaves are alternating, drooping, and pinnately unique. One species or variant of the Lamiaceae family of plants is *Ocimum tenuiflorum L*. It has contributed to science from ancient times to the present day in current practices because of its many restorative potentials. In conclusion, *Clitoria ternatea* (leaves), Black pepper (seeds), *Glycyrrhiza glabra* (root), and Tulsi (leaves) exhibited the numerous pharmacological potentials. Therefore, these herbs are promising research moiety which can be utilized in the management of various deadly ailments.

Keywords: *Clitoria ternatea, Glycyrrhiza glabra, Piper nigrum, Ocimum tenuiflorum,* pharmacological properties.

INTRODUCTION

1. Aparajita (*Clitoria ternatea)*

The twining plant *Clitoria ternatea* grows in four different countries every year: India, China, the Philippines, and Madagascar. It belongs to the family Fabaceae. Acute bronchitis, asthma, and frantic fever can all be alleviated with the administration of the roots because of its laxative, diuretic, anthelmintic, and anti-inflammatory effects. Paste is commonly used to treat mucous problems, sore throats, and stomach

inflammations; root was historically used to cause abortions. *C. ternatea* had nootropic, anticonvulsant, and anti-inflammatory effects. It improves memory and raises rat acetylcholine levels [1].

Flower is the aesthetically pleasing portion of the plant. These are available in single or paired configurations in several hues, including mauve, white, and both dark and light blue. The pedicles and bracteoles can reach lengths of 4-9 mm and 12 m, respectively, while the corolla has one regular petal, two keels, and two wing petals. The standard petal is the biggest among all the petals [2].The flower is generally bilateral; nevertheless, petal mutations exist in nature, resulting in a radial appearance of the bloom. The leaves have pinnate venation with seven leaflets. The terminal leaflet is larger, while the base leaflet is smaller.

The pods are flat, linear, and exhibit olive, brown, and black hues, measuring around 5-7 cm in length and holding 6-10 seeds per pod [3].

a) Plant

b) Flowers and Seeds

Fig 1. Depiction of *Clitoria ternatea* plant

Taxonomy

Kingdom:	Plantae
Family:	Fabaceae
Subfamily:	Faboideae
Genus:	*Clitoria*
Species:	*ternatea*

It contains the alkaloids, glycosides, flavonoids, resin, saponins, phenols, triterpenes, proteins, and carbohydrates [4].

Pharmacological properties

Anti-inflammatory & analgesic

The methanol extract of C. ternatea exhibited significant antipyretic activity. When administered orally to mice, C. roots methanol extract was shown to reduce acetic acid-induced vascular permeability and carrageenin-induced paw edema [5]. In a different investigation, C. ternatea flower petroleum ether extract (60-80ºC) showed significant anti-inflammatory activity at both dosage levels.

Anxiolytic

Oral administration of an alcoholic CT extract to rats at a dosage of 460 mg/kg significantly reduced the amount of time it took for them to escape the chlorpromazine maze. Evidence of a nootropic effect from *C. ternatea* was seen in a considerable rise in the discrimination index and inflexion ratio at 100 mg/kg [6].

Antimicrobial

The antibacterial activity of alcoholic and aqueous extracts from in-vitro produced calli was tested using the agar well diffusion technique. The results showed that Salmonella spp. and S. dysenteriae, which cause enteric fever, exhibited antibacterial activity [7].

Nephroprotective

It has been discovered that administering *C. ternatea* ethanol extract has a nephroprotective effect against APAP-induced nephrotoxicity. It provides experimental proof that *C. ternatea* retained histoarchitecture, raised myocardial enzyme levels (antioxidants), and enhanced heart function following APAP dosage [8].

Anti-stress

The effectiveness of airborne components in alleviating stress was examined in rats and mice under a variety of situations, including those that cause ulcers (cold restraint stress), twitching of the head (Li), hypothermia (clonidine), respiratory failure (sodium nitrite), and catalepsy (haloperidol) [6].

Larvicidal

The most encouraging aspect of the research was the effectiveness of C. ternatea against mosquito larvae. A. stephensi, A. aegypti, and C. quinquefascitus larvae were all effectively killed by methanol extracts of *C. ternatea* seed, with LC_{50} values of 65.2, 154.5, and 54.4 ppm, respectively [7]

CNS depressant

The calming effects of *Clitoria ternatea* on the brain make it useful for treating symptoms including vertigo, syncope, and brain weakness. The effects of *C. ternatea* on seizures, tension, anxiety, depression, and mental performance were the focus of the study. The methanolic extract of *C. ternatea* showed nootropic, anxiolytic, depressive, anticonvulsant, and antistress effects when tested with Pentylenetetrazol and maximal electroshock [10].

Proteolytic

In cotyledons, endopeptidases rose at day 3 before decreasing, but carboxypeptidase and aryl amidase increased and peaked at day 9. Arylamidase was low, while endopeptidase and carboxypeptidase activity in the axial tissue rose until day 9 before declining. Acidic endopeptidases and carboxypeptidases are involved in the degradation of storage proteins, as evidenced by their enhanced activity in germinating cotyledons [6].

Antioxidant

In Thailand, *C. ternatea* flower extracts are used as a cosmetic agent, and the flowers' chemical makeup raises the possibility that they contain antioxidant qualities. Higher antioxidant activity was demonstrated by C. ternatea water extracts compared to ethanolic CT extract.

Anthelmintic

We tested the inhibitory potential of C. ternatea leaf extracts in both water and methanol on free-living nematodes. Using mature P. posthuma Indian earthworms, another study looked at the anthelmintic effects of

C. ternatea's stems, roots, flowers, and leaves. Among the several extracts tested, the methanolic root extract paralyzes and kills worms more quickly and effectively than any of the others. Roots, stems, blooms, and leaves all contribute to a rise in potency [9]

Respiratory system

Because it calms the respiratory organs and serves as an expectorant, it is used to treat coughs, asthma, and common colds. The entire plant is smoked aside from that. Decoction is used to relieve symptoms of garglingin throat. Asthma and coughing up sticky mucus might be relieved by combining root juice with milk. When taken orally, it can also be used to treat whooping cough [11].

Anti-cancer

Recent research has shown that plants and their constituents can function as apoptotic inducers in cancer cells, tumor suppressors, and the most popular herbal remedy can inhibit the growth of tumors, disrupt the course of the cell cycle, and stimulate the immune system. Extracts from Clitoria ternatea are closely linked to previous findings on the anti-carcinogenic or cancer-suppressive properties of several plant extracts [12]. Using the trypan blue dye exclusion method, the cytotoxic effects of petroleum ether and ethanolic CT flower extract were assessed in vitro. The plant extract concentrations utilized were 10, 50, 100, 200, and 500 g/ml, with a control also included. In both cases, increasing the concentration of the extract caused a decline in the cell count. Every concentration examined showed an increase in cytotoxic activity that was dose-dependent. The petroleum ether extract was reduced by 8% at a concentration of 10g/ml and by 100% at a concentration of 500g/ml. The cell count fell by 1.33% at 10 g/ml and by 80% at 500 g/ml [13].

Anti-convulsant

An ethanolic extract of aerial portions of CT was tested for its anticonvulsant activity in rats using the maximum electroshock seizure test and the pentylenetetrazol test. There were no noticeable effects in the 230 and 460 mg/kg groups. How a component in a methanolic extract from the air might alleviate stress. Ulcers brought on by cold-restraint stress were subjected to CT scanning. twitching in the brain caused by lithium, hypothermia in rats and mice caused by clonidine, respiratory failure caused by sodium nitrite, and catalepsy caused by haloperidol. Using CT scans was part of the treatment plan. Doses of100,200, and 400 mg/kg considerably decreased the ulcer index. CT reduced ulcer index in a dose-dependent manner and exhibited anti-stress properties. At a dose of 100 mg/kg, CT dramatically reduced the occurrence of head injuries [14].

Anti-diabetic

C. ternatea leaf extracts in methanol, water, petroleum ether, and chloroform were studied for their acute and subacute hypoglycemic effects in rats that had diabetes caused by streptozotocin. in streptozotocin-induced diabetic rats. between two hundred and four milligrams per kilogram of carbon. Blood glucose levels were markedly decreased by ternatea extract. The hypoglycemic effect was most noticeable at 400 mg/kg, while 200 mg/kg had a smaller impact. When it comes to controlling blood glucose levels over the long term, 200 mg/kg is significantly more effective than 100 mg/kg, according to subacute activity.

Anti-hyperlipidaemic

Rats with experimentally generated hyperlipidemia were shown to benefit from the anti-hyperlipidemic effects of Vigna mungo and *C. ternatea*, as well as from hydro-alcoholic extracts of the latter's root and seed. The hydroalcoholic preparations of CT's roots and seeds demonstrated this. Following therapy, the HDL/LDL ratio and the atherogenic index were also improved in rats with diet-induced hyperlipidemia.

Anti-histaminic

The antihistaminic properties of CT roots were tested using the mice's clonidine-induced catalepsy and the haloperidol-induced catalepsy paradigm. Histamine H1 receptor antagonists prevent catalepsy in mice caused by the 2adrenoceptor agonist clonidine, but not H2 receptor antagonists. A number of asthmatic symptoms are brought on by the production of histamine by mast cells, which is triggered by clonidine. ECTR and CPM, however, do not prevent catalepsy brought on by haloperidol. The results show that ECTR has antihistaminic qualities [15].

Learning and memory

This study demonstrated that oral administration of CT root extracts to rats considerably improved their memory. Newborn rats were tested for improved learning and memory using the open field behavior test, passive avoidance test, and spatial learning test. CT aqueous root extract was used in the treatments. The memory-enhancing characteristics of CT root extract were demonstrated at both time points of the behavioral testing. It boosted retention and spatial learning ability, but had no impact on general motor activity.

Antidepressant

Using the tail suspension test, research found that methanolic CT extract of the aerial section has antidepressant properties at dosages of 100 and 400 mg/kg. When CT was administered orally, the duration of immobility was significantly shortened. While improving cognitive abilities, CT decreased total immobility time and did not result in sleepiness or behavioral toxicity. An alcoholic extract of the aerial section of CT was tested for its soothing effects in rats using the conditioned avoidance response test [16].

Hepatoprotective

According to studies on paracetamol-induced liver damage, mice given the ME of CT leaf (200 mg/kg) had far lower levels of ALT, AST, and bilirubin compared to the paracetamol group, which had significantly higher levels of all three. Researchers have also shown that CT leaf extract treatment protects against changes in histology [17].

Wound healing

The effectiveness of CT seed and root extracts in speeding wound healing was tested in rats using excision, incision, and dead-space models. Cotrimoxazole ointment was associated with these outcomes. Results showed that CT had an effect on the wound healing processes of proliferative, remodeling, and inflammatory phases [18].

Antipyretic

Rats' yeast-induced fever was lowered by Clitoria ternatea, suggesting an antipyretic effect. At both doses studied, the extract decreased the number of writings by 50.1% and 63.8%, respectively, whereas 150 mg/kg of aspirin induced a reduction of 70.9%. The overall results indicate that C. ternatea methanol extract possesses potent analgesic and antipyretic qualities.

LAs

An alcoholic CT extract (of the aerial component) was examined for its LA activity. A 10% alcoholic extract solution of the CT aerial component eliminated the foot withdrawal response in frogs, while the rabbit's cornea showed no signs of surface anesthesia. An alcoholic extract of the CT aerial component was nearly as effective as xylocaine in inducing local anesthesia [14].

2. Black pepper *(Piper nigrum)*

In reality, black pepper, green pepper, and white peppercorns are all the same fruit (Piper nigrum); the color differences are due to different phases of maturation and processing techniques. When the pepper berries are half-ripe and on the verge of turning red, they are picked to make black peppercorns. After that, they are allowed to dry, which makes them shrivel and turn dark. On the other hand, white peppercorns are picked when they are extremely ripe and then soaked in brine to remove their dark outer shell, leaving only the white pepper seed6, whereas green peppercorns are picked while still unripe and green in color. In reality, pink peppercorns come from a different plant species called Schinus molle, which is related to ragweed. Of all the pepper varieties, black pepper is the strongest and most tasty. It can be purchased as whole or broken peppercorns or processed into powder [19].

Taxonomy

Kingdom: Plantae

Class: Magnoliopsida

Order: Piperales

Family: Piperaceae

Genus: *Piper*

Species: *nigrum*

a) Black pepper plant with raw fruits

b) Dried fruits

Fig 2. Depiction of Black pepper plant

Pepper contains the alkaloids like piperine (5-9%), Volatile oil (1-2.5%), is responsible for the aroma of pepper and comprises of terpenes, like α- and ß-pinene, dipentene, Phenllandrene and sesquiterpenes., pungent resin (6%), Piperidine and starch (30%). The pepper volatile oil which is yellowish in colour contains mainly L-Phenllandrene and caryophyllene. The resinous content along piperine also contributes to the pungency of the drug [19].

Pharmacological properties

Antioxidant

Piperine and *P. nigrum* sustain superoxide dismutase, glutathione peroxidase, catalase, glutathione-S-transferase, and glutathione levels, therefore mitigating oxidative stress induced by a high-fat diet. The effectiveness of *P. nigrum* components has been established in many screens employing diverse solvent systems. The ethanolic extract of *P. nigrum* had an antioxidant activity of 74.61±0.02% and an IC_{50} value of

14.15 mg, indicating that it is a promising contender. In an amyloid-(1-42) rat model of Alzheimer's disease, a methanolic extract of *P. nigrum* fruits was investigated for its memory-enhancing and antioxidant properties at dosages of 50 and 100mg/kg, administered orally for 21 days. Consequently, it will be pivotal in neutralizing free radicals and postponing the aging process. According to reports, *P. nigrum* exhibits anti-oxidant properties, which could be attributed to the presence of flavonoids and phenolic compounds [20][21].

Anti-inflammatory

The anti-inflammatory capabilities were evaluated in vitro using interleukin-1 activated fibroblast-like synoviocytes derived from rheumatoid arthritis patients, while the anti-arthritic and analgesic effects were examined in rats utilizing a carrageenan-induced acute paw model of pain and arthritis. Prostaglandin E2, cyclooxygenase-2, interleukin-6, and matrix metalloproteinase levels were quantified using ELISA (enzyme-linked immunosorbent assay) and RT-PCR (reverse transcription polymerase chain reaction). A dose-dependent response is found at concentrations of 10-100µg/ml. Even at 10µg/mL, it significantly decreased prostaglandin E2 production. The expression of interleukin-6 and matrix metalloproteinase 13 was also inhibited. Piperine reduced the migration of activator protein 1 into the nucleus in interleukin 1-treated synoviocytes, but it did not affect the migration of nuclear factor B. Piperine significantly reduced pain and arthritic symptoms in rats. Piperine demonstrated anti-inflammatory, analgesic, and anti-arthritic properties in a rat model of arthritis [22].

Analgesic

The analgesic effectiveness of piperine was evaluated in vivo in mice. A tail-flick experiment was employed to evaluate analgesic efficacy generated by acetic acid-induced writhing. The acetic acid-induced writhing in mice was considerably reduced ($p > 0.01$) following intraperitoneal (i. p.) administration of piperine (30, 50, and 70mg/kg), akin to the effects of indomethacin, a nonsteroidal anti-inflammatory drug (20 mg/kg, i. p.). Morphine (5mg/kg, i. p.) and piperine (30 and 50mg/kg, i. p.) substantially prolonged the response time of mice in the tail-flick experiment ($p > 0.01$). Pre-treatment with naloxone (5 mg/kg i. p.) negated the analgesic effects of both morphine and piperine in these subjects. These investigations indicate that piperine possesses analgesic effects perhaps mediated by the opioid system [23].

Immunomodulatory

Piperine was shown to be cytotoxic to Ehrlich ascites carcinoma cells and Dalton's lymphoma ascites at a dose of 250 µg/ml when its immunomodulatory and anticancer properties were investigated. At 50 µg/ml, piperine showed cytotoxicity in L929 cells in vitro. Total white blood cell counts rise in Balb/c mice treated with piperine. Alpha-esterase-positive cells and bone marrow cellularity were increased by piperine injection [24].

Anti-cancer

Piper nigrum has demonstrated antitumor efficacy in many experimental animals. Numerous research have demonstrated the anticancer effects of oral ingestion of P. nigrum or piperine. The alcoholic extracts of peppercorn and piperine have significant immunomodulatory and anticancer effects. Piperine has been demonstrated to reduce lung cancer risk by altering lipid peroxidation and activating antioxidative defense enzymes [25][26].

Hepatoprotective

Numerous experimental studies in both animal and human models reveal that P. nigrum possesses a hepatoprotective effect. The methanolic extract of black pepper fruits (100 and 200 mg/kg orally for 15 days) and piperine (50mg/kg orally for 15 days) were evaluated for their efficacy against ethanol-CCl_4 induced hepatotoxicity in Wistar rats. The results indicated that black pepper significantly reduced hepatic biomarker levels, including triglycerides (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and bilirubin. Furthermore, MEPN and piperine effectively restored the diminished levels of superoxide dismutase (SOD), glutathione reductase (GSH), and catalase (CAT) caused by ethanol-CCl_4 treatment. The results were comparable to the Liv-52 reference standard (1 mL/kg, orally, for 15 days) [27].

Anti-convulsion

A separate study employed D-galactosamine to induce hepatic injury in mice, subsequently administering piperine in a dose-dependent manner. This intervention resulted in a reduction of serum levels of GOT (glutamic oxaloacetic transaminase) and GPT (glutamic pyruvic transaminase), suggesting that the effect was contingent upon hepatocytes and diminished sensitivity to tumor necrosis factor-alpha. The findings indicate

that P. nigrum possesses significant hepatoprotective properties that may be utilized as a therapeutic intervention for liver illness [28].

Anti-obesity

Numerous plants possess anti-obesity qualities, with P. nigrum being one such example. Black pepper extract and piperine significantly inhibited the adipocyte differentiation of 3T3-L1 cells in an antiadipogenesis study including 3T3-L1 preadipocytes, without affecting cytotoxicity. The expression of the master adipogenic transcription factor SREBP-1c, CCAAT/enhancer-binding protein beta (C/EBP-beta), and peroxisome proliferator-activated receptor gamma (PPAR-gamma) mRNA was significantly reduced. Piperine suppresses the rosiglitazone-dependent interaction between PPAR-gamma and cofactor CBP in a GST pull-down assay. Moreover, genome-wide studies employing microarray technology demonstrate piperine's significant role in the regulation of lipid metabolism genes.

Anti-depressant

The antidepressant efficacy of piperine and its potential mechanisms were examined in a corticosterone-induced depression model in mice. Following three weeks of corticos-terone injections, the mice exhibited depression-like behavior. The forced swim test and tail suspension test indicated depression by a significant reduction in sucrose consumption and an elevation in immobility duration. Moreover, corticosterone-treated rats exhibited significantly reduced levels of brain-derived neurotrophic factor protein and mRNA in the hippocampus [29].

Bronchodilator

Black pepper exhibited antitussive and bronchodilator properties recognized in traditional medicine; hence, P. nigrum is frequently included in herbal cough syrups. Numerous senior individuals and herbalists contended that including a little quantity of powdered peppercorn into green tea significantly alleviated asthma symptoms. Piperine injections in mice at various dosages decreased hyperresponsiveness, eosinophil infiltration, and inflammation, potentially due to lower production of histamine, immunoglobulin E, interleukin-4, and interleukin-5 [30].

3. *Glycyrrhiza glabra* (Mulethi)

The ancient Greek words glykas, which means sweet, and rhiza, which means root, are the sources of the word glycyrrhiza. In northern India, Glycyrrhiza glabra is known as mulethi. G. glabra is native to the Mediterranean and certain regions of Asia. Sweet wood, licorice, madhuk, and kalitak are some names for it. Cough, cold, pain, edoema, and other conditions have historically been treated with G. glabra [31].

The plant is a herbaceous perennial that reaches a height of one to two meters and has a long, robust main taproot. The taproot is 15 cm long and has three to five offshoot taproots. New stems are produced every year. The leaves are alternating, drooping, and pinnately unique. The inflorescence resembles an erect spike and is 10–15 cm long. The blooms are bluish to pale violet in color and have a short pedicle that is 1-1.5 cm long. The fruit is a 1.5-2.5 cm long pod with a tiny, bell-shaped calyx. Three to five brown reniform seeds [32].

Fig 3. *Glycyrrhiza glabra* plant

The roots of Glycyrrhiza glabra Linn contain a saponin called glycyrrhizin, which is 60 times sweeter than cane sugar and rich in flavonoids. Four new isoprenoid-substituted phenolic constituents—licoriphenone, 1-methoxyficifolinol, isoangustone A, and semilicoisoflavone B—were isolated from roots. Liquorice contains proteins, amino acids, polysaccharides, simple sugars, and mineral salts (such as calcium, phosphorus, sodium, potassium, iron, and others). magnesium, silicon, selenium, manganese, zinc, copper, pectin, resins, starches, sterols, and gums). Oestrogens, tannins, glycosides, coumarins, phytosterols (stigmasterol and sitosterol), vitamins (B1, B2, B3, B5, E, and C), and oestrogens have all been reported [33].

Pharmacological properties

Anti-cancer

Approximately 250,000 people die from cervical cancer each year, making it the fourth most common malignancy in women globally. The anti-cervical cancer properties of ISL have also been studied in a number of studies. By causing HeLa cells to undergo intrinsic apoptosis, ISL demonstrates its anticancer ability. Oxidative stressors, mitochondrion-dependent signalling pathways, and estrogen receptor stress-triggered signalling pathways all contributed to HeLa cell apoptosis. In HeLa cells and cancer U14 cells, isoliquiritigenin treatment decreased cell proliferation and increased apoptosis. When administered in combination with cyclophosphamide, ISL enhanced anticancer efficacy and decreased micronucleus production of DNA strand breaks in KM mice carrying U14 in an in vivo experiment; the findings suggested that ISL could be a promising option to prevent and treat cervical cancer [34].

The efficacy of licorice extract's anticancer activity both by itself and in conjunction with cisplatin, as well as its protective effect against cisplatin-induced toxicity, were examined using a mouse xenograft model. This model demonstrated a substantial reduction in tumor formation when BALB/C mice implanted with CT-26 colon cancer cells were given licorice extract. Additionally, the combination of licorice extract with cisplatin significantly increased the licorice extract's anticancer activity while decreasing the therapeutic efficacy of cisplatin. Furthermore, therapy with licorice extract considerably reduced oxidative damage brought on by cisplatin. Therefore, when combined, licorice extract reduces the toxicity of cisplatin and inhibits the growth of colon cancer in mice without producing any negative side effects. Licorice extract may therefore be utilized as a chemopreventive and anticancer agent. However, licorice extract supplements should not be used by patients undergoing cisplatin treatment [35].

Respiratory Tract Infection

Isoliquiritigenin is a natural flavonoid that is derived from the root of the licorice. Isoliquiritigenin has exhibited anti-inflammatory and antioxidant properties. Researchers had tested the effect of isoliquiritigenin in a mice study on cigarette smoke-induced COPD. This study’s outcomes have demonstrated that isoliquiritigenin has lessened inflammatory cells’ infiltration and inflammatory cytokines. In addition, isoliquiritigenin regulated the NF-κß and Nrf2 signaling pathways and protected against cigarette smoke-induced COPD [36].

Effect on Cardiovascular system

hree hundred active components are found in licorice, used for thousands of years. The principal functioning component of licorice is glycyrrhizin. Glycyrrhizin is a prodrug of licorice transformed 3ß-monoglucuronyl-18ß glycyrrhetinic acid (3MGA) and 18ß-glycyrrhetinic acids in the intestines. 3MGA and GA suppress the enzyme 11ß-hydrogenase type II (11ß-HSD2) that changes cortisol to cortisone. High cortisol levels result from a modest mineralocorticoid abundance in the kidney and boost systemic vascular resistance by provoking mineralocorticoid receptors. Continuous suppression of 11 beta-HSD2 due to excessive licorice consumption results in hypernatremia, hypokalemia, and high fluid content, leading to significant life-threatening consequences, particularly in individuals with cardiovascular disease. Meta-analyses with 26 and 18 investigations have reported that licorice consumption and blood pressure significantly increase systolic and diastolic [37].

Hepatoprotective

GA has shown anti-inflammatory and antiapoptotic properties through the inhibition of TNF-α and caspase-3 that explains the hepatoprotective effect of GA. Liver regeneration could be aided by the expression of proliferating cell nuclear antigen that GA increases. Glycyrrhizin might be a potent medication protecting the liver from endotoxin-induced damage, particularly after a large hepatectomy [38].

Anti-microbial

Ethanolic and aqueous extracts of the leaves of licorice were examined to evaluate the antimicrobial potency. Serial dilution method and paper disc evaluation method was applied to measure the minimum inhibitory concentration (MIC) and minimum bacterial concentration (MBC) to test the antimicrobial activeness of *Klebsiella pneumoniae*, *Candida albicans*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*. The results have confirmed that licorice' ethanolic extract has antimicrobial potential against *Candida albicans* and gram-positive bacterial depending upon dose. Licorice's ethanolic extract of leaves is potent against gram-positive bacteria; therefore, it can be the probable alternative medication against diverse strains [39].

Anti-inflammatory

Wang et al. carried research to examine the consequence of glycyrrhizin in mice for anti-inflammatory treatment and investigate the possible actions of mechanism. The study results have exhibited that expression levels of iNOS, COX-2, TNF-α, and IL-6 were significantly decreased by the glycyrrhizin, a triterpene of licorice. The study results found that glycyrrhizin acts as an analgesic by attenuating the expression levels of COX-2, TNF-α, iNOS, and IL-6 [40].

In dental carries

One of the most prevalent health problems in children is dental caries. 60 percent of children in the middle-ages of 5 and 17 years have deteriorated, rotten or lost, or misplaced permanent teeth problems in the US. In a pre-school setting, a pilot study for young children was conducted to investigate the consequence of using the protocol of herbal caries-prevention to suppress the *Streptococcus mutants*. Licorice root extract containing sugar-free lollipops were formed and were administered three weeks twice daily to children. SM counts were determined by analysing saliva for specific monoclonal antibodies. Three groups were formed low, medium, and high-risk employing SM extent as to risk index. Bacterial counts were compared during the treatment and after nine weeks of treatment. The trial results revealed that administering herbal lollipops two times a day lessened bacterial count and relative percent in high-risk children [41].

4. Tulsi *(Ocimum tenuiflorum)*

Tulsi is one of the most important plants in Ayurveda. Tulsi is the finest Ayurvedic knowledge tonic for the body and mind, and it may treat a variety of contemporary disorders. It is a key component in the conventional Ayurvedic" and "Unani" systems. One species or variant of the Lamiaceae family of plants is *Ocimum tenuiflorum L*. It has contributed to science from ancient times to the present day in current practices because of its many restorative potentials [42].

Fig 4. *Ocimum tenuiflorum* plant

Tulsi is an upright, aromatic plant with many branches. 30 to 60 cm tall, fragrant plant. The oval leaves have a basic green or purple color, a gently serrated or dented edge, and a blade length of 5 cm. The blooms have a short, hairy stalk and are violet. The plant produces reddish-yellow seeds and little fruit. It has a harsh and caustic taste [43].

Taxonomy

Kingdom: Plantae

Order: Lamiales

Family: Lamiaceae

Genus: *Ocimum*

Species: *tenuiflorum*

Molludistin, orientin, luteolin, apigenin-7-O-glucuronide, ursolic acid, and luteolin-7-Oglucuronide are some of the additional compounds found in Tulsi leaf extract. This species of *Ocimum* also contains a number of monoterpenes and sesquiterpenes, such as bornyl acetate, ß elemene, neral, pinenes (α and ß), camphene, sitosterol, cholesterol, campesterol, and stigmasterol. The five types of fatty acids found in O. sanctum are stearic, palmitic, oleic, linoleic, and linolenic acid. Tulasi is rich in vitamin C, beta carotene, and calcium ions. In addition to tannins, camphor, and flavonoids such luteolin, orientin, vicenin, and triterpene; urolic acid; zinc, manganese, and sodium ions are all found in plant extracts [44].

Traditional uses

Tulsi was traditionally drunk as a herbal tea, dried powder, fresh leaves, or with honey or ghee. Tulsi's dried leaves are used to keep insects away from grains that have been kept. Tulsi has been used as a therapy for common colds, coughs, wounds, exhaustion, headaches, flu, fever, sore throats, and skin conditions or allergies from ancient times in "Ayurveda" and tribal medicine. To treat skin allergies, crushed leaves in goat urine combined with coconut oil are utilized. The "Charaka Samhita" states that it is used to cure scorpion stings (leaf paste) and snake bites (whole plant). Onion bulb-pounded leaves are used to treat headaches, coughs, and colds. It improves food digestion, lessens respiratory issues, and helps maintain blood glucose levels (powdered leaves with honey). Ghee and dried leaves may be used to cure piles, colic, and dysentery. Fever and diarrhoea are treated with a paste made from leaves and black pepper. Bronchitis is treated by combining the juice of flowers with honey, ginger, and onion leaves. In Thailand, the whole plant or a leaf is used to alleviate vomiting. Additionally, the plant leaves are used to heal oral infections and ulcers, improve memory, strengthen nerves, and purify drinking water [45].

Chemical Constituents

Among the detected phenolic chemicals are isoeugenol, apigenin, rosameric acid, circimaritin, cirsilineol, and eugenol (in high concentrations). Orientin and vicenin were the two types of flavonoids extracted from the water-based leaf juice. Molludistin, orientin, luteolin, apigenin-7-O-glucuronide, ursolic acid, and luteolin-7-Oglucuronide are some of the additional compounds found in Tulsi leaf extract. This species of *Ocimum* also contains a number of monoterpenes and sesquiterpenes, such as bornyl acetate, ß elemene, neral, pinenes (α and ß), camphene, sitosterol, cholesterol, campesterol, and stigmasterol. The five types of fatty acids found in O. sanctum are stearic, palmitic, oleic, linoleic, and linolenic acid. Tulasi is rich in vitamin C, beta carotene, and calcium ions. In addition to tannins, camphor, and flavonoids such luteolin, orientin, vicenin, and triterpene; urolic acid; zinc, manganese, and sodium ions are all found in plant extracts [44].

Pharmacological properties

Antioxidant Activity

Numerous studies reported on this behavior. Flavonoids have been shown to have antioxidant qualities and to play a part in protecting membranes. Radiation-induced lipid peroxidation in the mouse liver was significantly reduced as a consequence of the flavonoids' (orientin and vicenin) in vivo antioxidant activities. High reactive free radicals have been considerably scavenged by tulsi extract [45]. Phenolic substances and strong antioxidant properties were found in the Tulsi leaf and stem extract. The extracted phenolic combination is known as apigenin, eugenol, cirsilineol, cirsimaritin, isothymusin, and rosemarinic acid [46].

Anti-diabetic Activity

Oral administration of Tulsi extract lowers blood sugar levels in streptozotocin-induced diabetic rats as well as glucose-fed hyperglycemic rats. Tulsi extract enhances the physiological mechanism for insulin release by modifying the intracellular Ca+2 channel, which in turn activates the pancreatic ß-cell. Clinical research using placebo-controlled shows a drop in blood glucose levels, which is also seen in urine glucose levels. Additionally, tulsi has aldose reductase activity, which helps prevent diabetic side effects including cataracts and retinopathy. In contrast to glibenclamide, a hydro-alcoholic extract of Tulsi was shown to be significant against streptozotocin (250mg/kg) and nicotinamide (500mg/kg). Tulsi ethanol extract lowers hyperglycemia in mice with alloxan-induced diabetes [47].

Antimicrobial

It has been claimed that Tulsi's essential oil and leaf extracts have antibacterial properties. Tulsi works well against a variety of bacterial and fungal types. It has been discovered that tulsi alcoholic extract works well against Vibrio cholera. Both Gram-positive and Gram-negative bacterial strains may be effectively combatted by the aqueous extract. The most effective treatment for candidiasis, which is brought on by Candida species, is linalool. By blocking proton pumps, it lowers the development and metabolic rate of candida. The linolenic acid and ß-caryophyllene in fixed oil inhibited the growth of several bacteria, including Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, and Bacillus pumilus. On top of that, it doesn't become sick from certain types of Neisseria gonorrhea.

Chemopreventive

The hepatic/extrahepatic GST consecration in mice was used to detect the chemopreventive efficacy of Tulsi extract. Mice given Tulsi extract had increased amounts of deflated GSH in their hepatic, pulmonary, and gastric tissues. Significant anti-proliferative and chemopreventive effects were observed in mice when exposed to high quantities of Tulsi seed oil. To its antioxidant and cancer-preventive properties, seed oil owes its latent chemopreventive action [48].

Anticancer

Experimental evidence has shown that Tulsi has anticancer properties, and numerous studies have pointed to this fact. Enzymes and chemicals that metabolize carcinogens, including aryl hydrocarbon hydroxylase, glutathione S-transferase (GST), cytochrome P450, and cytochrome b5, were significantly impacted by the alcoholic Tulsi leaf extract [49].

Radioprotective

Impact of Tulsi phytoconstituents on radioprotectivity, initially noted in 1995. Orientin and vicenin, two flavonoids isolated from Tulsi leaves, show a stronger radioprotective effect than their synthetic or artificial counterparts. They have shown that human lymphocytes are significantly protected from the clastogenic effects of radiation at low, harmless doses. Combining Ocimum tenuiflorum extract with WR-2721 decreases the toxicity and injury of WR-2721 at higher doses and demonstrates the great protective action of bone marrow cells [49].

Hepatoprotective

To modify the hepatotoxicity implicated by dimethylnitrosamine, Tulsi leaf extracts in methanol work well. Male Wistar albino rats were protected from paracetamol-induced liver damage by an oral administration of 200 mg/kg of a hydro-ethanolic extract of Tulsi leaves. In albino rats, *Ocimum tenuiflorum* cold water extract effectively protected the liver from carbon tetrachloride-induced damage [50].

Anti-fertility

The antifertility activity in female rats was considerable (80% with benzene and 60% with petroleum ether) when exposed to Tulsi leaf extracts in these solvents. Also, male rats have shown a decrease in sperm count, testicular weight, and sperm motility after ingesting benzene extracts. One of the main ingredients in tulsi, ursolic acid, has an action that prevents fertility. The absence or halting of male rat spermatogenesis is caused by an anti-estrogenic mechanism, which is associated with this impact [51].

Antipyretic

Antipyretic effects were observed in the fixed oil of Tulsi (*Ocimum tenuiflorum*). In order to test it, researchers used the typhoid-paratyphoid A/B vaccine to make rats pyrexia. The significant decrease in the febrile response following intraperitoneal (IP) injection of oil demonstrated its antipyretic properties. In addition to prostaglandin, the fixed oil inhibits its production. An antipyretic effect of 3 milliliters/kg of oil was found to be on par with those of aspirin and ibuprofen [52].

Adaptogenic or Antistress

An adaptogenic impact cannot be achieved without tulsi's capacity to boost the immune system. An alcoholic extract of the whole plant reduced the incidence of stress ulcers in rats and milk-actuated leukocytosis in mice. It also increased the swimming mice's physical endurance, which may indicate a little better degree of acceptance [53].

Antiulcer

Aspirin, alcohol (50% C2H5OH), reserpine, serotonin, indomethacin, histamine, and stress-induced ulcers were all effectively treated by intraperitoneal administration of *O. sanctum* fixed oil in rats. Because of its lipoxygenase inhibitory, antisecretory, and histamine antagonistic actions, fixed oil at large doses showed antiulcer efficacy [54].

Anticoagulant

Similar to aspirin (100 mg/kg), the fixed oil of Tulsi (3 ml/kg, intra-peritoneal) prolonged blood clotting time and the overall reactivity. Tulsi oil's effect on platelets, which is anticipated to have an anti-aggregator effect [54].

Cardioprotective

Excellent cardioprotective effectiveness was established by the hydro-alcohol extract of Ocimum sanctum seeds. Numerous bioactive components of tulsi plants, including quercetin, diosgenin, carotinized, isoflavones, catechin, and sulforaphane, have been demonstrated to enhance cardioprotection and decrease the occurrence of cardiac issues. Efficacy of hydroalcoholic extract of tulsi in preventing myocardial infarction (MI) in rats following subcutaneous administration of isoproterenol (ISO) was investigated. Glutathione, superoxide dismutase, and liver damage factor (LDH) levels were significantly lower in rats. It also inhibits lipid peroxidation. At 50 mg/kg, tulsi demonstrates the greatest cardioprotective rate [55].

Antihypertensive

The Ocimum tenuiflorum Linn were able to avert both short-term cerebral ischemia (a condition similar to a stroke) and long-term cerebral hypoperfusion (a condition that causes swelling of cells, abnormal cell growth, and inflammation around blood vessels). The necessary fatty acids linoleic and linolenic are found in Tulsi fixed oil, which also suppresses the development of PGE-2, which raises blood pressure and hypertension, and creates PGE-1 and PGE-3, which are prostaglandins that regulate atrial pressure [56].

Anti-dengue virus

Through blocking viral replication and cytopathic (host cell-structural alterations) development, the methanolic extract of the Tulsi plant demonstrates antiviral characteristics toward dengue virus 1 [57].

Analgesic

In experimental studies, Tulsi was shown to have analgesic effects. It exhibited a dose-dependent reactivity to the writhing paradigm in rats that had been exposed to acetic acid. The combined inhibitory actions of prostaglandins, histamine, and acetylcholine proved that oil had an inhibitory effect [44].

Immunomodulatory

In rats with fair skin, the refined extract of *O. sanctum's* new leaves changed the humoral resistive response. The extract modifies the immunomodulatory effects through adjusting cellular receptivity, intervening in the immune system, and mediating GABergic pathways. To determine Tulsi's immunomodulatory effect, a randomized, double-blind control study is carried out in healthy participants. Increased levels of interferon-γ and interleukin-4, which include T-helper cells and natural killer cells, indicate the outcomes. Tulsi seed oil (3 ml/kg) significantly increased anti-sheep RBC antibody titers and decreased histamine release from activated

peritoneal mast cells in rats, indicating an immunological response; it also decreased the thickness and percentage inhibition of leukocyte migration. When taken orally, Tulsi aqueous extract speeds up the creation of white blood cells, red blood cells, and hemoglobin, as well as the production of antibodies, all without affecting the biochemical parameters [58].

Antiarthritic

Many different chemical components have been found to have anti-arthritic effects. The anti-arthritic properties of Tulsi essential oil were demonstrated in an extract of the flowers and leaves, which contained ursolic acid, apigenin, and luteolin. Rats were tested for the presence of turpentine oil-induced joint edema, Freund's adjuvant arthritis, and formaldehyde-induced arthritis [59].

Memory enhancer

Memory impairments were observed in developing mice when exposed to scopolamine (0.4 mg/kg) in combination with either the whole dried plant or an aqueous extract of Tulsi leaves, or the whole plant in its alcoholic form. Because of this, the acetylcholine esterase and down dormancy (SDL) restriction is greatly reduced or removed [60].

CONCLUSION

A natural source with potential for therapeutic use is piperine. In Asia, Piper longum Linn. has been utilised as a natural remedy for inadequate peripheral blood flow. Indian traditional medicine traditionally uses Piper longum Linn. and Piper nigrum Linn. as immune boosters. As a result, piperine's effectiveness has been demonstrated indirectly, while its exact mode of action is still unclear. In order to ascertain if piperine has therapeutic promise for the treatment of arthritis, we assessed its anti-inflammatory and antiarthritic properties.

In conclusion, *Clitoria ternatea* (leaves), Black pepper (seeds), *Glycyrrhiza glabra* (root), and Tulsi (leaves) exhibited the numerous pharmacological potentials. Therefore, these herbs are promising research moiety which can be utilized in the management of various deadly ailments.

CONFLICT OF INTEREST

Authors declare for none conflict of interest.

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