REVIEW ARTICLE

Nepeta cataria L. A comprehensive review of its phytochemical and pharmacological attributes

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Abstract

One of the most significant medicinal herbs is catnip *Nepeta cataria* (NC), which belongs to the mint family *Lamiaceae*. As a result of its naturalization in many nations across the world, it is known as an invasive species in the United States. It was described as a grass that smelled like orange, and the Greek names for it were Malsoonan and Maletana. Several diseases such as angina, heart illness, and black-bile vapors can all benefit from its cardiotonic properties, which make it a good supplement for all phlegmatic and black-bile-related ailments. In addition, it can help alleviate symptoms of stress, anxiety, and pain. There are many species of catmint, the most common and most researched of which is NC. As the name catmint suggests, cats have a great preference for this species. As a result, it is frequently employed in the pet toy business as a safe cat lure. Nepetalactone is the primary catalyst for this process in cats. Although *N. citriodora* or lemon catnip, a fragrant plant with a lemony-mint smell, resembles authentic catnip, it does not entice cats to use it. It is also used in the canning of vegetables and fruits. Since NC has a lengthy blooming period, as well as a high pollen and nectar output, it is ideal for beekeeping. NC has antioxidant, hepatoprotective, anti-diabetic, spasmolytic, anti-nociceptive, and anti-inflammatory properties. This plant contains anticancer and sexual activity-influencing characteristics that have been demonstrated in scientific studies. This article talks about the pharmacological properties of NC and also talks about the plant's phytochemistry and chemical elements.

Key words: Chemical constituents, *Lamiaceae*, *Nepeta cataria*, pharmacology, phytochemistry

INTRODUCTION

Plant secondary metabolites (SMs) have been used by humans since the dawn of time to treat a variety of ailments, keep pests at bay, preserve food, and enhance flavor.[1] Approximately 80% of the world's population, according to the WHO estimates, is heavily reliant on conventional drugs obtained from SMs for their medical care. Conventional medicine is based on the use of SMs derived from plants in countries such as India, China, and Egypt.[2] At present, in a variety of nations, 119 plant-derived compounds are utilized as major pharmaceuticals.[3] Over the course of time, synthetic chemicals have supplanted SMs of plant origin as the former has more precise actions and delivers earlier results. In addition, the use of synthetic chemicals has a number of negative side effects, including human health difficulties, gene mutation, insect and pest resistance, biodiversity loss, and environmental contamination.[4] Synthetic chemicals have been targeted for replacement with SMs derived from plants, which are more environmentally friendly, biodegradable, less poisonous, and cheaper than their synthetic counterparts. Alkaloids, carotenoids, flavonoids, phenolics, tannins,

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and terpenes are only some of the natural components that make up the SMs.[5] Phytomedicine has been increasingly popular in recent years. A wide variety of herbs and plants was employed, not only for the prevention and cure of sickness but also as natural ingredients in the diet. The role of essential oils (EOs) in phytomedicine has grown over the years.[6] It has been shown by several authors that EOs has antimicrobial, antifungal, and antiparasitic activities and also have antioxidant, anti-inflammatory, and anti-carcinogenic qualities. A member of the mint family, *Nepeta cataria* (NC) (also known as catnip or catmint), the family *Lamiaceae*, has been used for centuries to treat a variety of ailments. In Asia, Europe, and North Africa, the genus *Nepeta* includes perennial or annual plants. North American folk medicine and tea, dye, and infusions have traditionally relied on NC. In traditional medicine, *Nepeta* species are used for a variety of ailments due to their antispasmodic and expectorant properties, as well as their antibacterial, antiviral, antitussive, and anti-asthmatic properties.[7] Aside from that, the fresh or dried plant's juice, extract, and juice can cause cats to experience intense pleasure. In addition, NC plants or their components have been linked to depressive and anxiolytic effects in several studies. Other investigations have failed to duplicate the antidepressant properties of NC. A putative antidepressant-like action of NC was investigated in animal models of antidepressant medications because of these inconsistencies. Using commercial goods containing NC for a prolonged period of time has been shown to induce effects similar to antidepressants without impairing performance in the open field or the elevated plus-maze.[8]

With about 300 species, *Nepeta* is one of the biggest genera, mostly found in the temperate areas of Europe, the Near East, and portions of Africa. It has also been naturalized in North America. The majority of *Nepeta* species are endemics, particularly in the South-west Asian region (Turkey and Iran). Most people have heard of the plant NC, better known as catnip or catmint.[9] Because cats have a great preference for this species, the moniker "catmint" was coined. Cats, especially huge wild cats, have been reported to experience stupor or ecstasy when exposed to this plant, which makes it an obvious candidate for use as a behavioral changing medication (name catnip is derived from the words "nip," meaning a small quantity of liquor, that intoxicates cats). Nepetalactone and related compounds (iridoids) have been found in the EO and various extracts isolated from NC, which have been mainly responsible for the plant's various biological activities, such as cat attractant, insect pheromone, insecticide, and insect repellent. The rumor mill has it that the nepetalactone's biological activity is largely determined by its C-7 configuration.[10] In addition, lubber grasshoppers and coconut stick insects both contain a significant amount of the defensive compound nepetalactone in their secretions. These compounds are not the only ones found in the plant. The flavonoids (luteolin) and other compounds are related to natural products like apigenin 7-Glucuronide (as well as other phenolic acids like apigenin 7-Glucuronide) (caffeic, rosmarinic acids, gallic acid, etc.) To put it more succinctly, ursolic acid, oleanic acid, stigmasterol, β-sitosterol, β-amyrin, and other steroid hormones. In addition, terpenoids (such as 1,8-cineole, bisbolene, citral, caryophyllene, geraniol, humulene, α-terpineol, etc.) have been found to be important as well.[11] This article deals with the pharmacological properties of NC, and also emphasizes in detail about phytochemistry and chemical constituents of NC [Figures 1 and 2, Table 1].

CULTIVATION

Because of its extended blooming period (late May through late August or early September) and high pollen and nectar production, NC is well-suited for beekeeping. NC is also farmed on a large scale because of its application in the pharmaceutical and nutrition industries, as well as in the pet toy business. It is one of Egypt's, Ukraine's, and North America's most promising aromatic plants.[12] Commercially grown NC has an upright growth habit and greater biomass, EO, and Z, E-nepetalactone output than any other NC cultivar in North America. In addition, a variety of NC genotypes is employed in the germplasm collection and breeding program. Nepetalactone is absent or present at small levels in these strains, which have a unique citrus scent.[13] A forest-steppe variety called Melody and a steppe variety called Peremozhets were developed for cultivation in Ukraine's.

Seed is used to propagate NC. About 0.5 g is the weight of 1000 seeds. Seed is generally spread in the fall in open field settings. However, stratification is required if the sowing is done in spring. May is the time of year when greenhouse-grown crops are transferred into the field.[14] Egyptian researchers tested the influence of planting date on germination percentage by spreading NC seed in nurseries every month from October to April. Planting NC seedlings in the field began on April 15th, with hills spaced 30 cm apart and rows spaced 60 cm apart. On the June 15 and the September 20, two harvests were carried out. According to the findings, the germination rate ranged from 30 to 80%. Sowing seeds in the soil medium in February and March had the best germination rates. In this regard, the germination rate was between 70% and 80%.[15] Combinations of row width, density, and spacing were developed to offer cultural management information. A total of three-row widths and three intra-row spacing's were available (30, 60, and 90 cm). It has been demonstrated that plant spacing has a significant impact on plant size. Flower production was greatly increased when plants were spaced evenly at 90 × 90 cm. In addition, the oat straw treatment resulted in considerably higher NC plant heights than the two organic mulches (a flax straw mat and a non-woven wool mat) as compared to the positive (hand weeded) and negative (non-weeded) controls.[16] Nepetalactone concentrations were not affected by weed management therapy. Natural catariavar. var citriodora herbal yield was significantly affected by substrate moisture (50, 125, and 250 hPa). Additional factors

that affect EO content include drought stress, such as 50 hPa, which resulted in increased EO production.[17]

It is recommended to apply 100 kg/ha of N, 80 kg/ha of P_2O_5, and 120 kg/ha of K_2O in Poland. Nitrogen concentrations in nutrient solutions (50, 150, and 300 mg/l) were observed to have a significant impact on the herbal production of *N. citriodora* var. *citriodora*, as well as the amount and composition of the EO.[18] Nitrogen concentrations were shown to have the greatest impact on EO composition. The fresh yield of NC herb was reported at 138.5 and 180.0 g/plant in the first and second cuttings, respectively, throughout the growing season in Egypt. In this regard, the dry yield per hectare was between 1.98 and 2.77 t/ha. During both harvests, a total of 4.75 t/ha of dry weight was harvested from two cuttings. The first cut had the greatest oil percentage (0.25%), while the second cut had the lowest (0.19%). In addition to harming the plant, the devastation caused by dangerous insect pests and diseases in NC reduces the quality of the crop's therapeutic value. Insect pests and bacterial diseases have been found to be a problem for this particular plant. California has a case of Xantomonas leaf spot (*Xanthomonas campestris*), a disease that has been observed in the state. Infected leaves show microscopic brown specks that can be seen on both sides. Eventually, larger dark brown and angular specks eventually form. Toxic yellowish-white staining of the foliage is caused by the eating insects of the Eupteryxmelissae little leafhopper.[19]

TRADITIONAL USES

Researchers from several scientific disciplines have relied on understanding the traditional uses of a plant to help them gather more data and explore the full potential of the research plant for human well-being. There is a long history of NC being used in traditional medicine by many ethnic groups and nations all over the world. NC young leaves and shoots were used as a seasoning by the French.[20] During public executions in England, public hangmen chewed on this herb because of its hallucinogenic effects. As a traditional soporific and sedative, the tea made from the plant's leaves is also used to treat digestive and respiratory disorders, including diarrhea, coughs, and bronchitis.[21] Several North American Indian tribes, including the Chippewa, utilized this plant's leaves to make herbal tea. Indian groups in the Okanagan-Colville region of British Columbia utilized this plant to treat a variety of ailments, including respiratory issues and digestive issues. The Iroquois Indians, on the other hand, used this plant as a remedy for indigestion, vomiting, sore throats, and migraines. It was utilized by the Menominee, Rappahannock, and Cherokee for a variety of ailments, including fever and blood and female diseases. In addition, the Cherokee Indians utilized this plant to treat convulsions as well as boils, worms, and rheumatism by smoking the dried leaves.[10] Flowering tops, as well as dried leaves, have been used as diaphoretics, carminatives, and tonics, as well as stimulants and antiseptics in traditional medical systems, as well as against toothaches.

In Addition, NC has the Following Biological and Therapeutic Qualities

1. The extract from NC inhibited the enzyme and bacterial growth, generation, and adhesion. Juvenile hormone action from the catnip plant extract has been documented
2. Traditional English folk medicine has used NC to treat uncomfortable swellings
3. Scenting floral tips and leaves, fresh or dried, have been utilized in soups, cheeses, and as flavoring elements for prepared meals
4. It has been used to produce pheromones for insects as a component of insect pest management tactics
5. For sleeplessness, colds, flu, and fevers, a hot infusion of this plant might be helpful in promoting perspiration and relieving symptoms. Miscarriage and early delivery are two other possible outcomes of using this supplement.

PLANT DESCRIPTION

Plants of the genus NC are perennials. There are multiple quadrilateral stems ranging in height from 50 to 100 cm from the long and rod-shaped root. Short hair and sessile glands cover the stems, which are branching. Oval, solid pilose, with numerous sessile glands, truncate or serrated, the leaves are 3.5–8.0 * 2.5 cm, and the petioles are 7 mm long. The 35-flowered inflorescences on each branch form a thick spike-like structure. Flowers have five petals, are tiny, and have hairs on both sides. Perennial herbaceous NC is found in the wild. The root has a long, rod-like form. It grows into several 50–100 cm tall and erect quadrilateral stalks with branching, extorsively glandular pilose, short-haired pilose, with sessile glands. The five-petaled, double-haired flowers are the smallest of the lot. The calyx and bracteoles are both linear-oblong in shape and length. The calyx of this plant has an oblique calyx of 5–6 mm, is heavily pilose-pubescent, and with sessile glands. The 6–10 mm long corolla is white with blue-violet markings. Nutlets are elliptical, 1.5–1 mm in diameter, dull, matte, and somewhat tuberculate at the tip.[22]

PHYTOCHEMISTRY AND CHEMICAL COMPOSITION OF NC

A variety of factors, including plant age and development stage, organ, time of collection, climate, and soil composition, influence the content, quality, and the number of SMs collected from various extracts and EOs of different plants. Extracts and oils of the same composition must be taken from a plant organ that is obtained at a similar point in its life cycle and under similar environmental circumstances. The iridoids found in the *Nepeta* genus and species NC include nepetalactone, dihydronepetalactone, 5,

9-dehydronepetalactone, iridomyrmecin, and neptelic acid, all of which are terpenoids of the iridoids class. NC EO contains four chemical compounds, including glycerin, 1, 8-cineol, alpha-humulene, and alpha-pinene.[11] Nepetalactone was found in the plant's EO at every stage of development. Flavonoids (flavonols and flavones), glycosides, terpenes, isomers of napa lactone, and coumarins are all found in the leaves of NC.[23] Stearic acid, linolenic, lauric, oleic, and palmitoleic acids were found in the flower's fixed oil.[24] Flavonoids, tannins, glycosides, and sugars were found in the plant's aerial sections.[25] NC leaves and stems contain caffeoyl phenylethanoid glycosides (Lamiuside A and verbascoside) that should be included as constituent parts.[26] Nepetalactone and epinepetalactone are found in the whole plant.[27] The glandular trichomes on the leaf epidermis are where the fragrant volatiles are formed. As far as EOs are concerned, the NC EO is colorless, nontoxic, and odorless; the lemon catnip EO (CEO), on the other hand, is comprised of nerol and citronellal as well as nerol, citronellal, and caryophyllene oxide.

PHARMACOLOGICAL ACTIVITIES

It has been shown that the therapeutic properties of plants may be used to cure numerous ailments. For the most part, people in underdeveloped nations continue to employ age-old folk treatments made from medicinal plants. The use of NC as traditional medicine has been around for a long time; it is also commonly used to flavor food; it is used in tea to help alleviate gastrointestinal (diarrhea, stomach distress, and vomiting) and respiratory ailments; it is also used as a seasoning (colds, coughs, asthma, bronchitis, sore throats, and pneumonia). Fever and emmenagogue, as well as rheumatoid arthritis and other feminine illnesses, have all been treated with it.[10] The scientific validity of some of these uses in traditional medicine has been established. Studies have shown that NC has a wide range of health benefits, including hepatoprotective, anti-diabetic, antidepressant, spasmolytic, and anti-inflammatory properties. Studies have shown that this herb impacts sexual activity and has anti-cancer qualities. In addition, the antimicrobial and insecticide capabilities of the plant have been discovered.

Spasmolytic and Broncho Dilatory Activity

Gilani *et al*. 2009; investigated the phytochemicals and pharmacological potential of NC oil. The chemistry of NC was studied using GC-EIMS, 13C NMR, and a method known as the Kovats Retention Indices, whereas pharmacology was studied using isolated tissue preparations NC. Oil contains 27 different chemicals, of which 1,8-cineol (21%), α-humulene (14.44%), -pinene (10.43%), and geranyl acetate (8.11%) were found to be the most important. When administered to isolated rabbit jejunum in the presence of *NC*. Oil, papaverine, or verapamil, these compounds suppressed spontaneous and high K+ (80 mM) precontractions and moved the Ca^{++} concentration-response curves (CRCs) to the right, indicating calcium channel blockage. Carbachol precontractions were suppressed by NC. Oil and papaverine with equal strength, but verapamil was more powerful against K+ precontractions in guinea pig trachea. Papaverine-like PDE inhibitor activity was found in NC. Oil, which enhanced isoprenaline inhibitory CRCs NC. Oil, like papaverine, produced cardiodepression in isolated guinea-pig atria when concentrations were 25–80 times greater. Data from this study show that NC has spasmolytic and myorelaxant properties, which may explain its historic usage in the treatment of colic, diarrhea, cough, and asthma.[11]

Antibacterial Activity

Edewor and Usman 2011; revealed the antibacterial activity of NC. It was discovered that flavonoids (flavones and flavonols), coumarins, and glycosides were present in the dichloromethane and methanol extracts during the phytochemical screening process. *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Salmonella* typhi have been shown to be resistant to these SMs. For the TLC analysis of the dichloromethane extract, chloroform and methanol were used as solvents. The results showed that the dichloromethane extract was made up of three parts, with Rf values of 0.23, 0.46, and 0.69.[23]

Suschke *et al*. 2007; demonstrated the cytotoxic and antibacterial potential of NC. The oils were tested for cytotoxicity in human keratinocytes and skin cells to determine the safety of the topical application. The HET-CAM-test was used to assess the irritation threshold concentrations and cell lines of the bronchial epithelial cells. The GC and GC-MS were used to examine the composition of the EO. A broth test yielded their MICs and MBCs, which were then compared with clinical isolates with varying levels of sensitivity to the microdilution technique. The MTT test was used to measure cytotoxicity. In all reference strains except for *Pseudomonas aeruginosa* (MIC 2%), the MIC ranged from 0.016 to 0.25% (v/v) for the oils of catnip and lemon balm, which were shown to be toxic. Scientifically, regardless of where they came from, isolates were just as responsive to the oils (one serial dilution) as the matching reference strains. Common treatments that were cytotoxic to keratinocytes and bronchial epithelial cells at CC50 levels were found to be cytotoxic in the 0.0012–0.015% range. The largest concentration of monoterpene aldehydes was found in lemon balm oil. Catnip oil, which included mostly monoterpene alcohols and catnip, had antibacterial and cytotoxic properties. The oil has nepetalactone in it. The findings support the use of catnip and lemon catnip in veterinary medicine. Respiratory tract infections can benefit from the use of balm oils, which have a strong antibacterial action. Antibiotic-resistant bacteria of the respiratory tract including clinical isolates. However, in topical treatment, cytotoxicity must be taken into account.[28]

Larvicidal Activity

Giarratana *et al*. 2017; evaluated the larvicidal activity of NC. *In vitro* tests with Anisakis type, one L3 larvae showed that CEO has nematicidal action. Most fishbone zoonotic illnesses are caused by the consumption of nematode larvae from Anisakis, contraceacum, and hysterothylacium nematodes. Anisakidosis is one of the most significant fishbone diseases. Parasites were completely inactivated after 6 and 12 h of treatment, at 10% and 5% concentrations, in water. After 12 and 18 h at 10% and 5% concentrations, parasites were completely inactivated in the marinating solution. The results show that CEO has a big effect on Anisakis larvae, which means that more research needs to be done.[29]

Antidepressant Activity

Bernardi *et al*. 2010; investigated the antidepressant activity of NC. In male mice, the antidepressant, anxiogenic, and motor activity-enhancing effects of chronic, acute, and repeated administration of NC leaf apolar and polar extracts were studied. Repeated feeding and injection of apolar extract decreased immobility in the behavioral despair test, but it had no effect on the elevated plus-maze and open-field characteristics. Acute feeding or acute and repeated administration of polar extracts from NC. leaves had no effect on mice behavior. According to these findings, NC may be an effective antidepressant. Furthermore, the apolar extract exhibited this antidepressant action.[30]

Anticancer Activity

Fan *et al*. 2017; demonstrated anti-cancer treatment using NC. Because of its high throughput, great sensitivity, and low cost, microfluidic chip technology is becoming increasingly popular in scientific study. A microfluidic device and flow cytometry was used to examine the effects of TFS, a total flavonoid extract from NC, on A549 cells. As a result, qRT-PCR and western blot were used to examine the molecular processes of the partial PI3K-AKT pathway and the mRNA expression. Researchers discovered that TFS can inhibit miR-126 expression and modulate the PI3K-AKT signaling pathway to combat cancer. Based on these results, it seems likely that TFS will be used as a new way to treat NSCLC in the near future.[31]

Sexual Activity

Bernardi *et al*. 2011; evaluated the sexual activity with NC leaves. A chow supplemented with 10% NC leaves was given to male rats in the NC group for a period of 4 h, while ordinary chow was given to the controls. Abdominal erection and coordination were observed 15 min after the conclusion of four hours of NC feeding; general activity in the open field was measured at 0, 15, 30, and 60 min following treatment.

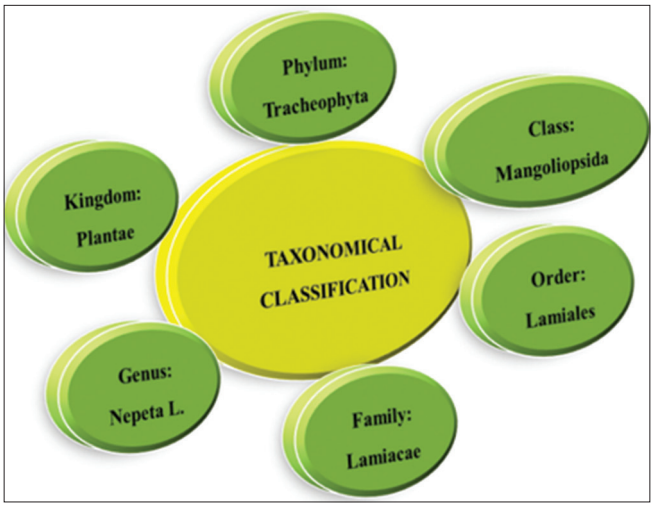

Figure 1: Taxonomical classification of *Nepeta cataria* L

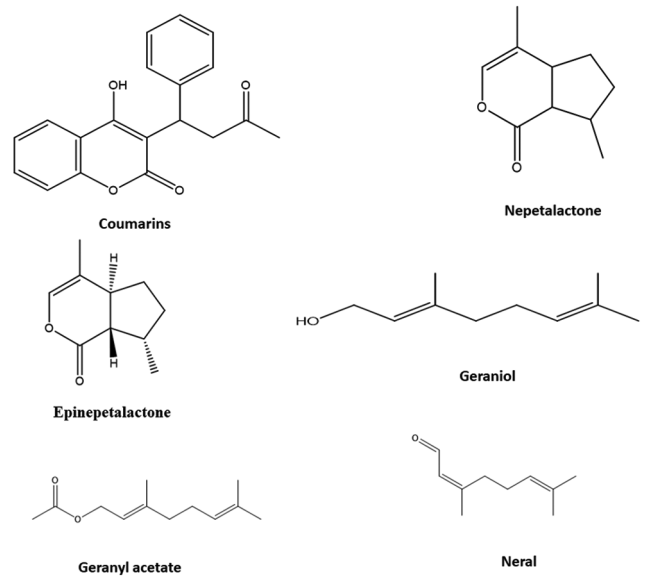

Figure 2: Chief chemical constituent of *Nepeta cataria* L

The male rat's penile erection was enhanced by NC therapy. Male rat sexual behavior was modestly facilitated and overall activity was reduced in NC-treated rats. In terms of yawning episodes or motor coordination, the NC therapy had no effect. By influencing dopaminergic systems, it has been hypothesized that NC enhances penile erection and somewhat enhances male rat sexual behavior.[32]

Bacteriostatic and Fungistatic Activity

Bourrel *et al*. 1993; NC EO was tested using GC/MS to determine its chemical composition. Besides the previously known nepetalactones 4a, 7a, 7a-nepetalactone; 3,4-dihydro-4a, 7a, 7a-nepetalactone; and -caryophyllene; five additional ingredients have been identified: dimethyl-3,7 oxa-1 bicyclo [3,3,0] oct-2-ene, piperitone, thymol methyl ether, hexenyl benzoate, and humulene oxide. The

Table 1: Numerous chemical components of NC have been found throughout the plant

Plant part	Chemical constituents	References
Leaves	Flavonoids, glycosides, terpenes, isomers of napa lactone, and coumarins	[25]
Flower	Stearic acid, linolenic, lauric, oleic, and palmitoleic acids	[26]
Stem	Caffeoyl phenylethanoid glycosides (Lamiuside A and verbascoside)	[28]
Whole plant	Nepetalactone and epinepetalactone	[29]
Aerial part	Palmitic, stearic, oleic, palmitoleic, linoleic, myristic, linolenic, and arachidic acid	[26]

nepetalactone concentration of the plant's EO was compared between two samples of the plant that were obtained at various phases of growth. Five bacteria and seven fungi were tested on the oil samples and a hexane extract, and the results were compared to those of natural substances known to have antimicrobiological properties.[33]

Anti-nociceptive and Anti-inflammatory Activity

Ricci *et al*. 2010; conducted a study of NC for anti-nociceptive and anti-inflammatory actions. Analyses of the phytochemical composition of NC-EO (NCEO) were conducted. Observations of the oil's overall activity and dosage and time responses were made on female mice administered with it in an open area. Using the tail immersion and acetic acid writhing reflex tests, researchers looked for anti-nociceptive effects. The carrageenan-induced edema test was used to examine the anti-inflammatory effects of the oil. A dosage of 0.0005 and 0.001 mL/kg of NCEO injected intravenously improved the overall activity of female mice, whereas 0.0005 mL/kg decreased their immobility. To add to this, the anti-nociceptive characteristics of NCEO (0.0005 mL/kg) were demonstrated in the treated rats, which showed enhanced tail withdrawal latency and decreased acetic acid-induced abdominal constriction. Peripheral anti-inflammatory effects of NCEO (0.0005 mL/kg) were also seen following carrageenan administration. Phytochemical research found the trans-trans and trans-cis nepetalactone isomers to be the most active constituents of nepetalactone, which may explain these effects.[34]

CONCLUSION

Despite the fact that numerous SMs have been found so far, nature must yet have a large number of other compounds. As a result, it is necessary to conduct a thorough and systematic investigation to identify and record the plants that have served as a source of medicinally significant SMs. NC, which belongs to the *Lamiaceae* family, has been a representative species of the genus *Nepeta*. Conventionally, it has been used to alleviate pain and treat a variety of diseases. Nepetalactone and its analogs have been the main chemical components of this species and the genus *Nepeta* because of the terpenoids, flavonoids, polyphenols, and steroids that make up the chemical variety of NC. Among the plant's many biological actions, its anti-inflammatory, anti-diabetic, antioxidant, and insecticidal chemical ingredients have been the most notable. However, there have been several areas of its use in traditional medicine that still requires pharmacological explanation. There are several uses for novel physiologically powerful chemicals obtained from plants. As a result, this study sheds light on NC by examining its chemical components and pharmacological effects in great detail.

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