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Catnip (*Nepeta cataria* L.): Recent Advances in Pharmacognosy, Cultivation, Chemical Composition and Biological Activity

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Abstract

Plant preparations are said to be medicinal or herbal when they are used to promote health beyond basic nutrition. It is indeed quite interesting to observe that our ancients were duly equipped with the vast, in depth and elaborated knowledge of drugs from the vegetable origin but unfortunately they possessed a scanty knowledge with regard to the presence of chemically pure compounds in most of them. The genus Nepeta L. (catmint), a large genus of the family Lamiaceae, is named after the ancient Italian City of Nephi It is also known as Glechoma and Cataria and it contains about 280 annual and perennial species, the majority of which are aromatic plants native to temperate Europe, Asia, North Africa, and North America. The wide variety and high content of terpenoid, flavonoid and phenolic compounds of Nepeta species provide diverse pharmacological effects, justifying its traditional utilization for medicinal purposes. *Nepeta cataria* (catnip or catmint, *N. cataria*), an aromatic perennial herb, belongs to genus *Nepeta* of Lamiaceae family and has been well known for its medicinal and therapeutic values. The name *Cataria* has been originated from Cathus, an old Latin word, which mean of cats. Like other aromatic plants which have showed flavoring and medicinal properties and act as renewable source for the same, *N. cataria* has also been known for its essential oil and secondary metabolites, which showed tremendous applications in pharmaceutical, agrochemical and food industries. It was shown by the different research groups that the essential oil and different extracts isolated from *N. cataria* have been a rich source of nepetalactones and related compounds (iridoids), which have been mainly responsible for different biological activities of the plant, viz. cat attractant, antioxidant, hepatoprotective, antidiabetic activities, as well as sedative, antidepressant, spasmolytic, anti-nociceptive and anti-inflammatory activities. Experiments show that this plant influences sexual activity, and expresses anticancer properties. Antimicrobial activity against a number of bacteria is also noted, as well as repellent and insecticidal properties. Nematodidal and allelopathic effects are also noted. This review emphasizes on latest information regarding the botany, distribution, cultivation taxonomy, traditional uses and more focused on phytochemistry, pharmacology.

Keywords: *Nepeta cataria,* Lamiaceae, Nepetalactones, Biological activities, Phytochemistry

INTRODUCTION

Medicinal plants and traditional medicines has a very long history: it is the sum total of the practices based on the theories, beliefs and experiences of different cultures and times, often inexplicable used in the maintenance of health, like prevention, diagnosis, improvement and treatment of illnesses. In every country traditional medicines find foundation in religious beliefs. WHO is engaged to establish definitive guidelines for methodology of clinical research and the appraisal of effectiveness of traditional medicines. Herbal medicine is the use of medicinal plants for prevention and treatment of diseases: it ranges from traditional and popular medicines of every country to the use of standardized and titrated herbal extracts. Generally cultural rootedness and widespread use in a Traditional Medical System may indicate safety, but not efficacy of treatments. In herbal medicine, tradition is almost completely based on remedies containing active principles at very low and ultra-low concentrations or relying on magical-energetic principles[1]. In modern medicines, plants occupy a significant place as raw material for some important drugs, although synthetic drugs and biotechnology have brought about a revolution in controlling different diseases. There is a growing tendency all over the world, to shift from synthetic to natural based products including medicinal and aromatic plants. Less than 5% of the plants have so far been analyzed as potential medicine and still there is a great scope of research in this field. There is a need to develop strong linkages between growers, collectors, health experts and pharmaceutical industries for developing scientific basis on which these systems of medicine are working[2]. The genus *Nepeta* is one of the largest from the Lamiaceae (labiatae or mint) family, with ca. 300 species, distributed in temperate regions, mainly in central and southern Europe, the Near East, central and southern Asia, and some parts of Africa and it is naturalized in North America, Himalayan region of India (Uttarakhand, Himachal Pradesh, Jammu and Kashmir, Leh-Ladakh), Pakistan (Khyber Pakhtunkhwa and Pakistani Kashmir), Nepal (Baglund district). Most *Nepeta* species are endemics, especially in

Southwestern Asia (Turkey and Iran) [3]. The essential oils and various extracts isolated from different species of this genus have been a wealthy source of special class of terpenoids known as iridoids along with other classes of secondary metabolites (SMs). These SMs showed a wide range of biological activities and have been used since prehistoric times in various traditional medicines. These have been used as diuretic, expectorant, antispasmodic[4-6], anti-inflammatory, antitussive, antiasthmatic, antiseptic[7,8], sedative, diaphoretic, febrifuge, antioxidant[9], insecticidal, antimicrobial[10], antiviral and fungicidal[11]. Further, these have also been used against scorpion and snakebites[4,6], stomach diseases[8], kidney and teeth troubles, liver diseases[12] and many problems of heart such as tachycardia, angina pectoris, cardiac thrombosis, and heart weakness and have showed numerous biological activities, viz. analgesic, antiasthmatic, anticancer, anti-inflammatory, antimicrobial, antioxidant, antipyretic, antiseptic, antispasmodic, diaphoretic, diuretic, fungicidal, herbicidal, insecticidal, sedative, and insect repellent. *Nepeta cataria* (catnip or catmint, *N. cataria*), an aromatic perennial herb, belongs to genus *Nepeta* of Lamiaceae family and has been well known for its medicinal and therapeutic values. It has acted as the representative plant of this genus because it has been the most studied species of this genus. The name catmint is derived from the strong attraction most cats have towards this species[13-16]. It is well known that this plant is a potent behavior-altering drug, i.e. provokes stupor or euphoria in domestic cats and large wild cats (name catnip is derived from words: nip meaning a small quantity of liquor, that intoxicates cats) [17, 18]. Because of this, it is often used in pet toy industry as a safe attractant for cats, especially for cats kept indoors in order to improve the quality of life and to attenuate stress [19, 20]. The main compounds responsible for this reaction in cats are nepetalactones. *N.cataria* has also been known for its essential oil and SMs, which showed tremendous applications in pharmaceutical, agrochemical and food industries. It was shown by the different research groups that the essential oil and different extracts isolated from *N. cataria* have been a rich source of nepetalactones and related compounds (iridoids), which have been mainly responsible for different biological activities of the plant, viz. cat attractant, insect pheromone, insecticidal and insect repellent, etc [18-24]. It has been reported that the biological activity of nepetalactone mainly depends upon the configuration at C-7[25]. Nepetalactone has also been found to be the major component in the defensive secretions of lubber grasshopper and the coconut stick insect[18]. Besides these compounds the plant also contains other compounds related to different classes of natural products like flavonoids (luteolin 7-O-glucuronide, 7-O-glucurono-glucoside, apigenin 7-O-glucuronide, etc.); phenolic acid (caffeic, rosmarinic acids, gallic acid, etc.) [26-30]; steroids (ursolic acid, oleanolic acid, β-sitosterol, stigmasterol, β-amyrin, etc.) [27] and terpenoids (1,8-cineole, α-bisbolene, α-citral, β-caryophyllene, β-farnesene, geraniol, α-humulene, α-terpineol, etc.) [28-30].The Taxonomy of *N. cataria* consists of Kingdom: Plantae, Subkingdom: Viridiplantae, Infrakingdom: Streptophyta, Superdivision: Embryophyta, Division: Magnoliophyta, Phylum: Magnoliophyta, Class: Angiospermae, Subclass: Asteridae,Category: Lamiids, Order: Lamiales, Superorder: Asteranae, Family: Lamiaceae, Subfamily: Nepetoideae, Genus: Nepeta, Species: cataria[31]. The vernacular names of the plant are English: catmint, French: cataire, Germany: echte Katzenminze,Italian: cataria, Japanese: chikumahakka, Spanish :albahaca and commonly known as catnip, catswort,catwort, field balmand catmint[32]. Therefore, in this study, the ethno pharmacological review of *N. cataria* was carried out aimed at providing a detailed precis of the botany, cultivation, ethnomedicinal uses, pharmacological activities and chemical composition of the species.

RESEARCH METHODOLOGY

To recognize pertinent information on the phytochemistry, cultivation, botany, medicinal uses and biological activities of *N. cataria*, a review was amassed based on scientific literature from a variety of sources including Google Scholar, Science Direct, PubMed, Scielo, Springerlink, Google Patents, Web of Science, Sci Finder, Scopus, Espacenet, BioMed Central (BMC) and Medline. The keywords used for recognition of relevant data included dissimilar scientific name and synonyms, common English names and the terms: biological activities, ethnobotany, medicinal uses, medicinal, ethnopharmacology, pharmacology, phytochemistry and therapeutic value, *N. cataria*, catnip, catswort, catwort, field balm and catmint ect. Further literatures were finding from books, book chapters, theses, websites and conference proceedings.

OCCURRENCE AND DISTRIBUTION

The genus *Nepeta* is distributed in temperate regions, mainly in central and southern Europe, the Near East, central and southern Asia and some parts of Africa and it is naturalized in North America. Most *Nepeta* species are endemics, especially in Southwestern Asia (Turkey and Iran).Most of the genus *Nepeta* species have been herbaceous in nature and are used for variety of medical purposes by local and tribal peoples of hilly regions of Turkey, Iran, Korea, Japan and particularly Himalayan region of India, China, Pakistan, Bhutan and Afghanistan[33].*Nepeta cataria* is native to southern Siberia, Central Asia, China and Eastern Europe. Plant widely grows outside to native area, especially in Eurasia, North America, and Africa. This plant prefers slightly alkaline soil to grow[34].

CULTIVATION

N. cataria is cultivated for ornamental purposes and because of the long flowering duration (late May through late August – early September) and large production of pollen and nectar it is very suitable for beekeeping[35-37]. Apart from this, because of its use in pharmaceutical and food industry, as well as in pet toy industry, *N. cataria* has been grown on a large scale. It is one of the most promising aromatic plants in Egypt[38], Ukraine and North America[39]. 'CR9' is the first cultivar of *N. cataria* in North America developed specifically for commercial agricultural production with a more upright growth habit and higher biomass, essential oil and *Z,E*-nepetalactone yield. Apart from that, in germplasm collection and breeding program different genotypes of *N. cataria* are used. These are characterized by completely devoid or producing little amounts of nepetalactone and by a distinct lemony aroma[39]. In Ukraine, there are two varieties of *N. cataria* var. *citriodora*: 'Melody' (for growing in the forest-steppe zone) and 'Peremozhets' (for steppe zone). *N. cataria* plants prefer slightly alkaline soil even though they are not very demanding about the soil-type, however, they prefer well drained ground. *N. cataria* is propagated by seed. Weight of 1000 seeds is 0.5 g. Under open field conditions seed is mainly sown in autumn, conversely, if the sowing is done during spring stratification is necessary[40]. Crops that are established by seedling in the greenhouse in April are transplanted into the field in May. In experiments conducted in Egypt, the seed of *N. cataria* was sown every month from October to April in nurseries to study the effect of date of sowing on germination percentage. Pure sand soil (S1), mixture of 1 vol. sand + 1 vol clay (S2) and mixture of 2 vol sand + 1 vol clay loamy (S3) were used as germination medium. Seedlings of *N. cataria* were planted in the field on 15th April in hills 30 cm apart in rows 60 cm in-between. Two harvests were performed on 15th June and 20th September. Results show that germination percentage varied between 30 to 80%. The highest percentage of germination was obtained when seeds were sown in February and March in the S3 soil medium. The germination percentage in this respect reached up to 70% and 80%[38]. Row width density spacing combinations were established to provide information on cultural management. There were three row widths (45, 90 and 135 cm) and three intra-row spacings (30, 60 and 90 cm). It is established that plant size was greatly affected by plant spacing. Uniform plant spacing of 90×90 cm produced significantly more flowers[36]. In addition, use of several organic mulches (oat straw, a flax straw mat and nonwoven wool mat) in comparison to positive (hand-weeded) and negative (non-weeded) controls, it is established that *N. cataria* plant height was significantly greater in the oat straw than the other treatments. However, there was no significant weed management treatment effect on the concentration of the nepetalactones[41]. Substrate moisture (50, 125 and 250 hPa) had a considerable effect on herbal yield of *N. cataria* var. *citriodora*. In addition, draught stress influenced the essential oil content, i.e. 50 hPa provided high yield of essential oil[42]. In Poland recommendation for fertilization is: 100 kg/ha N, 80 kg/ha P_2O_5 and 120 kg/ha K_2O[43]. Investigation on the impact of different nitrogen concentrations in nutrient solution (50, 150 and 300 mg/l) on herbal yield and content and composition of essential oil of *N. cataria* var. *citriodora* found that concentration of 300 mg/l was effective for herbal yield and favorable for maximum yield of essential oil. Furthermore, the essential oil composition was mainly affected by tested nitrogen concentrations[44]. The growth measurements of *N. cataria* plants during the growth season in Egypt showed that the fresh yield of *N. cataria* herb recorded 138.5 and 180.0 g/plant in the first and the second cut, respectively. Dry yield per hectare in this respect recorded 1.98 and 2.77 t/ha. The total yield of dry weight from two cuts was 4.75 t/ha in both harvests. The highest percentage of oil recorded (0.25%) during the first cut, against 0.19% in second cut[38]. Devastating effects of injurious insect-pests and diseases in *N. cataria* are not only harmful for the plant but also impair the quality of the produce, thus hampering its medicinal value[45]. One bacterial disease and one insect pest that affect this plant has been recorder. Xantomonas leaf spot (*Xantomonas campestris*) is a disease recorded in California. Symptoms consist of small brown flecks that are visible from both sides of the leaf. The flecks later develop into larger, dark brown, angular spots [46]. The feeding insects of small leafhopper *Eupteryx melissae* cause characteristic yellowish-white discoloration of the leaves and injury to the plants[47-50].

MORPHOLOGY

N. cataria grows to a height of 25 to 40 cm. The stem is opaque, hairy, and grey. The leaves are opposite, stalked, heart-shaped, incise-serrate, pointed, hairy underneath and 5 to 7.5 cm long. The flowers are calyx tubular, white with purple markings, approximately 0.5 to 1 cm long and arranged in compact spikes. The entire plant is harvested when in flower, which occurs from June to September. It has a mint like taste and odor and is strongly scented[51-54].

MICROSCOPY

Leaf: dorsiventral; transaction shows single layer of epidermis present on both upper and lower surfaces, leaf bearing glandular and non-glandular trichomes and caryophyllaceous stomata , stomata less frequent on upper surface. Non glandular trichomes are 3-4 cells long and uniseriate. Glandula trichomes are of 2 types: (a) small having unicellular head and unicellular stalk and (b) 4-celled head and unicellular stalk. Mesophyll is differentiated into 2-layered palisade and 4-6 layered spongy parenchyma. Midrib much pronounced towards lower surface, 2 layers of collenchyma present below both upper and lower epidermis in midrib region; vascular bundle in conjoint, collateral and arc shaped.

Petiole: transaction shows single layered epidermis with trichomes as in lamina; 2-3 layers of collenchyma present below epidermis; cortext parenchymatous; a comparatively large conjoint, collateral vascular bundle is present in the centre and flanked by two smaller bundles in the two projecting arm-like structures.

Stem: in transaction rectangular in shape with projecting corners; epidermis single layered with glandular and non-glandular trichomes as in lamina; ridges contain 6-8 layers of collechyma; cortex parenchymatous; pericycle is represented by pateches of sclerenchyma; xylem present in a continuous ring but narrowed at the furrows; phloem present beneath pericyclic patches; pith parenchymatous and having a central is hollow[55-59].

CHEMICAL CONSTITUENTS

Chemical analysis of the air dried flowering aerial parts of *N. cataria* showed 6.2% of moisture, 7.9% of ash, 15.6% crude fiber, 9.1% crude protein, 4.9% crude lipids and 62.5% carbohydrate. Fixed oil extracted from the air dried flowering aerial parts of *N. cataria* contained palmitic (20.3%), stearic (18.6%), oleic (14.2%), palmitoleic (9.6%), linoleic (9.3%), myristic (7.2%), linolenic (5.8%), arachidic (4.1%) and lauric (3.7%) acids. Unsaponifiable matter components are: henetricontane (26.0%), β-sitosterol (18.6%), hexacosane (10.2%), stigmasterol (8.9%) nonacosane (6.8%), campesterol (6.5%), α-tocopherol (5.3%), dodcane (4.0%), dotriacontane (3.0%) and pentacosane (0.8%)[60-74].The aromatic volatiles are produced in the glandular trichomes on the leaf epidermis. Essential oil of *N. cataria* is a colorless, mobile liquid with a pleasant herb-citrus aroma with tones of geraniums[75-81]. The main essential oil constituents of catmint were nepetalactones, geraniol and α-pinene, while nerol, citronellal, neral and caryophyllene oxide were the main constituents of lemon catnip[52,82]. Nepetalactones are a specific type of monoterpene known as iridoids. The stereochemical variation of the nepetalactones is contributed to the biosynthetic pathway. Four nepetalactone stereoisomers with differing stereochemistry at the 4α and 7α positions are observed at different rations in various *Nepeta* species (referred to as *Z,Z*-, *Z,E*-, *E,Z*- and *E,E*-)[53, 83]. However, metabolism of nepetalactone by *N. cataria* plants yielded a significant amount of dihydronepetalactone that were bound to plant components[54]. Also, nepetalactone was labeled from either nerol or citronellol[55, 84]. In the wild *N. cataria* essential oil from 45 compounds were isolated, and the chemical composition varies little during its life cycle. Essential oil is mostly composed of citronellal, neral, geranial, citronellol, nerol and geraniol. Small amounts of other oxygenated monoterpenes were isolated, while sesquiterpenes were *β*-caryophyllene and *α*-humulene. No nepetalactone were found in the oil. This may be explained by the variation of chemical composition during the hydrodistillation. In addition, drying the plant material before distillation did not affect the composition[85, 86].The composition of *N. cataria* essential oil at different growth stages (vegetative, floral budding, full flowering and fruit settings) shows that nepetalactones were the major constituents of all growth stages[57, 87]. There are noted seasonal variations of volatile compounds from different *N. cataria* plant tissues (stems, leaves and flowers). In the flower oil 65 components were recorded with sesquiterpenes as the dominant component (54.8%), while the leaf oil before and during flowering contains mainly monoterpenes (54.6% and 94.0%, respectively), with *Z,E*-nepetalactone as the most abundant components. As for the stem oil the dominant were acids. For instance, the aroma of fresh herb changes after drying due to losses of the most volatile constituents and consequently green aroma notes. In addition, differences in the quantitative composition of volatile compounds isolated by the different techniques were considerable[20, 88]. The changes in the essential oil composition were observed across harvests suggesting that ecological factors during growth stages may play a major role. Various drying methods had a significant effect on the essential oil content and composition[58, 89]. Research conducted in Poland confirmed that the essential oil of *N. cataria* var. *citriodora* is rich in monoterpene alcohols citronellol and geraniol, and the monoterpene aldehydes neral and geranial. The yield from steam distillation was better than that from hydro distillation, but lower concentrations of neral and geranial were obtained. Total monoterpene aldehydes were higher altering hydrodistillation whereas steam distillation gave oil richer in monoterpene alcohols[59, 90]. Apart of essential oil, *N. cataria* contain non-volatile compounds.

TRADITIONAL USES

The knowledge of traditional usage of any plant has been very important in order to attract different research groups belonging to different fields of science with an aim to get more and more and to explore extensive application of research plant in human well-being. *N. cataria* has a long history of association with the traditional medicine practices of the peoples of different tribes and countries[8, 91]. The French peoples used young leaves and shoots of *N. cataria* for seasoning. England's public hangmen chewed this plant while performing their duties due to its hallucinogenic properties. The tea prepared from its leaves traditionally has been used as soporific and sedative and against gastrointestinal and respiratory diseases, viz. diarrhea, asthma, cough, bronchitis, etc.[6, 12, 92]. Many Indian tribes from North America and Chippewa used leaves of this plant to prepare herbal tea. Iroquois, Cherokee, and Okanagan-Colville Indian tribes used this plant as a remedy to cure colds, coughs, and stomach upsets. On the other hand, Iroquois Indian tribes took this plant for the treatment of diarrhea, vomiting, sore throats, and headaches. Menominee peoples used this plant to induce sweating and for the cure of pneumonia, Rappahannock for pain relief, and Cherokee for ease of fever and blood and female disorders. Further Cherokee Indians took this plant for the treatment of convulsions, boils, and worms and Shinnecock used dried leaves for smoking to cure rheumatism[93]. Furthermore, flowering tops and dried leaves have been aromatic in nature and therapeutically used as diaphoretic, carminative, tonic, antiseptic, emmenagogue, refrigerant, soporific, and stimulant and against tooth ache in traditional medicine system.

Other biological and medicinal properties of *N. cataria* are the following:

- The extract isolated from *N. cataria* showed inhibitory activity on growth, production,and adhesion of enzyme and some bacteria. Juvenile hormone activity has also been reported from catnip plant extract.
- *N. cataria* has been employed traditionally for the cure of painful swellings in English folk medicine.
- Fresh or dried scented flowering tops and leaves have been used in soups and cheese and as flavoring agents particularly for cooked foods and sauces and in medicine.
- It has been used in the production of insect pheromones and a part of strategies for insect pest management.
- It has been used in popular medicine, dyes, and teas in North America.
- This plant has promoted sweating and has also been useful against insomnia, colds, flu, and fevers when taken as hot infusion. Further, it has been supposed to be helpful in allaying morning sickness and preventing miscarriage and premature birth.

Apart from these *N. cataria* showed many biological activities, viz. anti-inflammatory, anti-nociceptive activity, antimicrobial, antifungal activity, antioxidant activity, anthelmintic activity, cytotoxic activity, felineattractant activity, insect repellent, insecticidal activity, nematicidal activity, spasmolytic, bronchodilatory activities and trypanocidal activity[94].

Reported pharmacological activities of *N. cataria*

Activity	Plant parts/Solvent	Model	Ref
Anti-inflammatory, Anti-nociceptive	Leaves, essential oil	open field, Tail immersion test, Acetic acid writhing reflex, Carrageenan-induced edema	95
Anti-inflammatory	flowers, upper leaves and lower leaves, methanol	Inhibition of nitric oxide production	96
Cytotoxic	essential oils	bronchial epithelial cell lines and human keratinocyte by microculture tetrazolium (MTT) essay	97
Cytotoxic	herb's powder, ethanol	human lung cancer cell line A549	98
Antimicrobial	herb's powder, diethyl ether	44 *Staphylococcus aureus* strains,	99
Antibacterial	essential oil	*Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcuspneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*	100
Antibacterial	Whole plants, essential oils	*Escherichia coli*, *Staphylococcus aureus*, *Salmonella enteritidis*	101
Antimicrobial	essential oil and leaves methanol extracts	1 yeast, 24 bacteria, and 15 fungal stains	102
Antimicrobial	Leaf, dichloromethane and methanol	*Staphyococcus aureus*, *Kliebsiella pneumoniae* and *Salmonella typhii*	103
Antimicrobial	Leaf, methanol	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*, *Pasteurella multocida*,	104

		Klebsiella pneumonia, Aspergillus flavus, and *Candida albicans*	
Antimicrobial	aerial parts, essential oil	food-borne pathogens	105
Antimicrobial	aerial parts, essential oil	*S. typhi, S. paratyphi and E. coli, S. agalactiae and S. epidermidis,* S. mutans	106
Antimicrobial	essential oil, (*Z,E*)- and (*E,Z*)-nepetalactones	5 Gram-positive and 9 Gram-negative bacteria	107
Antioxidant	Leaves, methanol	DPPH radical scavenging	108
Antioxidant	Leaf, stem, Ethanol, methanol, water	DPPH, ABTS, FRAP assay	109
Antioxidant	Whole plant, ethanol	ferric thiocyanate method, Reduction power, DPPH, Superoxide anion radical scavenging activity	110
Antioxidant	70% ethanol, petroleum ether and chloroform	DPPH and nitric oxide (NO) free radical scavenging	111
Anthelmintic, Nematicidal, and Trypanocidal	Leaf, methanol; diethyl ether	*Haemonchus contortus* worms, gastrointestinal Nematodes; second-stage juveniles and egg hatchability of *Meloidogyne incognita;* epimastigotes of *Trypanosoma cruzi*	112, 113
Antidepressant, anxiogenic, and motor	Leaves, n-hexane and ethanol	*Behavioral despair test,Elevated plus maze,Open field test*	114
Hepatoprotective	Leaf, essential oil	Acetaminophen-induced Liver Dysfunction	114
Calcineurin inhibition	Leaves , stems, DMSO	Direct calcineurin assay, Calmodulin activated calcineurin assay	116
Sexual behavior and penile erection	Chow with leaves	Sexual behavior test, Penile erection and yawning tests, open field test, Motor coordination test	117
Spasmolytic and bronchodilatory properties	essential oil	*calcium channel blocking activity, Guinea-pig trachea, phosphodiesterase inhibitory effect, Guinea-pig atria*	118
Larvicidal	aerial parts, essential oils	*Aedes aegypti*	119

Insect Repellent, Attractant, and Insecticidal Activity

The essential oil isolated from different parts of *N. cataria* has been reported to protect well from several insect pests, cockroaches, and many mosquito species, which transmit several diseases[120-124]. Further, essential oil obtained from catmint plant repels about 13 families of insects[125]. Peterson and Coats (2001) reported that the *E,Z*-isomer of nepetalactone obtained from catnip oil has been more active in comparison to *Z,E*-isomer and DEET (N,N-diethyl-3-methylbenzamide) as insect repellent[120]. Schultz et al. (2004) evaluated catnip essential oil for its repellence activity against houseflies (*Musca domestica*) and American cockroaches (*Periplaneta americana*) and found that catnip essential oil has been good and in some cases better repellent as compared to citronellal or DEET. Catnip essential oil has shown more repellent activity than citronellal and DEET in the short-term bioassay[121]. Further, Chauhan et al. (2005) observed that compounds isolated from catnip oil have showed greater bite deterrence effect as compared to ethanol control against yellow fever mosquito (*Aedes aegypti)*, whereas racemic nepetalactone and their individual isomers have showed less effective deterrence effect as compared to DEET or (1*S*,2'*S*)-2-methylpiperidinyl-3-cyclohexene- 1-carboxamide (SS220) against biting of *A. aegypti*[126]. Amer and Mehlhorn (2006) tested the essential oil of catnip for its repellent activity and protection potential using the skin of human volunteers against yellow fever mosquito. The oil has shown protection time of 8 h with 100% repellent potential against all three tested species[96]. Gonzalez and Hallahan (2007) observed that dihydronepetalactone minor component of catnip essential oil has been more stable and has pleasant fragrance as compared to nepetalactone. Further, it has shown insect repellent activity with improved properties as compared to nepetalactone and in some cases this activity exceeded than synthetic compound DEET[128].

SAFETY AND TOXICITY

Zhu et al. (2009) evaluated catnip (*N. cataria*) essential oil for its dermal, acute oral, primary dermal, eye irritation, and inhalation toxicity[129].

Acute Oral Toxicity

Catnip oil has not caused any mortality and also not even induced any toxicity in treated male and female mice when exposed to a dose of 1000–2150 mg/kg BW (body weight) with exception of death of one male mouse. The study revealed that the catnip oil has showed medium lethal dose (LD50) at 2710 mg/kg BW in case of male and 3160 mg/kg BW in case of female mice.

Acute Dermal Toxicity

The test for acute dermal toxicity using single dose of catnip oil (5000 mg/kg BW) on Wistar rats showed that all rats have survived and remained active after the testing. It revealed that the catnip oil has not shown any acute dermal toxicity and no major abnormalities have been observed in any of the tested animals. The catnip oil has showed acute dermal LD50 >5000 mg/kg BW.

Acute Inhalation Toxicity

The catnip oil when applied at a concentration of 10 g/m3 to a group of mice has showed no toxicity effect and abnormalities in treated animals after two weeks. For acute inhalation LC50 >10 g/m3 has been observed in case of both sexes of mice.

Primary Skin Irritation

No signs of erythema or edema have been observed in four New Zealand white rabbits during first two days of the application at a dose of 0.5 g of catnip oil. On the third day of application minor erythema has been reported in one animal on the treated area, but in case of other animals it has been observed on fourth day. However no edema and skin irritation have been observed in case of any tested animals during the whole testing period.

Primary Eye Irritation

The catnip oil has not been exhibiting any signs of corneal opacity and iritis on three tested rabbits. During the first hour of test, conjunctival irritation has been observed, but it has not persisted for twenty four hours. During the testing period no gross toxicity signs have been observed in tested animals[130-136].

FUTURE PROSPECTIVE

It has been reported by different research groups that the different extracts obtained from *N. cataria* have showed prominent anti-inflammatory, anti-nociceptive, cytotoxic, anthelmintic, nematicidal, trypanocidal, spasmolytic, and bronchodilatory activity, but only a few papers have been published on these topics. Apart from these many species of genus *Nepeta*, viz. *N. juncea*, *N. hindostana*, *N. pannonica*, *N. nuda ssp. albiflora*, etc., have been known to show prominent vasorelaxant, platelet aggregation, anti-atherosclerotic, and phytotoxic activity. These species have comparable chemical composition to *N. cataria*. So, there has been remarkable scope for exploring ethnopharmacology of *N. cataria.* Nepetalactone and related iridoid compounds having 1-R configuration have acted as sex pheromones in many species of aphids, viz. *Megoura viciae*, greenbug (*Schizaphis graminum*), pea aphid (*Acyrthosiphon pisum*), black bean aphid (*Aphis fabae*), bird-cherry aphid (*Rhopalosiphum pad*), peach-potato aphid (*Myzus persicae*), potato aphid (*Macrosiphum euphorbiae*), and hop aphid (*Phorodon humuli*). Due to these aforementioned properties of nepetalactone and related compounds, there has been a great opportunity to use these compounds in integrated pest management strategies for the control of different harmful insect pest species, as this is the need of present world to explore the new compounds for this purpose due to the resistance developed by the insect pests against different chemicals used in present time. Further nepetalactone and its derivatives have been well known for their insect repellent properties. Iridoid compounds have acted as a key intermediate for the synthesis of different kinds of alkaloids, i.e., secologanin monoterpene glycoside has been the chief compound in the alkaloid biosynthesis. Iridoid loganin has acted as the biosynthetic precursor for the synthesis of secologanin. Nepetalactone and its isomers can act as the precursors for the synthesis of loganin and hence for the synthesis of different kinds of alkaloids. This opens the new field for the synthetic chemists for the synthesis of useful alkaloids from the precursor which have not been of amino acid origin. Apart from these essential oils and different extracts obtained from *N. cataria* may find many applications in cosmetic, pharmaceutical, and agrochemical industries[63].

CONCLUSION

Although many pharmacologically active secondary metabolites have been discovered so for, yet the nature must have many more in her basket. So, a detailed and systematic study is required in order to identify and document the plants, which have been pharmacologically important and provided a variety of secondary metabolites of biological importance. *N. cataria* has been a representative species of genus *Nepeta*, which belongs to family Lamiaceae. The plant has been known for its wide range of traditional usages and used to relieve pain, and for the cure of different gastrointestinal and respiratory ailments, female disorders, pneumonia, rheumatism, etc. The chemical diversity of *N. cataria* has mainly been represented by terpenoids, flavonoids, polyphenols, and steroids; out of these iridoid compounds (unique class of terpenoids) such as nepetalactone and its derivatives have been the representative chemical constituents of this plant and genus *Nepeta*. These chemical constituents have been chiefly responsible for the numerous biological activities shown by the plant, out of which their anti-inflammatory, antidiabetics, antioxidant, and insecticidal have been the most outstanding. Further, the toxicological studies of this plant have revealed that the essential oils and different extracts obtained from the plant have mostly been nontoxic in nature. In spite of this, there have been numerous areas of its usage in traditional medicine system that still need pharmacological justification. This review would be supportive in the enhancement of today's research in the development of new biologically potent compounds derived from plants (of genus *Nepeta*) and which would find many applications in the well-being of mankind.

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