Pharmacology and Toxicology of *Nepeta cataria* (Catmint) Species of Genus *Nepeta*: A Review

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Introduction

Peoples from ancient time use secondary metabolites (SMs) of plant origin in their everyday life for the treatment of many diseases, to keep away and eradicate insects, as food preservatives and flavoring agent, etc. World Health Organization in its survey estimated that 80% of the world's population largely depends on conventional drugs obtained from SMs for their health care (Gopal et al. 2014). Peoples in countries like India, China, and Egypt used SMs of plant origin as medicine, which forms the basis of the conventional medical system (Ravishankar and Shukla 2007). Nowadays, in different countries 119 chemicals isolated from 90 plant species are used as significant drugs (Siddiqui et al. 2014). With the course of time, synthetic chemicals have replaced SMs of plant origin as the former have more precise action and provide early results. However, these synthetic chemicals have many side effects and cause many serious problems, viz. human health issues, gene mutation, resistance developed by insects and pests, biodiversity reduction of agroecosystems, and environmental pollution. Due to these reasons in the present scenario, strategies have been made to replace synthetic chemicals with SMs of plant origin because these are ecofriendly, biodegradable, less toxic, and cost effective in nature. The SMs of plant origin belong to different classes of natural products, viz. alkaloids, carotenoids, flavonoids, phenolics, tannins, terpenoids, etc., and have been well known for their biological potential. The biological potential of secondary metabolites depends on their nature and composition (Celis et al. 2008). The plant families such as Apiaceae, Asteraceae, Cupressaceae, Lauraceae, Myrtacea, Piperaceae,

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M. Ozturk, K. R. Hakeem (eds.), *Plant and Human Health, Volume 3*,
https://doi.org/10.1007/978-3-030-04408-4_13

Poceace, Rutaceae, and Zingiberaceae have been known for their valuable and useful bioactive SMs and Lamiaceae is one of them.

Nepeta has been a multiregional genus of the Lamiaceae (labiatae or mint) family and have a rich source of bioactive SMs. 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 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 (Rapisarda et al. 2001; Dabiri and Sefidkon 2003; Formisano et al. 2011), anti-inflammatory, antitussive, antiasthmatic, antiseptic (Aggarwal et al. 2007; Sharma and Cannoo 2013), sedative, diaphoretic, febrifuge, antioxidant (Tepe et al. 2007), insecticidal, antimicrobial (Edewor and Usman 2011), antiviral, and fungicidal (Sharma and Cannoo 2016a). Further, these have also been used against scorpion and snakebites (Rapisarda et al. 2001; Formisano et al. 2011), stomach diseases (Sharma and Cannoo 2013), kidney and teeth troubles, liver diseases (Baser et al. 2000), 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), 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 *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 (Tapsell et al. 2006; Aggarwal et al. 2007) and act as renewable source for the same (Sherman and Hash 2001), *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, insect pheromone, insecticidal and insect repellent, etc. (Peterson and Coats 2001; Peterson et al. 2002; Baranauskiene et al. 2003; Herron 2003; Peterson and Ems-Wilson 2003; Chauhan et al. 2005; Amer and Mehlhorn 2006; Formisano et al. 2011). It has been reported that the biological activity of nepetalactone mainly depends upon the configuration at C-7 (Zimmermann et al. 2012). Nepetalactone has also been found to be the major component in the defensive secretions of lubber grasshopper and the coconut stick insect (Peterson and Coats 2001). 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.) (Modnicki et al. 2007); steroids (ursolic acid, oleanolic acid, *β*-sitosterol, stigmasterol, *β*-amyrin, etc.) (Jamila et al. 2011); and terpenoids (1,8-cineole, α-bisbolene, α-citral, β-caryophyllene, β-farnesene, geraniol, α-humulene, α-terpineol, etc.) (Sajjadi 2005; Rather et al. 2012; Sharma and Cannoo 2013).

The presence of medicinally active phytoconstituents in *N. cataria* and tremendous potential of these compounds in agrochemicals, food, cosmetics, and pharmaceutical industries allow us to write this review in order to provide valuable information regarding this plant to scientific communities.

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 (Kafaru 1994; Sharma and Cannoo 2013). 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. (Baser et al. 2000; Shafaghat and Oji 2010; Formisano et al. 2011). 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 (Sue Eland 2008). 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 (Nostro et al. 2001; Adiguzel et al. 2009). Juvenile hormone activity has also been reported from catnip plant extract (Louey et al. 2001).
- *N. cataria* has been employed traditionally for the cure of painful swellings in English folk medicine (Turner 1995).
- 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 (Leung and Foster 1996).

- It has been used in the production of insect pheromones and a part of strategies for insect pest management (Birkett and Pickett 2003).
- It has been used in popular medicine, dyes, and teas in North America (Ricci et al. 2010).
- 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 and anti-nociceptive activity (Ricci et al. 2010), antimicrobial and antifungal activity (Nostro et al. 2001; Suschke et al. 2007; Bisht et al. 2010), antioxidant activity (Adiguzel et al. 2009; Lee et al. 2010; Kraujalis et al. 2011), anthelmintic activity (Bandh et al. 2011), cytotoxic activity (Suschke et al. 2007), feline attractant activity (Formisano et al. 2011; Sharma and Cannoo 2016b), insect repellent and insecticidal activity (Peterson, 2001; Schultz et al. 2004; Bernier et al. 2005; Trongtokit et al. 2005; Zhu et al. 2006; Birkett et al. 2011), nematicidal activity (Pavaraj et al. 2012), spasmolytic and bronchodilatory activities (Gilani et al. 2009), and trypanocidal activity (Saeidnia et al. 2008).

Phytochemistry

The composition, quality, and quantity of secondary metabolites obtained from different extracts and essential oils of different plants depend upon the age and growth stage of plant, plant organ, time of collection of plant part, climate, and soil composition (Angioni et al. 2006). So, for the extraction of essential oils and extracts of identical composition again and again these have to be extracted from the same plant organ collected at the same time, age, and growth stage of plant under same climate conditions.

The genus *Nepeta* and the species *N. cataria* have been known for their special class of terpenoids known as iridoids, viz. nepetalactone, dihydronepetalactone, 5,9-dehydronepetalactone, iridomyrmecin, and neptelic acid. These compounds are present in higher concentration in essential oils isolated from different species of this genus and have been responsible for their biological activities.

Biological Activity (Pharmacology)

Anti-inflammatory, Anti-nociceptive and Cytotoxic Activity

Ricci et al. (2010) noted anti-nociceptive and anti-inflammatory action of the essential oil extracted from the leaves of *N. cataria*. Essential oil of *N. cataria* (EONC) at dosages of 0.0005 and 0.001 mL/kg has resulted in increased general activity of female mice but a dose of 0.0005 mL/kg reduced the immobility of test organism. Suschke et al. (2007) reported cytotoxicity of essential oils isolated from *N. cataria* and *N. cataria* var. *citriodora* against bronchial epithelial cell lines and human keratinocyte by microculture tetrazolium (MTT) essay. The essential oils have shown cytotoxic activity against both bronchial epithelial cells and keratinocytes at CC_{50} (cytostatic concentration) values 0.0012–0.015% (v/v). Further, it has been reported that the different extracts of *N. cataria* and *Teucrium chamaedrys* have acted as retardant for calcineurin (inflammation mediated through T cell). The bioactive fractions have been isolated with the help of HPLC and showed the presence of lamiuside A (teupolioside), verbascoside, and caffeoyl phenylethanoid glycoside teucrioside. These compounds have played an important role in calcineurin inhibition (both in the absence and presence of calmodulin).

Antimicrobial and Antifungal Activity

The essential oil isolated from *N. cataria* rich in β-caryophyllene, 4aα, 7α, 7aα-nepetalactone, and 4aα, 7α, and 7aβ-nepetalactone showed antimicrobial activity against seven fungi and five bacteria (Sharma and Cannoo 2013 and references therein). Further, Nostro et al. (2001) evaluated the diethyl ether extract isolated from same plant against 44 *Staphylococcus aureus* strains (some resistant to methicillin) and *S. aureus* 6538P (American Type Culture Collection) for their antibacterial activity by noting the effect of subminimum inhibitory concentrations on in vitro adherence, DNase, coagulase, thermonuclease, and lipase production. Thermonuclease, DNase, and lipase have been retarded at concentrations equal to 1/2 and 1/4 MIC (minimum inhibitory concentration). Suschke et al. (2006) tested the essential oil of *Melissa officinalis* (lemon balm), *N. cataria* var. *citriodora* (lemon catnip), and *N. cataria* (catnip) against clinical isolates of respiratory tract bacteria. The antibacterial activity has been tested in vitro with modified broth microdilution method. These results have indicated the occurrence of cross resistance towards standard antibiotics and natural resistance towards tested essential oils in these bacteria.

The essential oils obtained from *N. cataria*, *N. atlantica*, and *N. tuberosa* have been tested for their antimicrobial (against *Escherichia coli*, *Staphylococcus aureus*, *Salmonella enteritidis*) potential by Zenasni et al. (2008). The results have shown that the biological potential of genus *Nepeta* alters according to the chemical composition and concentration of nepetalactone plays an important role in case of antibacterial potential against tested bacteria. The tested essential oils have showed comparable antibacterial potential. Adiguzel et al. (2009) reported the biological potential of *N. cataria* essential oil and methanol extracts individually against 1 yeast, 24 bacteria, and 15 fungal stains. Only 5 bacterial and 7 fungal stains have shown sensitivity towards methanol extracts whereas essential oil has shown activity against 1 yeast, 11 bacteria, and 12 fungi. Maximal inhibition zones and MIC values in case of oil-sensitive bacterial stains range from 10–32 mm to 15.62–250 µL/mL, whereas in case of yeast and fungal stains it ranges from 10–39 mm to 15.62–125 μL/mL, respectively.

The presence of glycosides, coumarins, and flavonoids in *N. cataria* leaf extracts (dichloromethane and methanol) was reported by Edewor and Usman (2011). The extracts showed outstanding antibacterial activity against gram-positive bacteria compared to gram-negative. This biological potential of the different extracts of *N. cataria* against tested microorganisms has been attributed to the presence of different flavonoids in these extracts (Bisht et al. 2010; Sharma and Cannoo 2016a).

Bandh et al. (2011) analyzed antibacterial and antifungal potential of *N. cataria* methanolic extracts against animal pathogenic bacterial and fungal strains (viz. *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*, *Pasteurella multocida*, *Klebsiella pneumonia, Aspergillus flavus*, and *Candida albicans*). The extracts have possessed more antibacterial activity in comparison to its antifungal activity. Further, in the same year Bandh et al. (2011) evaluated the antimicrobial activity of aqueous extracts obtained from leaves of *N. cataria* at different concentrations against two fungal (*Candida albicans* and *Aspergillus flavus*) and five bacterial stains (*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumoniae*).

Antioxidant Activities

Lee et al. (2010) reported that rosmarinic acid has been one of the major antioxidants present in different extracts of *N. cataria.* Kraujalis et al. (2011) tested methanol extracts of *N. cataria* var. c*itriodora*, *N. transcaucasica, N. cataria*, and *N. bulgaricum* for their antioxidant potential and established that methanol extracts of *N. cataria*, *N. transcaucasica*, and *N. bulgaricum* retarded approximately 80% of DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals present in the reaction, while *N. cataria* var. *citriodora* retarded DPPH radicals present in the reaction only up to 44%. The strong antioxidant rosmarinic acid has been the chief component present in all extracts, while luteolin and caffeic acid have been present in lower amounts. Mihaylova et al. (2013) studied the antioxidant potential of three extracts obtained from *N. cataria*, viz. 70% ethanol extract obtained by heat reflux method and water and 70% ethanol extract obtained by ultrasonication-assisted method (UAE with water and UAE with 70% ethanol) with ferric-reducing antioxidant power (FRAP), 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging, and 2,2′-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical decolorization assay. The results indicated that the extract obtained from conventional heat reflux method showed highest antioxidant potential in comparison to UAE extracts, which have been further supported by the high-concentration polyphenol and flavonoid compounds in 70% ethanol extract obtained by heat reflux as compared to UAE extracts.

Anthelmintic, Nematicidal, and Trypanocidal Activity

Bandh et al. (2011) studied the anthelmintic activity of methanol extract obtained from *N. cataria* both in vitro and in vivo. Anthelmintic effects ($p > 0.05$) of methanolic extract on live *Haemonchus contortus* worms have been revealed from their death and/or paralysis after 8-h exposure by an in vitro study. On the other hand, in vivo study of extract in sheep (infected naturally with mixed species of gastrointestinal nematodes) has demonstrated a maximum (73.69%) egg count reduction on day 15 after treatment in treated sheep at a dose of 2 g/kg body weight. Pavaraj et al. (2012) evaluated the nematicidal activity of methanol extracts isolated from ten plants against second-stage juveniles and egg hatchability of *Meloidogyne incognita.* The nematode juveniles and eggs have been exposed to different concentrations of plant extract ranging from 10 ppm (*parts per million)* to 100 ppm for 24, 48, and 72 h. *N. cataria* and *Couroupita guianensis* extracts have shown mortality of 73–86% after exposure of 72 h. The egg-hatching capacity has been declined with increase in concentration of plant extracts. The extracts obtained from *N. cataria, Pentanema indicum*, and *Couroupita guianensis* have shown more reduction in egg hatching in comparison to extracts obtained from other tested plants. Nematode mortality and larval hatching have been affected strongly by selected plant species, concentration of extracts, and exposure duration of nematode and larvae. These activities of different plant extracts have been attributed to the presence of different oxygenated compounds and their derivatives, which interact with biomembrane and cytoplasm of the nematode. Saeidnia et al. (2008) evaluated diethyl ether extract of *N. cataria* isolated from young leaves for its trypanocidal activity against epimastigotes of *Trypanosoma cruzi*. The diethyl ether extract revealed strong trypanocidal activity with minimum lethal concentration of 6.2 μM.

Effects on Central Nervous System

Nepetalactone, nepetalic acid, and commercial sample of *N. cataria* oil have been screened for their behavioral and toxicological effects in rats and mice (Ali et al. 2012). Biphasic effect of alcoholic extract of *N. cataria* has been reported on the behavior of chicks by Fareed et al. (2013). High dose greater than 2 g/kg has induced sleep in a less number of chicks, whereas low and moderate dose greater than 25–1800 mg/kg has induced sleep in a large number of chicks. This agent has been very effective in promoting sleep, calming nervous system, and relieving pressure.

The antidepressant effect of 10% enriched chow with *N. cataria* leaves and apolar extracts has been evaluated in male mice by Bernardi et al. (2010) with the help of behavioral despair test (BDT), elevated plus maze (EPM), and open-field test (OF). The BDT essay revealed the reduction of immobility time in mice upon repeated feeding with chow-enriched leaves ($p < 0.0007$), whereas no differences have been observed with EPM or OF test in case of repeated feeding groups with chow-enriched leaves. Further, OF test in mice (treated acutely) with apolar extract of *N. cataria* leaves has shown reduction in rearing frequency ($p < 0.0042$) and locomotory activity ($p < 0.0001$) in comparison to control group. The time of immobility has been decreased in BDT, when mice have been treated with apolar extract repeatedly ($p < 0.001$) and acutely ($p < 0.0001$). Furthermore, when apolar extract has been administrated repeatedly it decreased the latency for the first immobility ($p < 0.0001$). The data revealed that apolar extract of *N. cataria* has antidepressant activity. Apart from this there have been many other reports attributed to anxiolytic and antidepressant properties of *N. cataria* plant (Bhat and Moskoviz 2009).

Feline Attractant

Different *Nepeta* species have been known for their feline attractant properties for a long time. These properties of different *Nepeta* species have been due to the presence of nepetalactone and its isomers in different extracts of aforementioned species. The unique behavior pattern has been observed in most of the species of Felidae family towards compounds obtained from *N. cataria*. These compounds have showed pseudo-narcotic effects and might either act as hallucinogens or cross-react with social odors of natural origin. Birkett et al. (2011) synthesized the unnatural (4aR,7R,7aS)-nepetalactone and enantiomer of (4aS,7S,7aR)-nepetalactone. These two molecules have been bioassayed against two American short-hair, three Abyssinian, and four Japanese cats. Almost all cats reacted strongly especially the female ones towards both the enantiomers. Female cats have been found to be extremely attractive even at the dose of 0.01 mg.

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 (Peterson 2001; Schultz et al. 2004; Bernier et al. 2005; Trongtokit et al. 2005; Zhu et al. 2006). Further, essential oil obtained from catmint plant repels about 13 families of insects (Maia and Moore 2011). 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. 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. 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*. 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. 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.

Spasmolytic and Bronchodilatory Activities

Gilani et al. (2009) evaluated essential oil of *N. cataria* for their spasmolytic and bronchodilatory activities on gastrointestinal and respiratory disorders. The essential oil, verapamil, and papaverine have suppressed spontaneous and high pre-contractions of K^+ (80 mM) in isolated rabbit jejunum and also shifted concentration–response curves of Ca^{2+} to right, indicating the blocking activity in calcium channel. Further, this essential oil and papaverine suppressed the K^+ and carbachol (1 μm) pre-contractions in isolated trachea of guinea pig. The oil has shown PDE (phosphodiesterase) inhibitor activity like papaverine. Furthermore, the oil at 25–80 times higher concentrations caused cardiodepression similar to papaverine in isolated atria of guinea pig. The above study indicated that *N. cataria* possesses myorelaxant and spasmolytic activities regulated through dual inhibition of PDE and calcium channels. This study has explained the traditional use of essential oil of *N. cataria* in cough, diarrhea, and asthma.

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.

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 (LD_{50}) 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 LD_{50} > 5000 mg/kg BW.

Acute Inhalation Toxicity

The catnip oil when applied at a concentration of 10 g/m^3 to a group of mice has showed no toxicity effect and abnormalities in treated animals after two weeks. For acute inhalation LC_{50} > 10 g/m^3 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.

Toxicology Study of Refined Oil of **N. cataria** *(Biochemical Pesticide)*

US Environmental Protection Agency has categorized the refined oil of *N. cataria* (hydrogenated catmint oil) into different toxicological category I, II, III, and IV depending upon the hazards recognized from the study of information given to the agency. Category IV indicates lowest whereas category I indicates highest toxicity.

The agency has categorized the technical grade refined oil into category III for primary eye irritation and acute oral toxicity and into category IV for acute dermal, skin, and acute inhalation irritation.

Future Prospective

Ethnopharmacological 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 (Suschke et al. 2007; Saeidnia et al. 2008; Ricci et al. 2010; Bandh et al. 2011; Pavaraj et al. 2012). 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 (Ashraf et al. 1999; Hussain et al. 2009; Mancini et al. 2009). These species have comparable chemical composition to *N. cataria*. So, there has been remarkable scope for exploring ethnopharmacology of *N. cataria.*

Integrated Pest Management (Sex Pheromone Defensive Secretions)

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*) (Goldansaz et al. 2004). Due to these aforementioned properties of nepetalactone and related compounds, there have 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.

Biosynthesis of Alkaloids

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.

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 non-toxic 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.

Acknowledgements The first author is grateful to DST (Department of Science and Technology), Govt. of India, New Delhi, for financial assistance under INSPIRE programme (INSPIRE Code IF120715).

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