ejpmr, 2017,4(4), 135-138

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

FURTHER CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF SOME *NEPETA* SPECIES FROM IRAN.

Prof. Abdolhossein Rustaiyan[1]*, Mahdieh Ariaee Fard MSc.[2] and Afsaneh Faridchehr PhD.[3]

[1,3]Department of Chemistry, Faculty of Basic Sciences, Science and Research Branch Islamic Azad University, Tehran, Iran.

[2]Faculty of Pharmaceutical Chemistry, Department of Phytochemistry and Essential Oils Technology, Islamic Azad University, Pharmaceutical Sciences Branch (IAUPS), Tehran, Iran.

***Corresponding Author: Prof. Abdolhossein Rustaiyan**

Department of Chemistry, Faculty of Basic Sciences, Science and Research Branch Islamic Azad University, Tehran, Iran.

Article Received on 31/01/2017 **Article Revised on 21/02/2017** **Article Accepted on 14/03/2017**

ABSTRACT

In this review, we will continue with the rest of the Iranian *Nepeta* species. Surely we will discuss their constituents and biological activities of *Nepeta kotschyi* Boiss., *Nepeta mirzayanii* Rech. F. et Esfand., *Nepeta menthoides* Boiss. and Buhse., *Nepeta mahanensis* Jamzad & Simmonds, *Nepeta macrosiphon* Boiss., *Nepeta meyeri* Benth., *Nepeta persica* Boiss., *Nepeta pogonosperma* Jamzad et Assadi, *Nepeta prostrate* Benth, *Nepeta pungens* (Bunge.) Benth., *Nepeta straussii* Hausskn. & Bornm., *Nepeta saccharata* Bunge., *Nepeta racemosa* Lam., *Nepeta rivularis* Bornm., *Nepeta schiraziana* Boiss. and *Nepeta sintenisii* Bornm.

KEYWORD: *Nepeta* species, Lamiaceae, Constituents, Biological activities.

INTRODUCTION

We have recently published a review article on some of the Iranian *Nepeta* species [1]. We will now continue about the rest of the *Nepeta* species from Iran. The feline attractant properties of several *Napeta* species have been known for a long time. *Nepeta cataria* L., commonly known as catnip, is the most intensively studied species. Nepetalactone was identified as the main constituent in the oil of the species [2]. Regnier et al. concluded from their studies that ants are strongly repelled from their natural food sources by the oils of *N. cataria*, *N. mussini* (syn. *N. racemosa*) and *N. citriodora* [3].

The extract of many *Nepeta* species are also used in domestic medicine because of their diuretic properties and slight bacteriostatic activity and in ointments to heal skin disorders of the eczema type [4].

In this review, we will discuss the rest of Iranian *Nepeta* species which we have mentioned in the abstract of this review.

Nepeta kotschyi Boiss.

The volatile constituents of the aerial parts of *Nepeta kotschyi* Boiss. growing wild in Iran have been examined by GC/FID and GC/MS. Eleven components were identified, constituting approximately 97.7% of the oil. The main constituents of the essential oil were 4aβ, 7α, 7aα-nepetalactone (92.0%), 1, 8-cineol (2.6%), β-pinene (0.9%), pulegone (0.4%) and bicyclogermacrene (0.3%)[5].

Nepeta mirzayanii Rech. F. et Esfand.

The essential oil from the aerial parts of *Nepeta mirzayanii* Rech. f. et Esfand was obtained by hydrodistillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass spectrometric detection. Twenty-two compounds were characterized in the oil of *N. mirzayanii* with 4aα, 7a, 7aα-nepetalactone (61.0%) and caryophyllene oxide (7.8%) as main constituents [6].

Nepeta menthoides Boiss. and Buhse.

The composition of the essential oils of *Nepeta menthoides* Boiss. and Buhse. was investigated by means of gas chromatography (GC) and GC- mass spectrometry (MS). 1, 8-cineole was the most abundant component in oil of *N. menthoides* (41.1%). Other significant components were dihydromyrcen-1-ol (9.2%), 4-terpineol (7.1%), and geranyl acetate (6.1%) were in the oil of *N. menthoides* [7].

In another study, the chemical composition of *Nepeta menthoides* oil which is an endemic species to Iran was extracted by Clevenger apparatus and its components were analyzed by means of GC-MS. From eighteen constituents representing 97.07% of the oil, 4aα, 7α, 7aα-nepetalactone (36.85%), 1, 8-cineol (31.29%), 1-terpinene-4-ol (4.39%), α-terpineole (4.2%), geranyl acetat (3.5%), neryl acetat (3.5%) and β-pinene (3.39%) were the major components of the oil [8].

In another study, the essential oil of aerial parts was obtained by hydrodistillation and analyzed by GC/MS. The present work describes *in vitro* cytotoxic activity of the essential oil evaluated against HT-29 (colon carcinoma), Caco-2 (colorectal adeno-carcinoma), T47D (breast ductal carcinoma) and NIH-3T3 (Swiss mouse embryo fibroblast) cell lines using the MTT method. Acetylcholinesterase inhibitory effect of the oil was assessed by Mata method and their antioxidant activities measured by DPPH and FRAP assays. Twenty-one components representing 92.86 % of the total oil were identified. The major components were 4a-α,7β,7a-α-Nepetalactone (18.39%), 4a-α,7α,7a-α-Nepetalactone (17.57%), 1,8-cineol (16.66%) and geranyl acetate (7.0%). The MTT test showed a significant effect of the essential oil against all three cell lines (IC_{50} were 19.37±4.92, 30.7±7.36 and 32.24±5.98 µg/ml for T47D, HT-29 and Caco-2 cell lines respectively). In acetylcholinesterase inhibitory test, the essential oil had desirable activity with IC_{50} value of 64.870 µg/ml.IC_{50} of DPPH test and FRAP value were 28.363 µg/ml and 68.902±1.37 µmol Fe^{2+}/g dry plant. These activities can be attributed to different components of *N. menthoides* essential oil and further experiments are necessary to investigate the main active compounds [9].

***Nepeta mahanensis* Jamzad & Simmonds**

The essential oil from the aerial parts of *Nepeta mahanensis* Jamzad & Simmonds was obtained by hydrodistillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass spectrometric detection. Eighteen compounds were identified in the oil of *Nepeta mahanensis* with nepetalactone (37.6%), 1,8-cineol (27.2%) and germacrene D (6.5%) as the main components. The results showed that, also the nepetalactone isomers are the main components of the essential oil of *N. mahanensis* [10].

***Nepeta macrosiphon* Boiss.**

The essential oil from flowering aerial parts of *Nepeta macrosiphon* Boiss. growing wild in Kermanshah Province, Iran, was analyzed by GC/MS. This essential oil was prepared by a modified Likens-Nickerson's simultaneous distillation-extraction (SDE) method. Forty-five compounds consisting 95.1% of the total components were identified from the oil obtained with a yield of 0.1%w/w. Among them, spathulenol (14.1%), germacrene D (9.2%) and caryophyllene oxide (8.1%) were the major components of the oil [11].

***Nepeta meyeri* Benth.**

The essential oil obtained by hydrodistillation of the aerial parts of *Nepeta meyeri* Benth. was analyzed by GC and GC/MS. The oil of *N. meyeri* was made up mainly of oxygenated monoterpenes, of which 4aα, 7α, 7αβ-nepetalactone (68.1%) was the major constituent [12].

Water-distilled volatile oil from the aerial parts of *Nepeta meyeri* Benth. was analysed by a combination of GC and GC–MS. Eighteen components were identified, constitute approximately 99.3% of the oil. The main constituents of the essential oil were 4a*α*-7*α*-7a*β*-nepetalactone (53.2%), 1, 8-cineole (29.3%) and camphor (4.1%) [13].

***Nepeta persica* Boiss.**

The essential oil from the leaf of *Nepeta persica* Boiss. analyzed by gas chromatography (GC) and gas chromatography (GC)/ mass spectrometry (MS), were shown to contain 4aα,7α,7aβ-nepetalactone (49.46%) and 4aα,7α,7aα-nepetalactone (14.18%). The other main constituents were n-octane (13.10%), n-decane (3.67%) and germacrene-D (2.04%). Antibacterial activities of the leaf oil were evaluated using the micro-dilution broth method. Inhibitory effects on *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi* and *Enterococcus faecalis* were recorded. The leaf oil has different activities against the test microorganisms. The antibacterial property of the essential oil might be ascribed to their high content of nepetalactone isomers [14].

In another study, the essential oil from aerial parts of *Nepeta persica* Boiss was obtained by steam distillation and was analyzed by GC and GC/MS. Fourteen components were identified as accounting for 97.3% of total oil composition. The 4aα,7α,7aα-nepetalactone (80%) and Spiro[5.6]dodecane (14.2%) were the main components of essential oil. Antimicrobial activity of essential oil against different kinds of microorganisms was determined by micro-broth dilution assay. The minimal inhibitory concentration and minimal lethal concentration values of oil were in the ranges from 1-8 to 1-16 µl/ml, respectively. Most of all, the oil was sensitive to *Candida albicans*, *Staphylococcus aureus* and *Klebsiella pneumoniae*. Antioxidant activity was evaluated by 2, 2'-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging. The IC_{50} values of *N. persica* essential oil and BHT were nearly 0.03%, 2.98%, respectively and in β-carotene/linoleic acid system, the essential oil did not show effective antioxidant activity[15].

***Nepeta pogonosperma* Jamzad et Assadi**

The essential oil was isolated by hydrodistillation from the aerial parts of *Nepeta pogonosperma* Jamzad et Assadi in 1.70% w/w yield. The oil was analyzed by capillary GC and GC/MS. Among the 28 compounds identified, the major components were 4aa, 7a, 7aβ-nepetalactone (57.6%), 1,8-cineole (26.4%) and β-pinene (3.7%) [16].

***Nepeta prostrate* Benth, *Nepeta pungens* (Bunge.) Benth., *Nepeta straussii* Hausskn. & Bornm. and *Nepeta saccharata* Bunge.**

The essential oils were obtained by hydrodistillation of the aerial part of *Nepeta prostrata*, flowers of *N. straussii*, which are endemic to Iran, and the aerial parts of *N. saccharata* and the leaves of *N. pungens* have been

analyzed by a combination of GC and GC-MS. The oils of *N. prostrata* and *N. straussii* were rich in 1,8-cineole (26.1% and 22.1%) and β-pinene (13.6% and 12.1%), respectively. The other main component of the first oil was myrtenol (11.8%) and in the latter one was germacrene-D (18.5%). The major components of the oil of *N. saccharata* were neo-isomenthol (18.6%), hexadecanoic acid (12.1%), 1, 8-cinole (11.7%) and germacrene- D (11.6%). (E)-Sesquilavandulol (39.5%), β-caryophyllene (14.7%) and caryophyllene oxide (11.6%) were the predominant compounds in the oil of *N. pungens*. All oils consisted mainly of oxygenated monoterpenes except that of the *N. pungens*, which was rich in oxygenated sesquiterpenes [17].

In another study, the oils obtained by hydrodistillation from fresh and dried aerial parts of *Nepeta pungens* Benth. at the flowering stage were analyzed by GC and GC/MS to investigate the variations of oil yields, oil components along with their percentages in fresh and dry stages. Forty-nine compounds (97.2%) were determined. The major compounds were geranyl acetate (17.0%), limonene (12.0%), eucalyptol (5.8%), bornylacetate (5.3%), citronellal (4.9%), spathulanol (4.2%), sabinene (3.9%), β-ocimene (3.9%), β-sesquiphellandrene (2.8%), nerylacetate (2.5%), α-humulene (2.4%), α-pinene (2.3%), humuleneoxide (2.2%), norsolanadione (2.1%) and terpinen-4-ol (2.0%). The yield of the oil was 1.1 (v/w) %. The essential oil showed antibacterial activity for *Staphylococcus aureus* [18].

***Nepeta racemosa* Lam.**

The water-distilled essential oil of *Nepeta racemosa* Lam. essential oil of was analyzed by GC and GC/MS. The main consitutents of the oil were found to be 4aα, 7α, 7aα-nepetalactone (64.9%), (Z)-β-ocimene (9.5%), (E)-nerolidol (8.8%) and 4aα,7α,7aβ-nepetalactone (7.4%) [19].

In another study, the essential oil composition of *Nepeta racemosa* Lam. was prepared by hydrodistillation and analysed by a combination of GC and GC/MS. Twenty-four components were identified, constituting approximately 99.3% of the oil. The major constituents of essential oil were 4aβ,7α,7aβ-nepetalactone (33.6%), 4aα,7α,7aβ-nepetalactone (25.6%), 4aα,7α,7aα-nepetalactone (24.4%) and 1,8-cineol (9%) [20].

***Nepeta rivularis* Bornm.**

The essential oil from the aerial parts of *Nepeta rivularis* Bornm. was obtained by hydrodistillation. The oil was analyzed by capillary gas chromatography, using flame ionization and mass spectrometric detection. Twenty-two components were identified in the oil of *Nepeta rivularis* with 1, 8-cineol (38.5%), sabinene (14.8%), β-pinene (10.7%) and γ-terpinene (5.1%) as the main constituents[10].

***Nepeta schiraziana* Boiss.**

The stems, flowers and leaves of *Nepeta schiraziana* were collected from Sepidan region in north-west of Fars province. The essential oils of stems, flowers and leaves of the plant were separately obtained by hydrodistillation and analyzed by GC and GC/MS. In each oils of the stem and flower, fourteen components were identified with 1, 8-cineol (45.6% and 39.4), germacrene-D (17.4% and 15.8%), and β-caryophyllene (11.7% and 10.6%) as the main constituent, respectively. Furthermore, 1, 8-cineol (38.5%), β-caryophyllene (14.2%) and caryophyllene oxide (11.7%) were the major components among the 18 constituents characterized in the leaf oil. As a result, 1, 8-cineol was the dominant compound in the investigated oils while nepetalactone isomers reported in many *Nepeta* species, were not identified in *Nepeta schiraziana* [21].

***Nepeta sintenisii* Bornm.**

The aerial parts of *Nepeta sintenisii* from Iran were subjected to hydrodistillation and the chemical composition of the isolated essential oil was analyzed by GC/MS method for first time. Forty constituents (96.5% of the total oil) were identified of which 4aβ, 7α, 7aβ-nepetalactone (23.4%), elemol (16.1%), E-β-farnesene (9.5%), 1,8-cineol (8.2%), cis-sabinene hydrate (6.5%), β-bisabolene (4.2%) and germacrene-D (3.5%) were the main components [22].

***Nepeta sessilifolia* Bunge.**

Water distilled essential oils from the aerial parts of *Nepeta sessilifolia* Bung. were analyzed by GC and GC/MS. Thirty-three compounds representing 97.4% of the *N. sessilifilia*. The major components of the essential oil of *Nepeta sessilifolia* were linalool acetate (14.7%) and linalool (14.2%). The oil was richer in oxygenated monoterpenes than sesquiterpenes [23].

CONCLUSION

As mentioned in this review constituents and biological activities of Iranian *Nepeta* species including *Nepeta kotschyi* Boiss., *Nepeta mirzayanii* Rech. F. et Esfand., *Nepeta menthoides* Boiss. and Buhse., *Nepeta mahanensis* Jamzad & Simmonds, *Nepeta macrosiphon* Boiss., *Nepeta meyeri* Benth., *Nepeta persica* Boiss., *Nepeta pogonosperma* Jamzad et Assadi, *Nepeta prostrate* Benth, *Nepeta pungens* (Bunge.) Benth., *Nepeta straussii* Hausskn. & Bornm., *Nepeta saccharata* Bunge., *Nepeta racemosa* Lam., *Nepeta rivularis* Bornm., *Nepeta schiraziana* Boiss. and *Nepeta sintenisii* Bornm.

Most attention has been focused on Nepetalactones and their biological activities.

ACKNOWLEDGMENT

The authors thank Dr. V. Mozaffarian for identification of the plant materials.

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