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Short communication

Antigenotoxic potential of *Nepeta grandiflora*

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Introduction

Nepeta grandiflora M.Bieb. (Lamiaceae), commonly known as a giant catmint, is an ornamental herbaceous perennial native to Caucassus and Crimea, displaying notable arthropod-repellent properties. Interestingly, this species produces no nepetalactone-type iridoids, which are the common group of compounds for catmints (Banjanac et al., 2026). On the other hand, it is a rich source of iridoid glycosides (IGs) and phenolic acids (Mišić et al., 2015). The objective of this study was to chemically characterize the *Nepeta grandiflora* methanol extracts (ME), hydrodistillation-derived essential oil (EO) and hydrolate (H), and further examine antigenotoxic potential in cell suspensions of *Saccharomyces cerevisiae*.

Materials and methods

Plant material

Nepeta grandiflora M.Bieb. (Lamiaceae) was cultivated in the experimental field of the Institute for biological research „Siniša Stanković“- National Institute of the Republic of Serbia, University of Belgrade. Above ground parts with flowering tops were harvested in July 2025, dried at the room temperature until constant mass, and mechanically grinded into a fine powder.

Hydrodistillation of EOs

Plant material (200g) was disolved in 2l of distilled water, and subjected to hydrodistillation in a Clevenger-type aparatus for 3 hours. The procedure was repeated and the average yield was around 50 µl NgEO per 200 g DW. In addition, hydrodistillation by-product hydrolate (NgH) was collected.

Extraction in methanol

Plant material (10 g) was dissloved in 96% methanol (w:v = 1:10), vortexed for 1 min, and extracted in an ultrasonic bath for 1 h at 4 °C, which was followed by overnight extraction at 4 °C. Following centrifugation at 10000g for 10 min, supernatant was filtered, and dried using a vacuum evaporator.

GC/MS profiling of VOCs

Profiling of volatile organic compounds (VOCs) was perfomed using Agilent 8890 gas chromatograph (GC) coupled to a Mass Selective Detector (5977B GC/MSD, Agilent Technologies, Santa Clara, USA) and connected to an automated

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sample extraction and enrichment platform (Centri®, Markes International Ltd., Bridgend, UK). VOCs were chromatographically separated on a HP-5MS column (30 m × 0.25 mm, 0.25 mm film thickness) as previously described in Banjanac et al. (2026).

HPLC/Orbitrap MS profiling of polar compounds

An LC-HRMS/MS instrument (Thermo Scientific™ Vanquish™ Core HPLC system coupled to the Orbitrap Exploris 120 mass spectrometer, San Jose, CA, USA) was used to identify methanol-soluble metabolites in hydrolate and methanol extracts. Liquid chromatography system was equipped with a Hypersil GOLD™ C18 analytical column (50 × 2.1 mm, 1.9 μm particle size). All chromatographic and mass spectrometry settings are previously described in Stojković et al. (2024).

Evaluation of genotoxicity and antigenotoxic potential

Combined treatment: Cell suspensions of *Saccharomyces cerevisiae* strain 551 were treated for 30 min with each of the extracts at a concentration 1μg/ml at optimal conditions for cell growth (30 ºC, 200 rpm). After that, the cells were washed, resuspended in YPD medium containing 1.76 mg/ml methyl methanesulfonate (MMS), a standard mutagen and carcinogen, and incubated for 30 min at optimal conditions. Three endpoints were measured: cell survival, induction of superoxide anions and Ty1 retrotransposition as described in Todorova et al. (2022).

Results and discussion

N. grandiflora EO, along with HE, and ME were subjected to metabolic profiling using GC/MS and/or LC/MS instruments. Sesquiterpenes were the predominant terpene group in EO, with caryophyllene oxide, caryophyllene, and germacrene D being the most abundant. Nepetalactones were not detected. The H contained both traces of EO constituents and water-soluble polar compounds, although in low amounts. Methanol extract, on the other hand, was a rich source of IG 1,5,9-*epi*-deoxyloganic acid, and of rosmarinic acid—the major phenolic compound.

All the samples (EO, H, and ME) displayed no genotoxicity against *S. cerevisiae*, and were equally efficient in protecting the cells from the genotoxic action of the alkylating agent MMS. The samples also reduced MMS-induced transposition, thus showing the promising anticarcinogenic activity.

Conclusion

Respectable antigenotoxic activities were recorded for hydrodistillation-derived products and by-products (EO and H) and for methanol extract (ME) of *N. grandiflora*, which positions them as versatile agents for various applications related to human and animal health. In the case of ME, these activities can be ascribed to high content of iridoid glycosides and phenolic acids, while bioactive potentials of EO and H rely on the high content of sesquiterpenoids.

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