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INTER- AND INTRASPECIFIC VARIABILITY AS A BASIS FOR DEFINING THE QUALITY OF HERBAL DRUG

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To define new herbal drug and its quality, it is important to know inter- and intraspecific variability of chemical constituents of certain species of one genus. In the case of potentially new aromatic herbal drugs, among others, variability of essential oils composition is examined. The aim was to investigate interspecific variability of essential oil composition of four *Seseli* L. species, Apiaceae and intraspecific essential oil variability of selected species *S. rigidum* Waldst. & Kit. Composition of oils was determined by GC-FID and GC-MS and results were statistically analysed (ANOVA, PCA, CDA, cluster analysis). Antimicrobial (broth-microdilution, checkerboard method), cytotoxic (MTT test, flow cytometry) and genotoxic/antigenotoxic activity (Comet test) of oils of selected populations of *S. rigidum* were investigated. Significant differences in oils composition of investigated *Seseli* species were observed. Monoterpene hydrocarbons dominated in oils of aerial parts of *S. rigidum* and *S. gracile* Waldst. & Kit. and sesquiterpene hydrocarbons in *S. annuum* L. and *S. tomentosum* Vis. Climate had significant influence on composition, higher than population and substrate (serpentine or calcareous). The best antimicrobial activity showed *S. rigidum* root oil of population with high falcarinol content against *Candida albicans* and MRSA. Synergistic effect of mentioned oil and antibiotics was observed. Oils of root, aerial parts and fruit showed cytotoxic activity against tumor cells HeLa, LS174 and A549**,** while genotoxic effects weren't observed. Oils of *S. rigidum* aerial parts and fruit manifested antigenotoxic effects. Conducted research indicated the potential of *S. rigidum* as a source of new herbal medicinal raw materials.

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INTER- I INTRASPECIJSKA VARIJABILNOST KAO OSNOV ZA DEFINISANJE KVALITETA BILJNE DROGE

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Za definisanje nove biljne droge i njenog kvaliteta važno je poznavati kako inter-, tako i intraspecijsku varijabilnost hemijskih sastojaka određenih vrsta jednog roda. U slučaju potencijalno novih aromatičnih biljnih droga, između ostalog, ispituje se varijabilnost sastava etarskih ulja. Cilj rada je bilo ispitivanje interspecijske varijabilnosti sastava etarskih ulja četiri vrste roda *Seseli* L., Apiaceae, kao i intraspecijske varijabilnosti etarskih ulja odabrane vrste *S. rigidum* Waldst. & Kit. Sastav etarskih ulja utvrđen je GC-FID i GC-MS metodom i rezultati su statistički analizirani (ANOVA, PCA, CDA, klaster analiza). Ispitane su antimikrobna (bujon-mikrodiluciona, *checkerboard* metoda), citotoksična (MTT test, protočna citometrija) i genotoksična/antigenotoksična aktivnost (Komet test) etarskih ulja odabranih populacija *S. rigidum*. Uočene su značajne razlike u sastavu etarskih ulja ispitivanih vrsta roda *Seseli*. U etarskim uljima herbi *S. rigidum* i *S. gracile* Waldst. & Kit. dominirali su monoterpenski ugljovodonici, a u uljima herbi *S. annuum* L. i *S. tomentosum* Vis. seskviterpenski ugljovodonici. Na sastav etarskih ulja najznačajnije je uticala klima, a znatno manje ispitivana populacija i podloga (serpentinit ili krečnjak). Najbolju antimikrobnu aktivnost pokazalo je etarsko ulje korena *S. rigidum* populacije sa visokim sadržajem falkarinola prema sojevima *Candida albicans* i MRSA. Takođe, uočen je sinergistički efekat navedenog ulja i određenih antibiotika. Etarska ulja korena, herbe i ploda *S. rigidum* ispoljila su i citotoksičnu aktivnost prema tumorskim ćelijama HeLa, LS174 i A549, dok genotoksično delovanje nije uočeno. Dodatno, etarska ulja herbe i ploda *S. rigidum* ostvarila su antigenotoksično delovanje. Sprovedeno ispitivanje ukazalo je na potencijal vrste *S. rigidum* kao izvora novih biljnih lekovitih sirovina.

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