Chemical and pharmacological characterisation of 9 taxa of the genus *Heracleum* L. (Apiaceae), autochthonous for Southeastern Europe

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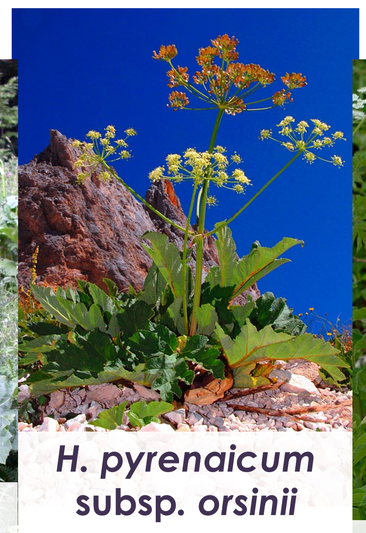
H. sphondylium

H. sibiricum

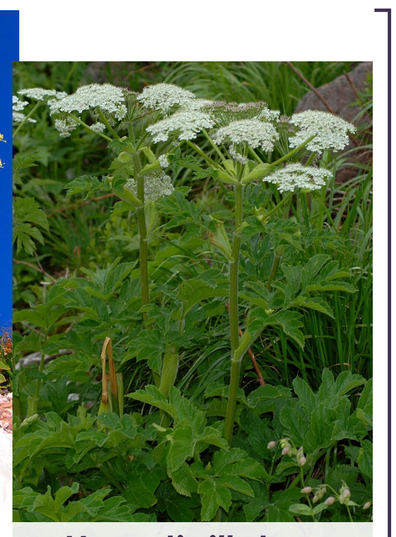
H. montanum

H. ternatum

H. pyrenaicum subsp. *pollinianum*



H. pyrenaicum subsp. *orsinii*



H. verticillatum

H. sphondylium group

sect. Heracleum

Methods and Results

- ✓ **Plant material:** collected in 2009-2016 at 14 localities in SE Europe (*H. sphondylium*, *H. montanum* and *H. austriacum* in Slovenia, *H. sibiricum* and *H. verticillatum* in Serbia, *H. ternatum* and *H. pyrenaicum* subsp. *orsinii* in Montenegro, *H. pyrenaicum* subsp. *pollinianum* and *H. orphanidis* in North Macedonia).
- ✓ **Essential oils composition:** GC-FID and GC-MS analysis revealed 19-113 components in 59 hydrodistilled root, fruit, leaf or flower oils. Dominant were monoterpenes/phenylpropanoids (*H. sphondylium* group root oils), (Z)-falcarinol (*H. orphanidis*/*H. austriacum* root oils), aliphatic esters octyl hexanoate (*H. austriacum* fruit oil)/octyl acetate (other fruit oils and *H. orphanidis* leaf oil) and sesquiterpenes/phenylpropanoids (other leaf and flower oils) [**1-5**].
- ✓ **Antimicrobial activity of essential oils:** 17 of 30 tested oils showed strong activity in microdilution test (MIC values lower/around 100 μg/mL) on at least one of 8 tested bacteria (4 Gram(+) and 4 Gram(-), incl. *Bacillus cereus* and *Enterobacter cloacae* clinical isolates) and/or 8 tested fungi (4 *Aspergillus* spp., incl. *A. fumigatus* clinical isolate, 3 *Penicillium* spp. and *Trichoderma viride*) [**1-4**].
- ✓ **Cytotoxic activity of essential oils:** 13 of 26 tested oils showed strong effect in MTT test (IC_{50} values lower/around 30 μg/mL) on HeLa, LS174 and/or A549 cancer cells; oils generally did not inhibit growth of normal MRC-5 cells [**1-4**].
- ✓ **Anti-DPPH activity of essential oils:** 8 of 14 tested oils showed weak potential; composition of active zones in TLC-DPPH test was analyzed by GC (oxygenated terpenes and phenylpropanoids were dominant).
- ✓ **Safety profile of essential oils based on determined furanocoumarin (FC) content:** daily intake of tested *Heracleum* oils containing FCs (32 samples), not contributing significantly to overall risk, determined according to EMA/HMPC recommendations (Doc. Ref. EMEA/HMPC/317913/2006), ranges from 1.94 to 15.68 mL [**6**].
- ✓ **Furanocoumarins (FCs) composition:** 12 FCs identified in root and fruit CH_2Cl_2 extracts of all 9 *Heracleum* taxa (by LC-MS using FC standards or based on UV, MS, ^1H and ROESY NMR spectra); dominant were pimpinellin, bergapten, byakangelicol, heraclenin and/or imperatorin [**7**].
- ✓ **Fatty oil constituents:** 18 fatty acids (dominant petroselinic), 9 sterols (dominant β-sitosterol) and α-amyrin identified by GC-FID and GC-MS in oily supernatants of fruit CH_2Cl_2 extracts of all 8 sect. *Heracleum* members [**9**].
- ✓ **Chemosystematic significance:** for essential oil components (in the case of roots and fruits also for headspace fraction components) and FCs, chemosystematic significance was demonstrated using multivariate statistics (PCA, nMDS and UPGMA). Investigated taxa were grouped according to their taxonomy [**7,8**].

H. orphanidis

sect. *Wendia*

H. austriacum subsp. *siifolium*

➢ These results constitute **PhD thesis** of the first author (L. U.) and are published in **8 papers in international journals**, **1 paper in national journal**, **7 abstracts presented at international** (M34) and **5 abstracts presented at national conferences** (M64).

Food & Function **1. (M21)**

PAPER

Essential oils of three cow parsnips – composition and activity against nosocomial and foodborne pathogens and food contaminants

Ljuboš Ušjak,[a] Silvana Petrović,[*a] Milica Drobac,[a] Marina Soković,[b] Tatjana Stanojković,[c] Ana Ćirić[b] and Marjan Niketić[d]

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DOI 10.1007/s13197-017-2610-z

ORIGINAL ARTICLE

Edible wild plant *Heracleum pyrenaicum* subsp. *orsinii* as a potential new source of bioactive essential oils

Ljuboš Ušjak[1] · Silvana Petrović[1] · Milica Drobac[1] · Marina Soković[2] · Tatjana Stanojković[3] · Ana Ćirić[2] · Marjan Niketić[4] **2. (M22)**

Chem. Biodiversity **2016**, *13*, 466 – 476

3. (M22) FULL PAPER

Chemical Composition, Antimicrobial and Cytotoxic Activity of *Heracleum verticillatum* Pančić and *H. ternatum* Velen. (Apiaceae) Essential Oils

by Ljuboš J. Ušjak[a]), Silvana D. Petrović[*a]), Milica M. Drobac[a]), Marina D. Soković[b]), Tatjana P. Stanojković[c]), Ana D. Ćirić[b]), Nađa Đ. Grozdanić[c]), and Marjan S. Niketić[d])

NPC Natural Product Communications 2016 Vol. 11 No. 4 529 - 534

Chemical Composition and Bioactivity of the Essential Oils of *Heracleum pyrenaicum* subsp. *pollinianum* and *Heracleum orphanidis*

Ljuboš Ušjak[a], Silvana Petrović[a,*], Milica Drobac[a], Marina Soković[b], Tatjana Stanojković[c], Ana Ćirić[b] and Marjan Niketić[d] **4. (M23)**

DOI 10.1007/s10600-018-2356-5
Chemistry of Natural Compounds, Vol. 54, No. 2, March, 2018

CONSTITUENTS OF THE ESSENTIAL OILS OF *Heracleum austriacum* subsp. *siifolium*, AN ENDEMIC PLANT OF THE SOUTHEASTERN ALPS

Lj. Usjak,[1] S. Petrovic,[1]* M. Drobac,[1] and M. Niketic[2] **5. (M23)**

PhD thesis (19.3.2019):
1 × M21
4 × M22
3 × M23
1 × M52

Arh. farm. 2019; 69: 165 – 175 *Originalni naučni rad /Original scientific paper*

Evaluation of safety profile of the essential oils of eight *Heracleum* taxa (Apiaceae) related to determined furanocoumarin content

Ljuboš Ušjak[1*], Milica Drobac[1], Marjan Niketić[2], Silvana Petrović[1]

6. (M52)

DOI: 10.1002/cbdv.201800412 FULL PAPER **7. (M22)** CHEMISTRY & BIODIVERSITY

Chemosystematic Significance of Essential Oil Constituents and Furanocoumarins of Underground Parts and Fruits of Nine *Heracleum* L. Taxa from Southeastern Europe

Ljuboš J. Ušjak,[a] Milica M. Drobac,[a] Marjan S. Niketić,[b] and Silvana D. Petrović*[a]

Plant Systematics and Evolution

ORIGINAL ARTICLE

Chemosystematic evaluation of leaf and flower essential oils of eight *Heracleum* taxa from Southeastern Europe

Ljuboš Ušjak[1], Marjan Niketić[2], Milica Drobac[1], Silvana Petrović[1] **8. (M22)**

Original Article

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Fatty Acids, Sterols, and Triterpenes of the Fruits of 8 *Heracleum* Taxa

Ljuboš Ušjak[1], Ivana Sofrenić[2], Vele Tešević[2], Milica Drobac[1], Marjan Niketić[3], and Silvana Petrović[1] **9. (M23)** SAGE

Conclusions

1. Performed **chemical characterisation** significantly contributes to the knowledge on the composition of secondary and primary metabolites of **8 selected sect. *Heracleum* members**; investigations of ***H. austriacum* subsp. *siifolium*** from **sect. *Wendia*** were done for the first time.
2. Investigated taxa are potential **new herbal sources of compounds** significant for pharmaceutical, cosmetic, food and chemical industries.
3. **Essential oil components** and **furanocoumarins** have **chemosystematic significance** for investigated taxa.
4. Observed **pharmacological activities** of the **essential oils** justify further research of these potential novel herbal raw materials, with respect to determined maximum daily intakes for those essential oils in which furanocoumarins were detected.

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