

Review

***Tanacetum vulgare* L. – A Systematic Review**

Milica Ćimović ^{1,*} and Nikola Puvača ²

¹ Department of Alternative Crops and Organic Production, Institute of Field and Vegetable Crops Novi Sad, Maksima Gorkog 30, 21000 Novi Sad, Serbia

² University Business Academy, Faculty of Economics and Engineering Management, Department of Engineering Management in Biotechnology, Cvećarska 2, 21000 Novi Sad, Serbia

* Correspondence: milica.acimovic@ifvcns.ns.ac.rs; Tel.: +381-21-780-365

Received: 5 April 2020; Accepted: 1 June 2020

Abstract: *Tanacetum vulgare* L. (syn. *Chrysanthemum vulgare* L.) commonly known as tansy, is a perennial herb of the Asteraceae family, native to temperate Europe and Asia, where it grows along roadsides, hedgerows and waste places. It was introduced into North America for medicinal and horticultural purposes and now grows wild throughout many USA states. It has two varieties: var. *vulgare* (distributed in N Europe and N America, however in Corsica, Sardinia and Sicily ssp. *siculum* grows, in some cases reported as a separate species) and var. *boreale* (distributed in Russia, China, N Korea and Japan). Aerial plant parts contain essential oil divided into chemotypes, and the environmental adaptability of the plants can be assumed from essential oil contents. *T. vulgare* is also rich in phenolic acids, flavonoids and their derivatives which contribute to the pharmacological actions of the plant.

Keywords: tansy; *Asteraceae*; essential oil.

1. Introduction

Tanacetum vulgare L. (syn. *Chrysanthemum vulgare* L.) commonly known as tansy, comes from the Greek word “athanasia” which means “immortality”, probably originating from the fact that its flowers do not wilt when dry [1]. This is a perennial herb of the Asteraceae family, native to temperate Europe and Asia, where it grows along roadsides, hedgerows and waste places. It was introduced into North America for medicinal and horticultural purposes and now grows wild throughout many USA states [2, 3, 4]. However, *T. vulgare* has two varieties: var. *vulgare* which is widely distributed in northern Europe and North America and var. *boreale* distributed in Russia, China, North Korea and Japan [5]. Regional variability of the chemical composition of *T. vulgare* essential oils is well-known and many essential oil chemotypes have been reported in literature [4]. In Corsica (France), Sardinia and Sicily (Italy), plants grow with finely dissected leaves; these are regarded by some as a separate species (ssp. *siculum*) [6, 7].

2. Botanical features

T. vulgare is a perennial herb with deep green leaves, 15-25 cm long, pinnatipartite to pinnatisect, glabrous to sparsely hairy and glandular-punctate. The lower cauline leaves are more than 5 cm long, petiolate, oblong to oblong-ovate and the segments pinnatisect to pinnatilobed. They are linear-lanceolate to oblong-elliptical. The upper cauline leaves are similar but sessile. *T. vulgare* has button-like corymbs, with 10-70 yellow capitulate flowers, each showing an involucre of 5-8 mm in diameter. In the outer ring, the florets are tubular, mostly female and zygomorphic, bright yellow. They are 3-toothed, rarely shortly ligulate, or actinomorphic (some flowers are 5-toothed and hermaphroditic). The inner florets are tubular and 5-toothed. The achenes are 1.2-1.8 mm long, 5-ribbed, possessing scattered epicarpic, sessile, transparent, non-mucilaginous glands; the pappus is a short unevenly

toothed membranous cup, 0.2-0.4 mm wide [8, 9]. However, its strong scent stems from the essential oil containing glands in leaves and flowers [10]. Cytogenetical studies of the *T. vulgare* show that it is diploid ($2n=18$) [11].

3. Chemical composition

Aerial plant parts of *T. vulgare* harvested in full flowering stage usually contain between 0.1 and 0.5% of essential oil [12, 13, 14], but in some cases it is reported up to 1.9% [15]. *T. vulgare* essential oil is a yellowish to orange olive liquid with a warm, almost sharp and spicy, dry and herbaceous odour. The taste is very sharp, pungent and bitter. It should not be used in flavours or any food preparations. *T. vulgare* essential oil is mainly high in thujone, a poison that can cause convulsions, vomiting and uterine bleeding [12]. Apart of essential oil it contains bitter components and sesquiterpene lactones [16].

Ecological role of essential oils is reflected in the interaction of plants with environmental factors. Environmental adaptability of the plants can be assumed from essential oil contents [17]. According to the cluster analysis the essential oil *T. vulgare* from Lithuania is divided into four groups: 1,8-cineole, *trans*-thujone, camphor and myrtenol [18]. However, the last one is produced by *T. vulgare* plants very rarely [19]. In Norway, seven chemotypes of *T. vulgare* could be identified: α -thujone, β -thujone, camphor, chrysanthenyl acetate/chrysanthenol, chrysanthenone, artemisia ketone/artemisia alcohol, and 1,8-cineole [15]. Furthermore, more than 15 distinct chemotypes have been described from Scandinavia and the Baltic so far [10], and the correlation between the genetic distance matrices of the same genotypes was highly significant [20]. The majority of the results from literature identified β -thujone, respectively *trans*-thujone, camphor and chrysanthenyl acetate as the most common main components of the essential oils of *T. vulgare* from 11 different habitats throughout the world [21].

Table 1. Composition of the aerial parts of *T. vulgare* essential oils.

	Canada	Romania (Sibiu)	Romania (Alba)	Serbia (Belgrade)	Slovakia	Italy (Sicily)	Estonia (Harju)	Estonia (Tartu)
Reference	[4]	[22]	[22]	[1]	[16]	[6]	[14]	[14]
α -Pinene	4.43	nd	nd	1.81	2.44	nd	5.0	1.9
Camphene	7.29	nd	nd	0.46	2.17	nd	0.4	0.1
1,8-Cineole	10.80	3.50	3.27	3.88	8.32	11.8	9.6	1.4
Artemisia ketone	nd	2.19	7.88	2.94	9.36	nd	0.3	nd
α -Thujone	0.08	24.81	13.21	5.28	nd	23.8	0.2	0.4
Chrysanthenol	nd	nd	nd	15.05	nd	nd	nd	nd
β -Thujone	3.66	14.41	12.79	9.04	21.00	18.0	nd	47.2
Chrysanthenone	3.76	nd	nd	0.40	nd	1.3	41.9	1.0
Camphor	30.48	1.16	10.17	4.90	19.69	nd	nd	nd
Borneol	14.80	0.93	9.34	2.10	4.55	nd	1.3	nd
α -Terpineol	0.69	nd	nd	nd	nd	nd	1.5	tr
Chrysanthenyl acetate	0.10	25.84	20.06	41.62	3.17	0.6	0.4	nd

tr-trace; nd-not detected

The inflorescences and leaves of *T. vulgare* plants produce oils with the same dominating constituents, however in some cases, the leaves produced oils of the 1,8-cineole chemotype, while the inflorescences biosynthesized oils of the camphor or myrtenol. Amounts of the 1,8-cineole in all leaf oils were greater than in inflorescence oils [18].

Many investigations are shown that *T. vulgare* is rich in the phenolic acids, flavonoids and their derivatives which contribute to the pharmacological actions of the plant (Table 2). Furthermore, yellow-orange flavonoids and carotenoids can be obtained from *T. vulgare* used as alternative colourants [23].

Table 2. Phenolic compounds found in *T. vulgare* extracts.

Compound	Reference
Ferulic acids	
3,5-dichlorogenic acid	[24]
4,5-dichlorogenic acid	[24]
chlorogenic acid	[1, 24]
neochlorogenic acid	[1, 24]
Hydroxycinnamoylquinic acids	
1,5-dicaffeoylquinic acid	[25]
1-caffeoylquinic acid	[1]
3,4,5-tricaffeoylquinic acid	[1]
3,4-dicaffeoylquinic acid	[1, 25]
3,5-dicaffeoylquinic acid	[1, 25]
3-caffeoylquinic acid	[25]
4,5-dicaffeoylquinic acid	[25]
4-caffeoylquinic acid (=Cryptochlorogenic acid)	[1]
5-caffeoylquinic acid	[25]
Flavonoids	
Apigenin	[1, 24]
Baicalin	[1]
Casticin	[26]
Eupalitin	[25]
Eupalitin	[1]
Hispidulin	[1]
Hyperoside	[24]
Isoquercetin	[1]
Kaempferol	[24]
Luteolin	[1, 24, 25]
Nepetin	[1]
Quercetagetin dimethyl ether	[25]
Rutin	[24]
Saponarin	[1]
Scutellarin	[1]
Flavonoid-O-glucuronides	
Apigenin-7-O-glucuronide	[25]
Chrysoeriol-7-O-glucuronide	[25]
Eriodictyol-O-glucuronide	[25]
Homoeriodictyol-O-glucuronide	[25]
Luteolin-7-O-glucuronide	[1, 25]
Quercetin-3-O-glucuronide (=Miquelianin)	[1, 25]
Flavonoid-O-glucosides	
Acacetin-7-glycoside	[24]
Gossypetin-8-O-glucoside	[1]
Kaempferol-O-(caffeoyl)glucoside	[25]
Luteolin-7-O-glucoside	[1, 25]
Petunidin-3-O-glucoside	[1]
Quercetin-3-O-glucoside	[25]
Organic acid	
Citric acid	[25]
Dihydroxybenzoic acid derivative	[25]
Gluconic acid	[25]
Quinic acid	[25]

4. Biological activity

T. vulgare is a well-known herbal plant widely used in traditional medicine in south-eastern Serbia. Tea is used as an antihelminthic, carminative, antispasmodic, stimulant to abdominal viscera,

tonic, emmenagogue, antidiabetic, diuretic and antihypertensive [27]. Furthermore, *T. vulgare* is conventionally used in balms, cosmetics, dyes, insecticides, medicines, and preservatives [1].

4.1. Antioxidant activity

The methanolic extract of the aerial parts of *T. vulgare* and its fractions were investigated for antioxidant activity. The crude extract displayed DPPH radical scavenging effects with an EC₅₀ value of 37 µg/mL. Activity guided fractionations of the crude extract resulted in the isolation of three antioxidant compounds; 3,5-*O*-dicaffeoylquinic acid (3,5-DCQA), axillarin and luteolin. 3,5-DCQA was the major constituent with antioxidant activity (IC₅₀ = 9.7 µM) comparable with that of the standard quercetin (IC₅₀ = 8.8 µM) [3]. *T. vulgare* showed antioxidant activity in correlation with the total phenolic content of the extracts [26]. The *T. vulgare* essential oil possesses anti-inflammatory activity inhibiting NO production. It also inhibits intracellular DCFH oxidation induced by tert-butylhydroperoxide [4].

4.2. Anti-inflammatory activity

The CHCl₃ extracts of *T. vulgare* were found to have significant wound healing activity and anti-inflammatory activities. Parthenolide content of the CHCl₃ extracts of *T. vulgare* were found in the value of 177.51 µg/100 mg plant material. According to the results, the other secondary metabolites present in the aerial parts of the *T. vulgare* possibly exerted synergistic effects on the observed healing of the wounds [28]. Anti-inflammatory activity of essential oil appears driven mainly by α-humulene while antioxidant activity is provided by α-pinene and caryophyllene oxide [4].

4.3. Antimicrobial activity

Essential oil from *T. vulgare* showed better activity against Gram-positive bacteria than against Gram-negative ones. Among the bacteria tested, *Bacillus subtilis* was the most sensitive [29]. Contrarily, *T. vulgare* methanol extract exhibited antimicrobial effect against the tested Gram-positive bacteria and fungi [26].

Furthermore, essential oil from *T. vulgare* was active against both *Escherichia coli* and *Staphylococcus aureus* with camphor and caryophyllene oxide responsible for antibacterial activity [4]. The essential oil and ethanolic extracts of *T. vulgare* exhibited moderate action against *Staphylococcus aureus* and *Bacillus subtilis* and low action against *E. coli* and *Pseudomonas aeruginosa* [30]. *T. vulgare* essential oil showed strong activity against most of the tested fungi and was efficient as bifonazole and ketoconazole, while the most sensitive bacteria were Gram-negative *E. coli* and *E. cloacae*. All methanol extracts showed fungistatic and fungicidal effects against all of the eight tested fungi, however, the antimicrobial activity was higher against Gram-positive bacteria [1].

The inhibition zone of chlorhexidine against *C. albicans* was 30.3-19.3 mm, however, in combination with EthOAc extract of *T. vulgare*, this inhibition was from 32.7-30 mm, indicating that this combination exerted a marked synergistic effect against *C. albicans*. The inhibition zone of sodium hypochlorite (69.7–65 mm) was higher than the inhibition zone of EthOAc extract and chlorhexidine. The combination of EthOAc extract with sodium hypochlorite resulted in a loss of antifungal activity. Furthermore, the activity of the EthOAc extract against *C. albicans* was decreased after mixing the extract with dentine at a concentration of 25 mg/50 µL [31].

4.4. Citotoxic activity

T. vulgare essential oil was slightly cytotoxic against the human healthy cell line WS1 while α-humulene and caryophyllene oxide were moderately cytotoxic against human lung carcinoma A-549, human colon adenocarcinoma DLD-1, and human skin fibroblasts WS1 [4].

Methanol extract of *T. vulgare* expressed strong cytotoxic activity against both cancer (HeLa) and healthy (Vero) cell lines [26]. Methanol extract of *T. vulgare* leaves and flowers exhibited a strong antiproliferative effect on human cervical adenocarcinoma (HeLa) cells, causing cell shrinkage and detachment [1].

Cytotoxic activity of dichloromethane extract from the flowers of *T. vulgare* growing in Sicily was tested *in vitro* on A549 (human lung carcinoma epithelial-like) and V79379A (Chinese hamster lung fibroblast-like) cells using the tetrazolium salt reduction (MTT) assay. All five sesquiterpene lactones with the eudesmane skeleton have been isolated from dichloromethane extract induced high time- and concentration-dependent cytotoxic effects [7].

Four polysaccharide fractions were isolated and purified from aqueous extracts of *T. vulgare* florets and investigated their effects on innate immune cell function. It was found that Tansy polysaccharides had potent immunomodulatory and anti-inflammatory activities, including modulation of macrophage and neutrophil functions, as well as complement-fixing activity. Thus, the immunomodulatory activities of *T. vulgare* polysaccharides could likely contribute to the known therapeutic effects of *T. vulgare* extracts [2].

4.4. Organic agriculture

Dry flowers from *T. vulgare* were extracted with methanol, evaporated, and then the concentrates were divided into liquid and soft fractions. The liquid fraction was diluted in water up to 24 h before the assay, while the soft fraction was diluted in water just before the assay. These two fractions were used for establishing antiviral effect against CMV and PVY in tomato plants. Results show that treatment with 5% liquid fraction reduced development of PVY symptoms, while 3% had no effect on the virus infection. Furthermore, 20 % of soft fraction reduced the DAS-ELISA values, but 10% reduced development of PVY symptoms. Contrarily, concentrations from 3% of liquid fraction and 5 % soft fraction of methanol extracts from *T. vulgare* reduced development of virus symptoms, but DAS-ELISA values of CMV remained above the cut off [32].

The probing and feeding activity of the peach potato aphid (*Myzus persicae*) on plants treated with preparations of potassic horticultural soap, alone and in combination with extracts of *Allium sativum* and *T. vulgare*, was monitored by using the Electrical Penetration Graph (EPG) technique. The total probing time in peripheral tissues and the proportion of sap ingestion activity among all aphid activities in plant tissues were similar in all aphids irrespective of an applied treatment. The lowest proportion of probes that contained phloem phase, the longest duration of the first phloem salivation period, and the highest proportion of salivation in aphid activities in the phloem occurred in aphids on garlic+tansy-treated leaves. The results demonstrate that these preparations show postingestional deterrent activity [33].

Acknowledgments: This research was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia, grant number: 451-03-68/2020-14/200032.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Devrnja, N., Anđelković, B., Arandelović, S., Radulović, S., Soković, M., Krstić-Milošević, D., Ristić, M., Čalić, D. Comparative studies on the antimicrobial and cytotoxic activities of *Tanacetum vulgare* L. essential oil and methanol extracts. *S Afr J Bot* **2017**, *111*, 212-221.
2. Xie, G., Schepetkin, I.A., Quinn, M.T. Immunomodulatory activity of acidic polysaccharides isolated from *Tanacetum vulgare* L. *Int Immunopharmacol* **2007**, *7*, 1639-1650.
3. Juan-Badaturuge, M., Habtemariam, S., Jackson, C., Thomas, M.J.K. Antioxidant principles of *Tanacetum vulgare* L. aerial parts. *Nat Prod Commun* **2009**, *4(11)*, 1561-1564.
4. Coté, H., Boucher, M.A., Pichette, A., Legault, J. Anti-inflammatory, antioxidant, antibiotic, and cytotoxic activities of *Tanacetum vulgare* L. essential oil and its constituents. *Medicines* **2017**, *4*, 34; doi:10.3390/medicines4020034
5. Uehara, A., Akiyama, S., Iwashina, T. Foliar flavonoids from *Tanacetum vulgare* var. *boreale* and their geographical variation. *Nat Prod Commun* **2015**, *10(3)*, 403-405.

6. Formisano, C., Senatore, F., Bruno, M., Rosselli, S., Bellone, G., Spadaro, V. Essential oil composition of *Tanacetum vulgare* subsp. *siculum* (Guss.) Raimondo et Spadaro (Asteraceae) from Sicily. *Nat Prod Commun* **2009**, 4(4), 567-570.
7. Rosselli, S., Bruno, M., Raimondo, F.M., Spadaro, V., Varol, M., Koparal, A.T., Maggio, A. Cytotoxic effect of eudesmanolides isolated from flowers of *Tanacetum vulgare* ssp. *siculum*. *Molecules* **2012**, 17, 8186-8195; doi:10.3390/molecules17078186.
8. Clapham, A.R., Tutin, T.G., Warburg, E.F., eds, **1952**. Flora of the British Isles. Cambridge, UK: Cambridge University Press.
9. Heywood, V.H. **1976**. Plantaginaceae to Compositae (and Rubiaceae). In: Tutin TG, Heywood VH, Burges NA, Moore DM, Valentine DH, Walters SM, Webb DA, eds. Flora Europaea, Vol. 4. Cambridge, UK: Cambridge University Press, 169-171.
10. Dragland, S., Rohloff, J., Mordal, R., Iversen, T.H. Harvest regimen optimization and essential oil production in five tansy (*Tanacetum vulgare* L.) genotypes under a Northern climate. *J Agric Food Chem* **2005**, 53, 4946-4953.
11. Lokki, J., Sorsa, M., Forsen, K., Schantz, M. Genetics of monoterpenes in *Chrysanthemum vulgare*. *Hereditas* **1973**, 74, 225-232.
12. Cruz, O.A., Guerrero, J., Podea, R., Batiu, I. Composition of the essential oil from the leaves of palma real (*Tanacetum vulgare* L.) from Perú. *Chem Bull "POLITEHNICA" Univ (Timișoara)* **2008**, 53(67), 10-12.
13. Alizadeh, M.A., Jafari, A.A., Sayedian, S.E. Evaluation of aerial biomass yield and essential oil content of seven species of *Tanacetum*. *Journal of Horticultural Research* **2017**, 25(1), 19-25.
14. Raal, A., Orav, A., Gretchushnikova, T. Essential oil content and composition in *Tanacetum vulgare* L. herbs growing wild in Estonia. *J Essent Oil Bear Plants* **2014**, 17(4), 670-675.
15. Rohloff, J., Mordal, R., Dragland, S. Chemotypical variation of tansy (*Tanacetum vulgare* L.) from 40 different locations in Norway. *J Agric Food Chem* **2004**, 52, 1742-1748.
16. Vaverkova, S., Birosova, L., Luptak, P., Brazdovicova, B. Content of essential oil obtained from flowerheads in selected species of *Tanacetum* L. genus and identification of selected components. *Herba Polonica* **2008**, 54(2), 22-29.
17. Stevović, S., Surčinski Mikovilović, V., Čalić-Dragosavac, D. Environmental adaptability of tansy (*Tanacetum vulgare* L.). *Afr J Biotechnol* **2009**, 8(22), 6290-6294.
18. Judzentiene, A., Mockute, D. The inflorescence and leaf oils of *Tanacetum vulgare* L. var. *vulgare* growing wild in Lithuania. *Biochem Syst Ecol* **2005**, 33, 487-498.
19. Mockute, D., Judzentiene, A. The myrtenol chemotype of essential oil of *Tanacetum vulgare* L. *vulgare* (tansy) growing wild in the Vilnius region. *Chemija* **2005**, 14(2), 103-107.
20. Keskitalo, M., Pehu, E., Simon, J. Variation in volatile compounds from tansy (*Tanacetum vulgare* L.) related to genetic and morphological differences of genotypes. *Biochem Syst Ecol* **2001**, 29, 267-285.
21. Mureșan, M.L. Variability of chemical composition in *Tanacetum vulgare* L. essential oils over the world. *Acta Medica Transilvanica* **2015a**, 20(4), 163-164.
22. Mureșan, M.L., Oniga, I., Georgescu, C., Paltinean, R., Gligor, F., Crăciunaș, M.T., Oprean, R. Botanical and phytochemical studies on *Tanacetum vulgare* L. from Transylvania. *Acta Medica Transilvanica* **2014**, 2(4), 300-302.
23. Räisänen, R., Primetta, A., Nikunen, S., Honkalampi, U., Nygren, H., Pihlava, J.M., Berghe, I.V., Wright, A. Examining safety of biocolourants from fungal and plant sources-examples from *Cortinarius* and *Tapinella*, *Salix* and *Tanacetum* spp. and dyed woollen fabrics. *Antibiotics* **2020**, 9, 266; doi:10.3390/antibiotics9050266.
24. Zolotaikina, M.Y., Hontova, T.M., Kotov, A.H., Ilyina, T.V., Kryvoruchko, O.V. Study of dry extract of tansy (*Tanacetum vulgare*) using the method of High-Performance Liquid Chromatography. *Der Pharma Chem* **2017**, 9(11), 1-4.
25. Vasileva, A.M., Iliev, I.A., Lozanov, V.S., Dimitrova, M.B., Mitev, V.I., Ivanov, I.P. *In vitro* study on the antitumor activity of *Tanacetum vulgare* L. extracts. *Bulg Chem Commun* **2019**, 51829, 249-255.

26. Ivănescu, B., Tuchiluș, C., Corciovă, A., Lungu, C., Mihai, C.T., Gheldiu, A.M., Vlase, L. Antioxidant, antimicrobial and cytotoxic activity of *Tanacetum vulgare*, *Tanacetum corymbosum* and *Tanacetum macrophyllum* extracts. *Farmacia* **2018**, 66(2), 282-288.
27. Stojković, M., Mitić, S., Pavlović, J., Stojanović, B., Paunović, D. Antioxidant potential of *Tanacetum vulgare* L. extracts. *Biologica Nyssana* **2014**, 5(1), 47-51.
28. Özbilgin, S., Akkol, E.K., Öz, B.E., İlhan, M., Saltan, G., Acikara, Ö.B., Tekin, M., Keleş, H., Süntar, I. *In vivo* activity assessment of some *Tanacetum* species used as traditional wound healer along with identification of the phytochemical profile by a new validated HPLC method. *Iran J Basic Med Sci* **2018**, 21(2), 145-152.
29. Mikulášová, M., Vaverková, Š. Antimicrobial effects of essential oils from *Tanacetum vulgare* L. and *Salvia officinalis* L., growing in Slovakia. *Nova Biotechnologica* **2009**, 9(2), 161-166.
30. Mureșan, M.L. Antimicrobial effects of the ethanolic extracts and essential oils of *Tanacetum vulgare* L from Romania. *Acta Universitatis Cibiniensis Series E: Food Technology* **2015b**, 19(2), 75-80.
31. Kameri, A., Koçani, F., Hashani, Z., Kurteshi, K., Kamberi, B., Kurti, A., Haziri, A. Antifungal and synergistic effects of the ethyl acetate extract of *Tanacetum vulgare* (L.) against *Candida albicans*. *Med Sci Monit Basic Res* **2019**, 25, 179-186.
32. Petrov, N., Stoyanova, M., Valkova, M. Antiviral activity of plant extract from *Tanacetum vulgare* against Cucumber Mosaic Virus and Potato Virus Y. *J BioSci Biotechnol* **2016**, 5(2), 189-194.
33. Dancewicz, K., Gabryś, B., Przybylska, M. Effect of garlic (*Allium sativum* L.) and tansy (*Tanacetum vulgare* L.) extracts and potassic horticultural soap on the probing and feeding behaviour of *Myzus persicae* (Sulzer, 1776). *Aphids and Other Hemipterous Insects* **2011**, 17, 129-136.



© 2020 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).