Anti-inflammatory and Anti-oxidant potential of Root Extracts and New Compounds from *Doronicum austriacum* Jaqc.

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Doronicum austriacum Jacq., Asteraceae, is a plant growing in many European regions. Historical sources describe the use of root extracts in traditional alpine medicine as vermicidal and laxative agent but also as a heart strengthening preparation (Tabernaemontanus, 1625). Considering the high interest in the identification of new anti-inflammatory and anti-oxidative compounds of natural sources we evaluated *D. austriacum* root extracts (dichloromethane and methanol) *in vitro*, in macrophages and astrocytes cell lines (Pepe et al., 2015). Investigations of potential anti-inflammatory activities of the extracts of the roots of *D. austriacum* were performed on lipopolysaccaride from *E. coli* (LPS)-stimulated J774.A1 macrophages.

Our results showed that both extracts exerted a strong inhibition of nitiric oxide (NO) release by macrophages. Those results incited a phytochemical reinvestigation (Bohlmann and Zdero, 1970) of this plant, which led to the isolation and structure elucidation of three known dihydrobenzofurane derivatives: 6,12-dihydroxytremeton (**1**), 6,12-dihydroxytremeton-12-*O*-isobutyrate (**2**), 6,12-dihydroxytremeton-12-*O*-(2-methyl)butyrate (**3**) of the DCM extract. Investigations of the methanolic extract yielded two unknown tremeton derivatives and three new diterpene acid derivatives: 12-*O*-ß-D-glucopyranosyl-6,12-dihydroxytremeton, 12-*O*-ß-D-[6-(3-hydroxy-3-methyl-glutaryl)-glucopyranosyl]-6,12-dihydroxy-tremeton; 4-carboxy-2-*O*-β-D-[2-(3-isopropyl-malat-1-methyl-ester)-glucopyranosyl]-atractyligenin, 4-carboxy-2-*O*-β-D-[2-(3-isopropyl-malat-1-methyl-ester)-isorhamnosyl]-atractyligenin and 2-*O*-β-D-[2-(3-isopropyl-malat-1-methyl-ester)-glucopyranosyl]-atractyligenin. All tested compound revealed a significant activity in inhibiting nitric oxide (NO) and reactive oxygen species (ROS) release as well as tumor necrosis factor-α (TNF-α) and interleukine-6 (IL-6) release. Among tested compounds numbers **1**-**3** exerted the highest anti-inflammatory and anti-oxidant potential on macrophages. Due to these promising results the isolated compounds were also investigated for their anti-inflammatory anti-oxidant potential on C6 astrocyte cell line. Our results showed a weaker, despite always significant, inhibitory effect on NO- and ROS-release in astrocytes, respect to macrophages. Again compound **1**-**3**, in particular **1**, showed the highest effects. Anti-proliferative assay revealed that all tested extracts and compounds at tested concentrations (50 to 5 μg/ml and 50 to 5 μM) did not affect cell viability.

Those results identified an anti-inflammatory and anti-oxidant potential for *D. austriacum* roots. Among the tested extracts the investigated DCM extract showed the highest potential which might be related to the exclusive presence of the more active compounds **1**-**3**.

Tabernaemontanus (1625). Neuw Vollkommentlich Kreuterbuch. online version: www.kraeuter.ch.
Pepe et al. (2015). Food Chem. Jan 15 (167):153-61.
Bohlmann and Zdero (1970) Tetrahedron Lett. 11(41): 3575-6.