New abietane-type diterpenes from *Perovskia abrotanoides* and their anti-inflammatory activity

Zahra Alizadeh[1,2], Mahdi Moridi Farimani[1], Massimiliano D'Ambola[2], Stefania Marzocco[2], Shara Francesca Rapa[2], Alessandra Braca[3], Nunziatina De Tommasi[2]

[1]Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, Tehran, Iran. [2]Department of Pharmacy, University of Salerno, Via Giovanni Paolo II 134D, 80084 Fisciano, Italy [3]Department of Pharmacy, University of Pisa, Via Bonanno 33, 56126 Pisa, Italy e-mail: alessandra.braca@unipi.it

Perovskia is a small genus in the Lamiaceae family, which is represented in Iran by three species: *P. abrotanoides* Karel., *P. atriplicifolia* Benth., and *P. artemisoides* Boiss [1]. *P. abrotanoides* is locally used for the treatment of cutaneous leishmaniosis, gonorrhea, typhoid, headache, toothache, motion, vomiting, cardiovascular diseases, atherosclerosis, liver fibrosis, and cough [2-4]. It has been reported that tanshinones with a *nor*-abietane skeleton are the most abundant and important bioactive compounds obtained from the roots of this species [2].

In the present work, we have undertaken a phytochemical investigation of the ethyl acetate extract from the plant root. Preparative isolation by a combination of silica gel column chromatography and HPLC afforded 15 abietane-type diterpenes, including six new compounds, 15,16-dehydrolatifolionol, 1-hydroxyneocryptotanshinone, 1β-hydroxycryptotanshinone, 8β-hydroxy-9(11),13(14),15(16)-abietatrien-12-one-4,16-olide, 1-oxo-neocryptotanshinone, and 3-oxo-1,2-en-1-deoxoarucadiol. Their structures were established using comprehensive spectroscopic data analysis, 1D and 2D-NMR, HRMS and comparison with the literature data.

Since tanshinone derivatives demonstrated to have anti-inflammatory activity [5], the isolated compounds (50-12.5 μM) were subjected to bioassays, indicating that all of them were able to significantly inhibit both nitric oxide release and inducible nitric oxide synthase expression in J774A.1 macrophages, during inflammatory conditions. In particular, among the tested compounds, 8β-hydroxy-9(11),13(14),15(16)-abietatrien-12-one-14,16-olide, 15,16-dehydrolatifolionol and 1β-hydroxycryptotanshinone showed to have the best activity in affecting both the pro-inflammatory parameters.

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