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Title: Protective action of saharian *Anvillea radiata* extracts against diabetic neuropathy progression, inflammatory processes and oxidative stress in high-fat-fed mice. An electrophysiological, biochemical and EPR investigation.

Anne Mercier¹, Chouaib Kandouli^{1,2}, Marcel Culcasi¹ and Sylvia Pietri¹

anne.mercier@univ-amu.fr

¹Aix Marseille University, CNRS, ICR UMR7273, SMBSO, Marseille, France

²Laboratoire de Biologie et Environnement, Faculté des Sciences de la Nature et de la vie, Université des Frères Mentouri, BP 325, route Ain El Bey, 25017 Constantine, Algeria.

Abstract

We have recently investigated the antioxidant, anti-inflammatory and antidiabetic properties of polyphenol-enriched extracts of the Saharian traditional medicine *Anvillea radiata* Coss & Dur (Kandouli et al., 2017). Diabetic neuropathies (DN) are of the major and earliest complications in diabetic patients, taking complex and multiple forms and are associated with reactive oxygen species (ROS) production, mitochondrial dysfunction and inflammatory-mediated damage in neurons and glial cells. In our search of natural medicines against diabetic-induced complications, we then investigated the protective effect of *Anvillea radiata* (AR) extracts against neural damages. Experiments were first conducted *in vitro* in human neuroblastoma cells exposed to high glucose medium. In the presence of selected aqueous or organic extracts at doses as low as 5 µg/mL, caspase and NADPH oxidase activities and ROS production were significantly reduced. Then, two selected extracts were given orally for 12 weeks at the dose of 150 mg/kg in High-Fat-Diet (HFD)-C57BL/6J diabetic mice. A significant hypoglycemic action, a reduced oxidative stress in blood and muscles and improved hyperlipidemic and inflammatory status were demonstrated. Interestingly, oral treatment with both AR extracts were found protective against DN damage including i) apoptosis in sciatic nerves, ii) conduction velocity and motor nerve conduction impairment, iii) infiltration of T cells, iv) inflammation and oxidative stress. Taken together, the use of AR extracts may prove to be of therapeutic value in the management of diabetes complications.