

Pharma Europe 2020: New therapeutic agents from selected medicinal plants against disease - Djebbar Atmani - University of Bejaia

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Abstract

Reactive oxygen species (ROS) are byproducts of the normal metabolism of oxygen and have important roles in cell signaling and homeostasis. However, their accumulation in cells, as in oxidative stress, may cause damage to biological molecules and cell membranes, ultimately leading to cell death. The present study was designed to investigate the anti-inflammatory, antidiabetic and anticancer potential of *Pistacia lentiscus* (Anacardiaceae) and *Fraxinus angustifolia* (Oleaceae) extracts, as well as identification of active compounds, using appropriate methodology. Evaluation of antioxidant activity was undertaken to support the anti-inflammatory effects.

The results indicated that *P. lentiscus* and *F. angustifolia* extracts, exhibited a promising anti-diabetic activity in streptozotocin (STZ)-induced diabetic rats, by a significant reduction (55%) of blood glucose level, a result confirmed by the inhibition of alpha-amylase activity (65%). The results of the anti-inflammatory activity of *P. lentiscus* and *F. angustifolia* showed significant reduction of the paw edema induced by carrageenan. Furthermore, *P. lentiscus* extracts showed a significant reduction of pro-inflammatory cytokines (IL-1 β) in activated macrophages. Moreover, the extracts of *F. angustifolia*, significantly inhibited ear edema induced by single and multiple doses of 12-*O*-tetradecanoylphorbol 13-acetate (TPA) and suppressed the cellular infiltration. In vivo, the vesicles loaded with the crude extract of *F. angustifolia* and especially penetration enhancer-containing vesicles (PEV) inhibited oxidative stress in human keratinocytes against H₂O₂ and attenuated edema and leukocyte infiltration by stimulating the repair of TPA-induced skin damage. Chromatographic and spectroscopic analyses allowed the identification of known and new phenolic compounds, some of which are endowed with highly interesting biological activities. Finally, the different extracts of leaf and fruit exhibited strong and promising antioxidant activity.

In light of the obtained results, we can conclude that *Pistacia lentiscus* and *Fraxinus angustifolia* could be beneficial in the treatment of inflammatory conditions and diabetes complications.

Introduction:

Plants are a large source of new bioactive molecules with therapeutic potentials. Many studies carried out have shown that the medicinal properties of plants come from the presence of bioactive agents in their extracts. The most important elements are alkaloids, flavonoids, vitamins, tannins, essential oils, organic acids, resins, fat oils, saponins and polysaccharides. Reports indicate that there is an inverse relationship between the dietary intake of antioxidant-rich foods and the incidence of human disease. However, synthetic antioxidants, such as (BHT) and (BHA), have been widely used as antioxidants in the food industry and may be responsible for liver damage and carcinogenesis. For this reason, interest within the use of natural antioxidants has increased. Epidemiological studies have indicated the relationship between the plant antioxidants and reduction of chronic diseases. Therefore, the development and utilization of more effective and non-toxic antioxidants from natural products are recommended, not only for the food and drug storage, but also for the nutritional and clinical applications. A great deal of effort has focused on using available experimental techniques

to identify natural antioxidants from medicinal plants. The Mediterranean region is relatively rich with plants (between 15,000 and 20,000 species). Algeria, a North African country with a large variety of soils (littoral, steppe, mountains and desert) and climates, possesses a rich flora (more than 3,000 species and 1,000 genders), it has an immense biodiversity. *Pistacia lentiscus* L. is an aromatic evergreen shrub belonging to the Anacardiaceae family, largely distributed in the Mediterranean basin. Aerial parts of *P. lentiscus* have traditionally been used in the treatment of hypertension, coughs, sore throats, eczema, stomach aches, kidney stones and jaundice. They possess stimulant and diuretic properties. The fruits, galls, resin and leaves of *P. lentiscus* have an extended tradition in folk medicine dating from the days of the traditional Greeks. Several studies focused on the phytochemical composition of the resin, the leaves and therefore the

galls volatile oil of *P. lentiscus* and also on its antioxidant activity but in contrast, fewer studies are associated with the composition and antioxidant activity of the berries of *P. lentiscus*.

Antioxidant activity is a superb example of a functional benefit that plant extracts can deliver. Plants are known to contain a spread of natural antioxidants that protect and preserve their physical and metabolic integrity also as their heredity by way of their seeds. Many of those extracts and compounds from plants are emerging as candidates for moderating the consequences of the aging process on skin by limiting biochemical consequences of oxidation.

Compounds like vitamin C, vitamin E and rosmarinic acid (RA) are commonly utilized in foods also as cosmetics for his or her potent antioxidant activity that aids in product stability. Reduction in oxidation features a clear benefit for the merchandise also as for skin, and therefore the consumer perception of antioxidants may be a positive one, making them particularly attractive as cosmetic ingredients. The danger is that the utilization of one antioxidant is usually positioned as a panacea. The phenomenon of the merchandise that contains the "most potent antioxidant ever discovered" belies the scientific understanding that antioxidants add synergy. The physiological codependence of water soluble vitamin C and lipophilic vitamin E is well accepted. Plant antioxidants differ not only in redox potential and solubility, but also in their mechanism of action. Some quench one or more ROS like superoxide, hydroxyl radicals, or singlet oxygen. Others inhibit activity or expression of oxidative enzymes, or enhance activity or expression of antioxidative compounds or enzymes like catalase, or chelate oxidizing metal ions, or act by other mechanisms, known and unknown. Given the variability of chemical structures and biological mechanisms of antioxidants described from plants, it's not surprising that not all antioxidants confer an equivalent degree of functional protection to the skin.

Recent Publications:

1. Salima Sebaihi-Harzoun, Dina Atmani-Kilani, Nadjet Debbache-Benaid, Frédéric Nana, Emilie Evain-Bana, Gilbert Kirsch, Jessica Tabart, Claire Kevers, **Djebbar Atmani** (2018). Phytochemical composition, antioxidant and anti-proliferative properties of *Genista ferox* Poirret. aerial parts. *European Journal of Integrative Medicine*, 23 : 6-13.

2. AZIB Leila, ATMANI-KILANI Dina, DEBACHE-BENAIIDA Nadjet, **ATMANI Djebbar** (2019). *Pistacia lentiscus* L. leaves extract and its major phenolic compounds reverse Aluminium-induced neurotoxicity in mice. *Industrial Crops and Products*, 137: 576-584.
3. Nadja AHMANE, Dina ATMANI-KILANI, Nassima CHAHER, Karima AYOUNI, Meriem RAHMANIBERBOUCHA, Grégory DA COSTA, Nadjet DEBBACHE-BENAIIDA, Tristan RICHARD, **Djebbar ATMANI** (2019). Identification of bioactive compounds from *Fraxinus angustifolia* extracts with anti-NADH oxidase activity of bovine milk xanthine oxidoreductase. *Turkish Journal of Biology*, 43: 133-147.
4. AJA Iris, DA COSTA Grégory, PEDROT Eric, IGLESIAS Marie-Laure, PALOS-PINTO Antonio, VALLS Josep, CHAHER Nassima, RUIZ-LARREA M.Begoña, MÉRILLON Jean-Michel, **ATMANI Djebbar**, RUIZ-SANZ José Ignacio, RICHARD Tristan. Unusual stilbene glucosides from *Vitis vinifera* roots. 2019 International Viticulture and Enology Society-IVES 573-579.
5. OURABAH Asma, ATMANI-KILANI Dina, DEBACHE-BENAIIDA Nadjet, KOLESOVA Olga, AZIB Leila, YOUS Farah, BENLOUKIL Malika, BOTTA Brono, GIOVANNA Simonetti, **ATMANI Djebbar**. Anti-*Candida albicans* biofilm activity of extracts from two selected indigenous Algerian plants: *Clematis flammula* and *Fraxinus angustifolia*. *Journal of Herbal Medicine (in press)* 2019.

Biography

Professor Djebbar Atmani is a senior lecturer at the Faculty of Nature and Life Sciences, University of Bejaia (Algeria). He obtained his Master of Science degree from California State University, Los Angeles (USA) in 1987 and his PhD from the University of Sétif (Algeria) in 2004. His research interest is natural products from medicinal plants. He published over thirty papers in high impact scientific journals and attended several seminars and symposia worldwide.