

Plant phenolics as new therapeutic agents in the treatment of diabetes and inflammation

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Phytochemicals are well known plant components which have discrete bio-activities towards animal biochemistry and metabolism are being broadly studied for their extensive ability to provide health benefits. It is important to establish the scientific rationale to defend their use in foods, as potential nutritionally active ingredients. Scientists estimate there are more than 5,000 phytochemicals, and we're only beginning to understand what the compounds may do for human health.

Phytochemicals, including phenolic compounds present in many plants have received much attention in recent years due to their health benefits. Plant polyphenols are a diverse group of secondary metabolites predominantly synthesised through the shikimic acid and acetate/polyketide pathways. The common perception of polyphenols' pharmacological effect is that they are mediated through a nonspecific interaction with proteins/enzymes and general antioxidant mechanisms. Numerous specific biological effects at sub-micromolar concentration are however common for many polyphenols. One of the distinct advantages of polyphenols is in their therapeutic potential for complex diseases like diabetes and obesity, where a one drug → one target → one disease approach offers limited efficacy. Through their multifunctional actions, plant polyphenols could ameliorate the various components of such diseases and offer a better outcome through the one drug → multitarget → one/multidisease principle. They could also work in a synergistic manner, with their crude mixtures often showing a higher activity than the isolated pure compounds (multidrug → multitarget → one/multidisease approach). Since both diabetes and obesity cases are now growing in the world with epidemic proportions, our desperate search for safer drugs from natural sources must continue. In this regard, polyphenols are best placed and this Special Issue is designed to scrutinise recent developments in the chemistry, pharmacology, and medical implications of polyphenols as potential therapeutics for diabetes and/or obesity. We are thus inviting colleagues to join us by making their valuable contributions to Molecules.

This study was conducted to investigate the anti-diabetic and anti-inflammatory activities of *Pistacia* and *Fraxinus angustifolia*, two plants traditionally used in Algerian folk medicine. 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 biological activities.

So far, the evidence indicates that phytochemicals have promising benefits. For example: Carotenoids in red, orange, yellow, and green plants (cooked tomatoes, carrots, squash, and broccoli) may inhibit cancer growth and cardiovascular disease, and boost immunity, Flavonoids in berries, apples, citrus, onions, soybeans, and coffee may fight inflammation and tumor growth, Anthocyanins in berries and red wine are associated with lower blood pressure, Resveratrol in red wine, grapes, dark chocolate, and peanuts is associated with longevity in some animals, Proanthocyanidins and flavanols in grapes, apples, cocoa, and red wine are linked to better function of the lining of the arteries and reduced blood pressure., Sulfides and thiols in onions, garlic, leeks, olives, and scallions may help decrease "bad" LDL cholesterol, Isothiocyanates (sulforaphane) in cruciferous vegetables such as broccoli, cabbage, and kale may help protect us against cancer and cardiovascular disease, Quercetin in apples, onions, and citrus fruits may help decrease inflammation and blood pressure, Terpenes in cherries and citrus fruits may help slow cancer cell growth and fight viruses, Lutein and zeaxanthin in dark, leafy greens are linked to eye health. The benefits aren't yet conclusive. They have been derived from associations between people's diets and health outcomes (which does not show a direct cause and effect), and from laboratory studies of human cells or lab animals (resveratrol, for example, has been shown to help prevent cancer and heart disease in lab mice, but at levels of consumption much higher than found in a human diet).