Atherosclerosis is related to inflammatory conditions, which are initiated by invasion of low density lipoprotein (LDL) cholesterol (“the bad cholesterol”) into the artery wall. The early atherosclerotic lesion is characterized by the accumulation of cells loaded with cholesterol, which gain the appearance of foam cells. Elevated plasma levels of LDL-cholesterol are major risk factors for cardiovascular disease, because this is associated with cholesterol deposits in the arterial wall, which lead to a blockage of blood flow to the heart and a consequent heart attack. However, beyond the quantity of the LDL-cholesterol, its quality is also an additional major risk factor for atherosclerosis. For instance, the oxidative stress to which the human body is constantly exposed, can modify LDL to form oxidized LDL (Ox-LDL). Oxidized LDL is taken up at an enhanced rate by cells of the arterial wall leading to a massive cholesterol accumulation in the arteries. Intervention to reduce the levels of LDL cholesterol in the blood, or to inhibit LDL oxidation are thus widely used in order to inhibit the progression of atherosclerosis, the major cause of morbidity and mortality in the western world.

LDL can be protected from oxidation by dietary antioxidants, such as vitamin E (tocopherol), β-carotene and lycopene, and by plant-derived flavonoids. Human serum contains additional antioxidants which protect LDL from oxidation. These antioxidants include vitamin C (ascorbic acid) and polyphenolic flavonoids found in red wine, pomegranate juice, tea, ginger and licorice roots.

Research continues to indicate that fruits and vegetables are prime sources of antioxidants. Dietary consumption of flavonoids was shown to be inversely related to morbidity and mortality from coronary heart disease. Flavonoids compose the largest and most studied group of plant phenols. Over 4000 different flavonoids have been identified to date. They are usually found in plants as glycosides (linked to sugars), and large compositional differences exist between different types of plants, even between different parts of the same plant.

Glycyrrhiza glabra, the licorice plant, is known as a healthy nutrient for more than 3000 years. The licorice roots have long been used as flavoring and sweetening agents. Licorice root has also been used medicinally for a wide range of therapeutics, such as antibacterial, antiviral, antiinflammatory, antiallergic, and antiepileptotic. Minor components of licorice, mostly flavonoids from the isoflavan and chalcon subclasses, were shown to possess potent antioxidative properties. Among these compounds, glabridin constituted the major flavonoid in the licorice root extract (5 g/kg of root).
Recently, we used licorice crude extract and the main isolated purified flavonoid, glabridin, to test their antioxidant capacity in protection of LDL against oxidation. We found that licorice root extract, as well as purified glabridin, were able to protect LDL from oxidation. Upon LDL incubation with glabridin, the later was shown to bind to the LDL, and subsequently to protect it from oxidation.

The protective capabilities of licorice against LDL oxidation, were also investigated in healthy humans, and in patients who suffer from high levels of cholesterol in their blood. We administered 100 mg of licorice root ethanolic extract per day, for a period of two weeks to ten healthy volunteers and to ten hypercholesterolemic patients. Then, LDL was isolated from the plasma and analyzed for its resistance to oxidation. We found that LDL isolated from the blood after consumption of licorice root extract was more resistant to oxidation by 44% in comparison to LDL isolated prior to licorice supplementation. Furthermore, we have observed that consumption of licorice root extract resulted also in a 10% reduction in the patients’ systolic blood pressure.

Thus, dietary consumption of licorice root extract by hypercholesterolemic patients may act as a moderate reducing blood pressure nutrient and as a potent antioxidant agent, which confer its beneficial health benefit against cardiovascular disease.

In order to study directly the effect of licorice root extract consumption on the development of atherosclerosis, we administered licorice root extract to a specific strain of mice that were created by gene target technique, so that they lack the apolipoprotein E and because of that they accumulate large amounts of cholesterol in their blood, and develop atherosclerotic lesions (apolipoprotein E deficient (E0) mice). We supplemented the mice via their drinking water with 200 µg of licorice extract/day/mouse for a period of six weeks. Then, we analyzed the resistance of their LDL to oxidation, and found out an 80% reduction in the susceptibility of their LDL to oxidation, in comparison to LDL isolated from placebo-treated mice.

Most importantly, inhibition of LDL oxidation in E0 mice following licorice root extract consumption, was associated with a substantial reduction in the formation of macrophages loaded with cholesterol and in the development of atherosclerosis.

We conclude that licorice represent a source of some of the most potent nutrients, which can attenuate the development of atherosclerosis secondary to its antioxidative properties against lipid peroxidation in cells and in lipoproteins.

References
About the Author

Education: Dr Bianca Fuhrman, Senior Adjunct Lecturer in Biochemistry, obtained her DSc degree in Medical Sciences at the Technion Faculty of Medicine, Haifa, Israel. Since then, Dr Fuhrman was appointed as a senior scientist in the Lipid Research Laboratory, Rambam Medical Center, Haifa, Israel, which is affiliated with the Technion Faculty of Medicine and the Rappaport Institute for Research in the Medical Sciences.

Teaching: Dr Fuhrman is teaching elective courses on lipids, lipoproteins, antioxidants and atherosclerosis to medical students, and supervises graduate students (for MSc and DSc/PhD degrees), as well as physicians in basic and clinical research.

Research: Dr Fuhrman’s research focuses on the mechanism responsible for foam cell formation and atherosclerosis. The hypothesis of LDL oxidation as a major risk factor for atherosclerosis development raised an extensive investigation on the role of antioxidants against LDL oxidation as a preventive treatment of atherosclerosis. The contribution of Dr Fuhrman to the understanding of the mechanisms involved in the beneficial effects of nutritional antioxidants is reflected in many published articles, demonstrating that dietary supplementation with nutrients rich in polyphenols such as licorice root extract, red wine, ginger, carotenoids and pomegranate juice is associated with increased resistance of plasma LDL to oxidation and reduced development of atherosclerosis.

Awards: In 2003, Dr Fuhrman was awarded the Israel Society for Clinical Biochemistry Annual Award for Scientific Achievements.

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