# Macromolecular Antioxidants: Importance in Health and Perspectives

## Antioxidantes macromoleculares: importancia en salud y perspectivas

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#### Antioxidants

Antioxidants are dietary constituents that play an essential role in the prevention of chronic diseases (neurological, cardiovascular, cancer) and processes associated with aging ((insulin resistance, increase in inflammation, cognitive and memory decline, aorta thicker and less flexible, deterioration of the skin and others).

The antioxidants in the diet are a complex mixture of hydrophilic and lipophilic substances, consisting mainly of three vitamins (A, C, E), a few dozens of carotenoids (beta-carotene, lycopene, lutein, zeaxnthin,...) and several hundred of polyphenols (flavonoids, anthocyanins, resveratrol, hydroxytyrosol, quercetin, phenolic acids....). They are characterized by their ability to protect from oxidative damage to DNA, proteins and lipids, and to prevent the pathogenesis of numerous risk factors associated with chronic diseases (oxidative stress, inflammation, hypertension, hyperglycemia, dyslipidemia). Its mechanisms of action are complex, including free radical counteraction, modulation of gene expression, modulation of the colonic microbiota and strengthening of the endogenous antioxidant system.

The natural source of antioxidants are foods and beverages of vegetable origin, which usual and abundant consumption provides the amount and variety of antioxidants adequate to maintain a suitable antioxidant status. It should be take into account that the positive effects of antioxidants result not from a particular antioxidant but from the synergistic and additive action of a high number of substances, including vitamins A, C and E, carotenoids and polyphenols. A good antioxidant status contributes significantly to protecting health and achieving quality-of-life aging.

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#### Macromolecular antioxidants<sup>1</sup>

The strong scientific evidence of health effects of antioxidants has been established through biological and medical research exclusively focused on the small molecular size or low weight antioxidants (mA) mentioned above: (Vitamins A.C and E, carotenoids and polyphenols).

However, recent findings has shown that plant foods - in addition to mA - contain abundant amounts of other type of high molecular weight antioxidants, named macromolecular antioxidants (MA). They are high molecular weight proanthocyanidins and tannins and polymeric structures of low molecular weight polyphenols and carotenoids bound to polysaccharides and proteins

MA have so far been ignored due to the fact that it is not possible to extract them from the plant material using the current technologies and, in addition, they are not detected by the usual methods of analysis of antioxidants. That is why the scientific community has focused research exclusively on mA, ignoring MA. However, we ingest significant amounts of both mA and MA daily.

It should be noted that the daily intake of MA in our usual diet is higher than to that of mA.Therefore, it is very possible that in all the health effects currently attributed exclusively to Am there is a major contribution of MA.

Macromolecular antioxidants have a high biological and antioxidant activity and they exhibit promising health related properties. Their greater molecular size confers them some specific physiological characteristics and mechanisms of action, which differentiates them from mA.

Most Am are absorbed in the small intestine during digestion and pass to the blood stream between 0.5 and 2 hours after intaking, producing an increase in antioxidant status (blood antioxidant concentration) and being distributed to target cells and organs Contrary, MA crosses intact the stomach and small intestine and reaches the colon where they interact with the colonic microbiota in a fermentative process that breaks the macromolecules, resulting a high intestinal antioxidant status

**Correspondence:** Fulgencio Saura Calixto E-mail: fsaura@ictan.csic.es and the production of antioxidant metabolites. These metabolites are absorbed through the colonic mucosa and reach the bloodstream about eight hours after ingestion, being distributed to cells and tissues where they may have systemic effects. This indicates that MA may increase and prolong antioxidant status and the health effects associated to dietary antioxidant intake.

Several biological assays, animal experiments and clinical studies have been carried out, obtaining positive results indicating that macromolecular antioxidants may play an important role in gastrointestinal health - especially in relation to prevention of colon cancer - derived from increased antioxidant status and also in protection against various risk factors for chronic diseases due to metabolites absorbed through the colonic mucosa

The publications resulting from this research have had a high impact in recent years, as shown by the high number of references and by the recognized research impact indicators published in the Web of Science (WOS).

Current research focuses on the development of clinical trials to study the potential effect of macromolecular antioxidants in the prevention of metabolic syndrome. This syndrome is one of the major public health problems and occurs in people who have several of the most common risk factors in Western countries (hypertension, obesity, hyperglycemia, abdominal obesity, hypercholesterolemia).

Nevertheless, they are preliminary studies that require a great increase of research at national and international level for its consolidation. We must bear in mind that the scientific evidence of the effects of low molecular weight antioxidants has been established by hundreds of research teams over a century of work and even this topic has been awarded with several Nobel Prizes, while there are still very few research groups working on macromolecular antioxidants. The increase of number of researchers in this field along with the extraordinary advances in experimental methodologies and technological equipments, can allow the establishment of a complete knowledge of the properties and healt effects of macromolecular antioxidants in a few years

Technological studies are also being carried out to obtain macromolecular antioxidants and the development of applications as a new type of ingredient for the food and pharmaceutical industries. In fact there are already in the international market some products with MA.

#### Perspectives in nutrition sports

There is a growing market for antioxidant supplements to prevent muscle damage resulting from the intensive and strenuous exercise of sportsmen, produced by free radicals and inflammation and prolonged days after workouts and competitions. The most commonly used supplements are drinks or products rich in several types of low molecular weight polyphenols (mA), obtained from fruits or herbs rich in polyphenols (blueberries, pomegranate, ginger, green tea, etc.).

The use of MA in sports medicine would allow a more complete and balanced intake of antioxidants, currently focused exclusively on Am. Some positive effects in general wellness and in protection of muscle damage could be expected, derived from the specific characteristics of MA, previously mentioned: longer antioxidant action and strengthening of intestinal health resulting from its interaction with the colonic microbiota.

#### Bibliography

 Importance of macromolecular antioxidants in human nutrition and health. F. Saura-Calixto, Editor. Royal Society of Chemistry, UK (in press, to be published at January 2018).

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