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# NUTFRUIT

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## THE ENTIRE NUT AND DRIED FRUIT INDUSTRY MEETS IN CHENNAI

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## A HANDFUL OF NUTS EVERY DAY TO MODULATE THE ACTIVITY AND FUNCTION OF microRNAs

*Some of the health effects of nuts may be explained by the modulation of the activity of miRNAs, small regulatory RNA molecules which control several molecular processes at the cellular level.*

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The discovery in 1993 of small regulatory RNA molecules, called microRNAs (miRNAs), represented a break with the central dogma of molecular biology. From that moment on, RNA would not be considered simply a messenger between DNA and protein, but an active regulator of gene expression.

MiRNAs are a conserved family of 18-25 nucleotide small RNA molecules which are involved in posttranscriptional gene repression. There is evidence to suggest miRNAs play a key role in almost every cellular process, such as cell cycle control, development, immune response and metabolism. Due to their pivotal role in cell biology, miRNA deficiencies and excesses have been linked to a number of clinically important diseases and chronic conditions. In fact, miRNA profiling studies have demonstrated that aberrant miRNA expression patterns, detected in biofluids and/or tissues, were specific to various types of cancers, cardiometabolic diseases, obesity and diabetes<sup>1</sup>.

Changes in miRNA expression and/or in their mechanisms of action show a great plasticity and respond to environmental signals, including dietary factors. The description of the interplay between genes and diets has its roots in the last century, however it has recently been discovered that nutrients can exert their beneficial effects by acting on the biogenesis, processing and action of miRNAs<sup>2</sup>.

The scientific community has come to a global consensus regarding the health properties of nuts. A growing body of scientific evidence, from epidemiological observations to several clinical trials, both in animal models and in humans, has established the inverse associations between nut consumption and the risk of

developing coronary heart disease, type 2 diabetes, cancer and, more generally, with reduced risk of mortality<sup>3</sup>.

The beneficial effects of nuts are ascribed to their unique nutrient profile, which is high in unsaturated fatty acids, especially omega-3 polyunsaturated fatty acids, high-quality vegetable proteins, vitamins, minerals, fibers, plant sterols and phytochemicals. This profile makes nuts a source of bioactive molecules.

Owing to their complex matrices of fats and non-fatty constituents, recent scientific evidence has demonstrated that, behind the control of gene expression observed related to nut consumption, the regulation of miRNAs plays an important role.

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In this context, the recently published study of Tsoukas et al. found that a diet enriched with walnut significantly changed the miRNA expression profile in localized colorectal cancer tissue in a mouse model<sup>4</sup>. As for human beings, in the frame of the PREDIMED study, we found an association between an miRNA target site variant in the miR-410 and stroke incidence, observing

that the association was modulated by monounsaturated fatty acids and polyunsaturated fat intake, nutrients which are found in high quantities in extra-virgin olive oil and nuts<sup>5</sup>. In 2015, Ortega et al. reported for the first time the modulation of 11 plasma miRNAs in healthy subjects following 8 weeks of a 30 g nut-enriched normocaloric diet. Furthermore, the changes observed mirrored the improvement of the lipid and inflammatory profile<sup>6</sup>.

Even more specific is the study published in 2016 by Hernández-Alonso of our research group. Following the results obtained in the EPIRDEM study where we demonstrated how in pre-diabetic patients chronic pistachio consumption led to improved glucose and insulin metabolism as well as cardiovascular risk markers, we also demonstrated a shift towards a healthier profile in circulating

miRNAs which have been linked to diabetes as well as glucose and insulin metabolism<sup>7</sup>.

Taken together, the results of the few studies published so far settle the critical issue of understanding the molecular mechanisms behind the beneficial health effects of nut consumption. Walnuts, pistachios, almonds and other tree nuts can control biogenesis, processing and activity of the miRNAs which play a pivotal role in the definition of the physiological nature of the cell. 

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