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NUT CONSUMPTION AND MICROBIOTA MODULATION: NUTS ARE NOT ONLY GOOD FOOD FOR HUMANS

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The human gastrointestinal tract contains 10-fold more cells than the rest of the body and encodes 100-fold more unique genes than our own genome [1]. These data lead us to view ourselves as *holobionts* [2]. Approximately only 50 species belonging to five or six genera and two phyla account for 99% of microbiota biomass [3]. Moreover, nearly 90% of the bacteria in the human gut belongs to *Bacteroidetes* or *Firmicutes*, with *Actinobacteria*, *Fusobacteria*, *Cyanobacteria*, *Verrucomicrobia* contributing to a small fraction of the total bacteria, being this set of phyla which predominantly influence human nutrition and metabolism [4]. Even though most people have similar proportions of these phyla, subjects with obesity, type 2 diabetes (T2D), inflammatory diseases or other major health problems have a suboptimal and less diverse gut microbiota profile compared with healthy controls [5]. However, whether lower richness of gut microbiota can be prevented or treated by changes in the lifestyle is still unknown [6].

The increased interest in the study of gut microbiota has generated an improvement of its associated molecular tools. High-throughput 16S rRNA and full-genome sequencing (metagenomics) aim to describe which microbes are present in the human gut, and what is its potential role in human health. However, to further explore what the microbes are "doing", we need to apply other omic approaches such as metatranscriptomis (RNA level), metaproteomics (protein level) and metabolomics (compounds level) [7].

It has been established that long-term dietary patterns and shorter-term dietary interventions may influence gut microbiota composition [3]. However, these interventions does not necessarily result in permanent compositional shift, at least at phylum level [8]. Therefore, understanding which foods or dietary components strengthen or weaken the integrity of the human gut microbiota may assist in adapting diets to prevent or to promote microbes (and their associated metabolites) from accessing tissues and causing or palliating several chronic conditions.

Nuts could exhibit prebiotic effects by enriching potentially beneficial microbes such as bifidobacteria or lactic acid bacteria.

Many potential prebiotic components can be present in a particular food. For example, the fermentation of fiber to beneficial end-products (e.g. butyric acid) and the biotransformation of phytochemicals by the intestinal flora have been reported to be associated with the transition to a healthier microbiota. Other dietary components, as polyphenols have also been related with gut microbiomes [9]. Concerning that, nuts are a complex matrix of nutrients especially rich in fiber, unsaturated fatty acids and different bioactive compounds such as tocopherols, phytosterols, and phenolic compounds [10]. Thus, nuts could exhibit prebiotic effects by enriching potentially beneficial microbes such as bifidobacteria or lactic acid bacteria.

Along with this potential prebiotic properties, nuts have been proved to be beneficial for protecting against different metabolic disorders such as diabetes, dyslipidemia, coronary heart disease, among others [10–13]. The amount of fiber contained in nuts is also able to decrease postprandial glycaemic levels and this could be a strategy for increasing insulin sensitivity ameliorating several cardiovascular risk factors for chronic disease [14, 15]. Moreover, their content in bioactive compounds could explain the protective antioxidant properties of nuts [10]. The set of minerals present in nuts could explain the relationship observed between the consumption of some of them (e.g. magnesium or calcium) and a lower risk of type 2 diabetes and overall death [16, 17].

Almonds and pistachios have different protective properties modulating insulin resistance, glucose metabolism and lipid profile (reviewed in [18] and [19]). However, their prebiotic properties were not well-characterized until a few years ago. Mandalari et al. founding that almond's fiber significantly altered the composition of gut bacteria *in vitro*, thus suggesting a potential prebiotic use of almond skins [20]. Later, in two separated randomized, controlled, cross-over feeding studies with either almond or pistachio (1.5 or 3 servings/day) and a free-nut diet, showed that both interventions with nuts significantly affected gut microbiota [21]. However, the prebiotic effect of pistachio intake on gut microbiota composition was much stronger than that of almond consumption. Moreover, pistachio's microbiota modulation increased the number of butyrate-producing bacteria, identified as potentially beneficial, whereas bifidobacteria was not affected [21]. As these results were obtained from healthy volunteers, regardless of any specific disease or condition, it will be interesting to explore the potential prebiotic role of nuts linking such changes in microbiota with improvements in specific health outcomes such as obesity or T2D.

Undoubtedly, this pioneer medium-term study has set the basis for future long-term research on the modulation of nuts over the microbiota and thus, on different health outcomes. However, further research regarding nuts and microbiota-disease axis is needed in order to find new physiological pathways explaining the beneficial effects of nuts on human health, and thus contributing to strengthen the image of nuts as a healthy part of a daily diet.

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