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PISTACHIO NUT CONSUMPTION IMPROVES INSULIN RESISTANCE AND REDUCES GLUCOSE LEVELS IN PRE-DIABETIC SUBJECTS

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Type 2 diabetes is a worldwide problem that affects a huge part of world's population. Its current prevalence is nearly 400 million people (more than 5% of current population), and it is estimated that by 2035 there will be almost 600 million people living with type 2 diabetes (T2DM). However, prediabetes condition could be even worse because of its alarming current prevalence (almost 900 million people) and because it is a silent state associated with a higher risk of several deadly conditions, including T2DM, heart disease, hypertension, strokes and early death [1]. However, with lifestyle changes such as following a healthy diet, physical exercise and maintaining a healthy weight, blood sugar levels can go back to normal values.

Since the publication of the results of the Adventist Health Study showing that nut consumption was inversely associated with coronary heart disease [2], many evidences from epidemiological studies and controlled clinical trials (RCT) have demonstrated the beneficial impact of nut consumption on health outcomes and total mortality [3]. Nevertheless, the association of nuts with T2DM, as one of the most common cardiovascular risk factor, have been evaluated in different epidemiological studies including the PREDIMED study [4, 5]. However, even though we did find a significant protective effect of nuts over T2DM in the PREDIMED, the association of diabetes with nut intake is less conclusive [4, 6]. For this reason, some RCT have assessed the effect of nuts on glucose and insulin metabolism. Thus, there is a consensus in acute feeding studies as all of them reported beneficial effects on glucose and insulin parameters after nuts consumption, however, inconsistent results have been found in medium- and long-term clinical trials.

Nuts are a complex matrix of different nutrients (healthy unsaturated fat, minerals such as magnesium, vitamins (folate, tocopherols), low-GI fiber, antioxidants (phytosterols and polyphenols)) [4] that could have potential modulatory properties such as regulating postprandial glucose clearance, improving pancreatic secretion and decreasing insulin resistance [4, 7] thus leading to a potential beneficial role on both prediabetes and diabetes. Within nuts, pistachios are less energetic, have high amounts of polyunsaturated fatty acids, and are rich in fiber and bioactive compounds such as procyanidins and carotenoids. So, it can be hypothesized that chronic intake of pistachios will improve glucose metabolism and insulin resistance status in pre-diabetic subjects.

Investigators from our Unit of Research (Human Nutrition Unit, Rovira i Virgili University, Reus, Spain) have in the last two years conducted a clinical trial in order to examine whether a pistachio-rich diet reduces glucose and lipid profile and improves its metabolic risk profile, including inflammation and other related markers.

This study whose acronym is "EPIRDEM" (Effect of Pistachio Intake on Insulin Resistance and Type 2 Diabetes Mellitus) was headed by Dr. Mònica Bulló. The research team, recruited fifty-four individuals with prediabetes and recommended to consume two diets: a pistachio-supplemented diet (PD; including 57 g/day of pistachios) or a control diet (CD, lacking of any type of nuts), each for four months in a crossover manner. The periods were separated by a two-week washout period. Diets were isocaloric and matched for protein, fiber, and saturated fatty acids.

Results from EPIRDEM study have been recently published in the prestigious scientific journal *Diabetes Care* the 14th of August [8]. After the pistachio period, there were significant decreases in fasting glucose, insulin, and homeostasis model assessment of insulin resistance compared with the control diet. Importantly, there were no significant between-intervention changes in body mass index, which supports the fact that nuts are not fattening. Participants in the pistachio diet also showed a non-significant decrease in glycosylated hemoglobin (a measure of glucose control), and a higher non-significant reduction in serum low-density lipoprotein (LDL) cholesterol levels (but cholesterol), compared with participants in the CD. Compared with the control diet, after the pistachio diet there

were significant decreases in other cardiometabolic emergent risk markers such as fibrinogen, glucagon-like peptide-1, oxidized LDL, and platelet factor-4, showing an improvement in the inflammation, coagulation and platelet function. In addition, the study demonstrated a significant decrease of interleukin-6 and resistin gene expression in lymphocytes after the pistachio intervention, whereas SLC2A4 (glucose transporter) expression increased by 69% in CD. This implies that the beneficial systemic changes performed by the pistachio consumption are also present at the molecular level. Finally, cellular glucose uptake by lymphocytes decreased by 78.8% also during the pistachio diet, suggesting an improved glucose regulation.

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The results of this important study have demonstrated that the inclusion of pistachios into a balanced diet can be a safe nutritional strategy to reverse the risks associated with prediabetes. This research adds more evidence to the recent literature showing beneficial effect of nuts on glycemia and insulin levels, because few of them have focused on pistachios in particular, and none have studied people in the prediabetes stage in particular.

Along with the recent publication, this research funded by the American Pistachio Growers (U.S.) and Paramount Farms was previously selected for presentation in the European Congress on Obesity (ECO 2014) held in May 28th to 31st in Sofia (Bulgaria), and have had a high impact in science and a great media coverage worldwide.



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