

## Dietary Nucleotides in Neurodegenerative Diseases

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There has been an explosion of scientific interest in the health enhancing role of specific foods or physiologically-active food components, the so-called functional foods [1]. It is believed that diet play an important role against neurodegenerative diseases and some functional foods can help to prevent the onset of the disease or reduce the degree of progression, once established. The nutritional recommendations for most neurodegenerative diseases are an adequate intake of energy and protein, as well as vitamin E, for its antioxidant character, and vitamins of the B group (folic acid, B6, B12, choline), for its ability to prevent the accumulation of homocysteine. Other physiologically-active food components such as polyunsaturated fatty acids and gangliosides have been postulated.

During the last three decades numerous evidences of the benefits of dietary nucleotides have accumulated. Exogenous nucleotides, which are absorbed as nucleosides, are incorporated into the intracellular pool and thereby increase the availability of metabolites involved in the generation of energy (ATP GTP, etc.) and in many biosynthetic processes (CDP-choline, UDP-glucose, etc.) [2]. On the other hand, the nucleotide pool is closely related to rRNA and in lesser extent mRNA pools and the lack of dietary nucleotides originates a metabolic deactivation [3]. In addition, nucleotides have an active role as modulators of gene expression, not only of the elements involved in its metabolism (enzymes, transporters, etc.) [4,5], but a variety of genes not related (for example with the expression of genes of the inflammation and apoptosis) [6], by a mechanism that involves changes in many transcription factors [7]. Of especial importance are the functions as signaling molecules, the so call purinome or nucleotidome, is a complex interplay among ligands, degrading enzymes, receptors and transporters not fully characterized yet [8]. Through the above mechanisms, dietary nucleotides play an important role in the development of the immune system and are also important for proliferation and tissue development, particularly for tissues with a rapid turnover, as the skin, intestinal mucosa, bone marrow cells and lymphocytes. They have been considered as semi-essential nutrients and food supplemented with them considered as functional food [9]. Currently, there are numerous preparations containing nucleotides for infant and parenteral nutrition.

The relationship between the nucleotides and the central nervous system is well known; so the lack in salvage pathway of purines by the HGPRT deficit causes the Lesch-Nyhan Syndrome,

but the relationship with the nucleotides of the diet had barely been studied until very recently, in that many effects have been described. Thus, inosine, a purine nucleotide, induces the growth of the neurites and increases the formation of new projections in certain circumstances, especially after cortical infarcts [10]. Uridine, a pyrimidine nucleotide, increases the phospholipids and synaptic proteins and the size of the neurites; accelerate the synthesis of phospholipids and increases the levels of the neurofilaments, thus stimulating growth and preventing the formation of tangles [11-13]. The consumption of uridine and other precursors of CDP in rats stimulate the release of dopamine and acetylcholine in the corpus striatum, indicating an important role in neural functionality [14]. Very striking is the study of Cansev observed that a single dose of UMP increases levels of CDP-choline, indicating that this nucleotide reaches the brain quickly [15]. In treatments in situ (normally intracranial injection) with nucleotides, adenosine acts as a neurotransmitter and the pharmacological blockade of receptor A (2A) confers neuroprotection against different neurotoxic situations such as the one originated by 25-35 fragment of amyloid-beta protein [16,17]. In general, adenosine receptors in synapses, induced by nucleotides or other similar substances such as caffeine can help prevent loss of memory associated with neurodegenerative diseases. In addition, in these conditions of inflammation cell renewal is blocked, hindering the recovery of the affected areas [18,19]. Encouraged by these studies, the industry has begun to design and test specific diets for people with neurodegenerative diseases risk, especially for Alzheimer's disease.

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