Aporphine Alkaloids and their Antioxidant Medical Application: From Antineoplastic Agents to Motor Dysfunction Diseases

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Abstract: One of the biggest challenges in the modern medicine and the food industry is to provide chemical agents that, incorporated in the foods, could have some pharmacological properties, but mainly that can protect and preserve our health from oxidative stress, and could be used in clinical treatments against some chronic diseases with minor side effects. In this sense, aporphine alkaloids have been the group of nitrogen compounds more studied in nature, incorporated in many foods and with a wide therapeutic application. Examples such as (−)-bolamine (12), (−)-liridine (15), (−)-liridolidine (16) and glauconine (24) have been studied for their interesting antioxidant activity and, in case of 24, synthetic modifications have managed to generate derivatives that exhibit more efficient antioxidant activity. Therefore, clinical treatment against oxidative stress-related diseases, such as Parkinson’s disease, anticancer, antinociceptive, therapeutic applications among other mentioned in this review, gives the possibility of using these aporphine alkaloids of low cytotoxicity as an excellent alternative in the development of new therapeutic patterns using the duplicity; biologically active ingredient-antioxidant.

Keywords: Aporphines, oxoaporphines, antioxidant, free radical scavengers, oxidative stress, Parkinson’s disease, anticancer, antinociceptive.

1. INTRODUCTION

Oxygen is the molecule that for nature allows the living organisms to be able to develop the cellular and morphologic activities that they need for their survival. Although this molecule can be combined with atoms of the same specie to give reactive molecules such as ozone (O₃), for the adequate protection of the biosphere by ultraviolet radiation, also it is carried out by different atoms to generate complex structures in the cellular metabolism. Nevertheless, some species of oxygen can be absolutely harmful and their effects can be dangerous when acting continuously and permanently in the living systems.

As mentioned by Cai et al. [1], reactive oxygen species (ROS) carry out an important role in the signal transduction, nevertheless when ROS exist in a high concentration, cellular damages in lipids and proteins may occur, affording an imbalance between antioxidant and the in vivo formation of ROS [2]. Therefore, oxidative stress is related to a series of diseases of different nature as cancerous tumors, complaints to the vision, neurodegenerative diseases and motor dysfunctions, cardiovascular affections and the effects of the aging [3].

Thus, an antioxidant is defined as "a substance in low concentrations compared with the oxidizable substances, which can afford the partial or complete oxidation of a compound to be oxidized" [4]. In this way, antioxidants have the property to be ROS specific scavengers through hydrogen atoms and inhibiting some oxidants. As a whole with these antioxidant systems that are present in the living organism, there are biomolecules of different chemical classes and complexity that help to avoid the cellular oxidation by ROS. Notwithstanding, Shabas et al. [5] mentions that there are enzymatic antioxidants and non-enzymatic antioxidants and that they are in our living organism. Indeed, the enzymatic antioxidants can be divided in primary and secondary [6]. The primary enzymatic defense prevents the formation of free radicals being glutathione peroxidase, catalase [7], and superoxide dismutase, the most important examples. The secondary enzymatic defense are glutathione reductase [8] and glucose-6-phosphate dehydrogenase.

In this sense, food and some pharmaceutical substances contain synthetic antioxidants to extend the useful life as drugs. These compounds have been added in food to extend the half-life, by preventing the oxidation of unsaturated fatty acids. Also antioxidants are added to improve the stability of therapeutic agents by oxidation. Indeed, there are synthetic antioxidants used in food and pharmaceutical drugs as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and tert-butyldihydroquinone (TBHQ).

At present, most food and pharmaceutical products contain synthetic antioxidants. These compounds are added to food products in...