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Original Article

TOXICITY STUDIES OF SELOL – AN ORGANIC SELENIUM (IV) COMPOUND- *IN VITRO* RESEARCH

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ABSTRACT

Objective: Selol is a mixture of selenitriglycerides, which contain selenium at the +4 oxidation state. Here we present the results of assessing the cytotoxic properties of Selol on BJ and PNT1A normal human cell lines as well as the LNCaP transformed cell line compared to the cytotoxic activity of sodium selenite.

Methods: *In vitro* studies included measuring cell viability using the MTT assay, measuring total protein levels using the Bradford assay as well as measuring pro-apoptotic properties using flow cytometric methods with annexin V and propidium iodide staining.

Results: Based on the results of MTT and Bradford assays, the drop in survival of BJ and PNT1A cells under the influence of Selol was low for a wide range of concentrations. There was also no observable pro-apoptotic or necrotic effect of Selol (for Se concentrations of up to approximately 500 µM) on both normal cell lines investigated.

There is a marked difference in the levels of cytotoxic activity of Selol between normal (BJ and PNT1A) and transformed (LNCaP) cell lines. In all the assays performed, Selol, for the assessed range of concentrations, was more toxic towards transformed cells compared to normal cell lines. The cytotoxicity was dependent on the concentration of selenium used, as well as the incubation time. In the case of sodium selenite, it has been shown that it is highly toxic for both normal and transformed cell lines (IC50: 10.87; 19.3 and 9.89 µM Se for PNT1A, BJ and LNCaP cell lines respectively), as well as having a pro-apoptotic and necrotic effect.

Conclusion: The results of this study suggest that, taking into account safety as well as the effectiveness of applying selenium to intracellular processes, Selol displays more favourable properties when compared to sodium selenite.

Keywords: Selol, Sodium selenite, Cytotoxicity, BJ, PNT1A, LNCaP

INTRODUCTION

Selenium (Se) is a trace element which is necessary for the correct functioning of the human body and is found in its every cell. Various analyses showed a link between an insufficient level of selenium in a diet and the occurrence of various illnesses, such as Keshan and Kashin-Beck disease as well as disorders of the circulatory system [1-4]. It is suggested that supplementing the diet of patients in critical condition (e.g. patients suffering from widespread burns or in cases of systemic inflammatory response syndrome - SIRS) with high levels of selenium results in a significant drop in mortality and reduces time to recovery [5-7]. As an important antioxidant, selenium also displays anti-inflammatory properties. It has been reported that in cases of chronic inflammation, such as in patients with mucoviscidose and cystic fibrosis of inflammatory bowel disease, a lowered serum level of selenium is observed [8,9].

A lot of attention has been paid to selenium with regards to anti-tumour prophylaxis. A link has been observed between levels of selenium in the body and the incidence of certain neoplastic diseases (e.g. prostate cancer) along with a positive effect of selenium supplementation, especially in patients with low plasma levels at the outset [10,11].

Selenium occurs naturally in various foods, which results in a relatively low incidence of acute selenium deficiency. The overall levels of selenium within a population, however, are dependent on geographical location. Individual levels of selenium depend on, amongst others, the form in which it is ingested, daily dose, individual metabolism and genotype, i.e. the incidence of single nucleotide polymorphisms (SNPs) in genes responsible for selenoprotein synthesis [1,12]. In general terms, organic selenium compounds are easier to absorb when compared to inorganic compounds, whilst inorganic selenium compounds display increased toxicity when compared to organic compounds [13]. Compounds containing selenium at the +4 oxidation state display higher tissue affinity. They are capable of forming complexes with proteins as well as being more effectively incorporated into active sites of selenodependent enzymes, including glutathione peroxidase which is responsible for protecting cells from oxidation [14].

Currently research is being carried out in a number of centres into a compound of selenium (IV) called Selol, a mixture of selenitriglycerides obtained by the chemical modification of sunflower oil (Fig.1) [15].

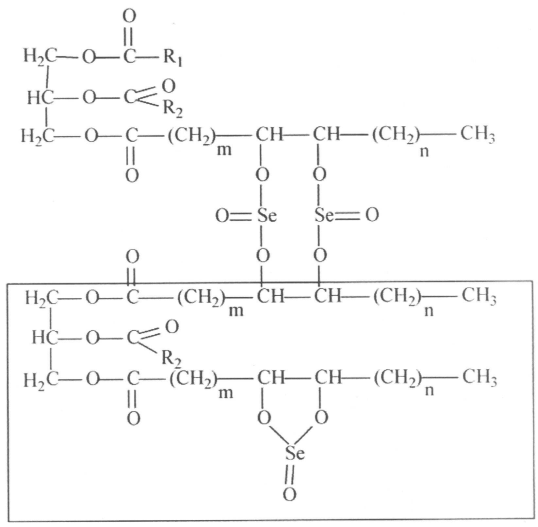

Fig. 1: Probable structure of Selol containing 5% Se (IV) built into fatty acid chains of sunflower oil [17].