

EVALUATION OF ELEMENTAL SELENIUM IN ANTIOXIDANT FORMULATIONS IN INDIA

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ABSTRACT

Background: Deficiencies of micronutrients are a major global health problem. A number of antioxidant preparations containing multiple micronutrients in varying amounts are available in the market. Recently, selenium has been included in the composition of many such formulations. However, high selenium levels are associated with many adverse effects.

Methods: All formulations of antioxidants available in the Indian market were evaluated. Selenium content of these formulations was noted. A comparison was done with the safe upper limit of intake of selenium.

Results: A total of 473 formulations containing multiple micronutrients were analyzed. 187 (39.5%) formulations contained selenium. Of these, 13 (7%) contained significantly high content of selenium in comparison to safe upper limit of intake.

Conclusion: Special attention needs to be paid regarding choice of selenium containing antioxidant formulations to avoid the risk of overdosing.

Keywords: Selenium antioxidants micronutrients

INTRODUCTION

Selenium is a trace mineral that is essential to good health but required only in small amounts.^{1,2} It is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes and help regulate thyroid function and play a role in the immune system.^{3,4}

Keshan's disease is a selenium-responsive endemic cardiomyopathy that mainly affects children and women of child-bearing age in certain areas of China.⁵ The major histopathological feature of the disease is a multifocal myocardial necrosis. Kashin-Beck's disease is an endemic osteoarthropathy that has also been linked with low selenium status.⁵ This disease primarily affects children between the ages of 5 to 13 years living in certain regions of China and the former Soviet Union. Advanced cases of the disease are characterized by enlargement and deformity of the joints. The pathological effects of pure selenium deficiency (i.e. independent of vitamin E deficiency) have been recognized in animals.⁵

While selenium is an essential nutrient at appropriate levels in the diet, it is toxic at higher doses.⁶ Its recommended daily allowance is 60 µg in pregnant women, 20 µg in children and 55 µg in adults.⁷ Its safe upper limit of intake in various age groups is shown in Table 1.⁷ The 'Lowest Adverse Effect Level' (LOAEL), defined as the 'average daily selenium intake causing individuals within a population to develop overt signs of toxicity,' is believed to be in the order of 1540 ± 653 µg/day.⁸ Early signs of selenium poisoning include vomiting, diarrhea, fatigue, irritability, garlicky smelling breath, and numbness and loss of control in the arms and legs. Chronic selenium poisoning in people is characterized primarily by loss of hair and changes in fingernail morphology.⁶ The biochemical mechanisms of selenium toxicity have not been clearly established. Some features of its deleterious effects reflect the chemical form of the particular selenium compound to which exposure has been excessive.⁹ It has been suggested that excessive selenium exposure plays a role in a variety of conditions (dental caries, reproductive problems, amyotrophic lateral sclerosis), but the evidence is not convincing.¹⁰

Table 1: Tolerable Upper Intake Levels for Selenium for Infants, Children, and Adults⁷

Age	Males and Females (µg/day)
0-6 months	45
7-12 months	60
1-3 years	90
4-8 years	150
9-13 years	280
14-18 years	400
19+ years	400

In recent years, concerns have been raised regarding the toxic potential of selenium in dietary supplements.¹¹⁻¹³ Therefore, we examined the marketed antioxidant formulations regarding their selenium content.

MATERIAL & METHODS

All formulations of antioxidants available in the Indian market were evaluated. Selenium content of these formulations as mentioned in the package label was noted. A comparison was done considering the safe upper limit of selenium intake as 400 µg/day for adults.

RESULTS

A total of 473 formulations marketed as antioxidants were evaluated. 187 (39.5%) formulations contained selenium. Selenium content of these formulations is shown in Table 2. 13 formulations (7%) contained significantly high content of selenium in comparison to the safe upper limit of intake. Ten formulations contained more than 40 times the safe upper limit of intake. Type of selenium salts used in these antioxidant formulations are shown in Table 3. Salt was not specified in 92 (49.2%) formulations. Inorganic salts were used in 91 (95.8%) out of 95 formulations for which salts were specified.

Table 2: Selenium content of antioxidant formulations

Amount	Number of formulations
3.5-100 µg	139
101-400 µg	11
400 µg -2 mg	3
2-20 mg	0
21-80 mg	6
80-150 mg	4
Not specified	24

Table 3: Selenium salts used in antioxidant formulations

Salt	Number
Elemental selenium/salt not specified	92
Selenium dioxide	69
Sodium selenate/selenite	19
Selenious acid	3
L-selenomethionine	3
Natural selenium monophenine	1

DISCUSSION

Our study indicates that 13 (7%) out of 187 antioxidant formulations contain significantly high amount of selenium. According to the American Association of Poison Control Center

(AAPCC) data (2006), there were a total of 972,073 exposures to pharmaceutical products resulting in adverse events, of which there were 6,809 major outcomes and 507 deaths.¹³ Of these exposures, 76,364 (7.9%) were due to dietary supplements and vitamins, with 42 major outcomes (0.6% of all major outcomes) and 3 deaths (0.6% of all deaths). Hence, serious adverse effects and death from these products are relatively uncommon.

Isolated cases of acute selenium toxicity due to nutritional supplements are reported in the literature.^{11,12} In 2008, US FDA reported adverse reactions to liquid nutritional supplements containing excess selenium and chromium in 201 individuals resulting in an epidemic of selenosis in the United States.¹³ In a case series performed on nine patients, supplement testing revealed almost 200 times the reported amount of selenium.¹⁵

A public perception that nutritional supplements are inherently safe, leads to the propensity of such products to be consumed without any medical advice and for prolonged periods, which can cause selenium toxicity. Also, dietary supplements such as vitamins, minerals, and herbal products are not subject to premarket review or approval for safety, efficacy, or Good Manufacturing Practices (GMPs) in several countries including India and United States. Global standards for vitamin and mineral supplements have been developed and adopted at an international level by the Codex Alimentarius Commission. However, these guidelines do not specify upper limits for vitamins and minerals in supplements, but provide criteria for establishing maximum amounts of vitamins and minerals per daily portion of supplement consumed, as recommended by the manufacturer.¹⁶

This study shows that 10 formulations contained more than 2000 µg per dose (Table 2). This is a very high amount in comparison to the safe upper limit of intake of 400 µg/day for adults and even with LOAEL of 1540 ± 653 µg/day.⁸ So far, there are no reports of selenium overdose/toxicity in India. However, this could be due to non-specific clinical features, lack of awareness among clinicians and lack of documentation. Special attention needs to be paid regarding the choice of selenium containing antioxidant preparations to avoid the risk of overdosing.

A recent Cochrane review suggests that there is no convincing evidence that individuals, particularly those who are adequately nourished, will benefit from selenium supplementation with regard to their cancer risk.¹⁷ Further, some authors suggest that beneficial effects in most studies have been reported with organic forms of selenium and not with inorganic forms.¹⁸ In this study, about 95 % of the formulations for which salt was specified contained inorganic form of selenium.

In conclusion, we suggest, since there is no clinical condition warranting use of very high doses of selenium, the formulations containing such high selenium levels should not be allowed to be marketed. Further, prescribers need to be educated regarding the risks of prolonged administration of high dose selenium formulations.

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