Ascorbic Acid and Selenium Interaction: Its Relevance in Carcinogenesis

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Abstract

Ascorbic acid and selenium are two nutrients that seem to have a preventive potential in the process of carcinogenesis; because of a possible synergistic action that may produce an enhanced anticarcinogenic effect. Interaction between these nutrients have been reported. Results indicate that the protective effect of the inorganic form of selenium (Na Selenite) was nullified by ascorbic acid, whereas the chemopreventive action of the organic form (seleno-DL-methionine) was not affected. A possibility exists that Selenite is reduced by ascorbic acid to elemental selenium and is therefore not available for tissue uptake. In experiments using Selenite; plasma and erythrocyte glutathione peroxidase enzyme activity was directly related to the level of ascorbic acid fed.

Indexing Key Words
Selenium, Carcinogenesis, Ascorbic Acid.

Introduction

Vast epidemiological data have pointed out possible cancer preventive foods; providing basis which has led to the study of specific vitamins, minerals and nutrients such as vitamins A, C, E, mineral selenium and provitamin A pigment beta-carotene and their role in the carcinogenesis process. These nutrients to some extent have shown some anticarcinogenic potential in experimental models.

The assessment of each of these nutrients as cancer prevention agents and the possibility to be used as cancer therapeutic agents is of great value and ultimate importance. For the past years intense research has focused on elucidating possible mechanisms of action of each of these nutrients in carcinogenesis. But this aspect, although very important, represents only one part of the complexity involved in nutrient-cancer interaction. This brings into context the need for studies of interaction between these specific nutrients that have shown anticarcinogenic potential. It is tempting to speculate of a possible synergistic effect when these nutrients are given or found together in either food or supplementation. It is conceivable that the anti-cancer potential could be enhanced significantly if this synergistical effect takes place in vivo in affected organisms.

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Discussion

Many experimental models studying carcinogenesis have used animal species with the capacity of producing their own vitamin C (as for example mice and rats). Thus, ignoring completely a possible nutrient interaction of the endogenous vitamin C and the exogenous nutrient exists. This by the way, can give rise to results which can not be extrapolated to non-producing ascorbic acid species. Ascorbic acid (AA) is an essential nutrient for the guinea pig, primates and other species.[1] We should remember that experimental animal models can only serve as guidelines for biochemical pathways in humans; but none the less of immense relevance to the understanding progress and development of nutritional and biochemical research.

It is documented that a combination of vitamin A and selenium produces an additive chemopreventive effect on mammary carcinogenesis.[2] Similarly, recent studies have shown that a high vitamin E intake is able to potentiate[3] while a low vitamin E intake tends to diminish[4] the protective effect of selenium (Se). It is therefore of ultimate importance to examine the interrelationship between nutrients and its effect on disease.

The interaction of AA and minerals at the intestinal level is varied and not fully understood. AA enhances iron absorption

in the gastrointestinal tract,[5] but reduces the intestinal transport of copper.[6]

Data about Se and AA are inconsistent. Shils and Levander[7] observed that AA could lead to a reduction of Selenite to a presumably unavailable form. Combs and Pesti[8] found that AA promotes dietary Se (organic) utilization in the chick, to which AA is not an essential nutrient. Combs and Scott[9] suggested that AA acting as an antioxidant might increase the biological utilization of dietary Se in chicks. Also dietary AA elevated the Se containing glutathione peroxidase enzyme activity and reduced the dietary Se requirement of the vitamin E deficient chick.[8] This work indicated that dietary AA promoted enteric absorption of vitamin E. Combs and Pesti[8] suggested that AA, which inhibits the oxidation of dietary Se, promotes its absorption and perhaps its utilization after absorption.

In contrast, high levels of AA can reduce the toxicity of (inorganic) Se in chicks[10] [11] and moderate doses of AA inhibit intestinal absorption of sodium Selenite in chicks.[12] Ip[13] compared the efficacy of inorganic and organic forms of Se compounds (2-4 ppm) in the protection against mammary tumorigenesis induced by 7,12 dimethyl-benz(a) anthracene (DMBA) in rats. Ip also examined the interaction of AA with Selenite (inorganic) and seleno-DL-methio-nine (organic) in his model. Ip found that both forms of Se compounds supplemented after induction had the same efficacy in mammary cancer prophylaxis and that the inhibitory response in mammary tumorigenesis with Se supplementation was dose dependent. A slight reduction in growth was observed at the higher concentration of Se (4 ppm).

Of great interest is the fact that the tumor incidence and yield was consistently but not significantly higher in rats given seleno-DL-methionine than in those given Selenite at each level of supplementation, although supplementation of this organic form by itself raised tissue Se concentration about 4-fold suggesting that seleno-DL-methionine might be more effective than Selenite in maintaining Se at an elevated state.

In other experiments AA with either inorganic or organic forms of Se were tested. Results demonstrated that the protective effect of Selenite in tumorigenesis was nullified by AA, whereas the chemo-preventive action of seleno-DL-methionine was not affected. It is possible that Selenite is reduced by AA to elemental Se and is, therefore, unavailable for tissue uptake. Ip[13] suggested that high levels of AA can interfere with the accumulation of tissue Se and actually decrease the anticarcinogenic effect.

It is likely that the organic form of Se might be a better therapeutic agent since it is less toxic to the liver at high levels in comparison with the inorganic form.[13]

The use of a combined regimen of inorganic Se and AA was studied in dime-thylhydrazine-induced colon cancer in rats.[14] In this model the combination of these two nutrients increased the tumor incidence (83%) even higher than in controls (64%).

It is relevant to point out that these experiments were done using two incompatible forms of nutrients (inorganic Se and AA) also, the experimental animal used was the rat, which can produce its own vitamin C; how this genetic characteristic can interfere with the results obtained in these experimental models with this vitamin mineral interaction is yet to be determined.

Recently the interaction of dietary AA and Se has been studied in the guinea pig,[15] a species not able to produce its own AA. Poovaiah, Potter and Omaye found that plasma, erythrocyte and liver AA concentrations were directly related to the levels of AA fed. Also erythrocyte and liver Se concentrations were dependent on dietary intake. Dietary AA had no effect on erythrocyte or liver selenium levels. In addition liver, plasma and erythrocyte glutathione peroxidase activity were directly related to the level of AA fed. This data indicates that in the guinea pig dietary AA has no influence on tissue levels of Se but increases plasma, liver and erythrocyte glutathione peroxidase activity.[15]

Machlin and Gabriel[16] have implied that AA might "spare" Se in a manner similar to the action of vitamin E and Se. A recent report noted that the intragastric AA supplementation to rats resulted in

elevated plasma glutathione peroxidase activity.[17] However, because no difference in deposition of Se was found into tissues. Poovaiah et al[15] speculated that the elevated glutathione peroxidase activity found with increased dietary AA might be due to some undefined direct stimulation.

It is still premature to postulate a mechanism for the AA and Se interaction which has not been delineated clearly yet. But definitely, nutrient interaction studies will have an important role in our understanding of biochemical physiological mechanisms involved in cancer prevention and possibly convey to new avenues of complementary less toxic cancer treatment in the near future.

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