



## Single or whole antioxidants in metal toxicities

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Toxic metals are able to interact with DNA and nuclear proteins causing oxidative damage of biological macromolecules. Antioxidants can be used in metals induced toxicity. However, consumption of fruits and herbal extract is preferred compared to single supplements such as vitamins C or E.

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It has been estimated that chronic diseases will account for more than 75% of all deaths worldwide, by 2020. Low intake of vegetables and fruits significantly increase the risk of most types of cancer and other hard curable diseases, as compared to high intake (1).

Antioxidants can also be used in metals induced toxicity. Several essential metals including iron, copper, zinc, manganese and cobalt participate in various signaling and metabolic pathways. However, they may escape out of control mechanisms such as homeostasis. Breakdown of these mechanisms may lead to displacement of other metals from their normal binding sites or attachment of these metals to protein sites other than those tailored for that purpose. Furthermore, toxic and carcinogenic metals are able to interact with DNA and nuclear proteins causing oxidative damage of biological macromolecules. Metals such as iron, copper, chromium, mercury, cadmium, vanadium and nickel are capable of producing reactive radicals, resulting in lipid peroxidation, DNA damage and other effects (2).

Free radicals enhance lipid peroxidation, cause various modifications to DNA, and alter calcium and sulfhydryl homeostasis. Lipid peroxidation occurs by attack of free radicals to polyunsaturated fatty acids producing mutagenic and carcinogenic compounds (3). The main factor in toxicity and carcinogenicity of metals is production of

free radicals, especially reactive oxygen species (ROS) and reactive nitrogen species (RNS). Arsenic directly binds to critical thiols, but, other mechanisms including formation of hydrogen peroxide have also been proposed. Arsenite causes DNA damage and Nitric oxide (NO) has been proposed to be involved in this toxic effect. Whilst iron, copper, cobalt vanadium, and chromium undergo redox-cycling reactions, the primary route for the toxicity of nickel, mercury and cadmium is binding to sulfhydryl groups of proteins as well as glutathione depletion. Common mechanisms including generation of hydroxyl and superoxide radicals also seem to be involved in iron, copper, vanadium, cobalt and chromium toxicity (2). Degenerations can be prevented or ameliorated by dietary intake of natural antioxidants. Dietary intake contains variety of antioxidants which play a vital role in protection of a variety of disorders (4). Antioxidants are endogenous or exogenous molecules which act against oxidative stress and its complications (1). Although they neutralize the free radicals induced oxidative stress and have therapeutic potential, but no single antioxidant is able to protect the body from all kinds of free radicals which are frequently generated in the body. Although single antioxidants such as vitamins C and E are effective in neutralizing some free radicals, but it seems that the complex compounds with wide range of antioxidant activity have better effect, because the can

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neutralize more kinds of free radicals (5). Millions of chemicals such as flavonoids and other phenolic compounds, carotenes, lipoic acid and vitamin C have antioxidant activities and are used as metabolic supplements which keep all our vital organs free from oxidative stress. Most of them are present in herbal medicines (1). Therefore, consumption of fruits and herbal extract is preferred compared to single supplements such as vitamins C or E.

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MRK prepared the first draft, SA edited it. MRK and SA read and confirmed the final version.

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