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BIOMETALS: NEW TOOLS FOR OBESITY TREATMENT AND ITS RELATED METABOLIC DISORDERS

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Abstract: *Objective:* Overweight and obesity have become an increasingly serious clinical and socioeconomic problem of world, and one of the greatest health challenges to man kind. It is estimated at least 1.1 billion adults are overweight, including 312 million individuals who are obese. Overweight and obese patients are at an increased risk for developing numerous cardiometabolic complications and certain types of cancers. There is much need to develop some newer pharmacological approaches for the treatments of obesity. One such pharmacological treatment for obesity may be through inorganic salts; these inorganic salts have been used in the treatments of various diseases. The inorganic salts of Vanadium, Chromium, Magnesium, Selenium, Calcium and Zinc etc., have been evaluated for their pharmacological activity. The present article is an effort on these inorganic salts to correlate and utilize them in the treatment of obesity.

Key words: Obesity, cardiometabolic disorders, inorganic salts, biometals.

Introduction

Obesity is defined as increased body weight caused by excessive accumulation of fat (1). The etiology of obesity may involve genetic, environmental and psychological factors. However, it is a disorder of energy imbalance (Fig. 1) (2). Obesity predisposes to increased risk of a number of medical conditions including type II diabetes mellitus, hypertension, coronary heart disease, osteoarthritis, respiratory problems and cancers of breast, endometrium, prostate and colon (3). The current therapeutic approaches for obesity can be lifestyle modifications, pharmacotherapy and bariatric surgery among them lifestyle modification is the first-order treatment (4).

Pharmacological targets for the treatment of excess weight include appetite (sibutramine), fat absorption (orlistat), weight-regulatory brain circuits (cannabinoid receptor-1 (CB1) antagonists), and metabolism (CB1 antagonists; drugs that stimulate uncoupling proteins). With recognition of obesity as an epidemic, there is an urgent need to improve the quality and effectiveness of available treatments.

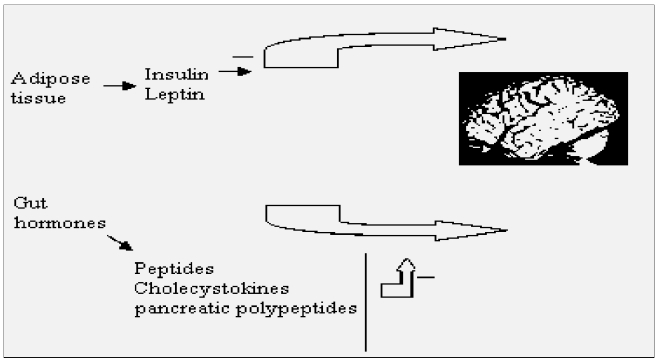

Figure 1. Appetite-modifying peptides from the gut and the adipose tissue. (+) Increasing appetite; (-) decreasing appetite

Inorganic salts in the treatment of various diseases

Most of the medicinal therapies are of organic composition. Therapeutic efficacy of inorganic salts has been evaluated in some diseases. The vanadium and its salts is the most common element studied for various diseases, both in organic and inorganic form. Hypoglycemic, insulin reserve actions, enhances insulin sensitivity and cholesterol lowering properties are already proved. Further the treatment of diabetes has

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also been confirmed with clinical trials (5-6). Vanadium ions mimic the biological actions of insulin and in sulphate form it regulates glucose and lipid metabolism. Vanadium ions translocates glucose transporter, increases intrinsic activity or changes in the insulin signaling pathway (7). Recently, vanadium and selenium salts were studied to observe the several physiological insulin-like effects by a post-insulin receptor kinase mechanism.

Biomedical importance of Molybdenum and Tungsten compounds, is mostly based on their interaction with proteins, enzymes and cellular constituents (8), antidiabetic activity (9), normalization of blood lipid profile (10), protection against oxidative stress (11), antiobesity effect (12) and hepatoprotective role have widely favored important role in modern day medical science.

Chromium is an essential nutrient involved in the metabolism of glucose, insulin and blood lipids (13). It improves insulin binding to cells and activates insulin receptor kinase leading to increased insulin sensitivity (14). Chromium supplementation during the transition period may increase immunity and reduce the incidence of retained placenta (15). Chromium binding with niacin has shown the ability to restore insulin function, metabolism of fat, muscle formation, and conversion of glucose into energy. Chromium supplements, particularly niacin-bound chromium or chromium-nicotinate, may be effective in attenuating insulin resistance and lowering plasma cholesterol levels (16).

Calcium ions are involved in weight management by increasing lipid metabolism (17). Calcium provided as a food supplement can decrease low density lipoprotiens and triglyceride concentrations (18). Hypolipidemic mechanisms of calcium may be due to inhibition of fat absorption accompanying an increased fecal fat excretion by a mechanism of conversion of cholesterol to bile acids (19).

Magnesium salts are used in the treatment of alcoholism, eclampsia, hypertension, atherosclerosis, cardiac diseases, diabetes and asthma (20). Hypomagnesemia is associated with diabetes mellitus. Reduced intracellular magnesium content might contribute to the impaired insulin response and action which occurs in Type 2 diabetes mellitus. Magnesium supplementation can improve Beta-cell response and insulin action in non-insulin-dependent diabetic subjects. Manganese and Selenium have a favorable effect on carbohydrate metabolism (21). Magnesium intake may be inversely related to the risk of hypertension and type 2 diabetes mellitus, and may decrease blood triglyceride and increase high-density lipoprotein levels (22).

Zinc is effective in prevention of mastitis that occurs predominantly in the first weeks of lactation, through enhanced antioxidant function and keratinisation of the teat canal. Zinc and Biotin are implicated in improving keratinisation of the hoof and prevention of this disease. Chronic dietary administration of zinc can lead to impairments in cognitive function (23). Selenium (Se) supplements are known to reduce the incidence of mastitis and retained placenta. Consumption of Se supplements at high doses may disturb the metabolism of carbohydrates and lipids. This may be due to adverse effects of dietary Se compounds and/or abundantly expressed selenoenzymes on the insulin sensitivity of major insulin target tissues and/or on the regulation of pancreatic insulin biosynthesis (24). Se is involved in the antioxidant system through glutathione peroxidase. Inadequate dietary Se decreases neutrophil function during the perpariturient period. Obese patients have significantly altered serum Se concentrations compared to non-obese patients (25).

Marginal Copper deficiency resulted in reduced neutrophil killing and decreased interferon production by mononuclear cells. The inorganic salts play a major role in Menkes disease treatment which is an X linked genetic disorder of copper intracellular transport (26). Copper reduces oxidative stress by reacting with the oxygen radical (O2–) and produce molecular oxygen and H2O2 (27). Chronic obesity may alter the nutritional requirements for trace metals such as copper (28).

Aluminium (Al) is present in medicines and is added to drinking water for purification (29). Al partly protects hepatocytes from Cd-induced depletion of acid soluble thiols (i.e.reduced glutathione) and from stimulation of lipid peroxidation. Al is a component of many consumer products as well as dental rinses and toothpastes used to reduce dentinal hypersensitivity (30). Al can alter plasma membrane properties by binding to membrane lipids or proteins which leads to modification of membrane permeability (31).

Conclusion

The above information can lead to conclude that inorganic salts can increases insulin sensitivity which generally occurs due to obesity as in case of Vanadium and Selenium. Mg may be used to lower the Blood Pressure. Salts of vanadate may play a good role in maintaining the lipid profile which is the primary target in the treatment of obesity. Some minerals and trace elements along with vitamins plays good role in the treatment impaired fertility. Magnesium intake also improves triglycerides and HDL levels. Higher BMI is associated with subclinical inflammation and increased systemic oxidative stress inorganic Se plays a defensive role in these conditions. Level of trace mineral Zinc, Copper, Aluminium, calcium, chromium and cadmium plays the pivotal role in the improvement of lipid profile. Hence from the existing studies it can be concluded that the inorganic salts may be the important tool and agents for the treatment of the obesity and other metabolic disorders. Obesity is still a major threat in terms of

disease, economic load and stress. However there is a need of hour to explore the efficacy and safety of these inorganic salts, whether they are safe in the treatment of obesity or not.

Conflict of interest: None of the authors had a conflict of interest in relation to this manuscript.

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