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CHROMIUM IN HEALTH AND DISEASES

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ABSTRACT
Chromium is found to have beneficial effects in a wide range of human ailments. Its beneficial effects have been studied extensively in DM, related to control of obesity, IR and OS. It is also found to have beneficial effects on cardiac, liver, renal, neuropsychiatric and immune systems. Its role in the curative aspects of PCOS, infertility and reproductive problems have also been studied. This review article brings into a nutshell the research findings during the last two decades on the role and beneficial effects of this important trace metal in all the diseases mentioned above. Further studies are required using large population size in each type of human disease and to establish a standardized procedure for measuring this metal on biological samples and to workout standard and easily implementation type protocol for supplementation based on its circulating level in blood.

KEYWORDS: Chromium, DM, IR, OS, PCOS, CVD.

INTRODUCTION

The naturally occurring biologically active form of chromium is chromodulin and it has been found to be beneficial to control carbohydrate, lipid and fat metabolism. Its deficiency has been observed in a host of human diseases starting with DM and extending to cardiac, liver, renal, reproductive and phychiatric disorders. This review article highlights the various research findings done during the last two decades.

Chromium and Diabetes Mellitus

Chromium (Cr) as an essential trace element in metabolism of carbohydrate, lipid and protein is currently prescribed to control DM. Glycated Hemoglobin (HbA1c) change in diabetic patients in Cr supplement therapy shows improvement. Cr lowers Fasting Plasma Glucose (FPG) but does not affect HbA1c, lipids and Body Mass Index (BMI)[1]. Chromium Picolinate (CrPic) is a widely available nutritional supplement marketed for a plethora of afflictions. There is some evidence, including results from human studies, that it has a role in glucose homeostasis and it continues to fall squarely within the scope of "alternative medicine," with both unproven benefits and unknown risks. It deserves closer scrutiny with additional prospective, randomized, double-blind, placebo-controlled trials to evaluate its efficacy in improving outcomes in patients with diabetes [2].

Cr appears to have a beneficial role in the regulation of insulin action and its effects on carbohydrate, protein and lipid metabolism and it is an important factor for enhancing insulin activity. Studies show that people with Type 2 Diabetes Mellitus (T2DM) have lower blood levels of Cr than those without the disease. Supplements containing 200-1,000 mcg CrPic a day have been found to improve glucose control and it is the most efficacious form of Cr supplementation supported by numerous animal studies and human clinical trials [3]. Cr has been established to be an essential trace element in mammals in regard to maintenance of normal carbohydrate metabolism. Supplementation studies in human subjects in documented deficiency showed improved glucose levels. However, controversy exists as to whether dietary supplementation with Cr should be routinely recommended in subjects without documented deficiencies. A clinical response to Cr (ie, decreased glucose and improved insulin sensitivity) may be more likely in Insulin-Resistant (IR) individuals with T2DM who have more elevated FPG and HbA1c levels [4]. Cr supplementation seems to improve glycaemic control in T2DM, which appears to be due to an increase in insulin action rather than stimulation of insulin secretion [5].

Intervention trials have shown the beneficial effects of Cr supplementation in T2DM. In population of elderly, diabetic patients undergoing rehabilitation, dietary supplementation with Cr is beneficial in moderating glucose intolerance. In addition, Cr intake appears to lower plasma lipid levels[6].Within the last 5 years, Cr has been shown to play a role in glucose intolerance, T2DM and Gestational Diabetes Mellitus (GDM). In addition, diabetes and the neuropathy of a patient on home parenteral nutrition were alleviated when supplemental Cr was added to Total Parenteral Nutrition (TPN) solutions. Supplemental Cr has been shown to have beneficial effects without any documented side effects on people with varying degrees of glucose intolerance ranging from mild glucose intolerance to overt T2DM[7].CrPic is a widely used nutritional supplement for optimal insulin function. A relationship among Cr status, diabetes, and associated pathologies has been established. Virtually all trials using CrPic supplementation for subjects with diabetes have demonstrated beneficial effects. The pooled data from studies using CrPic supplementation inT2DM subjects show substantial reductions in hyperglycemia and hyperinsulinemia, which equate to a reduced risk for disease complications. Collectively, the data support the safety and therapeutic value of CrPic for the management of cholesterolemia and hyperglycemia in subjects with diabetes[8].

Supplemental Cr had significant beneficial effects on HbA1c, glucose, insulin, and cholesterol variables in subjects with T2DM. The beneficial effects of Cr in individuals with diabetes were observed at levels higher than the upper limit of the Estimated Safe and Adequate Daily Dietary Intake [9].No significant difference in lipid profile was observed in the supplemented group; however, total cholesterol, HDL-c and LDL-c were significantly lowered, comparing pre- and post-treatment period, in the control group. CrPic supplementation had a beneficial effect on glycemic control in patients with poorly controlled T2DM, without affecting the lipid profile. Additional studies are necessary to investigate the effect of long-term CrPic supplementation [10].Strong association between serum Cr and Super Oxide Dismutase (SOD) in relation to HbA1c observed gives a strong point that these variables could be used as markers of cell injury with the intention in further part of life en route to progressive complications in T2DM [11].

Chromium and Obesity

The evidence from available Randomised Control Trails (RCTs) shows that Cr supplementation generates statistically significant reductions in body weight. The magnitude of the effect is small, and the clinical relevance is uncertain. Future trials should last at least 16 weeks and greater uniformity in the measuring and assessment tools for body composition is recommended [12].Cr supplementation may affect various risk factors for coronary artery disease (CAD) and T1DM, including body weight and composition, basal plasma hormone and substrate levels, and response to an oral glucose load. High levels of CrPic supplementation are contraindicated for weight loss in young, obese women. Moreover, exercise training combined with Cr nicotinate supplementation may be more beneficial than exercise training alone for modification of certain CAD and T1DM risk factors [13].The use of Cr-containing dietary supplements is widespread among patients with T2DM. Cr's effects in patients at high risk for developing diabetes, especially those with Metabolic Syndrome (MetS), is unknown. CrPic had no significant effect on other measures of glucose metabolism, body weight, serum lipids, or measures of inflammation and OS. CrPic at 1000 ug/day does not improve key features of the MetS in obese nondiabetic patients [14].

The Importance of Cr is actually challenged due to lack of clear manifestations of Cr deficiency in humans and animals. The recent clinical trials provided evidence both in favor and against the importance of Cr in healthy and ill organisms. Unfortunately, also the molecular mechanism by which Cr affects glucose and lipid metabolism is still unclear. Beneficial effects of diet supplementation with different sources of Cr can be potentially explained by rather pharmacological than nutritional effects [15].There were no statistically significant differences in the percentage change of FPG, Immune Reactive Insulin (IRI) or lipids between the Cr groups after 90 days of supplementation. However, those individuals within the Cr group with initial fasting IRI levels greater than 35 pmol/L had a significant decrease in IRI level after supplementation despite no significant changes in serum lipids. These subjects may benefit from Cr supplementation by improving insulin sensitivity and cardiovascular risk over time [16].

Chromium and Insulin Resistance

Cr deficiency in diabetic patients is a debatable problem. The prevailing opinion suggests the presence of low serum Cr in such patients and therefore an early, long-term addition of Cr to the standard therapy is recommended. The serum level of Cr was significantly lower in diabetic patients than in the healthy individuals used as controls A significant decrease of IRI and the IR index was observed after a two-month application of Cr 30 ug daily and Cr included early in the complex therapy of diabetes is beneficial in the reduction of the degree of IR [17].Most of the currently available drugs that improve insulin sensitivity have adverse effects. Therefore, attractive strategies to alleviate IR include dietary supplements. One such supplement is Cr, which has been shown to reduce IR in some, but not all, studies [18].

No changes were seen in glucose level, insulin level, or HOMA-IR after 6 months of Cr at either dosage level (500 mcg or 1000 mcg daily) when compared with placebo. None of the secondary outcomes improved with either Cr dosage compared with placebo. Cr supplementation does not appear to ameliorate IR or impaired glucose metabolism in patients at risk for

T2DM and thus is unlikely to attenuate diabetes risk [19].Various systematic reviews have been unable to demonstrate any effects of Cr on glycaemic regulation (possibly due partly to the low dosages used), but there is a slight reduction in body weight averaging 1 kg. In a double-blind randomised placebo-controlled trial in a Chinese population with T2DM, supplementation with 1000 ug of Cr led to a fall in the HbA1c by 2%. Toxic effects of Cr are seldom seen; recently, however, the safety of one of the dosage forms of Cr, CrPic, has been questioned. One should be aware that individual patients with T2DM may have an increased risk of hypoglycaemic episodes when taking Cr supplements as self-medication [20].

Supplementation at 50 and 200 µg of CrPic did not promote glycemic control, increase insulin sensitivity, or change the lipid profile of subjects with diabetes [21].Following Cr-supplementation, there were no significant changes in either insulin sensitivity or glucose tolerance. There was a significant improvement in serum HDL cholesterol concentration in the group supplemented with Cr. CrPic supplementation at this level was well-tolerated, but overall was not an effective therapy for IR in HIV-infected subjects [22].

Chromium and Oxidative Stress

Cr–VI induced more pronounced oxidative damage in p53 deficient mice. This in vivo study highlighted that apoptotic regulatory protein p53 may play a major role in Cr–VI induced OS and toxicity. Taken together, OS and oxidative tissue damage, and a cascade of cellular events including modulation of apoptotic regulatory gene p53 are involved in Cr-VI-induced toxicity and carcinogenesis [23].The biological mechanisms responsible for the initiation and progression of diseases resulting from exposure to Cr-VI are not fully understood. In the last two decades, there has been increasing evidence of the correlation between Cr–VI induced generation of Reactive Oxygen Species (ROS) and carcinogenic actions [24].

The significant increases observed in liver total protein and RNA concentrations, as well as protein/DNA and RNA/ DNA ratios in diabetic rats supplemented with the high dose of Cr, compared to untreated diabetics, may be related to the improvement in the glycemic status of the diabetic animals rather than the direct effect of CrPic on protein anabolism [25].The GPx activity for females increased in all treatments, which revealed that the damage power of Cr - VI was increased with the increase of Cr - VI concentrations in terms of GPx, but the effect was not so remarkable. There was no consistent trend of GPx activities for males in all treatments of Cr – VI and changes in antioxidant enzymes were different for SOD, Catalase Activity (CAT) and GPx, of which the tendency was that activities generally changed with increase of concentrations of Cr - VI suggesting SOD, CAT, and GPx could serve as indices of Oxidative Stress (OS) to some extent [26].Cr supplementation prevents the increase in TNF-alpha levels and OS caused by the high levels of glucose in cultured U937 monocytic cells. Similarly, Cr supplementation prevented elevated TNF-alpha secretion and lipid peroxidation levels in H(2)O(2)-treated U937 cells. Cr supplementation inhibits TNF-alpha secretion in U937 monocytes cultured in high-glucose medium, which appears to be mediated by its antioxidative effect providing evidence for a novel molecular mechanism by which Cr supplementation may increase insulin sensitivity and glycemic control in diabetic patients [27].

Recent studies have demonstrated that both Cr -VI and cadmium (II) induce an OS, as determined by increased hepatic lipid peroxidation, hepatic glutathione depletion, hepatic nuclear DNA damage, and excretion of urinary lipid metabolites. However, whether chronic exposure to low levels of Cr-VI and Cd(II) will produce an OS is not shown. Low dose Cr administration of sodium dichromate and cadmium chloride induces an OS resulting in tissue damaging effects that may contribute to the toxicity and carcinogenicity of these two cations[28].Cr undergoes redox cycling, while cadmium depletes glutathione and protein-bound sulfhydryl groups, resulting in enhanced production of ROS such as superoxide ion, hydroxyl radicals, and hydrogen peroxide. These ROS result in increased lipid peroxidation, enhanced excretion of urinary lipid metabolites, modulation of intracellular oxidized states, DNA damage, membrane damage, altered gene expression and apoptosis. Enhanced production of nuclear factor-kappaB and activation of protein kinase C occur. Furthermore, the p53 tumor suppressor gene is involved in the cascade of events associated with the toxicities of these cations indicating that although different mechanisms lead to the production of ROS by Cr and cadmium, similar subsequent mechanisms and types of oxidative tissue damage are involved in the overall toxicities [29].

Chromium and Liver Diseases

Cr supplementation prevented progression of NAFLD and the beneficial effects were accompanied by reduction of hepatic triglyceride accumulation, elevation of hepatic lipid catabolic enzyme, improvement of glucose and lipid metabolism, suppression of inflammation as well as resolution of OS, probably through enhancement of insulin signalling and hence Cr could serve as a hepatoprotective agent against NAFLD [30].In the automobile mechanics, the levels of Cr, cadmium and lead were significantly higher when compared with controls. In the motor painters, Cr and cadmium were significantly higher when compared with controls. Levels of manganese, copper, cadmium, lead and total antioxidants were significantly higher in panel beaters compared with controls. In the battery chargers, only total antioxidants were significantly higher compared with controls suggesting that metal toxicity is imminent in panel beaters, automobile mechanics and motor painters and that the metals involved vary with occupations. This raises the need for public awareness

about the hazards of different occupations in order to enable these professionals take necessary precautionary measures [31].

Chromium and Cardiac Diseases

Cr is an essential mineral that appears to have a beneficial role in the regulation of insulin action, MetS and cardiovascular disease (CVD). There is growing evidence that Cr may facilitate insulin signaling and supplementation therefore may improve systemic insulin sensitivity. Tissue Cr levels of subjects with diabetes are lower than those of normal control subjects, and a correlation exists between low circulating levels of Cr and the incidence of T2DM. Controversy still exists as to the need for Cr supplementation. However, supplementation with CrPic, a stable and highly bioavailable form of Cr, has been shown to reduce IR and to help reduce the risk of CVD and T2DM. Since Cr supplementation is a safe treatment, further research is necessary to resolve the confounding data. The existing data suggest toconcentrate future studies on certain forms as CrPic and doses as at least 200 mcg per day[32].

No statistically significant effects of Cr nicotinic acid supplementation were found on plasma insulin, glucose, or lipid concentrations, although Cr nicotinic acid supplementation slightly lowered fasting plasma total and LDL-C, triglycerides and glucose concentrations and 90-min postprandial glucose concentrations in individuals with T1DM[33].CrPic treatment was associated with improved coronary flow and recovery of myocardial contractility and relaxation following ischemia-reperfusion insult. Dietary CrPic treatment of SHR alters neither blood pressure nor vascular smooth muscle reactivity but causes enhancement of endothelium-dependent vasorelaxation associated with Nitric Oxide (NO) production/release. Additionally, while the treatment does not affect infarct size, it improves functional recovery of the viable portion of the myocardium following IRI[34].Diabetic men with CVD have lower toenail Cr than healthy control subjects. However, it could not distinguish between the effects of Cr on diabetes and those on CVD. Long-term clinical trials are needed to determine whether Cr supplementation is beneficial for preventing CVD among diabetic patients[35].

Chromium and Neurologic

Neuropathy and glucose intolerance may occur despite increased serum Cr levels and respond to Cr infusion. The previous use of drugs such as metronidazole should not exclude Cr as a potential treatment for neuropathy in hypertensive patients [36].Cr exposure dose via drinking water, calculated from the results of the water analyses and the questionnaire data, showed associations with blood and hair Cr levels and certain hematological and biochemical parameters. Groups of subjects whose hematological or biochemical parameters were outside the normal range were not correlated with Cr exposure dose, except for groups of subjects with high triglycerides or low sodium. Motor impairment score was not associated with exposure to Cr [37].Elevated levels of nickel and Cr can be measured after posterior instrumented spinal arthrodesis. The levels diminish rapidly with time from surgery but still remained above normal levels 4 years after surgery. Long-term implication of this metal ion exposure is unknown and should be studied further [38].

Chromium and Psychiatric

Main effect of Cr was on carbohydrate craving and appetite regulation in depressed patients and that 600 ug of elemental Cr may be beneficial for patients with atypical depression who also have severe carbohydrate craving. Further studies are needed to evaluate Cr in depressed patients specifically selected for symptoms of increased appetite and carbohydrate craving as well as to determine whether a higher dose of Cr would have an effect on mood [39].Studies designed to link the clinical effects of Cr with changes in underlying insulin, serotonin, and dopamine pathways may be especially informative. If efficacious, Cr supplementation may provide a useful, low-cost alternative to or augmentation strategy for selective serotonin reuptake inhibitors, which have partial efficacy in Binge Eating Disorder (BED) [40]. CrPic has been reported to benefit patients with symptoms of atypical depression shows promising antidepressant effects in atypical depression. Its mechanism of action may relate to 5HT2A down regulation, increased insulin sensitivity, or to other effects [41].

Cr treatment was associated with reduced mood symptoms and improved overall health satisfaction in most participants. In some cases, Cr alone was associated with marked clinical improvement; in others, Cr plus an antidepressant resulted in greater improvement than either Cr alone or an antidepressant alone. These preliminary observations suggest that Cr may be a useful monotherapy or adjunctive therapy for women suffering from significant menstrual cycle-related symptoms. Larger, controlled studies are needed to evaluate the efficacy of Cr treatment in this patient population[42].Cr supplementation led to remission of dysthymic symptoms. Single-blind substitution of other dietary supplements in each of the patients demonstrated specificity of response to Cr supplementation. Preliminary observations suggest that Cr may potentiate antidepressant pharmacotherapy for dysthymic disorder. Controlled studies are indicated to test the validity of these initial observations [43].

Chromium and Immune Response

Supplemental CrPic improved average daily gain of growing steers, regardless of whether they had been stressed by shipping. Supplemental Cr did not affect any of the immune responses that were measured [44].Cr modulates the expression of IFN-gamma and route has effect on the onset and duration of the response. Thus, the supplementation of Cr at appropriate dose might be

helpful to enhance the IFN-gamma mRNA expression in response to Newcastle Disease Virus [45].

Body temperature tended to be lower for calves supplemented with Cr-nicotinic acid complex than for control calves. Calves supplemented with either Cr source had lower serum cortisol concentrations at 5 d after challenge and Cr supplementation enhanced cell-mediated immune function [46].Cr is of significant importance in altering the immune response by immunostimulatory or immunosuppressive processes as shown by its effects on T and B lymphocytes, macrophages, cytokine production and the immune response that may induce hypersensitivity reactions [47].

Chromium and Infectious Diseases

Cr improved IR, metabolic abnormalities, and body composition in HIV+ patients. This suggests that Cr supplements alleviate some of the antiretroviral-associated metabolic abnormalities [48].A significant interactive effect of Cr and Cu supplementation on lymphocyte proliferation was observed with ConA 50 µg/ml stimulation. After 12 weeks of supplementation, ConA-stimulated (50 µg/ml) lymphocyte proliferation was significantly lower when Cu was added to the Cr supplementation group. Moreover, ConA-stimulated (100 µg/ml) lymphocyte proliferation was significantly lower in the Cu supplementation group compared to the Cr supplementation group after 12 weeks of supplementation. These results suggest that Cu blocks enhancement of lymphocyte proliferation by Cr supplementation and that Cu supplementation has potential suppressive effects on the immune function in these subjects [49].Lower levels of Cr and Mn may be predictors for secondary infections in HIV-1 patients. There was a significant decrease in mean values of Cr and Mn in whole blood and scalp hair, whilst higher concentrations were observed in urine samples of the three groups of AIDS patients as compared to a controlled healthy male group. Low Cr and Mn levels may be due to increased Cr and Mn losses. These data present guidance to clinicians and other professional investigating deficiencies of Cr and Mn in biological samples of AIDS patients [50].

Chromium and Poly Cystic Ovary Syndrome

Treatment with Cr has been shown to improve insulin sensitivity in adults with PCOS. Treatment of adolescents with PCOS remains a challenge. No significant change in BMI Standard Deviation Score (SDS) with Cr supplementation was noted. The number of patients with oligo/amenorrhea decreased with treatment. Significant reduction in mean ovarian volume, total follicular count and free testosterone was observed. No significant improvement in acne or hirsutim was noted. Supplementation with Cr to adolescents with PCOS is a promising treatment option [51].In women with PCOS, CrPic (200 ug/day) improves glucose tolerance compared with placebo but does not improve ovulatory frequency or hormonal parameters. Future studies in the PCOS population should examine higher dosages or longer durations of treatment [52].

Trivalent Cr (1000 ug), as CrPic, given without change in diet or activity level, caused a 38% mean improvement in glucose disposal rate in five obese subjects with PCOS who were tested with a euglycemichyperinsulinemic clamp technique. This suggests that CrPic, an over-the-counter dietary product, may be useful as an insulin sensitizer in the treatment of PCOS [53].Cr supplementation in women with PCOS resulted in significant decreases in serum insulin levels, HOMA-IR, HOMA-B and a significant increase in quantitative insulin sensitivity check index (QUICKI) score compared with the placebo. In addition, a trend towards a significant effect on decreasing serum triglycerides, VLDL-C and cholesterol concentrations was seen. Eight weeks supplementation among PCOS women had favorable effects on markers of insulin metabolism [54].Use of CrPic for 6 months was associated with significant reduction of BMI and fasting specific insulin. CrP significantly increased the chances of ovulation and regular menstruation by almost two fold after the fifth month of treatment and hence CrPic is useful in PCOS to reduce IR and stimulate ovulation [55].

Chromium and Infertility

The nutritional dietary supplement CrPic has gained much notoriety as a safe supplement that supposedly promotes fat loss and muscle enhancement in humans. Thus, a significant industry has materialized around the incorporation of CrPic in many sports foods and drinks and a variety of weight loss products [56]. The ingestion of trivalent and hexavalent Cr compounds by adult male and female mice would cause adverse effects on fertility and reproduction [57]. CrPic decreased FPG and insulin levels and, thus, increased insulin sensitivity in clomiphene citrate-resistance PCOS women. These effects were comparable with metformin; however, metformin treatment was associated with decreased hyperandrogenism. Overall, CrPic was better tolerated compared to metformin; nonetheless, the two study groups were not significantly different regarding ovulation and pregnancy rates [58].

Chromium and Reproduction

Hexavalent Cr is an environmental contaminant which may be associated with reproductive abnormalities in male rats. A dose-dependent increase in blood and testis Cr levels as well as an increase in FSH and a decrease in LH and testosterone serum levels were detected in treated rats. Histological analysis revealed pronounced morphological alterations with enlarged intracellular spaces, tissue loosening and dramatic loss of gametes in the lumen of the seminiferous tubules of treated rats. In addition, a decreased sperm motility and number of epididymal spermatozoa together with an increased sperm abnormality rate was found in Cr-treated rats in comparison to controls. In rats receiving the higher Cr dose, histological images presented considerably

increased areas filled with seminal vesicle and prostate secretions. The mucosal crypts of seminal vesicles and the typical invaginations of prostate were altered. The results suggest that subacute treatment of potassium dichromate promotes reproductive system toxicity and affects testicular function of adult male rats[59].

The mRNA levels of the prolactin-growth hormone (PRL-GH) family of genes were dose dependently reduced by Cr exposure. The mRNA levels of Pit-1a and b isotype genes that induce the expression of the PRL-GH family of genes were also reduced by Cr exposure. The PRL-GH hormonal concentration in the rat placenta, fetus and maternal blood were decreased by Cr exposure. In the middle stage of pregnancy (day 11), a high dose of Cr suppressed the differentiation of spongiotrophoblast cells that secret the PRLGH hormones. In the last stage of pregnancy (day 20), a high dose of Cr induced apoptosis of placental cells. Reproductive data, such as placental and fetal weights, litter size, were reduced, but the pregnancy period was extended in the group exposed to Cr compared with the controls.Cr- VI disrupts the ordered functions of the placenta, which leads to reproductive disorders in rats[60].

Less documented are reproductive effects for mercury, manganese, Cr, nickel, and arsenic for the same gender. More complex is the demonstration of effects on female reproduction and on pregnancy. The action of lead, arsenic, cadmium, Cr and mercury may in fact be relevant in several stages, beginning in fetal life, during early development or maturity and is characterized by subfertility, infertility, intrauterine growth retardation, spontaneous abortions, malformations, birth defects, postnatal death, learning and behavior deficits, and premature aging. Also, for females the evidences of specific aspects such as fertility or abortions are usually higher and clearer from animal experiments than from human studies[61].

Administration of Cr - VI to rats revealed a significant accumulation of cholesterol and a prolonged diestrus phase leading to impaired fertility in rats and significantly reduced the antioxidant markers such as SOD and reduced glutathione (GSH), along with significant increase in peroxidation markers such as malondialdehyde and protein carbonyls in ovaries. The functional marker in serum such as total protein was decreased, whereas other functional markers viz Alanine Transaminase (ALT), Urea and creatinine were increased. Prominent pathological changes were observed in the uterus and ovaries of Cr-treated group. Co-treatment with α-tocopherol significantly reversed the Cr-VI induced changes[62].

A decrease in the specific activities of antioxidants, serum testosterone and progesterone and an increase in the levels of H_2O_2, lipid peroxidation (LPO) and FSH in rats exposed to Cr-VI when compared to control. Cr-VI exposure also delayed the sexual maturation and extended the estrous cycle. Simultaneous administration of vitamin C significantly prevented the increase in LPO and enhanced the antioxidant status. These results suggest the protective effect of vitamin C against the Cr-VI exposure-induced toxicity and attest the significance of antioxidants in diet[63].

CONCLUSIONS

The outcome of this Review article on the trace metal Chromium has brought out new insights about its role in the curative aspects of this metal to improve DM,Cardiac,Renal,Liver Reproductive failure, PCOS and Neurologic problems. The beneficial effects on the outcome of the research done during the last 20 years have been compiled under each disease condition for the benefit of future researchers in this field to undertake further research based on the lacunae pointed out by various researchers and to include this metal as a special test for each category of disease condition when other laboratory diagnosis are in doubt. Further, more research are to be done using large population size and to work out uniform strategies for supplementation and to evaluate its beneficial effects based on the prognostic outcome.

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