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A Review On : Chromium Deficiency And Its Emerging Role In The Pathogenesis Of Type 2 Diabetes Mallitus

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ABSTRACT:

Chromium deficiency is now a pivotal player in the etiopathogenesis of Type 2 Diabetes Mellitus (T2DM), which is a long-term metabolic disorder manifesting with defective glucose metabolism and insulin resistance. Chromium (Cr), a trace element, is involved in carbohydrate and lipid metabolism through its action in potentiating insulin activity and enhancing glucose tolerance. This review emphasizes the clinical significance of chromium supplementation in controlling T2DM and its physiological action in insulin signaling. Trivalent chromium (Cr^{3+}) has been found to increase insulin receptor sensitivity, facilitate glucose uptake, and normalize blood glucose levels through studies. However, conflicting evidence is also reported by some randomized controlled trials with no improved insulin sensitivity or glycemic control with chromium supplementation. Chromium deficiency has been associated with enhanced insulin resistance, obesity, hypertension, and cardiovascular disease. The bioavailability of chromium complexes containing organic ligands like chromium picolinate and chromium nicotinate is considerably greater than that of inorganic complexes. Experimental data indicate that biologically produced chromium–zinc complexes could provide safer and more effective hypoglycemic action. In spite of favorable results, variable findings and the possibility of toxicity with supraphysiological doses necessitate careful clinical application. Future work needs to be directed toward optimizing chromium preparations, dose, and long-term safety assessment. In general, chromium supplementation has promise as an adjunctive treatment for T2DM, but continued large-scale, controlled studies are needed to determine its ultimate therapeutic efficacy and safety.

KEY WORDS :

Chromium deficiency, Glycemic control ,Trivalent chromium, Chromium supplementation , Insulin sensitivity, Glucose metabolism , Type 2 Diabetes Mallitus

INTRODUCTION :

Diabetes mellitus is a very common metabolic illness with a capacity to cause disastrous long-term complications. In diabetes mellitus, practically all the functions of metabolism, such as micronutrient metabolism, are affected. Among such micronutrients is chromium (Cr), the role of which in carbohydrate metabolism and in insulin action mechanism is still unknown even after a quarter of a century of relevant investigation.[5] Patients with type 2 diabetes mellitus (T2DM) account for 90% to 95% of all diabetic patients, and T2DM is thus a key field of investigation in the epidemiology of diabetes. Scientists have researched the etiology of diabetes and prevention thereof extensively, years after years; there is still no cure, since the etiology of the disease is not well understood, and its pathogenesis is very complicated.[6]The etiology of the chronic disease is multifactorial with genetic and environmental factors being the main source. Environmental factors are factors such as heavy metal exposure and air pollution in states that contribute to the development and progression of the condition. In addition, food constituents, such as the daily use of dietary supplements of various minerals, contribute to the pathogenesis of diabetes mellitus.[7]The management of diabetes consists of a rigorous drug regimen, diet modification, and life modification aimed at decreasing health risk and mitigating the long-term consequences of accompanying complications.[1]Type II diabetes, obesity, hypertension, and other elements of the metabolic syndrome are accompanied by insulin resistance. It is the leading risk factor for cardiovascular disease and one of the leading causes of death and sickness. Insulin resistance management has been shown to have a key role to play in reduced risk of cardiovascular disease. However, there are fewer such compounds that increase the sensitivity of insulin. Safer and higher bioavailability of low-molecular-weight organic chromium complexes than chromium salts (2–5% vs. 0.5–2%) have predisposed chromium to become introduced as a low-molecular-weight organic complex of chromium as a drug to reverse decreased insulin effect in type II diabetes[8]Chromium is a shiny metallic element used largely in glass and alloy industries with 3 valences—II, III and VI. It is a nutritionally relevant compound with a crucial man requirement of 0.005–0.2 mg/day and serum level of 2.3–40.3 nmol/L It is trivalent Chromium Cr3, which has been extensively researched.[5]

METHODS :

The study population was selected from those patients who came to the Diabetes clinic, S.S.K.M Hospital, Calcutta. They were 50 type 2 diabetic patients on diet only or diet and oral hypoglycaemic therapy with reasonably stable (not optimal in all cases) glycaemic control in the preceding 3 months as determined by fasting plasma glucose and glycated haemoglobin levels.[5]

1.QUANTITATIVE ANALYSIS :

We contrasted the net difference between the within-treatment (chromium supplement) effect and the within-placebo effect. For glycosylated hemoglobin, fasting glucose, and lipoprotein outcomes, we performed random effects model meta-analyses. For outcomes other than these, we did not carry out meta-analysis since we did not have homogeneity in measuring these outcomes.[9] A. aceti was grown in liquid medium made up of 64 mg/mL of chromium trichloride and zinc chloride where the initial concentration of the bacterial solution was 1 × 104 CFU/mL. After induction of the bacterial solution for 48 h, the culture media was changed and once induction was done. The levels of chromium and zinc in the bacteria were determined using inductively coupled plasma mass spectrometry, whereas NADH and glucose dehydrogenase content were quantified using an NAD/NADH kit and glucose dehydrogenase kit, respectively. [6]

2.SEARCH STRATEGY AND SELECTION OF RANDOMIZED CONTROLLED TRIALS (RCTs):

The research was carried out in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline (Moher et al., 2009).Systematic search of the scienti□c literature up

to January 15, 2024, was carried out using the databases Scopus, PubMed, ScienceDirect and Cochrane.Searches were performed using subject heading (MeSHs), abstracts, associated keywords, speci□ed language and type of study.

3. INCLUSION AND EXCLUSION :

Criteria Two authors selected appropriate articles through screening titles, abstracts, and full text of papers. The research question was formulated as the association of type 2 diabetes mellitus with chromium consumption, particularly through dietary supplementation. Any full text human RCTs available with treatment in the English language that reported the impact of chromium supplementation on type 2 diabetes mellitus were evaluated.

4. DATA EXTRACTION AND ANALYSIS :

Two reviewers independently evaluated the titles and abstracts of studies identified through the search strategy. Relevance of studies was determined by obtaining full texts and cross-checking for eligibility. Eligible studies were evaluated for data using pre-designed abstraction form, which consisted of 1st author with year of publication, study design, location – country of study, type of patient, duration of trial, total sample size, population characteristics, type, and dose of treatment of chromium.

5.EVALUATION OF QUALITY OF RANDOMIZED CONTROLLED TRIALS (RCT):

The quality of the studies was assessed using the Cochrane Risk of Bias tool for Randomized controlled trials (RCT) (Higgins et al., 2011). The quality assessment tool adopted by the results provides a framework to the analysis of risk of bias in the findings of any randomized trial. The assessment is divided into a series of six discrete domains, through which bias can be introducedinto a test.[7]

6.COLLECTION OF BLOOD SAMPLE :

Ten milliliters of blood was collected from every patient. Five milliliters were used in the HbA1c assay in tubes containing EDTA. Four milliliters were collected for lipid profiles and one milliliter for fasting blood sugar test analysis. Glucose assay was done on the spot, while the rest were centrifuged and stored in -21°C until measurement.[1]

7. BODY MASS INDEX MEASUREMENT (BMI) :

BMI was calculated using the formula advised by the World Health Organization: weight in kg divided by square of height in meters. The BMI result was classified into different categories: underweight (BMI<18), normal weight (BMI 18-24.9), being overweight (BMI 25-29.9), and obese (BMI>30).[1]

8. STATISTICAL ANALYSIS:

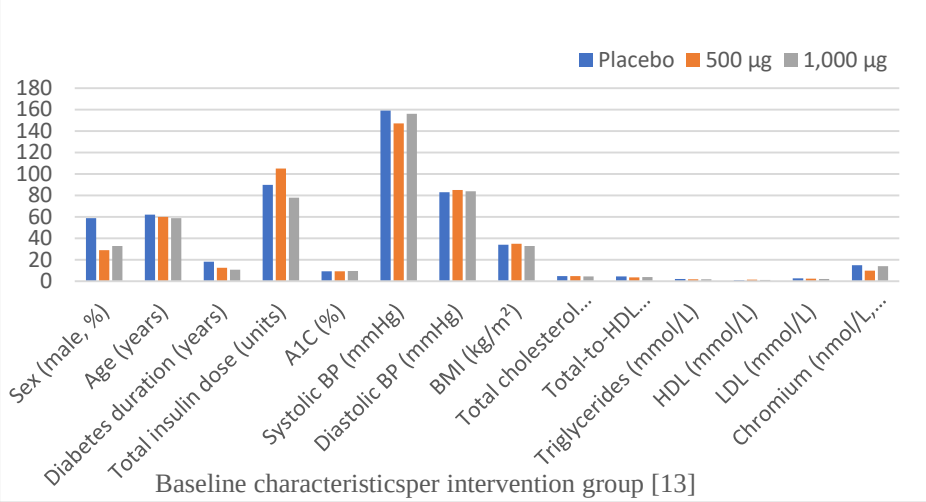
Data were collected with the help of Microsoft Excel and then analyzed with SPSS version 24. Categorical data were presented as numbers and percentages as well as analyzed through the chi-square test. Continuous data were presented as means and standard deviations.A p-value of less than 0.05 was considered to be statistically significant [1]

9. DNA CLEAVAGE REACTIONS:

DNA cleavage-catalyzed by chromium compounds was assessed as above. All of the solutions were prepared in Chelex-100 treated water to remove any remaining metal ions. Aliquots of pUC19 (about 40 μM in base pairs in 5 mM Tris, 500 μM EDTA buffer, pH 8.0) were mixed with ascorbic acid (5 mM) in the presence of the test compounds in phosphate buffered saline (pH 7.4), to a final volume of 15 μl. Reactions were allowed to proceed for 60 min and quenched with 2 μl of sample loading buffer nucleic acid. The samples were directly loaded onto a 1% agarose gel pre-stained with ethidium bromide and run electrophoresed at 60 V. The gels were taken under a UV transilluminator.[8]It was a randomized double-

blind placebo-controlled clinical trial that was done among the patients who referred to the institute of Endocrine and Metabolism of Iran University of Medical Sciences.[3]. Twenty-two diabetic women and 17 diabetic men, matched for age and treatment, and also in the process of rehabilitation, who had not received chromium picolinate supplements, constituted the control group.[10] The sample was roughly balanced at baseline within center by age (18–24, 25–30 years), gender, race (African American, Caucasian) and level of education (high school graduate or less, greater than high school)[11], new scientific data and grounds for health worries were first gained through a public consultation, including scientists, officials, and the overall population of the Nordic and Baltic nations[12]

DIAGRAM :



Baseline characteristicsper intervention group [13]

MECHANISM AND PHYSIOLOGY:

One of the proposed modes of action of Chromium in increasing insulin sensitivity is as follows. Chromium has been reported to increase the number of insulin receptors and also insulin binding with cells32. Chromium activity as a glucose tolerance factor and as an insulin sensitizer has been proposed to be the likely mechanism of action in type 1 and type 2 diabetes. Chromium's function in the everyday action and activity of insulin and in fat and carbohydrate metabolism is well established through various animal and human studies. Chromium also reduces insulin levels and leads to better glycemic control in obese populations of type 2 diabetics. Cr Pic occurs as a commonly used dietary supplement in the United States.[14] The body absorbs 0.5% of chromium in the diet by passive diffusion, and the remaining diet is passed in the faeces. Organic

chromium compounds are absorbed two to 16 times more than inorganic compounds, and chromium picolinate is more available than chromium nicotinate. Simultaneous ascorbate supplementation facilitates chromium absorption in humans and animals, whereas uptake of chromium is higher in zinc- and iron-deficient animals. The metal is transported in the blood bound to albumin and transferrin and is excreted mainly in urine. Urinary losses increase with metabolic stress and glucose intolerance may further add to this factor. Only in minute amounts is it eliminated via sweat and bile.Experimental chromium deficiency in previous animal studies resulted in impaired glucose tolerance in the face of regular insulin levels. The other deficiency signs in animals included diminished growth, elevated levels of serum cholesterol and triglycerides, high incidence of aortic plaques, lesions in the cornea, and lower fertility and sperm count.[12] The hexavalent (6+) and the trivalent (3+) forms are the two most common types of chromium. There is no naturally occurring Chromium 6+, which is toxic. Trivalent chromium is what occurs in food and in dietary supplements. Whole grains such as whole grain bread, vegetables, nuts, and spices are low in trivalent chromium. Supplements of chromium are available as chromium chloride, chromium

nicotinate, chromium picolinate, high-chromium yeast, or chromium citrate. Chromium chloride is said to have doubtful bioavailability but little is known about chromium absorption in man.[15]

DISCUSSION:

Chromium is also a part of insulin physiology, and chromium deficiency can lead to insulin resistance. Chromium supplementation can be beneficial in such rare instances of prolonged total parental nutrition when routine chromium supplementation is not possible[6]. In the lack of sufficient evidence that chromium supplementation improves glycemic control. chromium is also widely advertised as a beneficial supplement for improving glycemic control in type 2 diabetic patients.[16]Today, diabetes has become rampant with no cure in sight to man. The conventional treatment is long-term use of hypoglycemic drugs and symptom relief. However, in the course of long-term treatment, drugs are prone to resistance in non-compliant patients who fail to obey treatment guidelines. Therefore, apart from helping patients achieve blood sugar control in the long term, it is also important that we have clear identification of risk factors for diabetes so that diabetic patients are not exposed to the disease. One important area that can be vital both in the long-term management and prevention of diabetes is the use of supplemental micronutrients, as diabetic patients are deficient in B vitamins and micronutrients such as chromium, zinc, and selenium. the decisive function of zinc in glycemia regulation, a lack of zinc can lead to glucose metabolism's glycemic disorders, while excessive consumption could reduce the occurrence of glucose metabolism's glycemic disorders and diabetes. Above all, chromium and zinc supplementation could maintain blood glucose in an irreversible manner. The problem is how to supplement chromium and zinc through a proper, safe, and scientific pathway. In this study, A. aceti were co-cultured with chromium trichloride and zinc chloride to induce production of chromium- and zinc-enriched A. aceti using straightforward procedures with high yields. Chromium- and zinc-enriched A. aceti generated by this method not only induced A. aceti to exhibit the function of glucose decomposing but also enhanced the hypoglycemic effect exhibited in untreated A. aceti. Since the chromium and zinc was transformed by the bacteria, biological safety was ensured, hence implying that this could be utilized as a new hypoglycemic biological drug.[6]We examined the effect of chromium picolinate upon glucose metabolism mediated by insulin in a well-characterized group of non-obese non-diabetic volunteers. We saw no indication that chromium content in serum had a significant effect on insulin sensitivity in this population, or that increased chromium excretion was associated with insulin resistance. In investigating the feasibility of daily chromium picolinate supplementation as a modulator of insulin action, we saw no indication of a positive effect of the compound. Our principal finding was that the subjects with highest levels of serum chromium following treatment actually impaired insulin sensitivity and did not enhance it. This negative effect of chromium supplementation was demonstrated when we divided the chromium treated subjects into two groups on the basis of the medial serum chromium value of 3.1 μg/L – the subjects with higher value for chromium showed greater decline in insulin sensitivity than those with lower value for chromium. The research also utilized a wide range of chromium preparations, doses and durations of the therapy. Supplementation with 200 to 1000 μg chromium picolinate has been shown to improve glucose tolerance and lower insulin levels in circulation with an improvement in one trial in patients of type 2 diabetes more with 1000 μg dose than with 200 μg dose. The 1000 μg per day has been used in a number of other clinical trials and not associated with any toxicities.[4] Besides its action on diabetes, chromium supplementation has also been noted to be associated with reductions in blood pressure, cholesterol, and body weight and also reduced risk of metabolic syndrome. Most studies highlighted the role of chromium in not only managing type 2 diabetes and other metabolic conditions connected to its aetiology. chromium also plays a key role in the reduction of lipids. There are various studies that have demonstrated considerable reduction in triglyceride levels and reduction in the risk of central obesity without having any harmful impact on liver or kidney function.[1]It is the first study to explore the effect of a new chromium complex with d-phenylalanine amino acid on insulin signaling and glucose tolerance. Most significant findings of our studies are (i) Cr(pa)3 enhances insulin-stimulated glucose uptake by adipocytes, (ii) Cr(pa)3 potentiates insulin-signal transduction in cultured mouse adipocytes, (iii) oral treatment of Cr(pa)3 to

insulin-resistant animals restores glucose tolerance and (iv) Cr(pa)3 is non-toxic in generating hydroxyl radicals with DNA strand breakage under physiological conditions. A problem with chromium picolinate is that it is poorly soluble in physiological buffers that may contribute to poor bioavailability. Furthermore, the picolinate ligand has been shown to form hydroxyl radicals that are capable of causing genotoxic damage to DNA.[8]

PHARMACOLOGY:

Chromium deficiency was first reported in 1977. Some patients on long-term total parenteral nutrition had classic diabetic symptoms reversed by chromium.4 Plasma chromium levels in diabetic patients are 40% lower and the rate of urinary excretion three times normal of healthy patients. Normal plasma levels are ~0.1 µg/L. Tissue distribution of chromium is extensive, 10-100 times tissue levels of plasma levels. But plasma, urine, and tissue levels do not correlate well. High plasma chromium levels can occur with inadequate symptomatology and adverse chromium balance.[17] The majority (>80%) of US type 2 diabetics are overweight. Lean and especially obese type 2 diabetics are both characterized by daytime surges in plasma free fatty acid concentrations, which fail to fall normally following a mixed meal or oral glucose tolerance test.Fatty free acids (FFA) accumulate as triglycerides in the adipocytes and are an important source of energy during fasting states. Insulin is a potent inhibitor of lipolysis, and inhibits adipocyte release of FFA by inhibiting the enzyme hormone sensitive lipase. In type 2 diabetics insulin's suppression of lipolysis (as reflected by reduced suppression of radioactive palmitate turnover) and lowering of plasma FFA level is reduced quite significantly. It is currently known that extremely high plasma levels of FFA are likely to induce insulin resistance in muscle and liver and impair insulin secretion.[18]

DIETARY INTAKE :

Dietary intake was also assessed using the 24HR questionnaire to assess the interaction between diet, diabetes and glucose homeostasis. The 24HR questionnaire collected quantitative information concerning the number and amount of meals, foods and beverages consumed for breakfast, lunch and evening meal as well as morning, afternoon and evening snacks. Then, 24HR diet questionnaires were processed with the Nutrilog software (Version 3.20) (Nutrilog Europe Society, Marans, France) in the Research Unit of Obesity in National Institute of Nutrition & Food Technology of Tunis. The Nutrilog software allows transforming food and beverages into energy intake. As supplemented to that, it gives an estimation of the daily intake of every nutrient per day and of the distribution among macro and micronutrients. The calculated estimated average requirement (EAR) and recommended dietary allowance (RDA) were done in accordance with the European nutritional references [19] With exceptions occurring in specific instances only, oleic acid (cis C18:1n−9) accounts for more than 90% of MUFA in foods containing MUFA. vegetable oils from natural or genetically altered oilseed crops are the most concentrated sources of MUFA, followed by nuts (and spread fats or oils made from them), and all of these fatty foods contain low SFA levels. Two principles regarding high-MUFA foods need to be remembered for accurate interpretation of intervention and epidemiologic studies and for planning high-MUFA diets.[20]

DIABETES MELLITUS :GLUCOTOXICITY AND GLUCOLIPOTOXICITY ROLES :

Most clinicians would say that glucotoxicity is a part of β-cell function, amplifies lipotoxicity, and reduces β-cell mass. With current treatment paradigms, glucotoxicity could not be called a complication of type 2 diabetes because antidiabetes treatment is indicated only after a patient has reached some degree of β-cell failure, as evidenced by fasting hyperglycemia. [21] Oral glucose tolerance test A 75 g oral glucose tolerance test in fasting conditions was performed. Those with impaired fasting glucose or impaired glucose tolerance were excluded. Euglycemic hyperinsulinemic clamp: Euglycemic hyperinsulinemic clamp[18] was performed at baseline and at 16 weeks of chromium picolinate or placebo treatment Relation of chromium and insulin sensitivity at baseline: At baseline, placebo and chromium group participants had very low levels of serum and urinary chromium (range <0.5 to 0.6 µg/L and range 0-0.5

μ/g creatinine respectively).</mark> The correlation of insulin sensitivity with urinary and serum chromium was not significant (r = 0.24, p=0.1; r=0.08, p=0.79 respectively). Changes in insulin sensitivity by chromium absorption: Insulin sensitivity (M LBM/I) was not different significantly in the placebo and chromium groups at baseline (t= -0.22, p=0.83). After 16 weeks of treatment, the mean difference in insulin sensitivity was -1.63 mg/min/kg/mU insulin (-8.9 to + 5.57) in the placebo and -1.14 (-5.22 to + 4.11) in the chromium group (see Figure 1). The interaction between group and time was not significant [F(1,22) = 0.36, p=.54] suggesting the degree of change in insulin sensitivity from pre- to post-test did not statistically differ by group.[22]}

ADVERSE EFFECTS OF CHROMIUM :

Several beast and cell culture trials involving supraphysiological attention of chromium yielded results suggesting chromium could be accelerating DNA damage(20- 23). Chromium is n't unique in this respect; a number of other nutrients similar as vitamins A and D, nicotinic acid, and selenium have also been intertwined in causing toxin when taken in excess(24). Clinical trials involving oral chromium supplementation didn't demonstrate toxin in parenterally supported cases (24,25). Long- term chromium safety trials weren't discovered. The DNA damage in the case of supraphysiological trivalent chromium situations did n't do into potentially carcinogenic goods through a more physiological oral trivalent chromium cure in humans(23). Chromium supplements are considered safe with no poisonous responses noted during clinical trials. The U.S. EPA safe cure of exposure is 350 times the USDA adult upper position of estimated safe and acceptable diurnal salutary input.5 Rats were given several thousand times the fellow of 200 μg chromium without any adverse goods noted. One case of habitual renal failure redounded from 600 μg per day chromium picolinate supplementation for six weeks.14 Others challenged this opinion, including the vice chairman of exploration for Nutrition 21, the establishment which holds exclusive patent rights to manufacturing chromium picolinate.15 Another case reported renal failure, liver damage, and other problems after 1,200- 2,400 μg per day chromium picolinate for 4- 5 months.16 Acute, reversible cognitive, perceptual, and motor goods were reported an hour after another case taking 200- 400 μg chromium picolinate.17 Acute generalized exanthematous pustulosis was observed after 1,000 μg.18 The FDA has entered further than 500 adverse events involving chromium supplements, although utmost are salutary supplements with multitudinous sauces and other agents.(24).

CLINICAL EVIDENCE FOR CHROMIUM USE :

Andersonetal's intervention trial in 1997 was the first trial of chromium intervention among type 2 diabetic patients. Chromium picolinate supplements or placebo were administered to 180 Chinese type 2 diabetic patients in this trial. The patients were divided into three groups randomly and received placebo, 200 mg of chromium, and 1000 mg of chromium per day. At four months, hemoglobin A1c (HbA1c) in the placebo group remained unchanged (8.5%), while it decreased significantly in the 200 mg group from 8.5% to 7.5%, and decreased in the 1000 mg group, from 8.5% to 6.6%.[23]

ETIOLOGY OF TYPE 2 DIABETES :

In conjunction with observations of normalization of insulin secretion after bariatric surgery observations of the behavior of the pancreas and liver during dieting with hypocaloric intake bring about a hypothesis of etiology and pathogenesis of type 2 diabetes Infringement of fat in liver and subsequently in pancreas will result in self-reinforcing processes that interact to cause type 2 diabetes. Fatty liver causes defective fasting glucose metabolism and enhanced export of VLDL triacylglycerol which enhances fat delivery to all tissues including the islets. The cycle of liver and pancreas propels on after diagnosis with progressively worsening β-cell function. But noteworthy, findings of reversal of type 2 diabetes establish that if the major effect of positive calorie balance is eliminated, then the mechanisms are reversible[25]

RESULT:

3.1. Synthesis and characterization of Cr(pa)3 Stepwise synthesis of chromium complexes of l-phenylalanine and d,l-phenylalanine from aqua(isothiocyanato)bis(l-phenylalaninato) chromium and d,l- or l-phenylalanine as initial material is already given. A less complex, one-step reaction was used in the current work for the chromium(III) complex with d-phenylalanine in water solution. The synthetic route taken in the paper was closer to that of Abdel-Monem et al. for synthesizing identical chromium complexes of l-amino acids. The ratio of chromium to d-phenylalanine in the complex is 1:3 as confirmed by elemental analysis and spectroscopic studies. 3.2. Cr(pa)3 enhances insulin-stimulated glucose uptake in adipocytes Chromium was found to enhance insulin-stimulated glucose uptake in insulin-sensitive cells. 3.4. Cr(pa)3 enhances insulin-stimulated phosphorylation of Akt Akt has also been identified as a pivotal kinase, insulin receptor downstream that is essential for insulin action Insulin treatment of the adipocytes resulted in an increase in Akt (thr308) phosphorylation. Pretreatment of the adipocytes with the chromium complex induced further increases in the insulin-stimulated Akt phosphorylation both in time- and concentration-dependent fashion.[1] Mean age of patients was 52.3±6.3 years (range 40-60 years). Gender distribution was such that 46.7% of the sample was male and 53.3% were female. According to residence, 76.6% were urban and 23.4% were rural. According to BMI categories, 45% of the patients were normal weight, 21.6% were overweight, and 33.4% were obese. The mean BMI of the patients as a whole was 27.1±0.4. Weight and height were of mean values of 83.2±2.75 kilograms and 1.64±0.02 meters.[8]

CONCLUSION :

Chromium has a multifunctional role in human metabolism, especially in lipid and glucose regulation. Its potential in increasing insulin sensitivity and carbohydrate metabolism has made it a prime candidate for research in T2DM pathogenesis and treatment. While chromium deficiency has been associated with impaired glucose tolerance, the underlying biochemical processes are still unclear. Several clinical and experimental investigations have produced inconsistent results — while a few find enhanced glycemic control and diminished insulin resistance with chromium supplementation, others show small or even negative effects. The availability of chromium is mostly dependent on its chemical form, with organic complexes such as chromium picolinate and chromium–amino acid chelates demonstrating greater absorption and metabolic effect. New modalities, including chromium- and zinc-fortified biological preparations, have been identified as likely being safer and more effective alternatives for enhancing glucose homeostasis. Yet, the therapeutic utility of chromium supplementation as part of standard diabetes management is contentious owing to mixed clinical evidence and suspected safety issues. Thus, though chromium seems to be a trace element with obligatory function in insulin action and energy metabolism, it is not yet ready to become a standard antidiabetic treatment. Additional large-scale, properly controlled randomized trials are needed to define its biologic role, find optimal dosage, and ascertain long-term safety. Greater insight into the molecular mechanisms of chromium could open the way to specific nutritional or pharmacologic treatments for enhancing insulin sensitivity and metabolic health.

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