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## SPECIFIC FUNCTIONAL FOODS AND NUTRACEUTICALS IN THE MANAGEMENT OF METABOLIC SYNDROME

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**Abstract:** -Metabolic syndrome (MetS) is a world-wide epidemic disease associated with increased morbidity and mortality. Treatment strategies include pharmacologic and non-pharmacologic methods, with varying degrees of success rate all over the world. Nutraceutical interventions are currently being investigated on a large-scale basis as potential treatments for obesity and weight management. On the other side, it could be not convenient to use a nutraceutical to treat each metabolic syndrome component in each affected subjects. Many studies have focused solely on animal research, while others have implemented these nutraceuticals in controlled human trials. With recent marketing of products online, issues of safety should also be raised with respect to clinical treatment. Thus, this review tries to focus on widely marketed nutraceuticals with clinically demonstrated effects on more than one component of the MetS, namely omega-3 fatty acids, berberine, psyllium and other soluble fibers, cinnamon, chromium picolinate, banaba, and bitter gourd

**Keywords:** Metabolic syndrome, epidemic disease, psyllium, nutraceutical interventions.

### 1. INTRODUCTION

Metabolic syndrome has become a worldwide health problem and it affects a wide variety of population. It is a condition that includes a cluster of disorders such as obesity, hypertension, hyperlipidemia, diabetes, etc. mainly due to poor nutrition. In order to deal with this syndrome, researchers have made various interventions in the treatment methods as well in terms of nutrition. The term nutraceutical include nutritional and pharmaceutical aspects that work for the prevention and treatment of diseases and provide health and medicinal benefits. Researchers have identified presence of a wide range of phytoconstituents present in various traditional plants and spices. Certain plants such as Lagenaria siceraria, Trigonella foenum graecum, Curcuma longa, Vigna mungo etc. shows excellent properties in curing hypertension, obesity, diabetes and hypercholestromia. The current article reviews the importance of various nutraceuticals that we consume in our daily diet and their contribution in curing the metabolic syndrome.

Metabolic syndromes such as diabetes mellitus, obesity are rapidly increasing in the westernized world because of poor lifestyle habits favouring fat and sucrose enriched meals and low physical activity or sedentariness. Medical nutritional therapy is an integral component of diabetes mellitus, obesity and metabolic syndrome management. Pharmacological intervention is taken into consideration when diet associated physical exercise and healthy lifestyle is insufficient to control blood glucose, body weight and metabolic profile. In contrast, pharmacological intervention for obesity still remains a controversial issue because of only modest long term efficacy and concern about safety. Obesity is the major underline reason for metabolic syndrome. The worldwide incidence of obesity has been rapidly increasing in the last two decades. According to WHO report, obesity has been classified as a growing epidemic, and if immediate action is not taken, millions of people will suffer from serious weight related

disorders. Obesity counts a major health problem and common chronic disease. In health surveys conducted in the United States in 2005, 24.2% of men and 23.5% of women or over one-fifth of the respondents were classified as obese. Obesity mainly arises when there is an imbalance between energy intake, principally stored as triglycerides (food consumption), and energy expenditure (basal metabolic rate and biochemical processes). The excess energy is primarily stored in adipose tissue in the form of triglycerides. When adipose tissue function is compromised during obesity, the excessive fat accumulation in adipose tissue, liver, and other organs predisposes the individual to the development of metabolic changes that increase overall morbidity risks. Hence, the recent recognition of metabolic syndrome and its influence on health has led the researchers to consider the potential drug-food or nutrient-drug interaction here since nutrition therapy and pharmacological intervention are the major components in managing metabolic syndrome. An interaction is said to take place when the effects of one drug are changed by the presence of another food, drug, and drink or by some environmental chemical agents. Interactions between food and drug may inadvertently reduce or increase the effect of drug, resulting in therapeutic failure or increased adverse effect. The conventional clinically relevant food-drug interactions are caused by food induced changes in the bioavailability of drugs. Thus, in the field of metabolic disorders where nutrition plays a major role in the overall treatment, the potential influence of food and nutrient intake on drug therapeutic effect may be crucial.

Nutraceutical is defined as a food (or a part of food) that provides medical or health benefits, including prevention or treatment of a disease. Nutraceuticals are found in number of products emerging from (a) food industry, (b) herbal and dietary supplements and (c) pharmaceutical industry. Nutraceuticals covers most of the therapeutic areas that includes disorders related to sleep, digestion, cold and cough,

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prevention of cancer, blood pressure, pain killers, depression, hyperglycaemia and hypoglycaemia .

Nutraceuticals can be organized in several ways depending upon its easier understanding and applications i.e. for academic instruction, clinical trial design, and functional foods. Classification of nutraceuticals on the basis of food sources are as follows:-

- Dietary fibres (fruits, beans, barley, oats)
- Antioxidant vitamins (vitamin C, vitamin E and carotenoids)
- Polyphenols (tea, legumes)
- Spices (clove, garlic, turmeric)

a) Potential nutraceuticals b) Established nutraceuticals

A potential nutraceutical can only become an established one after sufficient data on its medicinal and clinical aspects are obtained. Pharmacokinetic interferences often occur as a result of change in drug metabolism. Cytochrome- P450 (CYP-450) system oxidises a broad spectrum of drugs by a number of metabolic processes that can be enhanced or reduced by various drugs (known as inducers or inhibitors). Other factors involved in drug interaction also involve age, sex, patient and administration.

## 2. MECHANISM OF ACTION

The antidiabetic effect of *Murraya koenigii* is due to increase in hepatic glycogen concentration and decrease in concentration of glycogen phosphorylase and gluconeogenic enzymes. It exhibits antioxidant activity by free radical scavenging activity. It is also known to induce apoptosis in human myeloid cancer cells and also a time dependent anti-proliferative in acute lymphoid and chronic myeloid leukemic cell lines. It is an inhibitor of lipooxygenase.

**Vigna mungo:** *Vigna mungo* is also known as black gram or black lentil. Grain legumes are the important source of food proteins. The leguminosae are the most important family in Dicotyledonae. These grams are the richest source of proteins and amino acids for human as well as animal nutrition.

Beneficial effects of black gram are:

**Cardiovascular disease:** The frequent intake along with a saturated fat poor diet can help in controlling the lipid homeostasis and consequently reduce the risk of CVD. The legume high fibre content, low glycemic index and the presence of minor components such as phytosterols, saponins, oligosaccharides etc. are considered the main responsible agents for this property.

**Diabetes:** Because of low glycemic index and high content of indigestible fibres, dry legumes are claimed to maintain glycemic control in diabetes individuals. Moreover, black grams also help to prevent insulin resistance which represents Type 2 diabetes.

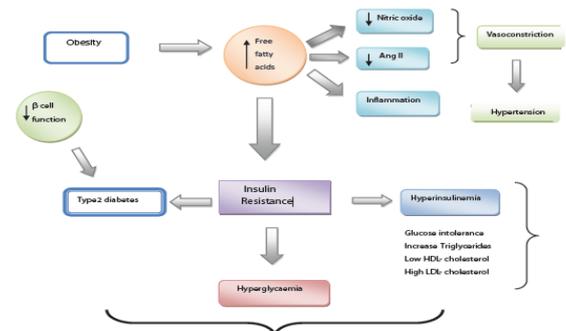
**Overall weight and obesity:** Despite their content of lipids, starch and proteins, dry legumes help in maintaining a regular body weight, and this is because of their satiety effects, thus limiting overall food daily intake.

## 3. METABOLIC SYNDROME MANAGEMENT

Metabolic syndrome is a clustering of at least three of five of the following medical conditions: abdominal (central) obesity,

elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, and low high-density lipoprotein (HDL) levels.

Metabolic syndrome is associated with the risk of developing cardiovascular disease and diabetes. Some studies have shown the prevalence in the USA to be an estimated 34% of the adult population, and the prevalence increases with age.



Metabolic syndrome is also known as metabolic syndrome X, cardiometabolic syndrome, syndrome X, insulin resistance syndrome, Reaven's syndrome (named for Gerald Reaven), and CHAOS (in Australia).

Metabolic syndrome and prediabetes may be the same disorder, just diagnosed by a different set of biomarkers.

The syndrome is thought to be caused by an underlying disorder of energy utilization and storage. The cause of the syndrome is an area of on-going medical research.

The first line treatment is change of lifestyle (e.g., Dietary Guidelines for Americans and physical activity). However, if in three to six months of efforts at remedying risk factors prove insufficient, and then drug treatment is frequently required. Generally, the individual disorders that compose the metabolic syndrome are treated separately. Diuretics and ACE inhibitors may be used to treat hypertension. Cholesterol drugs may be used to lower LDL cholesterol and triglyceride levels, if they are elevated, and to raise HDL levels if they are low. Use of drugs that decrease insulin resistance, e.g., metformin and thiazolidinediones, is controversial; this treatment is not approved by the U.S. Food and Drug Administration. Weight loss medications may result in weight loss. As obesity is often recognized as the culprit behind many of the additional symptoms, with weight loss and lifestyle changes in diet, physical activity, the need for other medications may diminish.

A 2003 study indicated cardiovascular exercise was therapeutic in approximately 31% of cases. The most probable benefit was to triglyceride levels, with 43% showing improvement; but fasting plasma glucose and insulin resistance of 91% of test subjects did not improve. Many other studies have supported the value of physical activity and dietary modifications to treat metabolic syndrome. Some natural compounds, like ursolic acid, have been suggested as a treatment for obesity/metabolic syndrome based on the results of extensive research involving animal models; it is argued, however, that there is still a lack of data regarding the use of ursolic acid in humans, as phase-II/III trials of that drug have not been carried so far. Restricting the overall dietary carbohydrate intake is more effective in reducing the most

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common symptoms of metabolic syndrome than the more commonly prescribed reduction in dietary fat intake.

The combination preparation simvastatin/ sitagliptin were introduced in 2011 and the use of this drug was to lower LDL levels and as well as increase insulin levels. This drug could have been used to treat metabolic syndrome but was removed from the market by Merck in 2013 due to business reasons.

High-dose statins, recommended to reduce cardiovascular risk, have been associated with higher progression to diabetes, particularly in patients with metabolic syndrome. The biological mechanisms are not entirely understood, however, the plausible explanation may lie in competitive inhibition of glucose transport via the solute carrier (SLC) family of SLC01B1, important in statin pharmacokinetics.

**Diagnosis:** A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity published a guideline to harmonize the definition of the metabolic syndrome.<sup>[36]</sup> This definition recognizes that the risk associated with a particular waist measurement will differ in different populations. Whether it is better at this time to set the level at which risk starts to increase or at which there is already substantially increased risk will be up to local decision-making groups. However, for international comparisons and to facilitate the etiology, it is critical that a commonly agreed-upon set of criteria be used worldwide, with agreed-upon cut points for different ethnic groups and sexes. There are many people in the world of mixed ethnicity, and in those cases, pragmatic decisions will have to be made.

The previous definitions of the metabolic syndrome by the International Diabetes Federation and the revised National Cholesterol Education Program are very similar and they identify individuals with a given set of symptoms as having metabolic syndrome. There are two differences, however: the IDF definition states that if body mass index (BMI) is greater than 30 kg/m<sup>2</sup>, central obesity can be assumed, and waist circumference does not need to be measured. However, this potentially excludes any subject without increased waist circumference if BMI is less than 30. Conversely, the NCEP definition indicates that metabolic syndrome can be diagnosed based on other criteria. Also, the IDF uses geography-specific cut points for waist circumference, while NCEP uses only one set of cut points for waist circumference regardless of geography. These two definitions are much more similar than the original NCEP and WHO definitions.

**Mechanism of Action:** Various studies suggest that proteins are more satiating than carbohydrates or fats. In this respect, an increased gram protein intake may have weight loss benefits, and it also has credits to the lower extent of kidney workload of plant proteins compared to animal proteins. A specific direct action of black grams on  $\alpha$  amylase protein inhibitors has been considered for its potential use in prevention of obesity and weight loss. To prove these studies were carried out on normal, obese and diabetic subjects by oral administration of wheat  $\alpha$  amylase inhibitor have shown delayed carbohydrate absorption, a reduction in peak

postprandial plasma glucose concentrations with no malabsorption or other symptoms. More recently, the binding parameters of the association between wheat  $\alpha$  amylase inhibitors and porcine pancreas  $\alpha$  amylase and the high thermal stability of the proteins inhibitor have confirmed the potentially for its use as a nutraceutical molecule.

Action on improved glucose intolerance: Decreased rate of diabetes was seen in subjects with habit of consuming >6 cups of green tea per day compared to those who drank less than one cup a week, in an epidemiological study conducted in Japan. Additional support was garnered from a cross-sectional study which showed green tea consumers had less impaired fasting glucose. However close association between green tea consumption and glucose tolerance was not found. The consumption of oolong tea containing 386 mg epigallocatechin gallate (EGCG) decreased plasma glucose and fructosamine levels in twenty type-II diabetics. Plasma glucose and insulin was found to decrease in healthy volunteers consuming green tea extract (300mg EGCG) for 12 weeks. These subjects experienced light weight loss which could have affected insulin sensitivity rather than EGCG. Green tea beverage consumption in Asia results in high EGCG ingestion. Green tea catechins have been proven to show anti-diabetic, cardioprotective and anti-obesity effects in both animals and humans. Further controlled long term human studies would help to decide the optimal dose for prevention, management and treatment of metabolic syndrome.

**Marketed preparations:** Marketed preparations of the above mentioned spices, herbs, etc. are available in the market in the form of tablets, capsules, powder etc.

## 4. TREATMENT OF THE METABOLIC SYNDROME

In this section, we will review the prevention and treatment of the MS. The importance of appropriate assessment of IR and MS, global risk factor evaluation, continuity of risk in CVD, the nutrient-gene interaction, nutritional recommendations and clinical nutrition trials, the role of weight management, exercise, nutritional supplements such as vitamins, antioxidants, minerals, micronutrients and pharmaceutical drug intervention will be discussed.

## 5. CONCLUSION

With this changing lifestyle, individuals are more prone to disorders such as diabetes, hypertension and obesity etc. These disorders are known to be silent killers. In order to prevent the wide spread of these disorder, researchers have understood the importance of nutraceuticals and their benefits on health. The potential nutraceuticals should be evaluated further to study their mechanism responsible for the beneficial effect in metabolic syndrome.

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