

# Therapeutic Dietary Modifications Can Modify the Devastating Consequences of Cardio-Metabolic Syndrome (CMS): A Scientific Analysis



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**Submission:** April 16, 2018; **Published:** July 18, 2018

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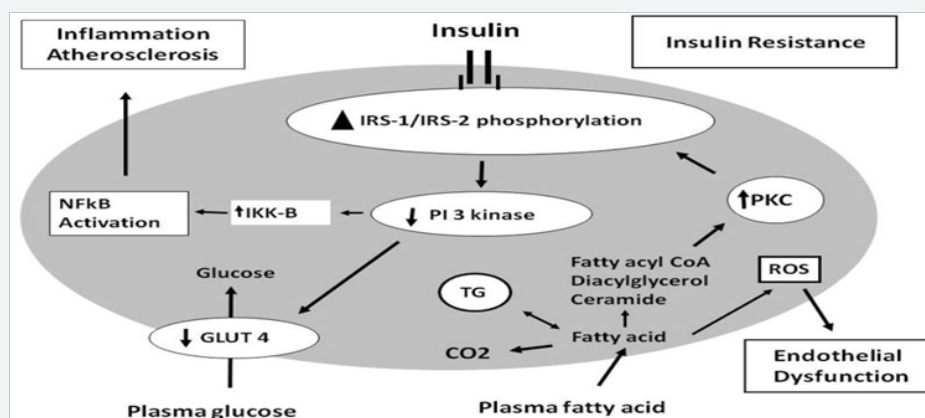
## Abstract

Cardio-metabolic syndrome (CMS) or Syndrome X is a disease of modern civilization. It is assumed that physical inactivity, obesity, sedentary life style, stressful life, shifting and drifting of socioeconomic status, changing the dietary pattern and tendency to cultural fission and fusion are prime factors associated with development of CMS. It has long term and devastating consequences and ultimate leads to death, if untreated. So, early diagnosis and proper treatment are necessary to combat the disease. By developing information, education and communication system to mass communities, changing the dietary pattern, therapeutic life style and adopt the different strategies, policies and interventions can reduce the mortality and morbidity of the sequential disease. It is an attempt to amalgamate the different therapeutic dietary modification strategies, techniques and policies to combat the CMS.

## Introduction

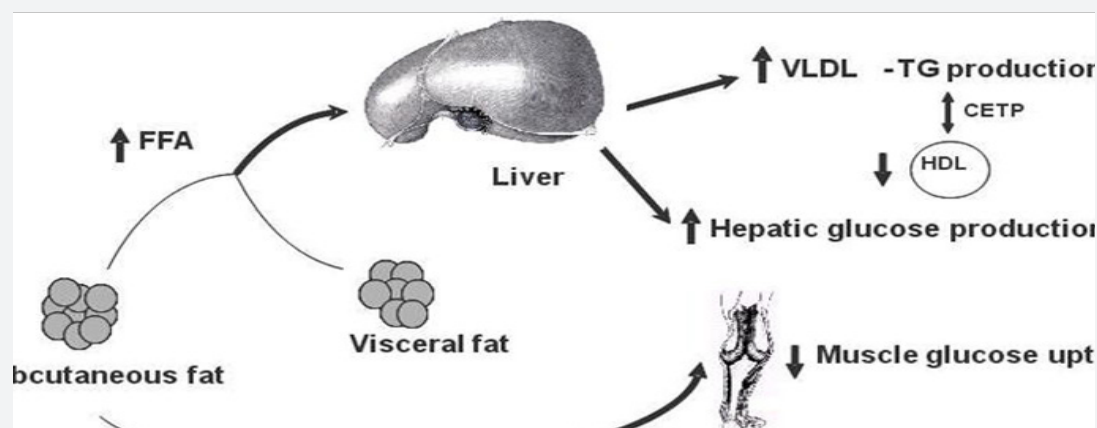
Cardio-metabolic syndrome or Syndrome X is a disease of modern civilization due to physical inactivity, obesity, sedentary life style, stressful life, shifting and drifting of socioeconomic status, changing the dietary pattern and tendency to cultural fission and fusion. The components of the syndrome are dysglycemia, raised blood pressure, elevated triglyceride (TG) levels; lower the high density lipoprotein (HDL-C)[1,2], central obesity and prothrombic state[3]. It is also associated with

cancer, chronic kidney disease and death. It has been proved that therapeutic dietary modification can reduce the devastating consequences of cardio-metabolic syndrome (CMS). It was estimated that approximately 47 million Americans were in high risk of heart disease because they were enrolled by a complex conditions like obesity, impaired glucose metabolism, hypertension and lipid disorders[4]. It is an attempt to amalgamate the different therapeutic dietary modification strategies, techniques and policies to combat the CMS.



**Figure 1:** Potential cellular mechanisms for fatty acid-induced insulin resistance.

IRS: Insulin Receptor Substrate; PI3 kinase: Phosphoinositide 3-kinase; PKC: Protein Kinase C; TG: Triglyceride; ROS: Reactive Oxygen Species; IKK $\beta$ : I-Kappa B Kinase Beta; NFKB: Nuclear Factor Kinase B4



**Figure 2:** Physiological relationships of fatty acid metabolism, insulin resistance and the features of the cardio-metabolic syndrome. CETP: Cholesterol Ester Transfer Protein; VLDL: Very-Low Density Lipoprotein Triglyceride; HDL: High Density Lipoprotein

### Mechanism of Development of CMS

(Figure 1 & 2).

#### Studies related to dietary pattern and cardio metabolic syndrome

Different studies found that the patients with metabolic syndrome trends to increase two folds risk of cardiovascular disease (CVD) and 5 folds increase the risk of type 2 diabetes mellitus (T2DM). Lifestyle changes like weight loss, increased physical activity and dietary modifications have been shown significant improvement of the marker of metabolic syndrome. It has been observed that low carbohydrate diets are more effective than low fat diets for resolving metabolic syndrome. It is recommended to reduce the consequences of Metabolic Syndrome by modification of diet such as carbohydrate diets <7% of total calories; trans-fat <1% of total calories, polyunsaturated fat up to 10% of total calories, monounsaturated fat up to 20% of total calories and fiber 20-30g/day, protein approximately 15% of total calories, cholesterol <200mg/day in total calories[5]. DASH (Dietary approaches to stop hypertension) dietary pattern emphasizes to consume more fruits, vegetables, low-fat dairy foods, whole grains, poultry, fish, nuts, seeds and legumes. Additionally, it is low in saturated fat, total fat, cholesterol, red meat, sweets, sugared beverages and refined grains. DASH was originally developed to manage or prevent high blood pressure[6]. Azadbakht et al. showed on clinical trial among the 116 men and women with MetS demonstrated that 6-months intervention with DASH diet significantly reduced body weight, waist circumference, triglyceride, systolic blood pressure, diastolic blood pressure, fasting blood sugar and also increased HDL-C (High density lipoprotein-Cholesterol) ultimately reduced the risk of the syndrome around 20%. In a randomized crossover clinical trial showed that DASH diet is reduced cardio metabolic risks among the type 2 diabetic patients and significant improvements in insulin sensitivity[7]. The Mediterranean diet (MD) which was first introduced by Ancel Keys in 1960s. It is used to follow by people in the different bordering countries

of the Mediterranean Sea including Greece, Spain, Southern Italy, Portugal and Turkey. This dietary pattern is characterized by daily consumption of non-refined cereals, vegetables (two or three servings per day), fruit (four to six servings per day), different olive oil products and nonfat or low-fat dairy products (one or two servings per day); weekly consumption of potatoes (four to five servings per week), fish (four to five servings per week), olives, pulses and nuts (more than four servings per week), more rarely poultry, eggs, and sweets (one to three servings per week), and monthly consumption of red meat and meat products (four or five servings per month with meals). Esposito et al. in a randomized clinical trial on 180 men and women for 24 month intervention with MD showed that prevalence of MetS was reduced by approximately 50%. The reduction in the prevalence of MetS was owed to significantly decrease in waist circumference, blood pressure, plasma glucose, total cholesterol and triglyceride concentrations, and a significant increase in HDL in the intervention group. A recent systematic review and meta-analysis of 50 studies including both observational studies and randomized controlled trials reinforced the benefits of MD on improving the MetS and it reduce the risk of developing the syndrome by 31%. Antioxidant and anti-inflammatory properties of the foods included in MD as well as high intake of vitamins and minerals reduce the incidence of MetS. Recently, it is shown that 2 months intervention with MD effectively increases total dietary antioxidant intake and plasma total antioxidant capacity. Olive oil is one of main food items of MD which has been shown to reduce cardiovascular risk factors, such as lipid profiles, blood pressure, postprandial hyperlipidemia, endothelial dysfunction, oxidative stress and antithrombotic profiles[8]. Phenolic compounds in olive oil have also shown antioxidant and anti-inflammatory properties that improve endothelial function[9]. Olive oil lowers NF-kB activation, thus leads to decrease in markers of inflammation (CRP, IL-6 and IL-8), oxidation and thrombosis[10]. Nuts are another high unsaturated fat food commonly consumed in the MD[11].

One study showed that forty-four healthy women and men (50-73 years, BMI 25-33, fasting glycaemia  $\leq 6.1$ mmol/L) participated in a randomized crossover intervention comparing a multifunctional (active) diet (AD) with a control diet (CD). Each diet was consumed during 4 weeks with a 4 weeks washout period. Active Diet (AD) included the following functional concepts: low glycemic impact meals, antioxidant-rich foods, and oily fish as source of long-chain omega-3 fatty acids, viscous dietary fibers, soybean, whole barley kernel products, almonds, stanols and a probiotic strain (*Lactobacillus plantarum* Heal19/DSM15313). AD promoted significant changes in total serum cholesterol ( $-26\pm 1\%$  vs baseline;  $P < 0.0001$ ), LDL cholesterol ( $-34\pm 1\%$ ;  $P < 0.0001$ ), triglycerides ( $-19\pm 3\%$ ;  $P = 0.0056$ ), LDL/HDL ( $-27\pm 2\%$ ;  $P < 0.0001$ ), apo B/apoA1 ( $-10\pm 2\%$ ;  $P < 0.0001$ ), HbA1c ( $-2\pm 0.4\%$ ;  $P = 0.0013$ ), hs-CRP ( $-29\pm 9\%$ ;  $P = 0.0497$ ) and systolic blood pressure ( $-8\pm 1\%$ ,  $P = 0.0123$ ) [12]. Williams et al. in a cross-sectional study demonstrated that a healthy balanced diet high in raw and salad vegetables, fruits, fish, pasta, rice and low in fried foods, sausages, fried fish, and potatoes was negatively associated with central obesity, fasting plasma glucose, and triacylglycerol and also positively associated with HDL-C [5]. Finally, scientific evidence suggested that reducing dietary carbohydrate is the prime approach for prevention or treatment of MetS. Increasing dietary protein as an approach to lowering dietary carbohydrates may be more effective than increasing fat.

### Clinical features of cardio-metabolic syndrome

- A. Dyslipidemia
- B. Type 2 Diabetes Mellitus
- C. Polycystic ovary syndrome
- D. Fatty liver resulting in inflammation and the potential for cirrhosis
- E. Micro albuminuria
- F. Obstructive sleep apnea
- G. Increased risk of dementia with aging
- H. Hypertension

According to the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart

Association (AHA), any three of the following criterias in the same individual can be diagnosed

as metabolic syndrome are:

1. Abdominal obesity: a waist circumference of 102cm (40in) or more in men and 88cm (35 inches) or more in women. For Asian Americans, the cutoff values are  $\geq 90$ cm (35in) in men or  $\geq 80$ cm (32in) in women.

2. Serum triglycerides 150mg/dl or above.
3. HDL cholesterol 40mg/dl or lower in men and 50mg/dl or lower in women
4. Blood pressure of 130/85 or more.
5. Fasting blood glucose of 100mg/dl or above.

### Laboratory tests suggested for CMS

1. Thyroid profile
2. Liver Function Tests
3. Lipid profile (Fasting)
4. CReactive Protein
5. Lipoprotein(a), apolipoprotein-B100(Apo)
6. Homocysteine
7. Hemoglobin-A1C levels
8. Uric acid
9. Microalbuminuria (Albumin/creatinine ratio)
10. Electrocardiography (rest/stress ECG)
11. Ultrasonography (vascular or rest/stress echocardiography) but fatty liver can be confirmed by nuclear magnetic resonance spectroscopy
12. Stress single-photon emission computed tomography (SPECT)
13. Cardiac positron emission tomography (PET)
14. Adipokine
15. Plasminogen Activator Inhibitor-1
16. Plasma glucose

### Management of CMS

#### Phyto-therapy for management of CMS

**Resveratrol (3, 5,4'-trihydroxystilbene found in grapes and other plant species):** Animal studies showed that resveratrol can reduce abnormal blood fat (cholesterol and triglycerides) and blood pressure and fight against inflammation [13].

**Alpha lipoic acid (spinach and broccoli):** An antioxidant that helps burn glucose to power the heart, brain and all other organs. It thus lowers glucose and insulin levels, reduces insulin resistance and slows the aging process [14].

**Gymnema sylvestre:** Treatment with DAGA (deacylgymnemic acid) resulted in a significant decrease in insulin resistance accompanied with a decrease in systolic blood pressure and improved glucose and lipid profile without decreasing body weight in a rat model of metabolic syndrome [15].

**Silymarin (Standardized):** An antioxidant flavonoid from the herb milk thistle, silymarin lowers/stabilizes blood glucose levels and protects the liver, the most important tissue involved in insulin utilization[16].

**Cinnamontree:** Bark (3gm) of the *Cinnamomumzeylanicum* (*Cinnamon*)-have shown reducepost prandial serum insulin and increased GLP-1 concentration without significantly affecting blood glucose in human[17].

**Wheat:** Fibers (24gm/day) of *Triticumaestivum* have shown increased short chain Fatty acid production and glucagon like peptide-1 secretion in human model for many days[18].

**Gardenia:** Fruit of the *Gardenia jesminoides* (*geniposide*) prevents the oxidative stress induced neuron apoptosis and improved glucose stimulated insulin secretion by activating glucagon like peptide 1 receptor in INS-1cell[19].

**CoQ10(Ubiquinol):** CoQ10 is a powerful antioxidant that modulates blood pressure apparently by reducing resistance to blood flow. It also is generally important for cardiovascular health. The body uses CoQ10 to convert food into energy and several trials have reported that supplementing with CoQ10 for 2.5-4 months significantly reduces hypertension[20].

**Fish oil (EPA/DHA):** EPA and DHA are key omega-3 essential fatty acids (EFAs) in the oil of fatty fish such as anchovies, sardines, salmon, herring, white albacore tuna, haddock and mackerel. The Journal of the American College of Nutrition 2002 has reported that EPA and DHA “may play an important role in the prevention and treatment of coronary artery disease, hypertension and other inflammatory disorders[21-23].

### Conclusion

Therapeutic dietary modification and life style change techniques can reduce the consequences of cardio metabolic syndrome. Though it is very difficult to change the dietary habit within in single intervention but continuous motivation can change the pattern of diet and life style. By modifying the dietary pattern, increasing the physical activities, avoiding sedentary life style and changing the life style can combat the morbidity and mortality of MetS.

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DOI: [10.19080/CRDOJ.2018.08.555726](https://doi.org/10.19080/CRDOJ.2018.08.555726)

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