Tocopherol Vs Tocotrienol (Vitamin E) in the Management of Metabolic Syndrome

Saima Rafique[1], Dilshad Ahmed Khan[2], Kulsoom Farhat[3], Mudassar Noor[3], Muhammad Asghar Khan[4], Mahjabeen Sharif[5]

ABSTRACT

Metabolic syndrome (Met-S) reflects a congregate of metabolic derangements including central obesity, hypertension, insulin resistance, dyslipidemia leading to enhanced risk of developing cardiovascular disease and diabetes. Both tocopherol (TCP) and tocotrienol (T3) have significant role in Met-S. However, it is still unclear regarding better clinical efficacy of either one in management of Met-S. This review compares clinical efficacy of different isomers of tocopherol with tocotrienol in stewardship of Met-S by search of human clinical studies only. Literature search was conducted till 20th May 2023 on PubMed, google scholar, open google search, pak- medinet and Cochrane data-bases. So far evidence revealed that Tocotrienol have been found safer and more beneficial as compared to tocopherol, having great potential in improving diabetes, hypertension and hyperlipidemia in Met-S patients and robust candidate for further future research regarding ameliorating obesity in metabolic syndrome.

Keywords: Metabolic Syndrome, Tocopherol, Tocotrienol, Obesity, Diabetes, Dyslipidemias.

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INTRODUCTION

Metabolic syndrome (Met-S) also known with the name of Syndrome X as well as Insulin Resistance Syndrome.[1] Met-S involves the presence of diabetes, systemic hypertension, obesity, hyperlipidemia leading to increased risk of cardiovascular disease.[2] It is a complex health disorder of metabolic abnormalities which is strongly linked to increased oxidative stress and inflammation. The initial approach for treating metabolic syndrome (Met-S) is lifestyle modification including healthy eating habits and regular intake of supplements.[3] Antioxidants are available in many food sources and can also be taken in the form of supplements, making them an accessible option for people looking to improve their overall health.[4] Research suggest that vitamin E has a positive impact on various cardiometabolic indices, including lipids, fasting blood sugar, blood pressure, obesity in patients with metabolic syndrome.[5] Vitamin E, two major forms, Tocopherol (TCP) and Tocotrienol (T3) with its various isomers have been found to have potential role as antioxidants in metabolic syndrome. Vitamin E comprises of tocopherol (TCP) and tocotrienol (T3). Each TCP and T3 consists of 04 isomers: α-, β-, γ-, δ- which are fat-soluble in nature. Natural source of TCP and T3 are oil seeds and nuts. TCP are found in oils of olive, nuts, almonds, soybean, corn, rapeseed, linseed and sunflower. Whereas T3 are found in hazelnuts, wheat germ, barley, oats, maize, annatto oil, palm and rice bran oil.[6] All isoforms of vitamin E have pro-apoptotic, anti-oxidative, anti-angiogenic, anti-proliferative and anti-inflammatory activity. Their beneficial role may be due to scavenge free radicals, modulate signal transduction and gene expression in inflammation.[7] Chemical structure of TCP contain saturated C16 side chain whereas T3 contain three unsaturated double bonds.[8] TCP and T3 being dietary antioxidants can prevent the damage caused by reactive oxygen species and chronic inflammation, thereby decreasing the negative impact of free radicals on human body.[9]

Based on current research, it appears that no study has compared the effectiveness of tocopherol (TCP) versus tocotrienol (T3) in the management of Met-S, making this study a unique contribution to fill the knowledge gap. The aim of current review is to present an update regarding comparison of efficacy of TCP with T3 in management of metabolic syndrome in humans.

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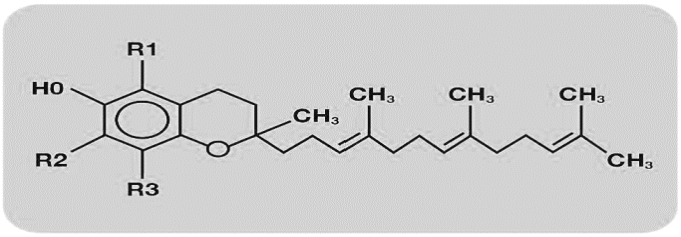
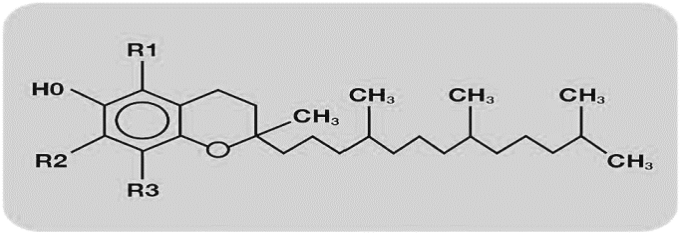


Tocotrienol Molecule



Tocopherol Molecule

Figure 1. Chemical structure of tocopherol (TCP) and tocotrienol (T3) isoforms.[8]

LITERATURE REVIEW

Abdominal obesity is the most frequently observed component of metabolic syndrome.[10] Obesity has increased globally with around 2.81 million people dying around a year due to being obese. Human obesity is now becoming prevalent world-wide. Obesity can be controlled by lifestyle changes, with less food intake and more physical workout. Anti-obesity drugs such as phentermine, orlistat & lorcaserin has been employed to reduce weight but these drugs can cause many adverse effects.[11] Increased adipose tissue leads to activation of inflammatory signaling pathways, increased synthesis of cytokines and immune response mediators cause chronic inflammation. Chronic inflammation in obesity results in increased oxidative stress leading to disturbance in balance of oxidants & antioxidants in human body.[12] As far as till the latest available research, it is the first review to compare efficacy of TCP with T3 in management of Met-S. Different studies have been done to show association of obesity with TCP and T3. In individuals with metabolically unhealthy obesity (MUO), a study discovered that the levels of certain antioxidant nutrients (retinol, beta-carotene, and Vitamin E) were inversely associated with metabolic alterations. This suggests that having higher levels of these nutrients may be favorable in declining the risk of metabolic complications in individuals with obesity.[13] Regarding tocopherol, one cross-sectional study found association between serum α-tocopherol levels and Met-S in Korean population by using multivariate logistic regression model on 2672 males and 3213 females. Dose-dependent association was revealed between serum α -tocopherol levels and Met-S. High levels of serum α-tocopherol showed association with increased threat of Met-S.[14] On the contrary, a clinical trial was conducted in Argentina on 13 males and 9 females to explore effects of combination of α- tocopherol with resveratrol & piperine on chronic inflammation in Met-S. Results revealed a decrease in chronic inflammation and adipogenesis by alpha tocopherol in Met-S patients[15] .Another research trial conducted on obese persons (n=60) with age of 18–54 years to determine relationship between 1.5 month weight loss program and α-tocopherol levels. This program included 03-day record method by using semiquantitative food-frequency questionnaire along with measurements of height (H), body weight (BW), hip circumference (HC), waist circumference (WC) and fat mass (FM). Significant reduction in carbohydrate and fat intake in all participants ($P < 0.001$) lead to decline in BW, WC, FM and body mass index (BMI) during 6 weeks weight loss program. Significant decline in serum α-tocopherol levels were observed within this period ($P < 0.006$) in 78% women and 68% males, after following 6 weeks of Antiox Obesity program. Males revealed more reduction in anthropometric measurements as compared to females. Serum α-tocopherol levels were reduced after weight loss program along with enhanced threat of oxidative stress in adults. Anti-obesity program requires monitoring in order to avoid deficiency of α-tocopherol in body. Supplements or diet with high dietary α-tocopherol should be given to obese people during weight loss programs.[12]

So far, no study has been done regarding effects of tocotrienol (T3) on human obesity, although various animal studies have been reported with anti-obesity effects of (T3) in animals.

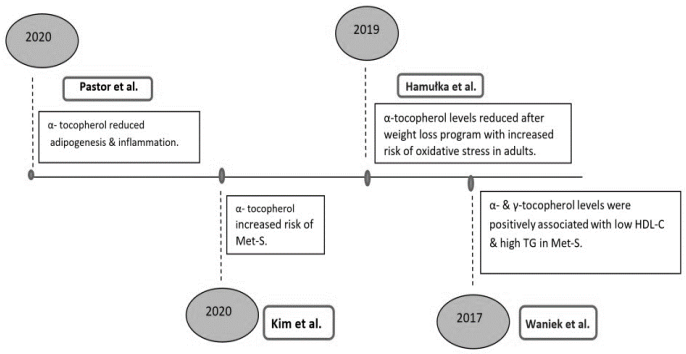


Figure 2. Timeline summary of human studies showing the association between Tocopherol (TCP) and obesity. [12,14,15, 21]

It is an important fact that diabetes occurs either by deficiency of insulin or due to resistance of insulin. Oxidative stress is the main culprit leading to progression of high blood sugar levels. Due to upsurge in free radicals' productions with downtrodden antioxidant defense processes result in damage at cellular level, enhanced lipidic peroxidation leading to development of insulin resistance.[16] There is a need for antioxidants to repress inflammation. Whereas, a randomized trial on 98 type 2 diabetes mellitus (T2DM) patients with vitamin A plus E supplementation combined with zinc showed improve β-cell function, glycemic control and insulin secretion.[17] Encouraging results have been observed with different isomers of tocotrienol on diabetes. The Venus randomized controlled trial (2011-2015) examined T3's effects on glycemic control of diabetics and neuroprotection. Among 229 diabetic individuals, 1-year oral supplementation of mixed T3 improved glycemic control but had no effect on neuropathic symptoms. The 400 mg/day dose was deemed safe, with no observed adverse

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effects.[18] In a randomized controlled trial (RCT) involving 110 T2DM patients taking oral hypoglycemic drugs were randomly assigned to either tocotrienol group or placebo group. They were administered 250 mg δT3 daily for a duration of 24 weeks. δT3 supplementation along with oral hypoglycemic drugs improved glycemic control in T2DM patients without adverse effects. It can be a beneficial supplement to avoid diabetic complications.[19]

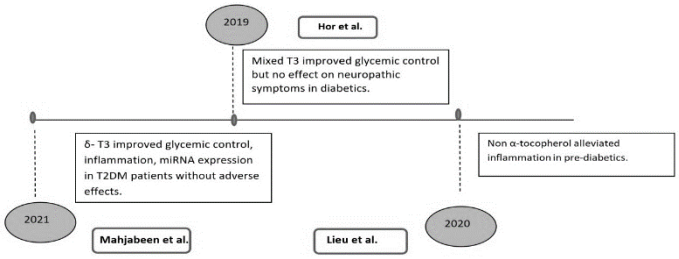

Figure 3. Timeline summary of human studies showing the association between Tocopherol (TCP) and Tocotrienol (T3) and diabetes.[17-19]

Dyslipidemia is the chief culprit for obesity, atherosclerosis, cardiovascular disease, ultimately leading to Met-S.[15,] Metabolic syndrome involves increased plasma triglycerides and decreased high-density lipoproteins (HDLs) leading to cardiovascular disease mainly myocardial infarction which have remained most common cause of mortality all over the world.[16] In human trial conducted by Podszun et al. showed reduction of intrahepatic triglyceride (IHTG) by intervention of α-tocopherol in (NAFLD) patients. Whereas combination of tocotrienol with polymethoxylated flavones (PMF–TT) showed no better effects on elevated LDL-C and high sensitive-C-reactive protein (hs-CRP) levels as compared to placebo.[20] Similarly, in a crosssectional study conducted in Northern Germany involving 641 individuals, researchers aimed to investigate relationship between circulating α and γ-tocopherol serum levels and various adiposity-related traits. The study found that higher levels of alpha- and gamma-tocopherol were having positive association with raised triglycerides and low HDL-C levels.[21]

Hypertension mainly involves increased oxidative stress in the body.[22] A randomized, placebo-controlled clinical trial was conducted in pregnant ladies to explore the effects tocotrienol-rich fraction (TRF) 100 mg daily in preventing pregnancy-induced hypertension. The results revealed reduction in incidence of pregnancy-induced hypertension.[23]

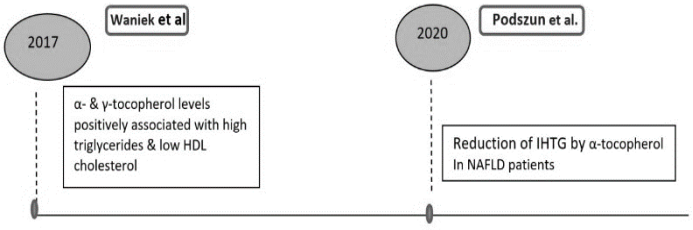

Figure 4. Timeline summary of human studies showing the association between Tocopherol (TCP) and dyslipidemia.[20,21]

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CONCLUSION

Tocotrienol (T3) may be a safe and effective option as compared to tocopherol (TCP) for treatment of individuals with metabolic syndrome (Met-S).

AUTHOR'S CONTRIBUTION

Rafique S: Acquisition of data, write up for entire manuscript, designing figures and drafting
Khan DA: Topic selection, critical review of finalization of entire manuscript
Farhat K: Supervision for Finalization of entire manuscript and final approval of version to be published
Noor M: Literature search for reference gathering**.**
Khan MA: Literature search and final approval of version to be published
Sharif M: Introduction write up and result summarization.

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