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Role of Curcuma Longa in Type 2 Diabetes and its Associated Complications

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Background: Occurrence of Diabetes and its related complications increased all over the world due to recent lifestyle trends. A higher proportion of ultra-processed foods in the diet have been associated with a higher risk of T2D. A lack of fiber and a surplus of refined simple carbohydrate are contributing to obesity and diabetes diagnosis. Hence there is need to evaluate different nutraceuticals for the management of Diabetes.
Methodology: A Scopus, pub Med/Medline and Google Scholar electronic database search was done by using the key word role of *Curcuma Longa* in diabetes type 2 and its associated complications to review the related articles.
Summary: Curcumin a yellow color powder is one of the most important components of *Curcuma Longa L*; and commonly utilized as food additive in Asian countries. Pre-treatment of human umbilical vein endothelial cells curcumin leads to decrease in intracellular MGO level induced by exogenous MGO and also modify the carboxymethyl cellulose formation. Curcumin nutritional supplement fully normalized arterial AGEs. Curcumin reduced AGEs increase in the heart of diabetic rats. Curcumin reduces the development of diabetes in pre-diabetic population.

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Conclusion: The literature review shows that the *Curcuma Longa L;* revealed anti-diabetic and antioxidant effects and prevent the development of diabetes associated complications in different animal model.

Keywords: Type 2 diabetes; curcuma longa; advance glycation end products (ages); carboxymethylcellulose.

1. INTRODUCTION

21 countries and territories including Pakistan are categorized as Middle East and North Africa (MENA) Region by International Diabetes Federation (IDF). As per IDF statement 55 million people are suffering from diabetes in MENA region that will increase up to 108 million by 2045. The prevalence of adult type 2 diabetes is 17.8% in Pakistan that is 148% more than formerly specified. In type 2 diabetic patients poor glycemic control is responsible for progression of advance glycation end products.

Occurrence of Diabetes and its related complications increased all over the world due to recent lifestyle trends. A higher proportion of ultra-processed foods in the diet have been associated with a higher risk of T2D [1].It has been estimated that 578 million in 2030 and 700 million in 2045 develop diabetes all over the world [2]. Resistance towards insulin is early sign for type II diabetes and associated with obesity, hypertension and circulatory disorder [3].

Several research reports have documented the effects of air pollution, walking, food and physical activity in the management of diabetes. A novel term of Geoenvironmental Diabetology has been invented for studying the interaction of diabetic patients with environment. It has been reported that green space and increased level of physical activity are associated with lower risk for type 2 diabetes whereas air pollution and high levels of noise are linked with greater risk for type 2 diabetes. Extreme weather and earthquake like natural events are responsible for extra stress in type 2 diabetic patients. Environment also has greater impact on factors like metabolic control, mortality, quality of life and health care utilization [4].Obesity is top most risk factor for diabetes type 2 that according to CDC affecting 93.3 million adult peoples in U.S [5].

Obese type 2 diabetic patients can manage their blood glucose better by dropping 5% to10% of their total body weight and people with pre-diabetes such modest weight loss could reverse their symptoms [6]. Sit less and move more is the first recommendation, according to 2018 physical activity guidelines issued by CDC as inactivity and increased body weight moving the persons towards type 2 diabetes diagnosis. Insulin receptors are present more on muscle cell than fat cells, one can by exercising decrease resistance towards insulin. Increase activity decreases blood glucose level also by increasing the efficacy of insulin [7]. More than 90% of type 2 diabetes peoples are overweight [8]. A lack of fiber and a surplus of refined simple carbohydrate are contributing to obesity and diabetes diagnosis. Switching to a diet centered on complex carbohydrates (brown rice, think sweet potatoes, lentils), fruits and vegetables richer with fiber (berries, leafy greens), lean protein (poultry, fish) and healthy fats (avocado, olives, seeds and nuts) can essentially prevent or reverse type 2 diabetes.

2. MATERIALS AND METHODS

A Scopus, pub Med/Medline and Google Scholar electronic database search was done by using the key word role of *Curcuma Longa* in diabetes type 2 and its associated complications to review the related articles. All the related articles those met with inclusion criteria were stated in this review article.

2.1 Inclusion Criteria

These includes controlled trials, clinical trials, systematic reviews, randomized controlled trials and meta-analysis dealing with *Curcuma Longa* as a single agent or in combination with other herbs.

2.2 Exclusion Criteria

This includes comments, Research protocols, articles without abstracts or having incomplete text and articles lacking related information.

3. DISCUSSION

3.1 Advanced Glycation End Products (AGEs)

Non-enzymatic glycation of lipids or proteins, due to hyperglycemia leads to formation of damaging

compounds known as advanced glycation end products (AGEs) [9]. These harmful glycated substances can be formed exogenously and endogenously by high temperature processing and hyperglycemia respectively. Receptor for advanced glycation end products (RAGE) and advanced glycation end product receptor 1(AGE-R1) are the two major classes of plasma membrane receptors those interfere with the impacts of AGEs. RAGE receptor stimulation leads to enhancement of oxidative stress, inflammation and cell growth [10] whereas AGE-R1 stimulation contributes in elimination and detoxification of advanced glycation end products [11].

AGEs are one of important pathway responsible for the development and progression of diabetes related complications including retinopathy, neuropathy and nephropathy. It has been also observed that the AGEs in tissues and blood are present in higher concentration in smokers [12]. AGEs those accumulate in retina, kidney and atherosclerotic plaques are responsible for diabetes related complications in diabetic patients [13,14,15]. Studies have reported that AGEs also play a very important role in diabetic retinopathy development (16) cataract formation [17] and in neuropathy that leads to diabetic foot [18]. It has been also revealed that heart failure and cardiomyopathy are more common in diabetic patients than non-diabetic populations [19].

Metabolic reaction that leads to formation of free radicals if not scavenged those leads to change the proteins, carbohydrate and lipid forms. Constant hyperglycemia increases the oxidative stress that is associated with energy metabolism and inflammatory mediator changes. Oxidative stress also plays a key role in the pathophysiology complications of diabetes [20].

In diabetes the medical challenge that still remain is the blood glucose maintenance in normal range. Largely the medicine that are used, responsible for enhancing sensitivity of insulin, maintaining the blood glucose level in normal range and decreasing the oxidative stress. Number of different therapies are tried for slowing the disease progression. It has been reported that in Indian traditional medicine different products from plant source are used in for diabetes management, having the hypoglycemic and anti-oxidant effects [21].

3.2 Curcuma Longa

Curcumin a yellow color powder is one of the most important components of *Curcuma Longa L*; and commonly utilized as food additive in Asian countries [22]. Curcumin possess major role as a medicinal herb with therapeutic characteristics in traditional medicine [23]. Curcumin is responsible for reducing the cholesterol, platelet aggregation, blood pressure, myocardial infarction, thrombus formation and inflammation in rheumatoid arthritis [24]. Curcumin has been found to possess anti-inflammatory effect in various rodent models. Its antioxidant effects have been found to produce beneficial effects in diabetes and prevention of insulin resistance by decreasing the death of beta cell and increasing their functions [25,26,27,28,29]. Curcumin has favorable effect on body weight due to its anti-inflammatory effect.

Turmeric commonly utilized in Southeast Asia countries as additive for giving flavor, color and adding the spice to different food preparation. In Siddha, Ayurvedha and Unani medicine, Curcuma Longa used as traditional therapy for management of numerous diseases as a home remedy. Curcuma longa consists 2-8% of curcumin. According to different studies *Curcuma Longa L*; has anti-inflammatory property [30], potent antioxidant [31] and also possess anticancer property [23]. The mouse model previous studies indicated that *Curcuma Longa* oral ingestion reverse inflammatory complications improve glycemic control and improve metabolic disturbance of obesity [32].

3.3 *In vitro* Studies

Hu et al. [33] have observed the curcumin effects on capacity of methylglyoxal MGO-trapping and carboxymethylcellulose protein expression, an AGEs member present in human umbilical vein endothelial cells. It has been also reported by authors that carboxymethylcellulose expression in human umbilical vein endothelial cells have significantly enhanced by exogenous MGO, whereas pre-treatment of human umbilical vein endothelial cells curcumin leads to decrease in intracellular MGO level induced by exogenous MGO and also modify the carboxymethylcellulose formation that induced by exogenous MGO in dose dependent manner. Sun et al [34] investigated the Curcumin effect on AGEs formation in human umbilical vein

endothelial cells with the help of two different methods. The investigators analyzed the reaction kinetics by incubation of MGO and human serum albumin with or without curcumin in different doses and conclude that MGO induced AGEs formation significantly inhibited by curcumin in dose dependent manner.

Li et al. [35] have observed Curcumin derivative inhibitory effect on non-enzymatic glycosylation and concluded that the all curcumin derivatives were responsible for inhibition of AGEs formation. Li et al. [35] observed the Curcumin effects including its MGO trapping capability, anti-glycation abilities and suppressing the AGEs formation.

3.4 Animal Studies

Fleenor et al. [36] observed Dietary Curcumin supplementation effects on AGEs in old and young mice by addressing aorta arterial AGEs expression. It was reported that young mice had low arterial AGEs related to old mice. Conversely Curcumin nutritional supplement fully normalized arterial AGEs. Sajithlal et al. [37] studied the Curcumin effect on advanced glycation in rat with diabetes. The Curcumin was administered in diabetic orally for 8 weeks. The AGEs level was observed in skin and tail tendon and concluded that the higher level of AGEs were present in diabetic rats as compare to control animal. Yu et al. [38] observed the Curcumin effects on controlling of diabetic cardiomyopathy on experimental diabetic rat. Orally diabetic rat were administered a 100 or 200 mg/kg/day of Curcumin for 16 weeks and noticed that Curcumin reduced AGEs increase in the heart of diabetic rats. Hassan et al. [39] studied the defensive effect of Curcumin– induced hemeoxygenase-1 against high blood pressure associated with diabetes. Daily injection of 5mg/kg of Curcumin was administered in experimental diabetic rats for 6 weeks and concluded that diabetic rats had significantly increased level of serum AGEs than control group.

3.5 Human Studies

Chilelli et al. [40] observed the effect of Curcumin with Boswelliaserrata (BSE) gum resin in randomized control trial on glycoxidation in regularly exercising athletes. 47 male athletes participating in the study were divided into two groups. Group 1 included 22 subjects on a Mediterranean diet (MD) only and group 2 included 25 number of subjects on Mediterranean diet (MD) along with curcumin and BSE gum resin for 3 months. It was concluded that in curcumin with BSE gum resin group AGEs was significantly decrease.

HomaHodaei et al [41] studied the effect of curcumin supplementation on weight and fasting blood glucose and concluded significant reduction in weight and fasting blood glucose. Bradford (42) has been also studied that the curcumin is responsible for the weight loss due to its anti-inflammatory effects.

240 pre-diabetic patients were observed in double blind randomized clinical trial by Chuengsamarn[43]. The subjects were divided into two group, one who is on 250 mg curcuminoid capsule/day and other taking a placebo capsule. After the 9 months not a single person on curcuminoid supplement diagnosed with diabetes and also showed decrease in insulin resistance along with increased adiponectin level where as 16.4% of patients on placebo were developed the type 2 diabetes.

According to Usharani et al [44] administration of 300 curcumin capsule supplements for 8 weeks in type 2 diabetic patients leads to improved antioxidant status as compare to atorvastatin.

Neerati et al [45] observed the effect of curcumin (475mg) supplementation in type 2 diabetic patients who are taking glyburide. Curcumin supplements leads to significantly improved lipid profile by decreasing the LDL, VLDL and triglyceride level and increasing the HDL level.

In type 2 diabetes patients Panhai et al [46] observed in randomized clinical trial the effect of curcumin 500mg/day in combination with piperine 5mg/day compare with placebo. There is significant improvement in glycemic control, reduction in C-peptide serum level and HBA1c in treated group compare to placebo.

According to one study [47] on 100 type 2 diabetic overweight/obese patients divided into 2 groups (300mg/day curcumin supplement group and placebo group) for three months, the curcumin supplement leads to significant decrease in HbA1c, reduction in fasting blood glucose level, along with improvement in activity of lipoprotein lipase and reduction of serum triglyceride.

According to one pilot study of Mexico curcumin dietary supplementation decreases the oxidative stress in proteinuric chronic kidney disease diabetic or non-diabetic patients [48].

Panahi et al. performed trial and concluded beneficial effect of curcuminoid plus piperine on hepatic parameter and glycemic control [49].

Vanaie et al. performed trial and revealed that oral curcumin administration presented beneficial effect on renal function by decreasing the albuminuria significantly [50].

4. CONCLUSION

The literature review shows that the *Curcuma Longa L;* revealed anti-diabetic and antioxidant effects and prevent the development of diabetes associated complications in different animal model. The in vitro studies also showed promising results for the management of diabetes type 2 and its associated complications. There is few clinical trials also studied its role as anti-diabetic agent and found promising results, but in most of the clinical trial curcumin is used in combination of certain other additive. There is shortage of studies about Curcuma Longa role in controlling the diabetes and its associated complications particularly as antiglycation agent in humans in real world setting outside the clinical trial. It is therefore needed to test the efficacy of Curcuma Longa in type 2 diabetes and its associated complications by using different dose as above studies showed that dose up to 15 gram of Curcuma Longa is safe.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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