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EVALUATING THE THERAPEUTIC POTENTIAL OF CURCUMIN IN THE MANAGEMENT OF DIABETES MELLITUS

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ABSTRACT:

Curcumin, found in Curcuma longa as a yellow pigment, is a bioactive chemical with tremendous medicinal potential for the treatment of diabetes mellitus. This metabolic condition is characterized by an inappropriate regulation of blood glucose levels brought on by inadequate insulin production and/or action. Curcumin targets the primary pathways that lead to diabetes, such as oxidative stress and β-cell dysfunction, using its antioxidant, anti-inflammatory, and anti-apoptotic capabilities. Findings of research suggest that curcumin effectively reduces fasting blood glucose and improves the activity of insulin and β-cells, thus preventing pancreatic damage. Interesting enough is the finding that curcumin has been reported to protect β-cells from oxidative damage and apoptosis by regulating the activities of NADPH oxidase, inflammatory cytokines, etc. This also revealed that curcumin might prevent the transition from pre-diabetes to type 2 diabetes and reduce insulin resistance in diabetic models. In vitro experiments further showed that curcumin protected the islet cells against oxidative stress through high glucose, and thus it adds further evidence to its potential role as a therapeutic agent. Despite the drawback of its poor bioavailability, the therapeutic efficacy of curcumin recently improved with some new formulations combined with excipients or synthesized analogy. Curcumin is considered a promising adjunct to the therapy of diabetes because it is safe and affordable and multi-beneficial, thus deserving further clinical research for optimization in the use of curcumin in the therapy of diabetes.

Keywords: Therapeutic Potential, Curcumin Management, Diabetes Mellitus, Turmeric.

INTRODUCTION:

An indication of diabetes is seen in those with high blood glucose levels. These people have deficiencies in the secretion and/or action of insulin, which prevents them from metabolising glucose. Numerous variables, such as inadequate physical exercise, excessive food and drink consumption, obesity, stress, and industrialisation, might contribute to the development of diabetes in addition to environmental and genetic factors. Chronic

hyperglycemia can lead to irreversible harm, impaired function, and organ damage, especially in the areas of the kidneys, heart, blood vessels, nerves, and eyes.

There are several different kinds of diabetes, including type 1 (T1D), type 2 (T2D), gestational diabetes, and others. Diabetes mellitus type 1 and type 2 are the two most common forms of the disease. The root cause of type 1 diabetes is an absolute failure of the immune system to secrete insulin. A significantly more prevalent form, type 2 diabetes, develops when insulin secretory response is inadequate and insulin action is resistant. Losing weight, exercising regularly, and/or taking oral drugs to reduce glucose levels can help diabetics achieve appropriate glycaemic control. On the other hand, individuals with severe β-cell breakdown and no residual insulin secretion cannot survive without insulin. Restoring and repairing the bulk of β-cells allows for the regulation of blood glucose levels through insulin production. Problems can develop throughout the body if a diabetic experiences oxidative stress. One of the reasons why the pancreatic β-cells secrete less insulin is the increase in oxidative stress and free radicals in the human body. The use of antioxidants in diabetic treatment may thus be essential. Research has shown that curcumin, due to its remarkable medicinal properties, can be an important component in diabetes treatment by attempting to halt the decrease of β-cell activity.

Turmeric contains the primary curcuminoid curcumin, which is structurally related to diferuloylmethane. Curcuma longa L., a perennial herb, is a member of the Zingiberaceae family. The tuberous rhizome of the turmeric plant has multiple uses, including as a spice (it can be used as a substitute for ginger), a dye, and a medicinal herb. It is a crucial component of many Indian curries. You won't find turmeric growing wild anywhere else than India. It was around 500 BCE that turmeric initially gained prominence in Ayurvedic medicine. The three main curcuminoids are curcumin, desmethoxycurcumin, and bisdemethoxycurcumin (Figure 1).

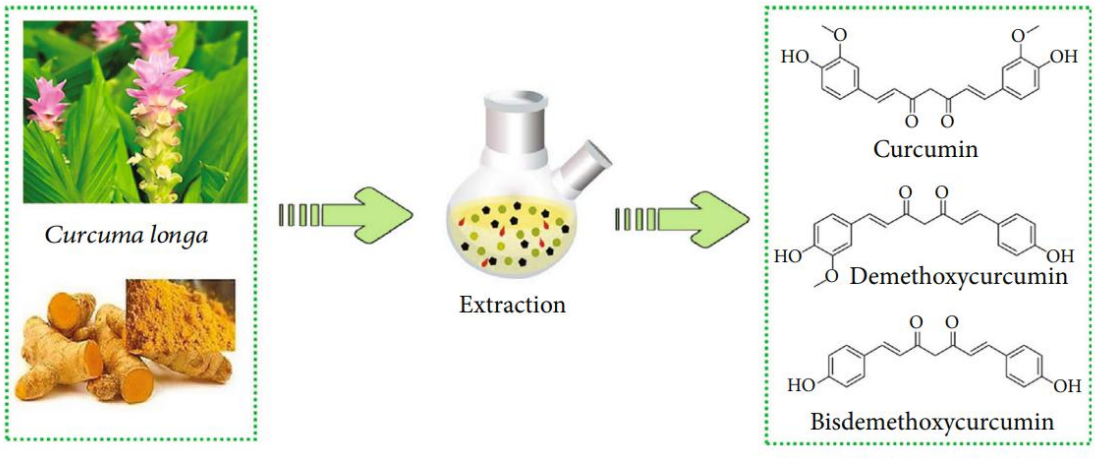

Figure 1: Chemical structures of most important curcuminoids

Curcumin is the most potent of them and has the greatest health impact. Admitting the distinction between turmeric and curcumin extracts or solutions is crucial. Curcumin is one of the curcuminoid chemicals found in turmeric, which are bioactive substances called curcuminoids. While turmeric does include some curcuminoids, the majority of these active curcuminoids are curcumin, which accounts for approximately 75% of them. Due to its ability to multitarget in numerous degenerative diseases, the curcumin molecule has medicinal and nutritional promise. Curcumin supports a healthy equilibrium in a variety of conditions, including anxiety, arthritis, metabolic syndrome, oxidative stress, inflammatory disorders, and hyperlipidemia. In addition to its antioxidant and anti-amyloid effects, curcumin also has antibacterial, anticancer, immune-modulating, and neuroprotective capabilities. By controlling the release of serotonin and dopamine, curcumin has shown antidepressant effects. It is well-known that medicinal curcumin has a number of drawbacks, including limited bioavailability, low stability, modest penetration, rapid metabolism, and targeted efficacy.

LITERATURE REVIEW:

Salehi et al. (2019) reviewed the promising therapeutic value of Curcuma longa L. and its major bioactive compound, curcumin, in traditional medicine practice for ages. There were documentations of health benefits of Curcumin in various in vitro, ex vivo, in vivo, and clinical trials to prevent diseases, promote health, and add it into treatments. The report scrutinized clinical studies that established the activity of curcumin on different types of diseases, including inflammation, dermatologic diseases, ophthalmologic diseases, central nervous system diseases, respiratory and cardiovascular diseases, gastrointestinal and urogenital disorders, metabolic dysregulation, as well as poisoning cases. There have been reports of curcumin's activity on several types of cancers. Although several clinical studies were conducted in the recent past, significant variations in the estimation of curcumin's biological effects were observed by the authors, highlighting the necessity for more standard approaches in further studies.

Yang et al. (2021) Only 2-9% of turmeric's curcuminoids are active curcuminoids, with curcumin accounting for around 75% of them. Given its capacity to multitarget in a range of clinical conditions, the curcumin molecule holds great promise as a therapeutic or nutraceutical agent. Curcumin can normalize hyperlipidemia, oxidative stress, inflammatory disorders, metabolic syndrome, anxiety, and arthritis. Curcumin has qualities that modulate the immune system, prevent tumors, kill bacteria, and reduce the effects of amyloid. It also has neuroprotective effects. As a result of its ability to modulate the release of serotonin and dopamine, curcumin has shown promise as an antidepressant. Curcumin has a number of well-known drawbacks when used therapeutically, including inadequate bioavailability, minimal penetration, rapid metabolism, low stability, and targeted effectiveness.

Quispe et al. (2022) conducted a comprehensive review of curcumin, a polyphenol compound from Turmeric with known bioactive properties that the therapeutic use of curcumin on diabetes mellitus - one of the chronic metabolic diseases, usually get long-term medications and lifestyle adjustments. Curcumin is an herbal supplement that has raised much interest in preventing diabetes and management due to its potential bioactive properties. However, some of the challenges it faces in exerting its potential are poor solubility, limited absorption, and low bioavailability. The review focused on nanotechnology-based formulations aimed at improving curcumin's pharmacokinetics to address these concerns. This study explored the use of nanocurcumin as a nanoparticle-based formulation of curcumin. PubMed/MEDLINE and ScienceDirect databases were searched, finding studies reporting pharmacological mechanisms whereby nanocurcumin reduces hyperglycemia-a core characteristic of DM. Thus, outcomes indicated that nanocurcumin improved therapeutic efficacy of curcumin by improving its bioavailability and biochemical pathways associated with enhanced antidiabetic effects. Conclusion Nanocurcumin could be promising as an adjunct for diabetes management strategies to afford a valid alternative for better glycemic control and improved outcomes for patients.

Marton et al. (2021) reviewed the literature on the effects of curcumin, a bioactive component found in the spice Curcuma longa, on diabetic mellitus (DM), a metabolic condition that is becoming more prevalent around the world. Diabetes mellitus (DM) is a complex disease with many facets; managing it mostly involves making lifestyle changes and taking medicine for an extended period of time. Curcumin is being considered as a possible therapeutic agent for the treatment of diabetes mellitus (DM) due to its antioxidant, anti-inflammatory, anticancer, neuroprotective, and anti-diabetic characteristics. The PUBMED and EMBASE databases were combed extensively by the researchers. The researchers included sixteen studies in their analysis after they met their inclusion criteria. The study's authors hypothesised that curcumin's ability to reduce inflammation and oxidative stress may explain its anti-diabetic benefits. Diabetic patients' fasting blood glucose, glycated hemoglobin (HbA1c), and body mass index (BMI) were all markedly decreased after taking curcumin. Another name for curcumin in its nanoparticle form is nanocurcumin. Plasma malonaldehyde, serum C-reactive protein, total cholesterol, triglycerides, VLDL-c, LDL-c, and HDL-c were all decreased by nanocurcumin. Based on these results, it seems that curcumin, particularly in its nanoform, may have positive effects on glycemic control and other diabetic problems by lowering risk factors.

COMPOSITION, STRUCTURE AND FUNCTIONS OF CURCUMIN:

Curcuma is a member of the Zingiberaceae group and is a perennial herbaceous plant with established

rhizomes. China and India are where it is primarily farmed. It was initially recognised for its use as a spice or food addition in cooking (curries, for example). The primary ingredient in curcuma (fig. 2), curcumin, provides significant health advantages. According to traditional Chinese medical belief, curcumin reduces pain. Abdominal distention, arm discomfort, fall injuries, amenorrhoea, and other illnesses can all be treated with it. According to current medical research, the phenolic compounds that are isolated from Curcuma longa's rhizome (fig. 3) have a number of preventive actions against metabolic diseases associated with diabetes and are crucial in lowering blood lipid levels. They also possess anticancer, anti-inflammatory, and antioxidant qualities. Curcumin's price, safety, and ease of extraction are further benefits. Nowadays, a variety of techniques have been used to increase curcumin's bioavailability, including mixing it with suitable pharmaceutical excipients, creating curcumin analogues, or altering dose formulations. Curcumin has promising therapeutic potential as a medication.

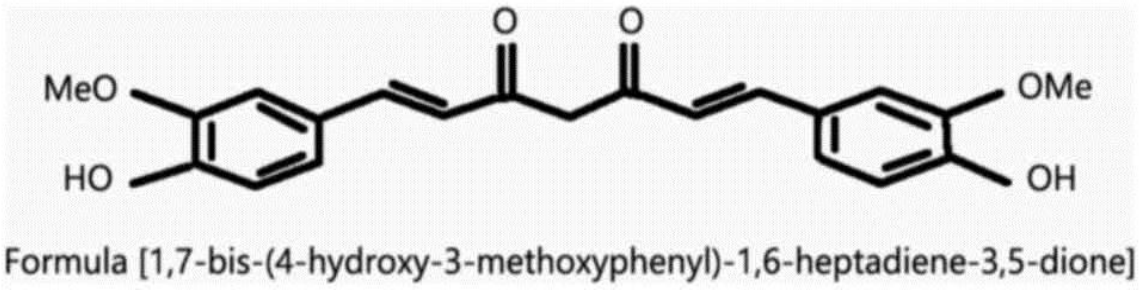

Figure 2: Chemical Structure of Curcumin

Figure 3: Rhizomes of Curcuma Longa and Powder Turmeric

THERAPEUTIC EFFECT OF CURCUMIN ON DIABETES:

One type of metabolic disorder is diabetes. Its prevalence has skyrocketed in recent decades (28), and as diabetes is a chronic condition that can harm multiple organs, prevention and treatment have become more and more important. According to studies, curcumin can shield cultured cells or diabetic individuals in vitro. Curcumin significantly reduces the number of patients who acquire type 2

diabetes after nine months of intervention in the pre-diabetic stage. In addition, research has shown that curcumin treatment generally improves β cell activity. The hypoglycemic effects of curcumin were found by Al-Saud in rats with diabetes caused by a high-fat diet and an injection of streptozotocin (STZ). Curcumin also improved the diabetic condition and reduced insulin resistance in tissues.

Fasting blood glucose levels in diabetic rats can be significantly reduced by curcumin, according to certain studies. Observations have shown that rats treated with curcumin show reduced levels of pancreatic tissue damage and IL-1, IL-6, MCP-1, TNF-α, Bax, and caspase-3 production, among other factors. Curcumin may help restore pancreatic function by lowering inflammation and protecting pancreatic islet cells from death, according to these results.

In vitro studies also show that curcumin has a significant protective effect on cells when exposed to high glucose levels (34, 35). An experiment that exposed insulin (INS)-1 cells to high glucose with or without curcumin found that the cells proliferated, the islet cells' morphology changed, ROS was produced, and superoxide dismutase and catalase activities were measured. Insulin levels were also recorded, as were the expression of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase subunits and apoptotic factors. The results showed that curcumin reduced INS-1 cell damage from high glucose-induced oxidative stress and proliferation as well as increased insulin levels and decreased apoptotic factor and NADPH oxidase subunit expression. These findings also showed that curcumin regulated the NADPH pathway, protecting islet cells from apoptosis and reducing oxidative stress due to high-glucose/palmitate. Xia et al. found that after administering curcumin, the activity of rat insulinoma RIN-m5F β-cells increased, their apoptotic rate decreased, and they were preserved. These results provide more evidence that curcumin may prevent diabetes by reducing blood glucose levels and protecting islet cells from the negative effects of high glucose through anti-inflammatory and anti-apoptotic pathways.

CONCLUSION:

Curcumin is a promising antidiabetic agent, for it also shows potent antioxidant, anti-inflammatory, and protective action on the β-cell. The therapeutic goal of diabetes treatment is approached from the root causes of this disease, which include oxidative stress and dysfunction of the pancreatic β-cell, both of which are pivotal factors in the pathogenesis of insulin resistance and hyperglycemia. Studies indicate that curcumin increases insulin sensitivity and preserves and restored function of β cells, thereby preventing the progression from pre-diabetes to type 2 diabetes and preventing most complications of the disease. Despite its potential, the bioavailability problem of curcumin remains a hurdle in drug development, although recent advances in formulating curcumin have led to higher therapeutic

efficacy that may turn curcumin into an effective adjuvant therapy in diabetes management. In conclusion, given that curcumin exerts its action in both directions, is relatively inexpensive, and is a naturally sourced molecule, curcumin is an attractive diabetes management agent most likely to improve the prognosis of treated patients in combination with traditional therapies.

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