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A Review on Curcumin in Metabolic Health and Disease

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ABSTRACT

In recent years, studies have suggested that metabolic disorders are nutritionally dependent. A healthy diet that is rich in polyphenols may be beneficial in the treatment of metabolic diseases such as lower blood level overweight subject metabolic syndrome, non-alcoholic fatty liver disease, , and, in particular, Cur cumin is a polyphenol found in turmeric and has been reported to have antioxidant, anti-inflammatory, hepatoprotective, and among others. This review summarizes the influence of supplementation with cur cumin on metabolic parameters in selected metabolic disorder.

Keywords: Curcumin, Metabolic Health and Disease

INTRODUCTION

Curcuma (1,7-bis(4-hydroxy-3-methoxy phenol)-1,6- heptadiene-3,5-dione) is a lipophilic polyphenol classified as a carcinoid. It has, among others, antioxidant, anti-inflammatory, and anticancer effects]. Indeed, today, its use is being explored in the course of many diseases; however, the history of the use of cur cumin dates back several thousand years [] due to its culinary use and health-promoting properties. The source of cur cumin is turmeric (*Curcuma longa*), a plant from the ginger family that grows in Asia, particularly in India. There, turmeric is often used as a spice due to its intense yellow colour, aroma, and flavor. Unfortunately, the cur cumin content in turmeric is only a few percent, and it has very low bioavailability]. For this reason, the use of cur cumin for therapeutic purposes occurs through standardized supplements, which have an increased bioavailability of cur cumin by up to 2000%. Hence, there is another limitation in establishing a proper therapeutic dosage of cur cumin. Cur cumin metabolism may be different from person to person due to the variety of microbiota.

One of the methods of enhancing the biological and pharmacological activity of cur cumin is Nano encapsulation. Over recent years, many formulations of cur cumin have been developed in order to increase its bioavailability and solubility and to shield it from inactivation through hydrolysis.

The most beneficial Nano formulations of cur cumin are with liposomes, polymers, gold nanoparticles, magnetic nanoparticles, solid lipid nanoparticles (SLNs), conjugates, cyclohexatrienes, solid dispersions, micelles, Nano spheres, Nano gels, and Nano disks. Each of these confirms its usefulness in the diagnosis of various diseases due to the very different outcomes. For example, liposomes have the ability to control the release of drugs with an optimal molecular ratio; they reduce side effects and toxicity in cells, and despite their short half-life, are rapidly removed by the reticuloendothelial system or due to their poor stability.

In turn, polymers (polymeric nanoparticles) are safe, effective, and biocompatible due to their small size, and thus have the ability to circulate in the blood for a long time. Gold nanoparticles are useful in prostate and colorectal cancer cell models due to their optical, catalytic, and non-toxic properties Magnetic nanoparticles also have some advantages. Their low production cost and the sustainable delivery of thiolate starch-coated iron oxide may indicate the compatibility of this system with lymphocyte cells. Additionally, magnetic nanoparticles may by manipulated in terms of their forms, shapes, sizes, and chemical properties To date, magnetic nanoparticles with cur cumin (MNP@PEG-Cur) have been established as a recommendation for drug carriers for antitumor medicines due to their high biocompatibility SLNs may also be useful for cancer treatment It has been shown that they enhance the solubility compared to that of native cur cumin and have the ability to reduce the activity of lipopolysaccharides (LPSs) Two or more molecules may be formed into conjugates Conjugation of cur cumin with molecules and hydrophilic polymers is efficient due to the increase in solubility and oral bioavailability. This formulation may be a potential treatment for Alzheimer's disease.

Cyclohexatrienes are used to enhance drug stability Cur cumin can help with metabolic diseases in a number of wand solubility and to deliver drugs to cancer cells in their active form. These forms have the ability to bear non-covalently bound drugs Other forms such as solid dispersions may decrease the particle size to the Nano range with improved wettability, pharmacokinetic properties, and oral biodistribution of the drugs. Micelles are widely used with curcuma to deliver poorly water-soluble drugs. Curcumas formulations with Nano spheres may present better cytotoxic effects against cancer cells and improve the solubility and stability in comparison to native curcumas, and they may also have great potential as a treatment for Alzheimer's disease Various other Nano formulations (Nano gels, Nano disks) enhance cur cumin's biological activity. These methods may be beneficial in controlling drug release and circulation and improving anticancer activity.

Plan of work

1. To evaluate the effects of curcuma on metabolic parameters (e.g., glucose levels, lipid profiles).

2. To explore the mechanisms underlying curcumin's effects on metabolic disease.

3. To assess the safety and bioavailability of cur cumin.

Review and literature

Here's a comprehensive overview of the literature on curcumin and its effects on health and metabolic diseases:

1. Anti-Inflammatory Properties

Curcumin is known for its strong anti-inflammatory effects. It inhibits pro-inflammatory cytokines and enzymes, making it beneficial in conditions such as metabolic syndrome, where chronic inflammation is a key factor.

2. Antioxidant Activity

Curcumin acts as a potent antioxidant, combating oxidative stress. This property is significant in metabolic diseases, as oxidative stress is implicated in the development of insulin resistance and other metabolic disorders.

3. Effects on Insulin Sensitivity

Research indicates that curcumin can enhance insulin sensitivity and lower blood glucose levels. Some studies show improved glycemic control in type 2 diabetes patients taking curcumin supplements.

4. Weight Management and Obesity

Curcumin has been found to influence adipogenesis, promoting the browning of white adipose tissue and reducing fat accumulation. Animal studies and some human trials suggest curcumin supplementation can aid in weight management.

5. Lipid Profile Improvement

Several studies have reported that curcumin can lower total cholesterol, LDL cholesterol, and triglyceride levels. This makes it a potential adjunct in managing dyslipidemia associated with metabolic diseases.

6. Metabolic Syndrome

Curcumin's ability to modulate metabolic pathways has led to interest in its role in managing metabolic syndrome. Studies indicate it may improve various components of this syndrome, including obesity, hypertension, keywords were used: "curcuma" and ("metabolic disease", obesity, lower blood lipid level ,overweight subject "non-alcoholic fatty liver disease") and ("clinical trials" or "human trials"). In addition,we used the website ClinicalTrials.gov to collect registered clinical trials of curcuma formetabolic diseases. After searching, we further examined the full text of the literature to determine eligibility for inclusion in this review. Editorials, conference abstracts and studies with incomplete or unavailable data were excluded Plant Sources and Chemical Properties of Cur cumin.

The genus Curcuma plants are the most important natural sources of cur cumin, such as Curcuma longa L. and Curcuma penguin Y.H. Chen et C. Ling, Curcuma photocells Val., and Curcuma angriness S.G. Lee et C.F. Liang Cur cumin was first isolated from

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The rhizomes of Curcuma longa L. in 1815 Curcuma longa is a perennial plant with fleshy, orange and tuberous rhizomes and is widely grown in India, China and Indonesia.

The content of cur cumin in Curcuma longa is usually between 1% and 9% Curcuma wenyujin, Curcuma photocells and Curcuma swankiness are native to China's Sichuan, Guangxi and Zhejiang provinces, respectively The content of cur cumin in the rhizomes of the three medicinal plants ranges from 0.068 to 1.720 mg/g The cost of cur cumin is about 6 USD per gram. The chemical structure of curcumin and its main sources are shown in Figure 1.

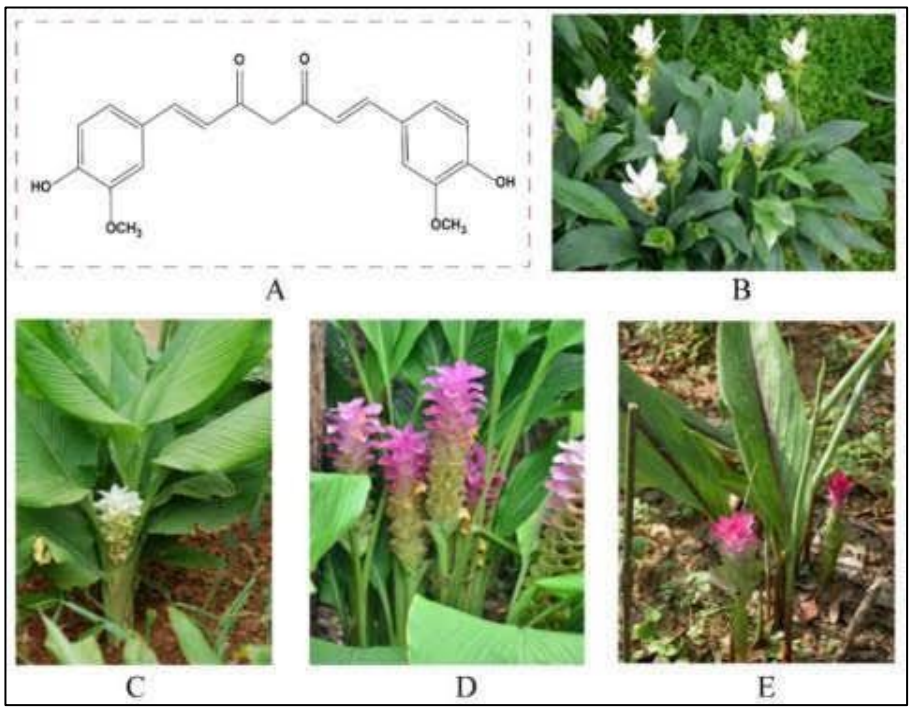

Figure 1. Chemical structure (A) of cur cumin and its main plant sources ((B) Curcuma wenyujin Y.H. Chenet C. Ling; (C) Curcuma longa L.; (D) Curcuma photocells Val; (E) Curcuma angriness S.G.Lee et C.F. Liang). The pictures are from the website: http://www.iplant.cn/frps, accessed on 21 September 2022.

Curcumin is a diketone in structure with the IUPAC name of (1E,6E)-1,7-bis(4- hydroxy-3-methoxyphenyl) hepta-1,6-diene-3,5-dione. Its molecular formula is C 21 H 2 0 6 and molecular weight is 368.38 g/mol. Cur cumin is an orange-yellow crystalline powder.

Curcumin for Treatment of Metabolic Syndrome

Metabolic syndrome (MS) is a highly prevalent and complex metabolic disorder that includes central obesity, elevated blood glucose levels, hypertension, and insulin resistance MS is currently estimated to affect approximately 20% of the global population. In diagnosing MS, there are some variations in the metabolic components thought to comprise it depending on (e.g., sex or ethnicity). Overall, the following are commonly recognized: impaired glucose tolerance or diabetes, obesity, hypertension, and/or dyslipidaemia. Cur cumin has been shown to have a role in decreasing angiogenesis and abiogenesis by suppressing CCAAT/enhancer-binding protein alpha and PPAR expression and by lowering cholesterol levels. Moreover, cur cumin has the ability to upregulate the gene expression of pancreatic glucose transporter 2 (GLUT2), GLUT3, and GLUT4, thus stimulating insulin secretion In a randomized and double-blinded clinical trial, Battani et al. investigated the effects of cur cumin Nano-micelles in patients with metabolic syndrome. The study demonstrated that supplementation with 80 mg/day of cur cumin Nano- micelles for 12 weeks significantly reduced the plasma TG levels in comparison to those of the placebo group (p = 0.03) as well as the homeostasis model assessment of ß-cell dysfunction (HOMA-ß). However, there were no beneficial effects on insulin, HOMA-IR, glycosylated haemoglobin (HbA1c), or fasting blood sugar (FBS). Moreover, no changes in anthropometric indices or blood pressure were reported. These results must be approached with some caution because of the limitations of the study. First of all, the inability to measure plasma levels of cur cumin in patients, which can be different due to the large range of body mass indices (BMIs), may have been a factor in the different responses to cur cumin. Second, the long-term effects of consumption of nano-curcumin formulations remain unknown. Furthermore, it is crucial to pay attention to the dose of nano-curcumin supplements. In another

study, it was observed that using 200 mg/kg of nano- curcumin had a greater therapeutic effect in diabetic rat samples in comparison to using 100 mg/kg of nano- curcumin Effect of metabolic diseases in human.

Cur cumin for Non-Alcoholic Fatty Liver Disease (NAFLD)

Non-alcoholic fatty liver disease (NAFLD)—the nomenclature of which was recently updated to metabolic-associated fatty liver disease (MAFLD)—is the most common chronic liver disease worldwide It is characterized by excessive fat accumulation that is greater than 5% of the total weight of the liver. The development of liver disease—and, in particular, NAFLD—involves oxidative stress processes and damage to lipids, proteins, and DNA as well as changes in functional signalling pathways Cur cumin and related phenolic have been linked with the inhibition of lipid peroxidation, free radical formation (e.g., neutralization of superoxide, peroxyl, and hydroxyl radicals (ROSs), nitric oxide, and peroxynitrite (RNS)) and DNA damage. Despite obesity and hyperlipidaemia it is also known that patients with type 2 diabetes have a high prevalence of NAFLD (up to 70%). The above diseases share multiple cardio metabolic risk factors and proinflammatory pathways Różański et al.] analysed databases and publications that have described the effects of using cur cumin supplementation on biochemical parameters in MAFLD. They concluded that cur cumin may have therapeutic potential in MAFLD patients; however, the analysed studies did not allow them to clearly determine its positive effects.

Effect of Cur cumin on Glycaemia and Lipid Levels in Obese or Overweight Subjects

Dysglycemia and dyslipidaemia are common features of obesity A double-blind, randomized, placebo-controlled clinical trial was conducted to investigate the effect of nano-curcumin on glycaemic and lipid profiles in overweight and obese patients The results showed that compared with the placebo group, administration of nano-curcumin capsules (80 mg/d) for 3 months significantly decreased the levels of FBG, HbA1c, HOMA-IR, TG, TC and LDL-C and increased the levels of HDL-C and the quantitative insulin sensitivity check index (QUICKI). Similarly, Karan dish et al. reported that cur cumin supplementation (500 mg/d) for 90 days in 21 obese subjects (5 men and 16 women) with PR diabetes significantly reduced FBG, 2 h postprandial glucose (2hpp), HbA1c and HOMA-IR levels and significantly increased insulin sensitivity In addition, two randomized controlled trials found that compared with placebo, administration of cur cumin C3 complex capsules (1000 mg/d) for 30 days in obese individuals or phytosomal cur cumin tablets (800 mg qd) for 8 weeks in overweight subjects resulted in a significant reduction in TG levels but no significant influence on other lipid parameters, including TC, LDL-C and HDL-C As noted, the current clinical trials suggest that cur cumin has a beneficial effect on glycaemia levels in obese or overweight subjects. It can lower blood glucose, increase insulin sensitivity and improve insulin resistance. However, in addition to TG, the effect of cur cumin on lipid levels cannot be reached with a definite conclusion due to the small number of clinical trials. In the future, more clinical trials with larger sample sizes are needed to determine its true effect on dyslipidaemia in obese subjects.

Cur cumin Lowers Blood Lipid Levels in Patients with NAFLD

Dyslipidaemia is an important risk factor for NAFLD. Some clinical studies have shown that cur cumin can significantly lower blood lipid levels in patients with NAFLD. For example, in a randomized controlled trial, 37 patients (19 men and 18 women) with NAFLD who took 500 mg of cur cumin (an amorphous dispersion preparation) daily for 8 weeks showed significant reductions in serum TG, TC and LDL-C levels compared with the placebo group . In addition, Panaji et al. reported that cur cumin supplementation (500 mg bid) for 8 weeks significantly reduced LDL-C, TG, TC and non- HDL-C levels in patients with NAFLD In another clinical study, 61 patients (37 men and 24 women) with NAFLD were randomly assigned to phospholipid cur cumin capsules (250 mg qd)and placebo groups. After 8 weeks of intervention, HDL-C levels in the phospholipid cur cumin group were significantly higher than those in the placebo group Likewise, a single- arm, before-and-after, controlled clinical trial found that supplementation of phospholipid cur cumin capsules (1500 mg/d) for 8 weeks significantly reduced LDL-C, TG and non-HDL-C levels in patients with NAFLD.

Obesity

Obesity, especially abdominal obesity, is closely associated with increased morbidity and mortality from cardiovascular disease . Clinically, several anthropometric measures, such as body weight, hip circumference, waist circumference and body mass index (BMI), are commonly used to assess obesity. In addition, obese people are often accompanied by dyslipidaemia and dysglycemia, such as elevated FBG, HbA1c, LDL-C, TG and TC levels. These abnormalities gradually cause inflammation and oxidative tress leading to cell, tissue and organ damage The effects of cur cumin on anthropometric parameters, dysglycemia, dyslipidaemia, inflammation and oxidative stress markers in obese or overweight people are reviewed below and shown in **Figure 3**.

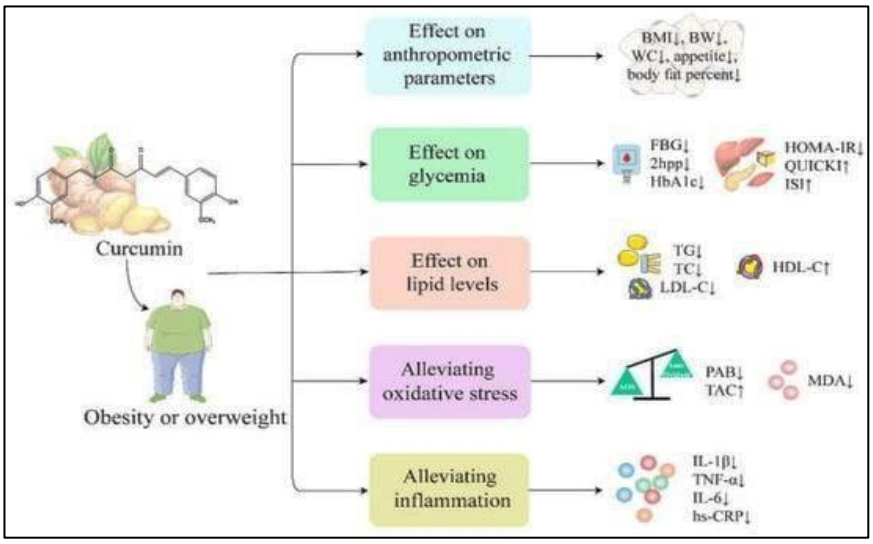

Figure 2. The therapeutic effects and potential mechanisms of cur cumin on obesity. ↑ indicates increase and ↓ indicates decrease. Specifically, cur cumin can alleviate inflammation by decreasing the levels of IL-1β, IL-6, TNF-α and has-CRP. Cur cumin alleviates oxidative tress by decreasing the levels of MDA and PAB and increasing the expression of the antioxidant's TAC.

Summary

Cur cumin supplementation in metabolic disorders has been the subject of many clinical studies in recent years. The results presented in this review suggest its beneficial effects on metabolic parameters in some metabolic diseases such as polycystic ovary syndrome, metabolic syndrome, glycaemic disorders, non- alcoholic fatty liver disease, and cardiovascular disease—particularly atherosclerosis. Mostly, improvements have been observed in fasting glucose, fasting insulin, HOMA-IR, and lipid profiles, which may be the result of cur cumin's ability to mediate many signalling pathways, decrease inflammatory response, or indirectly maintain cell homeostasis. Recent studies have found that the effects of nano-curcumin on serum lipid profiles are more effective than those of cur cumin. A possible explanation for these results may be the increased solubility and bioavailability of nano- curcumin, which are probably dose-dependent.However, the limitations of cur cumin supplementation prevent the establishment of therapeutic dosages of cur cumin in the treatment of metabolic diseases due to the poor bioavailability and rapid metabolism of cur cumin. Several limitations of the present studies should be mentioned. First, most of the results included had a small number of participants, and the number of studies was limited. Second, all studies lasted three months or less; as such, it is not possible to present the long-term effects of cur cumin and nano-curcumin supplementation on metabolic diseases and overall health. Third, a relatively high number of the studies included were conducted in Iran, and there was notable heterogeneity among the studies. Fourth, various dosages and sources of cur cumin and nano-curcumin were used in the included studies. Among the studies, the cur cumin dosages ranged from 40 mg of nano- curcumin to 1500 mg of per day, and the treatment periods ranged from two to three months.

Conclusion

Curcumin has received worldwide attention for its multiple health benefits, which appear to act primarily through its anti-oxidant and anti-inflammatory mechanisms. These benefits are best achieved when curcumin is combined with agents such as pipeline, which increase its bioavailability significantly. Research suggests that cur cumin can help in the management of oxidative and inflammatory conditions, Metabolic diseases. It may also help in the management of exercise-induced inflammation and muscle soreness, thus enhancing recovery and subsequent performance in active people. In addition, a relatively low dose can provide health benefits for people that do not have diagnosed health conditions.

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