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Mini review Article

Role of Curcumin and Fenofibrate on Cardiovascular Events in Type 2 Diabetes Mellitus

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ABSTRACT

Background and Aim Type 2 diabetes mellitus is associated with cardiovascular complications that account for a high percentage of mortality and increase the clinical burden on the healthcare system. Herbal products like curcumin and chemical drugs like fenofibrate were found to be effective in decreasing complications associated with heart in type 2 diabetes. The aim of this study is to evaluate the role of curcumin and fenofibrate on cardiovascular complications in type 2 diabetes in a minireview.
Method We reviewed the online databases PubMed, Science Direct, and Google Scholar for articles discussing the impact of curcumin or fenofibrate in improving lipid profile in patients with type 2 diabetes.
Results The prior studies demonstrated the impact of consuming curcumin or fenofibrate to improve the lipid profile in people with type 2 diabetes. Triglycerides (TG), low-density lipoprotein (LDL), and total cholesterol (TC) were reduced with either curcumin or fenofibrate. In contrast, high-density lipoprotein (HDL) levels were increased.
Conclusions: Curcumin or fenofibrate consumption in patients with type 2 diabetes enhances lipid profile, hence decreasing insulin resistance and reducing cardiovascular complications.

Keywords: Type 2 diabetes, Curcumin, Fenofibrate, Lipid profile, Cardiovascular complications.

1. INTRODUCTION

Diabetes has been a significant public health problem, affecting approximately 537 million adults in the world in 2021. The number of cases is expected to be 783 million in 2045.[1] Diabetes risk factors include age, family history, smoking, overweight, and physical inactivity. Moreover, complications associated with diabetes are heart disease, kidney disease, and neuropathy.[2] Concurrently, cardiovascular complications are considered the most significant complications associated with a higher percentage of morbidity in patients with type 2 diabetes mellitus (T2DM).[3] Hyperglycemia, lipid metabolism abnormality, and insulin resistance are related to the development of cardiovascular complications in patients with diabetes. Despite the efforts to decrease the mortality rate associated with cardiovascular complications (CVS) in diabetes, these complications remain a considerable challenge to the medical system due to the clinical burden of cardiovascular diseases on the healthcare system.[4] International Diabetes Federation (IDF) anticipated the cost of treating diabetes would be 673 billion dollars in 2015, increasing to 802 billion dollars in

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2040.[5] Herbal products were investigated for their benefits in metabolic disease, and one of these products is curcumin, which has been effective in treating type 2 diabetes. Research studies discovered that curcumin has antioxidant and anti-inflammatory properties.[6] In addition to that, curcumin was found to be effective in improving the lipid profile in type 2 diabetes, hence reducing cardiac complications.[7] In the same context, fenofibrate was proven to decrease cardiovascular complications in people with type 2 diabetes.[8] Fenofibrate is a peroxisome proliferator-activated receptor α (PPARα) activator with an anti-inflammatory action that might help in reducing cardiovascular complications.[9] Therefore, the purpose of the study is to explain the impact of curcumin and fenofibrate in improving cardiovascular conditions in patients with type 2 diabetes.

2. MATERIAL AND METHODS

The online databases PubMed, Science Direct, and Google Scholar were searched for articles discussing curcumin and fenofibrate in type 2 diabetes. The following keywords were used in the search: type 2 diabetes, curcumin, fenofibrate, lipid profile, and cardiovascular complications words. The inclusion criteria were studies on type 2 diabetes. In contrast, the exclusion criteria were as follows: studies on type 1 studies and studies published in languages other than English. Duplicate studies were eliminated from the study. The types of studies used were clinical trials.

3. RESULTS

3.1. Mechanism of action of curcumin

Curcumin improves lipid metabolism in diabetes patients by decreasing transcription factors' gene expression, that are implicated in hepatic lipogenesis. Curcumin reduces Sterol regulatory element-binding protein 1c (SREBP1c), which helps in cholesterol synthesis.[10] Curcumin decreases inflammatory markers such as interleukin-8 (IL-8), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-alpha), which have a crucial part in the development of cardiovascular diseases.[11]

3.2. Curcumin's impact on the lipid profile in type 2 diabetes

Curcumin was found to be effective in decreasing total cholesterol (TC), low-density lipoprotein (LDL), and triglycerides (TG).[12] This effect of curcumin is related to the high activity of lipoprotein lipase and changing genes for lipid and cholesterol expression.[13] Curcumin has antidiabetic, cardioprotective, anti-oxidant, and anti-inflammatory properties, which contribute to its effect on modifying lipid profile.[14] Based on the results of previous studies, **Table 1** illustrates the importance of curcumin in lowering lipid profile in patients with type 2 diabetes. According to the research in **Table 1**, curcumin effectively enhanced lipid profiles and decreased cholesterol, LDL, and triglycerides, and insulin resistance. Curcumin increased high-density lipoprotein.

3.3. Mechanism of action of fenofibrate

Fenofibrate stimulates peroxisome proliferator-activated receptors alpha (PPAR-alpha), which controls lipoprotein lipases, increases high-density lipoprotein production, and reduces apolipoprotein C production. Moreover, fenofibrate reduces triglycerides through clearance of triglyceride-rich particles and plasma catabolism. Fenofibrate reduces low-density lipoprotein (LDL) levels, which subsequently decreases triglycerides.[21]

3.4. Fenofibrate's impact on the lipid profile in type 2 diabetes

Fenofibrate markedly reduced triglycerides and increased high-density lipoprotein, which improved atherogenic dyslipidemia and hence significantly decreased cardiovascular events, according to research involving 9,795 people with type 2 diabetes.[22]

In research studies on patients with type 2 diabetes, fenofibrate effectively decreased insulin resistance, improved lipid profile, and decreased cardiovascular events **(Table 2)**.

4. DISCUSSION

In our research, we demonstrate the importance of medications that have the potential to improve cardiac complications in patients with diabetes. We examined the effects of the herbal product curcumin and the pharmaceutical medication fenofibrate. According to the American Diabetes Association, cardiovascular complications contribute significantly to the high mortality and disability rates in type 2 diabetes, and the added burden of cardiac events further affects the economic status of healthcare systems.[5] In this context, the early detection and prevention of these cardiac events play a major role in improving patients' quality of life and decreasing the economic burden associated with diabetes.[27] In this research, we discussed the benefits of curcumin supplements as a natural herbal product that has

Table 1: An overview of the curcumin randomized clinical trials (n = 6).

Study	Duration	Details	Results	Conclusion
(15)	12 months	Double-blind, randomized, placebo-controlled study. Human Three capsules of either curcumin or placebo for 12 months.	The curcumin group significantly reduced LDL-C and small-density lipoprotein cholesterol (sdLDL-C).	Curcumin could be effective as a cardioprotective agent against atherosclerosis in type 2 diabetes patients.
(16)	3 months	Double-blind, randomized, placebo-controlled study. Human Curcumins plus piperine (100 mg/10 mg) per day or placebo for 3 months.	The curcumin group significantly decreased TC levels and increased the serum level of HDL-C.	Curcumin could reduce cardiovascular complications in patients with type 2 diabetes.
(17)	12 months	Double-blind, randomized, placebo-controlled study. Human Curcumin 1500 mg or placebo one time per day for 12 months.	Insulin resistance levels were decreased in the curcumin group.	Curcumin treatment decreases insulin resistance, which is one of the factors responsible for cardiovascular disease.
(18)	3 months	A randomized trial Human Curcumin 1000 mg versus Atorvastatin 20 mg in the day for 3 months.	Curcumin was responsible for significant reductions in TC levels and increments in HDL-C.	Curcumin supplements were found to be effective in improving lipid profile and can be used as adjunct therapy in patients with type 2 diabetes.
(19)	2 months	Double-blind, randomized, placebo-controlled study. Human Three capsules of curcumin 500 mg per day or placebo for two months.	Curcumin decreases triglyceride levels after two months.	Curcumin supplements can decrease cardiovascular complications by decreasing triglycerides.
(20)	2 months	Double-blind, randomized, placebo-controlled study. Human Curcumin (700 mg) capsule or placebo three times a day for two months.	Significant reductions in triglycerides were observed, while no significant changes were found in TC. Reduction in LDL level.	Curcumin improved some of the lipid profile components. So, curcumin can reduce complications of atherosclerosis in diabetes patients.

Table 2: Summary of the randomized clinical trials of fenofibrate (n=4 studies).

Study	Duration	Details	Results	Conclusion
(23)	2 months	Micronized fenofibrate for 2 months. Human.	There was a significant decrease in triglycerides and an increase in HDL. Fenofibrate greatly reduces LDL cholesterol and triglycerides.	Fenofibrate therapy was effective in lowering lipid profile in type 2 diabetes, especially in patients with dyslipidemia.
(24)	3 months	250 mg/day fenofibrate once daily for 3 months. Human.	Fenofibrate decreased TC, TG, and VLDL. HDL was increased significantly. Serum-free fatty acids were decreased.	Fenofibrate treatment improves lipid profile, reduces insulin resistance in patients with type 2 diabetes, and hence decreases cardiovascular complications.
(25)	5 years	Randomized controlled trial Human Micronized fenofibrate 200 mg daily (or matching placebo) Human.	Fenofibrate therapy reduces levels of cholesterol, triglycerides, and LDL cholesterol. In addition to that, fenofibrate was effective in increasing high-density lipoprotein.	Fenofibrate was effective in reducing cardiac events in diabetes.
(26)	5 years	The study was done on participants of field trials of people with metabolic disease. Human.	Fenofibrate reduced cardiovascular events associated with low HDL-C levels in metabolic syndrome patients and those with T2DM.	Fenofibrate decreased cardiovascular events and reduced mortality associated with type 2 diabetes.

been used recently in type 2 diabetes. According to **Table 1**, studies that were done on curcumin illustrate curcumin's benefits for enhancing lipid profiles by increasing HDL and decreasing LDL, TC, triglycerides, and insulin resistance.[28]

The studies included for curcumin demonstrate improvement in lipid profile parameters, and these parameters are different in terms of significance. One study found a significant decrease in lipid levels, while another showed a smaller difference. However, all studies demonstrated the effectiveness of curcumin supplements in reducing cardiac events by improving lipid profiles. Fenofibrate also reduces triglycerides and increases HDL, hence decreasing cardiovascular events.[26] According to prior research, fenofibrate supplements resulted in a significant reduction of triglycerides and an increment in high-density lipoprotein. All these studies concluded the importance of adding fenofibrate or curcumin for patients with type 2 diabetes to improve lipid profiles and decrease the cardiac events associated with diabetes.

5. CONCLUSION

Clinical studies demonstrate the effectiveness of curcumin and fenofibrate in patients with type 2 diabetes mellitus as they reduce the risk of cardiovascular events by improving lipid profile and decreasing insulin resistance. Further studies are needed to compare the effect of curcumin versus fenofibrate in type 2 diabetes patients.

AUTHORS' CONTRIBUTIONS

All Authors reviewed the literature, conceived, and constructed the study design, as well the laboratory investigation. Writing and revision of the manuscript were done by all the authors. The final form of the manuscript was approved by all authors.

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DECLARATION OF CONFLICTING INTERESTS

Authors declare no conflict of interest.

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