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(REVIEW ARTICLE)

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A detailed review on some effects of turmeric curcuminoids on inflammation in obese individuals

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Abstract

Turmeric, derived from Curcuma longa, contains curcuminoids, notably curcumin, renowned for its anti-inflammatory and antioxidant properties. This review explores turmeric curcuminoids, focusing on curcumin, as potential remedies for obesity-related inflammation and associated disorders. The urgency to address obesity-related health risks is emphasized, with elevated BMI correlating with increased morbidity and mortality. Current obesity management strategies involve dietary changes, physical activity, and, sometimes, pharmacotherapy. Research suggests curcumin's role in significant weight loss and lean tissue mass augmentation, inhibiting adipogenesis-related proteins and increasing basal metabolic rate. The intricate connection between obesity and type 2 diabetes is examined, highlighting curcumin's impact on glucose homeostasis, hepatic gluconeogenesis, and lipid metabolism. Additionally, curcumin's anti-inflammatory effects, including modulation of pro-inflammatory cytokines and the NFkB pathway, demonstrate therapeutic potential. Clinical studies indicate curcumin's positive effects in reducing inflammatory markers and rebalancing adipokines in overweight and obese individuals, showing promise for addressing obesity-related inflammation and associated health risks. This review aims to investigate the potential role of turmeric curcuminoids, particularly curcumin, as remedies for obesity-related inflammation and associated disorders in obese individuals.

Keywords: Obesity; Turmeric; Weight loss; Curcumin; Type 2 diabetes; Anti-inflammatory

1. Introduction

Turmeric, derived from the dried rhizome of *Curcuma longa*, is a well-researched medicinal herb containing various phytochemicals (Soleimani et al., 2018). Its composition includes water (80–90%), carbohydrates (13%), proteins (2%), minerals (2%), and lipids (<1%). Curcuminoids, the key active components, make up about 10% of dry turmeric powder, with curcumin, dimethoxy-curcumin, and bisdemethoxycurcumin being the primary curcuminoids, present at 62–90, 9–23, and 0.3–14 mg/g in commercial turmeric products. Over 50 curcuminoids, including bisabocurcumin and cyclocurcumin, contribute to turmeric's yellow color (Meng et al., 2018). Curcumin, the most researched curcuminoid, was first extracted in 1815 and has the molecular formula C21H20O6 (Dumomangi et al., 2021). Though hydrophobic and insoluble in water, curcumin dissolves in substances like dimethyl sulfoxide and ethanol (Beyene et al., 2021). Turmeric contains 3–8% curcumin, with a typical 3 g serving providing 30–90 mg of curcumin (Fabianowska-Majewska et al., 2021).

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1.1. Obesity as a Global Public Health Problem

The global rise in overweight and obesity poses a significant public health issue. As of 2016, over 39% (1.9 billion) of adults were overweight, with more than 13% classified as obese (Singh et al., 2020). By 2030, it is projected that nearly 60% of the adult population, or 3.3 billion people, will face overweight or obesity (Islam et al., 2021). Obesity contributes to higher morbidity and mortality rates and is recognized by the WHO as a chronic non-communicable disease alongside cardiovascular diseases, diabetes, cancer, and gastrointestinal disorders, leading causes of death globally (WHO, 2003).

Body Mass Index (BMI) is a key measure, with a BMI of 25 or more indicating overweight and 30 or more indicating obesity (Kasprzak et al., 2018; Wadden et al., 2012). Rising BMI is linked to increased mortality due to cardiovascular diseases, diabetes, and cancer, particularly related to abdominal obesity (Després, 2006; Zhang et al., 2008). WHO attributes 80% of type 2 diabetes cases, 35% of ischemic heart disease, and 55% of hypertension to overweight and obesity. Addressing related health risks is crucial (Branca et al., 2007).

The primary treatment for obesity is a calorie-restricted diet and increased physical activity, with pharmacotherapy, such as orlistat and lorcaserin, considered in some cases. There is growing interest in natural compounds with fewer side effects for weight management (Singh et al., 2020), and curcumin, found in turmeric, has shown potential in preventing and treating obesity through various mechanisms (Singh et al., 2020; Alsharif and Almuhtadi, 2021). This review explores curcumin's anti-obesity potential based on in vitro and in vivo studies.

2. Role of turmeric curcuminoids in weight loss

Weisberg et al. conducted a study wherein dietary therapy involving curcumin in ob/ob mice led to noteworthy weight loss and an augmentation in lean tissue mass (Weisberg et al., 2008). The observed decrease in adipose tissue and weight loss in curcumin-fed C57/BL mice could be attributed to the inhibition of key transcriptional proteins linked to adipogenesis (Ejaz et al., 2009). Additionally, prior research has indicated a decline in pro-inflammatory cytokines and C-reactive proteins (CRPs) alongside increased weight loss (Corbi et al., 2002; Ziccardi et al., 2002). Both in vitro and in vivo studies involving high-fat-fed mice have provided evidence that supplementing with curcumin at a dose of 500 mg/kg in the diet can elevate the basal metabolic rate. This elevation contributes to heightened energy expenditure and subsequent weight loss (Ejaz et al., 2009). The consequential loss of body weight and an increase in the percentage of lean mass offer significant advantages in reducing insulin resistance and enhancing cardiovascular health among individuals with obesity (Ejaz et al., 2009; Weisberg et al., 2008). In light of these findings, it is suggested that, beyond its impact on lipid metabolism by reducing triglyceride synthesis and increasing fatty acid oxidation, curcumin may also influence body weight by enhancing the basal metabolic rate and modulating the release of certain cytokines.

3. Role in diabetes and insulin resistance

Type 2 diabetes mellitus (T2DM) is closely linked to obesity (Wang et al., 2009), with insulin resistance in obesity attributed to elevated free fatty acids in plasma and tissues (Han et al., 2008; Anderwald et al., 2007). Pro-inflammatory cytokines in the bloodstream are characteristic of insulin resistance in obesity and T2DM (Muller et al., 2002; Pitsavos et al., 2007). Lipid-induced insulin resistance is primarily due to NFkB activation by free fatty acids (Wang et al., 2009; Nguyen et al., 2005). NFkB plays a key role in insulin resistance, leading to TNF-a and IL-6 overproduction, impairing insulin signaling via IRS-1 and GLUT-4 (Wang et al., 2009; Liang et al., 2008; Rotter et al., 2003).

Curcumin is shown to be an effective anti-diabetic agent (Kuroda et al., 2005; Nishiyama et al., 2005), improving glucose homeostasis by activating glycolysis, inhibiting gluconeogenesis, and reducing lipid metabolism (Seo et al., 2008). Oral curcumin has been effective in treating hyperglycemia in diabetic animal models (Kuroda et al., 2005; Pari and Murugan, 2007). It mitigates insulin resistance by inhibiting NFkB (Wang et al., 2009) and has hypoglycemic effects by activating PPARg (Nishiyama et al., 2005). Curcumin also reduces ER stress in adipose and liver tissues, increasing expressions of Sirt1 and FOXO proteins (Weisberg et al., 2008). Synthetic curcumin analogs, like ferulamides, have been proposed for treating hyperglycemia (Yamazaki et al., 2008). Overall, curcumin is a promising antidiabetic agent, reducing free fatty acids, cytokines, and insulin resistance while controlling hyperglycemia.

4. Curcumin in inflammation

Inflammation is crucial in obesity-related complications. Macrophage infiltration, driven by monocyte chemoattractant protein-1, and TNF-a release from adipose tissue, contribute significantly to inflammation (Weisberg et al., 2008; Cancello and Clement, 2006; Christiansen et al., 2005). NFkB activation in adipocytes, triggered by TNF-a and macrophage Toll-like receptors, increases TNF-a gene expression, leading to lipolysis, cytokine release, and insulin

resistance (Gonzales and Orlando, 2008; Berg AH, Scherer PE, 2005; Souza et al., 2003; Hotamisligil et al., 1994). Obesity raises IL-6 levels in adipose tissue, promoting CRP synthesis, which heightens cardiovascular disease risk (Yudkin et al., 2000; Higdon and Frei, 2003; Heinrich et al., 1990; de Ferranti and Rifai, 2002). Chronic inflammation from adipose cytokines worsens obesity-related cardiovascular diseases and insulin resistance (Gonzales and Orlando, 2008). Increased BMI is linked to higher prostaglandin E2 serum levels (Berg and Scherer, 2005; Cottam et al., 2004; Fain et al., 2004). Deleting pro-inflammatory genes in obese mouse models prevents insulin resistance and hyperglycemia (Suganami et al., 2007; Tsukumo et al., 2007; Poggi et al., 2007).

Curcumin exerts therapeutic effects in inflammation-related diseases by inhibiting the JNK pathway, downregulating NFkB p65, and suppressing macrophage activation and infiltration into adipose tissue (Wang et al., 2009; Pendurthi et al., 1997; Weber et al., 2006; Chan et al., 1998; Weisberg et al., 2008; Woo et al., 2007). It also inhibits IKK phosphorylation, preventing NFkB translocation, and reduces TNF-a, IL-1b, IL-6, and cyclooxygenase-2 gene expression (Gonzales and Orlando, 2008). The reduction of IL-1b is crucial for maintaining IRS-1 function in adipocytes (Gonzales and Orlando, 2008). Curcumin may modulate adiponectin through PPARg, a regulator of adipocyte differentiation and adiponectin expression (Ohara et al., 2009), as the NFkB-PPARg complex limits PPARg's function, lowering adiponectin levels (Suzawa et al., 2003). Curcumin treatment has been linked to increased adiponectin mRNA expression and secretion (Weisberg et al., 2008). It also enhances Sirt1 gene expression, activating FOXO proteins, which are reduced in obese mice, with curcumin reversing this decline (Weisberg et al., 2008; Qiang et al., 2007). Curcumin and related compounds like N-arylalkylferulamides activate PPARg, stimulating adiponectin expression, thus lowering blood glucose and triglycerides (Yamazaki et al., 2008). Curcumin shows promise in reducing inflammation by modulating cytokines and adipokines through signal transduction pathways.

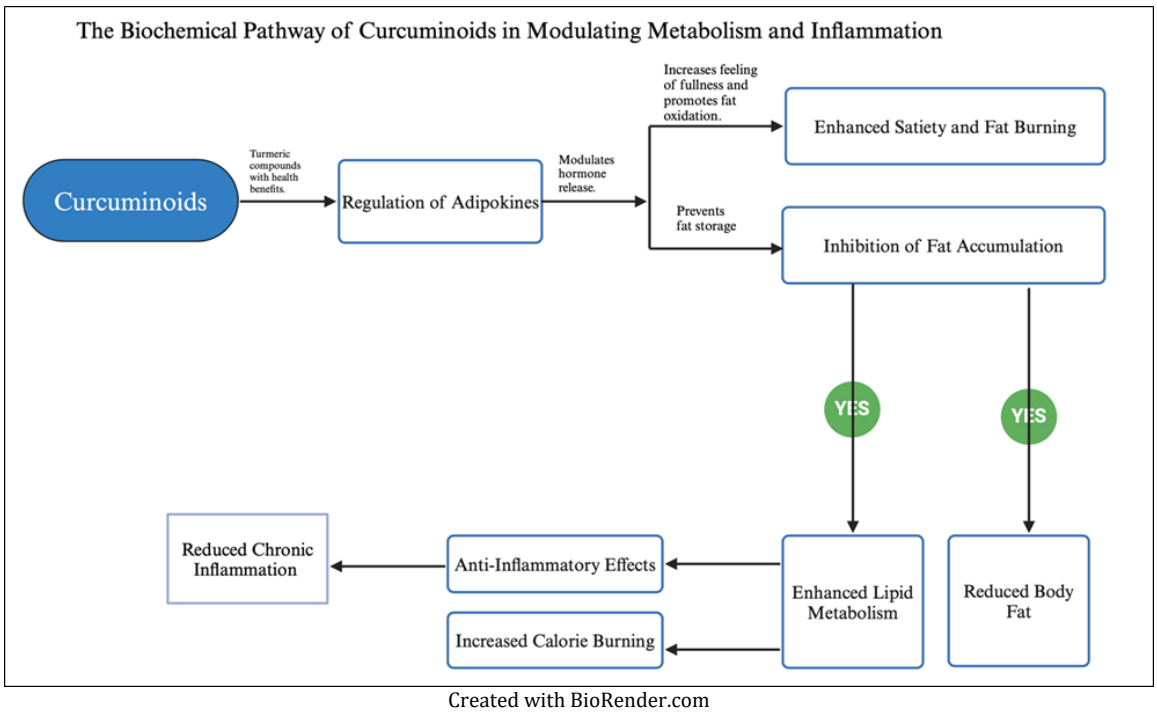

Figure 1 The Pathway of Curcuminoids in Modulating Metabolism and Inflammation

This diagram illustrates the multifaceted effects of curcuminoids on metabolism and inflammation. Starting with the regulation of adipokines, curcuminoids lead to enhanced satiety and fat burning, inhibition of fat accumulation, enhanced lipid metabolism, and anti-inflammatory effects. These interconnected pathways contribute to reduced body fat, increased calorie burning, and reduced chronic inflammation, highlighting the potential therapeutic benefits of curcuminoids in managing metabolic and inflammatory conditions.

5. Turmeric curcuminoids' impact on obesity-related inflammation

Over the past few decades, extensive research has been conducted on curcumin due to its beneficial effects in various diseases, including inflammatory and degenerative conditions, cancer, dyslipidemia, Metabolic syndrome (MetS), and obesity (Shimizu *et al*., 2019). Numerous studies have highlighted that its antioxidant and anti-inflammatory activities

are primarily responsible for these benefits. Obesity, resulting from an imbalance between energy intake and expenditure, leads to the accumulation of excess fat in Adipose Tissue (AT) (Thyagarajan *et al*., 2017). This condition is associated with chronic low-grade inflammation, which serves as a key link between obesity and the development of various diseases such as type 2 diabetes (T2D), dyslipidemia, heart diseases, stroke, and cancer (Schwartz *et al*., 2014). AT is recognized as an endocrine organ, secreting cytokines and chemokines with regulatory and immune functions. Dysregulation of AT's secretory activity likely plays a pathogenic role in obesity-related pathologies (Esser *et al*., 2014). Shimizu et al. have demonstrated that curcumin mitigates inflammation in obesity and related diseases by rebalancing the equilibrium between anti-inflammatory and pro-inflammatory factors through various mechanisms, including interactions with biomolecules like transcription factors, cellular receptors, growth factors, enzymes, cytokines, and chemokines (Shimizu *et al*., 2019). Additionally, Akbari et al. suggest that curcumin can enhance weight loss in overweight individuals with MetS through diet and lifestyle interventions (Akbari *et al*., 2019). However, the challenge of poor curcumin bioavailability has prompted the development of various delivery systems and the addition of piperine to enhance its effectiveness.

Emerging evidence supports the idea that curcumin treatment can alleviate altered pro-inflammatory mediator secretions associated with obesity and related pathologies. Studies on overweight and obese subjects supplementing with curcumin have shown positive outcomes. For instance, Jazayeri-Tehrani et al. demonstrated a reduction in inflammatory markers in overweight or obese patients with non-alcoholic fatty liver disease (NAFLD) after three months of curcumin supplementation (Jazayeri-Tehrani *et al*., 2019). Other studies on individuals with MetS revealed reductions in inflammatory markers following curcumin administration (Panahi *et al*., 2016). Moreover, curcumin has been found to modulate circulating levels of IL-1β and decrease circulating free fatty acid (FFA) levels in type 2 diabetes (T2D) patients (Arner *et al*., 2015)

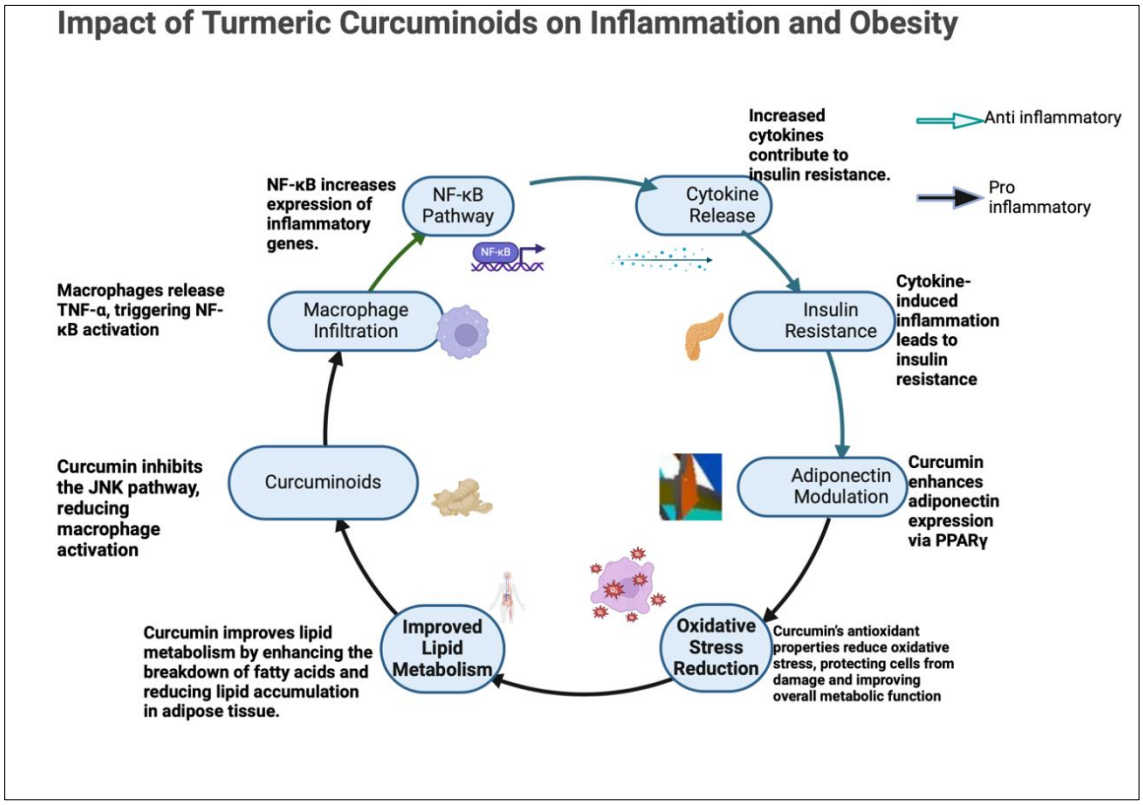

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Figure 2 Impacts of Turmeric Curcuminoids on Inflammation and Obesity

5.1. Clinical Studies

Liu et al. highlighted that obese-individuals often exhibit an imbalance in adipokines, characterized by low adiponectin and high leptin levels in plasma (Liu *et al*., 2020). Curcumin has been observed to increase adiponectin production, as indicated in systematic reviews and clinical trials (Simental-Mendia *et al*., 2019). These studies show that curcumin supplementation significantly increases plasma adiponectin concentrations while reducing pro-inflammatory markers like TNFα (Panahi *et al*., 2017).

Table 1 Impact of Curcumin on Inflammation in Obesity: Insights from Human Studies

Study Design	Subjects	Treatment	Duration	Outcomes	References
Randomized double-blind, placebo-controlled	Overweight/obese with NAFLD (males and females, n = 84)	42 curcumin (40 mg/day)	3 months	↓TNF-alpha and IL-6	Jazayeri-Tehrani *et al*., 2019
Randomized double-blind, placebo-controlled	Overweight/obese with MetS (males and females, n = 117)	59 curcumin (1 g/day)	8 weeks	↓TNF-α, IL-6, and MCP-1	Panahi *et al*., 2016
Randomized double-blind, placebo-controlled	Overweight/obese (adolescent girls, n = 60)	30 curcumin (500 mg/day)	10 weeks	↓IL-6	Saraf-Bank *et al*., 2019
Randomized double-blind, crossover	Obese (males and females, n = 30)	15 curcumin (1g/day + 5 mg bioperine)	4 weeks each treatment + 2 weeks wash-out between regimens	↓IL-1β, no changes in IL-6 and MCP-1	Ganjali *et al*., 2014
Randomized double-blind, placebo-controlled	Overweight/obese with T2D (males and females, n = 100)	50 curcumin (300 mg/day)	3 months	↓FFA	Na *et al*., 2013
Randomized double-blind, placebo-controlled	T2D (unspecified gender, n = 100)	50 curcumin (1 g + 10 mg piperine/day)	12 weeks	↓TNF-α and Leptin, ↑ Adiponectin	Panahi *et al*., 2017
Randomized double-blind, placebo-controlled	Overweight with T2D (males and females, n = 44)	21 curcumin (1500 mg/day)	10 weeks	↑ Adiponectin, ↓ weight	Adibian *et al*., 2019
Randomized double-blind, placebo-controlled	Obese (males and females, 29 adults, 29 children)	15 children curcumin (500 mg/day)	4 weeks	↓Leptin, ↓Resistin, ↑Adiponectin	Ismail *et al*., 2016
Randomized double-blind, placebo-controlled	Obese with MetS (males and females, n = 120)	40 curcumin (1 g/day)	6 weeks	↑ Adiponectin	Salahshooh *et al*., 2017
Randomized double-blind, placebo-controlled	Overweight T2D (males and females, n = 210)	107 curcumin (1.5 g/day)	6 months	↓ Leptin, ↑ Adiponectin	Chuengsamarn *et al*., 2014
Randomized double-blind, placebo-controlled	Overweight/obese with NAFLD (males and females, n = 46)	23 curcumin (3 g/day)	12 weeks	↓Leptin	Navekar *et al*., 2017
Randomized double-blind, placebo-controlled	Obese (males, n = 22)	11 curcumin (500 mg/day)	12 weeks	No change in Adiponectin	Campbell *et al*., 2019

Abbreviations: ↑ Indicates increase; ↓ Indicates decrease; IL-6 stands for interleukin-6; IL-1β represents interleukin-1β; MCP-1 refers to monocyte chemoattractant protein-1; TNFα denotes tumor necrosis factor α; FFA stands for free fatty acids; T2D signifies type 2 diabetes; MetS represents metabolic syndrome; NAFLD stands for nonalcoholic fatty liver disease

In conclusion, the discussed studies collectively demonstrate that curcumin supplementation contributes to rebalancing the production of pro- and anti-inflammatory factors, notably increasing anti-inflammatory adipocytokines like adiponectin and decreasing pro-inflammatory ones such as TNFα, IL-6, IL-1β, and MCP-1, thereby mitigating chronic inflammatory conditions in overweight/obese subjects (Table 1).

6. Conclusion

Research on turmeric curcuminoids, particularly curcumin, highlights its potential in reducing inflammation linked to obesity and related disorders. Curcumin, the most studied compound from Curcuma longa, has been shown to alleviate chronic low-grade inflammation associated with obesity, which contributes to conditions like type 2 diabetes, cardiovascular diseases, and certain cancers.

Studies reveal curcumin inhibits adipogenesis, suppresses pro-inflammatory cytokines, modulates pathways like NFkB, and boosts anti-inflammatory factors like adiponectin. Clinical trials support its effectiveness, showing reduced inflammatory markers (TNFα, IL-6, IL-1β, MCP-1) and increased adiponectin in obese individuals.

Curcumin also helps with insulin resistance and type 2 diabetes by improving glucose regulation in both animal models and humans. Overall, curcumin supplementation appears to be a natural strategy for reducing inflammation and associated health risks in obesity. More research is needed to optimize its therapeutic potential, bioavailability, and long-term effects. However, current findings emphasize curcumin's promising role in mitigating obesity-related inflammation.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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