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THE RELATIONSHIP BETWEEN DIETARY CURCUMIN SUPPLEMENTATION AND METABOLIC SYNDROME – A REVIEW

Mohamed E. Abd El-Hack[1♦], Reem Alazragi[2], Asmaa F. Khafaga[3], Alaa Qadhi[4], Khloud Ghafouri[4], Wedad Azhar[4], Abdulmohsen H. Alqhtani[5], Hanan Khojah[6], Ayman A. Swelum[5], Sylwester Świątkiewicz[7♦]

[1]Poultry Department, Faculty of Agriculture, Zagazig University, Zagazig 44511, Egypt
[2]Department of Pathology, Faculty of Veterinary Medicine, Alexandria University, Edfina 22758, Egypt
[3]Department of Biochemistry, Faculty of Science, University of Jeddah, Jeddah, Kingdom of Saudi Arabia
[4]Clinical Nutrition Department, Faculty of Applied Medical Sciences, Umm Al-Qura University, P.O Box 715, Makkah 21955, Saudi Arabia
[5]Department of Animal Production, College of Food and Agriculture Sciences, King Saud University, Riyadh, Saudi Arabia
[6]Department of Pharmacognosy, College of Pharmacy, Jouf University, P.O. Box 2014, Sakaka, Al-Jouf, Saudi Arabia
[7]National Research Institute of Animal Production, 32-083 Balice n. Kraków, Poland
♦Corresponding authors: dr.mohamed.e.abdalhaq@gmail.com; sylwester.swiatkiewicz@iz.edu.pl

Abstract

Metabolic syndrome is one of the most frequent diseases with the augmentation of the rapid changes in societies' lifestyles. On the other hand, various medicinal plants have recently been extensively used for plentiful therapeutics. Among these, curcumin and turmeric are the main components derived from the rhizome of plants, with significant effects on preventing metabolic syndromes. Due to their antioxidant and anti-inflammatory activities, the biological activities of turmeric and its bioactive element, curcumin, have antidiabetic properties via augmenting insulin release and anti-hyperlipidemia effects via enhancing fatty acids uptake, anti-obesity properties via declining lipogenesis, and antihypertensive properties via augmenting nitric oxide synthesis. Moreover, the dietary presence of turmeric and its bioactive element, curcumin, significantly affected poultry productivity, health and welfare. According to human and animal trials, turmeric or curcumin has important values as dietary supplementation and complementary therapy in some metabolic syndromes. This scenario highlights on the potential effects of curcumin (turmeric) on poultry health and its role in complementary therapy in metabolic syndrome. Additional high-quality clinical trial investigations are required to establish the clinical efficiency of the curcumin complement confidently.

Key words: curcumin, metabolic syndrome, hypertension, obesity, hyperlipidemia, diabetes

The last decades of gradual changes in our life accompanied by the Industrial Revolution increased the rapid fluctuations in societies' lifestyles (Abadi et al., 2022; Silveira Rossi et al., 2022). So, this change makes people consume processed foods, which are possible etiological issues for some metabolic syndromes (MS). The risks of MS are associated with manifold organ dysfunction and thus cause an augmentation in morbidity and mortality rates nowadays (Wang et al., 2022). MS is a cluster of multipart metabolic syndromes, including insulin resistance, hypertension, obesity, glucose intolerance, and dyslipidemia, risk issues for cardiovascular and metabolic-associated ailments (Silveira Rossi et al., 2022; Wang et al., 2022). As reported by Saklayen (2018), around 85% of women and 89% of men will be obese and overweight.

Consequently, avoiding or reducing the widespread of MS and treating MS efficiently is crucial. Scientists have recently focused on using some phytogenic molecules as a likely protection and therapy policy for MS (Wang et al., 2022; Abd El-Hack et al., 2016, 2018, 2020, 2021). On the other hand, the brilliant function of the poultry industry, such as broilers and layers, is to suffice the growing demand for providing us significant protein value in the form of eggs and meats (Raheem et al., 2020). Growth-boosting antibiotics are utilized to increase poultry species' productive efficacy to address this poor output issue. However, the extensive usage of antibiotics may produce microorganisms' resistance to antibiotics and some troubles of hostile impacts of their deposits in the human food chain. For many decades, scientists explored the potential efficacy of plant and herb extracts/metabolites in enhancing poultry health, production and welfare as an alternative to antibiotics (Bhardwaj et al., 2021; Jambwa et al., 2023; Mnisi et al., 2023). PFS (phytogenic feed supplements) are natural molecules that are procured from herbs and widely employed for several purposes in human and animal trials for preventing some metabolic syndromes (do Moinho et al., 2022; Wang et al., 2022) or improving their health status and wellbeing (Pandey et al., 2019). Commercially, the PFS can exist in various shapes *viz* herbs, essential oils, active compounds, and spices (Steiner and Syed, 2015). Many published treatises reported that the pure kinds of PAF and their various mixture had been applied in several *in vivo* and *in vitro* researches to uncover the immunomodulatory plausible, antibacterial, anthelmintic, coccidiostat, anti-inflammatory, antiviral, and antioxidant possessions (Oladeji et al., 2019; Vafaeipour et al., 2022; Wang et al., 2022). The beneficial properties of herbs on the productivity of poultry may be associated with the release of digestive enzymes secretions, thereby improving feed consumption and enhancing growth performance (Darmawan et al., 2022; Latek et al., 2022). Amongst these, curcumin is a bioactive polyphenolic constituent that exhibits antimicrobial, anti-inflammatory, anti-carcinogenic, anti-proliferative, and antioxidant actions (Abd El-Hack et al., 2020; Swelum et al., 2021; Hafez et al., 2022; Li et al., 2022).

In addition, dietary insertion of *Curcuma longa* (turmeric) has been found to display manifold usefulness in poultry welfare, health and productivity (Chen et al., 2023). According to plentiful studies on poultry (Alagawany et al., 2014, 2016; Saeed et al., 2017, 2018; Abdel-Moneim et al., 2020; Ogbuewu et al., 2022), dietary curcumin administration had considerable improvement in hepatic function by reducing liver and serum cholesterol levels, thus having the ability to control cholesterol levels and lipid profiles (Park et al., 2012; Chandran, 2021; Sasi et al., 2021; Kumar et al., 2022 a).

Curcuma longa (*C. longa*) is usually known as turmeric, a powdered form with different therapeutic possessions (Memarzia et al., 2022). The oleoresins, curcuminoid pigments (Raza et al., 2021), extracts, volatile oils and are the principal secondary molecules of turmeric that are accountable for the therapeutic activities of turmeric (Salem et al., 2022; Singh et al., 2022).

Turmeric is applied as a blood purifier and used in the retardation and medication of skin ailments (Firmansyah et al., 2023). Turmeric acid exhibited many biological activities, including; antiviral (Srivastava et al., 2022), antimicrobial (Singh et al., 2017; Ilangovan et al., 2018), anti-tumor (Abadi et al., 2022), antifungal (Hu et al., 2017), wound healing (Kumar et al., 2022 b), anti-venom (Sani et al., 2019), anti-inflammatory (Xiang et al., 2017), and hepatoprotective mediators (Sadashiva et al., 2019; Ibrahim et al., 2020). This therapeutic plausibility of *C. longa* crude extracts may be ascribed to their high contents of curcuminoids and polysaccharides as a supportive complement for cancer patients whose immune structures were wrinkled through chemotherapy management (Mehala and Moorthy, 2008). The aims of the current paper are to a) explore the potential uses of curcumin as a growth promotor in poultry feeding, b) describe the use of curcumin in treatment of some metabolic syndrome and obesity using animal and human models, and finally, c) highlight on the pharmacological curcumin effects in human health.

Curcumin as a phytogenic growth promoter

The green poultry industry tends to replace antibiotic growth promoters with natural growth promoters (NGP). Various natural growth enhancers are applied globally, derived from herbs to achieve this target. Probiotics, prebiotics, essential oils, organic acids, and herbs are virtuous antibiotic replacements (Abd El-Hack et al., 2019). Herbs, essential oils, and their extracts are brilliant substitute compounds due to the diversity of constructive actions (Wenk, 2003; Das et al., 2012; Rana et al., 2014). The NGP such as phytogenics are perfect mediators for the poultry sector because they are natural, eco-friendly, residue free, and have no side effects.

Moreover, phytogenics as NGP can primarily improve gut health for best functioning. Many biological activities of phytogenics are displayed, including insecticidal, antimicrobial, antifungal, antiparasitic, antiviral and antitoxic effects (Alagawany et al., 2022). Phytogenics boosted feed efficiency, enhanced digestion and growth indices, diminished the frequency of disorders and augmented farm profitability (Yitbarek, 2015). Curcumin is the most studied NGP known for its antimicrobial (Naz et al., 2010) and therapeutic properties (Tilak et al., 2004). Curcumin is acquired from *Curcuma longa,* also identified as turmeric acid. In addition, it is an instinctive herbal of Asia, and its stem is applied as a dye and in food flavoring as it abolishes oxidative stress and shields cells against various oxidation of proteins and lipids (Khan et al., 2012).

Owing to its different therapeutic possessions, the usage of curcumin in poultry nutrition developed broadly during the previous periods (Khan et al., 2012). Turmeric exhibits virtuous beneficial activities and can be a valuable NGP and safe antibiotic substitute. Recently, Ogbuewu et al. (2022) depicted that 0.5% turmeric powder addition had a very effective impact on production performance, serum biochemical variables and economic utility of broiler chicken rearing as a replacement for antibiotic. The usage of these antibiotics as NGF at preventive quantities is likewise dispirited globally, leading to severe arranging in some nations; therefore, other feed supplements are discovered as replacements (Durmic and Blache, 2012; Yadav et al., 2016). Many authors have evidenced the anti-parasitic activity of turmeric in poultry via abolishing sporozoites (Kim et al., 2013) or shifting oocyst's wall construction (Fatemi et al., 2015). Moreover, Pop et al. (2019) anticipated that turmeric not only affects parasites directly but also improves the competence and general performance by their valuable impacts such as antioxidative (Abdelnour et al., 2020), immunomodulatory, and anti-inflammatory machinery to protect against coccidia. Certain other typical functions of turmeric (Yadav and Jha, 2019) are to support feed absorption and digestion, prosperous positive intestinal microbiota, and thus sustain healthy intestinal assembly.

Composition of turmeric (curcumin)

Turmeric (*Curcuma longa*) is a commonly used natural medicine with numerous pharmacological characteristics. Concerning biochemical composition, 69.4% of turmeric is carbohydrates, 6.3% is protein, 5.1% is fat, 3.5% is mineral, and 13.1% is moisture (Abadi et al., 2022). Turmeric contains about 5% essential oils and 5% curcumin, a main bioactive molecule (Tajodini et al., 2015). Curcumin is a water- and ether-insoluble component but can disperse in ethanolic and other organic solvents (Ahmad et al., 2020). As illustrated in Figure 1, the most important bioactive ingredients in turmeric are curcumin, dimethoxy curcumin, tetrahydro curcuminoid and bis-methoxycurcumin (Tajodini et al., 2015). Curcumin is the vigorous component that represents around 1.5–2% of turmeric root. Various forms of curcumin have been reported in turmeric, comprising curcumin 77% diferuloylmethane, 18% dimethoxy and 5% bisdemethoxy and different pathways in humans (Ahmad et al., 2020).

Rhizomes of this herb are dehydrated to acquire turmeric powder, a yellow or gold-colored spice, which is also applied as a dye in the textile industry, food preservation, and health care. Besides, its color is due to a diferuloylmethane pigment found in turmeric. Curcumin is a water insoluble agent while highly soluble in dimethylsulfoxide, ethanol, acetone, and oils (Aggarwal, 2010; Priyadarsini, 2014). Turmeric constituents have various biological events owing to the presence of various bioactive molecules. Curcumin can display many biological actions such as antimicrobial, anti-inflammatory, antioxidant, and anticancer potential (Gull et al., 2022). Furthermore, curcumin increases insulin release and fatty acid uptake, decreases lipogenesis, and increases nitric oxide (NO) levels (Vafaeipour et al., 2022). About 326 biological activities of turmeric have been found (Ahmad et al., 2020; Kumar et al., 2022 a).

Use of curcumin in poultry nutrition

With the ban on antibiotics and the increased bacteria resistance, some natural molecules have been employed to support the health and welfare of poultry under extensive production (Wu et al., 2023). A bulk of investigations on poultry has reported the beneficial significance of dietary supplementation of curcumin in poultry production (Table 1). Turmeric addition at superior dose (1.0 and 1.5%) resulted in better growth indices and presented the greatest feed conversion ratio results. Hafez et al. (2022) reported enhanced FCR and body weight gain at 1.0 and 1.5% turmeric supplementation without the effect on feed efficacy. Likewise, Ogbuewu et al. (2022) described a decreased feed uptake at 0.5%, and Chen et al. (2023) found less feed utilization at 1–2% DM turmeric powder addition. Moreover, some studies showed curcumin's protective role against aflatoxins in broiler diets (Hafez et al., 2022; Li et al., 2022). This feature could be ascribed to curcumin's ability to improve immunity and reduce inflammatory genes such as IL-2 and IFN-γ mRNA in the spleen, thymus, and bursa of Fabricius. Moreover, curcumin addition enhanced the AFB1-triggered immune organs' damage via upregulated cytokines' expression in the broiler (Li et al., 2022).

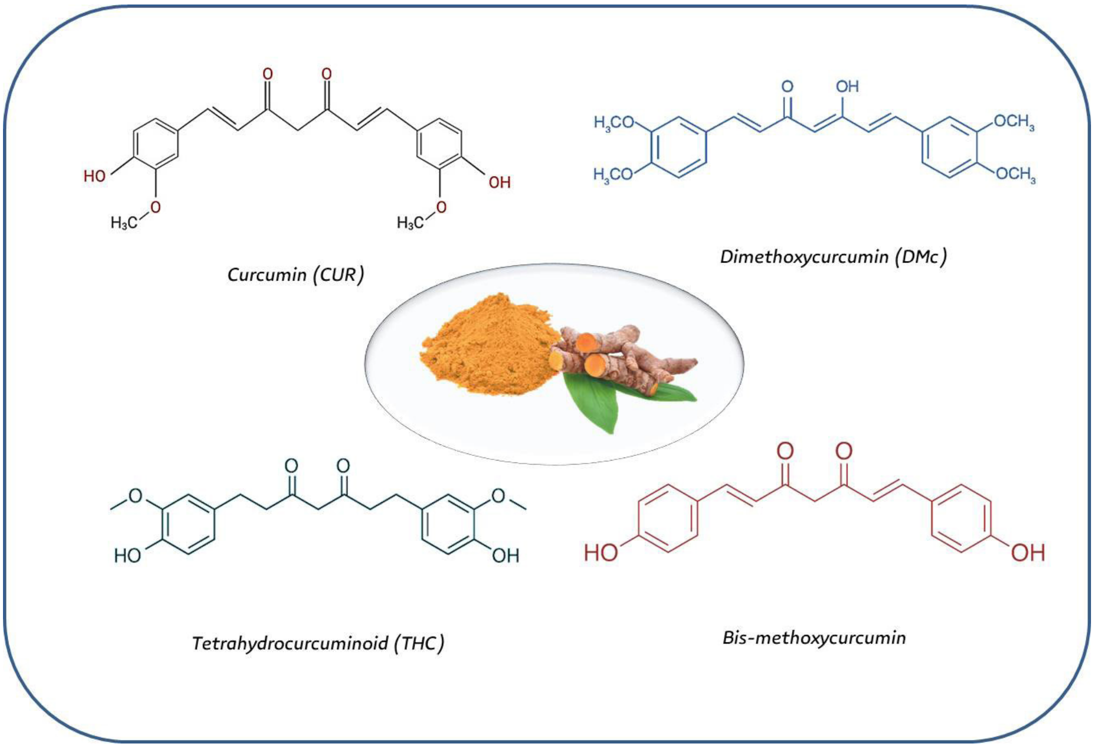

Figure 1. The most important bioactive ingredient in turmeric

Table 1. Effect of turmeric on poultry production

References	Form	Results
Lee et al., 2013	Turmeric oleoresin	– Enhanced the growth performance of broilers, resistance against avian necrotic enteritis, and reduced gut lesions.
Hussein, 2013	Dietary turmeric powder (7 g/kg)	– Improved relative growth rate and body weight, enhanced meat quality, and reduced serum concentration of cholesterol and triglycerides.
Akhavan-Salamat and Ghasemi, 2016	Dietary turmeric rhizome powder	– Enhancement of immune response in chicken, improvement in hematology, immune response, and better stress tolerance of broilers.
Chen et al., 2023	Dietary turmeric or *Curcuma longa* turmeric powder	– Good egg quality, like the improved thickness of eggshell and hardness, showed decreased yolk cholesterol levels.
Zhang et al., 2015; Yadav and Jha, 2019	*Curcuma xanthorriza*	– Improved meat quality, and increased carcass weight percentage.
Emadi et al., 2007	Turmeric rhizome powder	– Increase in total cholesterol level and hemoglobin, decrease in blood albumin content.
Galli et al., 2018	Curcumin	– Improved egg quality, and anticoccidial effect.
Zhang et al., 2015	Turmeric rhizome extract	– Improved antioxidant status, high growth performance, augmented breast muscle weight ratio, reduced fat in abdominal part.
Yadav et al., 2020	Curcumin (0.1−0.2 g/kg DM)	– Curcumin showed constructive replies on antioxidant status, lesion score and oocyst shedding. – Improved growth indices and intestinal permeability, decreased the lesion notches of the cecum, jejunum and duodenum. – Curcumin induced low-grade infection by *Eimeria maxima* in the broiler.
Salah et al., 2021	Curcumin (0.1−0.2 g/kg diet)	– Curcumin inclusion considerably augmented the breast harvest and decreased the proportion of abdominal fat. – Furthermore, both PUFAs and MUFAs in the thigh muscles and breasts were augmented. – Hepatic levels of ATP and CoQ10 were considerably improved by dietary curcumin inclusion.
Hafez et al., 2022	Curcumin (0.1−0.2 g/kg DM)	– Dietary curcumin inclusion in broiler diets improved behavioral patterns, growth indices, immune responses and growth-related gene expression of HSD. – Curcumin inclusion significantly diminished oxidative stress.
Cui et al., 2022	Curcumin (50, 150, and 250 mg/kg) for nine weeks	– Curcumin significantly reduced the absolute and relative abdominal fat weight – The levels of TG, MDA, and cholesterol in hepatic and spleen tissues were significantly reduced by supplemented 150 mg/kg. – The plasma and hepatic SOD, Gpx and catalase were boosted by curcumin addition. – Curcumin added also reduced ($P<0.05$) the mRNA expression of SREBP-1c, ACC, and FAS and significantly augmented the transcript of apolipoprotein-II and apolipoprotein B-100.

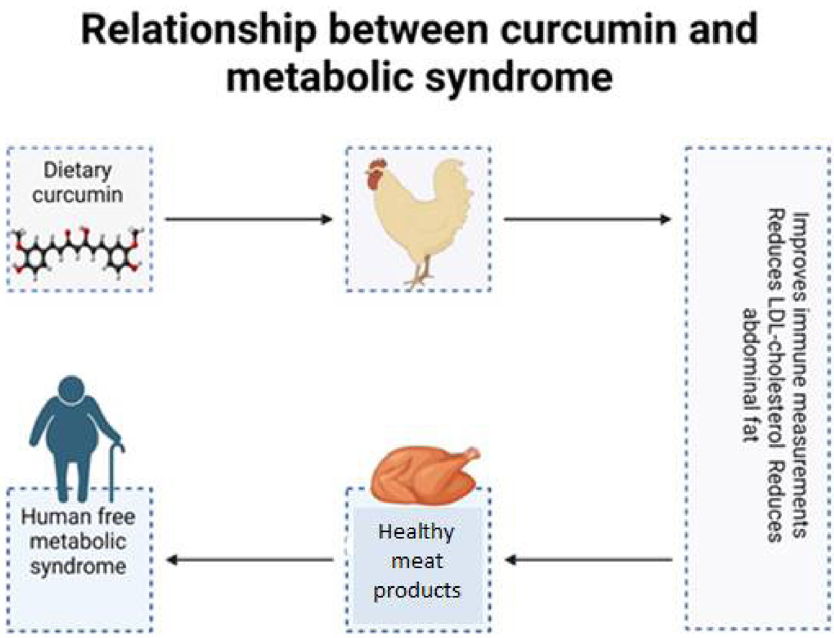

Figure 4. Relationship between curcumin and metabolic syndrome

Studies have reported the dietary inclusion of turmeric (1–1.5%) improved feed efficiency and final weight gains in various poultry species (Mondal et al., 2015; Hafez et al., 2022; Ogbuewu et al., 2022). These beneficial impacts of curcumin may be associated with enhancing intestinal integrity (Kpomasse et al., 2023) via increasing villi length and reducing pH of the intestine. Curcumin reduces the pathogenic microbes in the intestinal region, selectively augments *Lactobacillus* count (Durmic and Blache, 2012; Sasi et al., 2021) and improves digestive enzymes secretion, therefore supporting nutrient absorption, finally resulting in enhanced poultry productivity (Mondal et al., 2015). Moreover, the greater bile production was accredited to turmeric supplementation, thus improving the digestion of fats (Kheiripour et al., 2021). Two studies (Mondal et al., 2015; Kpomasse et al., 2023) showed that turmeric (1–2%) had no significant effects on the growth indices and feed competence of the broiler. Hernandez-Patlan et al. (2018) found that the addition of curcumin (0.1%) was capable of decreasing the intestinal permeability of microbial pathogenesis and total intestinal IgA while increasing significantly the activity of SOD in broilers infected with *Salmonella*. Poultry fed with turmeric had an improvement in immune measurements, D-LDL-cholesterol and reduced abdominal fat (Cui et al., 2022). Consequently, humans consuming poultry meat with lower LDL-cholesterol and fat as a functional food might be a better strategy for metabolic syndrome (Figure 4).

The discrepancy in the previous data might be associated with the difference in curcuminoids' levels of turmeric, which differs greatly (2–7%) from species to species. Moreover, collecting turmeric herbal at various phases of growth can affect growth phases and curcumin amounts (Hafez et al., 2022; Ogbuewu et al., 2022), which vary from 0.25 to 2.7% (Salem et al., 2022). Moreover, curcumin levels for precise turmeric makes between 0.58 to 3.14% of dry root weight depending on regions, soil factors, soil fertility and acidity (Ahmad et al., 2020; Salem et al., 2022; Singh et al., 2022). Turmeric powder was found to improve egg production and egg mass in chickens. According to Park et al. (2012), layers produced the most eggs when fed a meal comprising 0.50% turmeric powder, whereas those fed a control diet produced the least. But some reports showed that turmeric uptake did not significantly increase egg production. In the case of laying hens, turmeric was found to increase egg production by 10 or 30 g per kg of feed (Kosti et al., 2020), while annatto seed and turmeric with a concentration of 1% in the feed supported increased egg production (Laganá et al., 2011). Turmeric rhizome powder was given to laying hens and showed an increase in egg production, but when given to broilers, it reduced abdominal fat (Park et al., 2012; Darmawan et al., 2022). Together, curcumin, as a substitute for synthetic antibiotics in the poultry industry, has numerous benefits owing to its antioxidant and antimicrobial actions. According to the screening data, dietary inclusion of natural molecules such as curcumin could improve the growth indices, immune status, feed utilization, and digestibility of broiler and also verifies their effectiveness against pathogenic microbes such as *Pasteurella multocida* (Raheem et al., 2021).

Metabolic syndrome

Metabolic syndrome (MS) is a cluster of ailments associated with increased risk of diabetes and cardiac illnesses. The common characteristic in MS patients is related to the middle border and increased fat content in centric adipose tissues. Moreover, the chief constituents of metabolic syndrome are associated with decreased HDL cholesterol and raised triglycerides (≥150 mg/dl) (Ahmad et al., 2020). The National Health and Nutrition Examination Survey (NHNES) reported MS prevalence to rise from 28% in 1994 to 34% in 2004 (Mozumdar and Liguori, 2011). Besides, the escalation in the occurrence of type 2 diabetes can be closely related to the augmented epidemicity of obesity and it is estimated that around 90% of this illness is attributable to excess weight (Hossain et al., 2007). The pathophysiology involving diabetes and obesity is mainly attributed to two features: insulin deficiency and insulin resistance (Kaleta et al., 2022). Therefore, some types of management for metabolic syndrome can be realized by lowering the waist size and timely weight loss. Reduction in body weight by 5–10% can be achieved by many features such as lifestyle modifications and a healthy diet, which controls caloric uptake, augments physical activity, depresses all metabolic syndrome mediators and risk of cardiovascular and diabetes (type 2) diseases (Tian et al., 2022).

Metabolic syndrome is an extremely dominant and multifaceted metabolic disorder that comprises dyslipidemia, hypertension, central obesity, raised blood glucose amounts, and insulin resistance (Gholami et al., 2022). MS is presently predictable to influence around 20% of the total population. During the diagnosis of MS, there are certain differences in the metabolic mediators assumed to be contingent on many factors (e.g., ethnicity or sex). The following are normally documented: hypertension, obesity, disturbance glucose tolerance or dyslipidemia and/or diabetes (Rojas et al., 2020). As the target of this manuscript, curcumin molecule was described to have a part in declining adipogenesis and angiogenesis and by inhibiting C/EBPα (enhancer-binding protein alpha) and *PPAR* expression, thus depressing circulatory cholesterol values in the blood. Furthermore, curcumin can improve the expression of pancreatic glucose transporter (GLUT) cluster genes such as GLUT2, GLUT3, and GLUT4, therefore inspiring insulin excretion (Shehzad et al., 2012).

Recently, the study of Bateni et al. (2021) explored the likely impacts of curcumin nanoparticles (CUNA) in patients with metabolic syndrome. They reported that 80 mg/day of CUNA administered for three months suggestively decreased the blood triglycerides related to those of the placebo group, as well as the homeostasis model valuation of HOMA-ß (ß-cell dysfunction). The same results clarified that no useful impacts on HbA1c (glycosylated hemoglobin), blood pressure, HOMA-IR, insulin levels, anthropometric markers, or FBS (fasting circulating sugar) were found. These consequences must be approached with some caution due to the restrictions of the previous research. The explanations associated with the inability to determine curcumin in the plasma of patients, which can be variable because of the BMIs (body mass indices), might have been a feature in the changed responses to curcumin administration.

Moreover, the long-standing properties of the uptake of curcumin synthesis remain unidentified. Besides, it is critical to consider the optimum dosage of curcumin supplements. However, studies on curcumin as feed supplements are still unexplored and further explorations are needed. In this mean, the study of Shamsi-Goushki et al. (2020) detected that the utilized curcumin (200 mg/kg) had a superior therapeutic impact in diabetic rats in contrast to the control group or other groups with low dosage (100 mg/kg). The group of diseases described as metabolic syndrome is illustrated in Figure 2.

Curcumin and obesity

Curcumin is one of the most investigated phenolic components, due to its potential antioxidant and anti-inflammatory properties used in several therapeutic targets. Moreover, it is commonly considered for targeting many metabolic syndromes, including obesity treatment. This feature of the present molecule encourages weight loss, by helping to accelerate the basal metabolic pathway and decreasing the incidence of obesity-linked syndromes, due to its substantial anti-inflammatory action (Zamani-Garmsiri et al., 2022) that counteracts against the chronic low-grade metabolic inflammation of obesity (Alappat and Awad, 2010; Zamani-Garmsiri et al., 2022; Jambwa et al., 2023).

The white extended adipocytes mediate the direct achievement of curcumin in the overweight, which constrains inflammatory macrophage infiltration: they develop more plentiful and triggered. Thus, this inflammatory action of curcumin or its nanoforms might be linked with the suppression of inflammatory/cytokines pathways, including IL-6 and TNFα (Figure 3), which are non-traditional innovative risk issues for cardiovascular diseases (Ashraaf et al., 2023). By way of a systemic inflammation issue, the mediator TNFα can increase fat mass and insulin resistance (Raza et al., 2020; Parcha et al., 2022), thereafter triggering obesity. At the same time, the IL-6 mediator augmented the transcript of elevation-sensitivity CRP (C-reactive protein), which is principally related to abdominal obesity (Gui and Rabkin, 2022). Furthermore, the anti-inflammatory action of curcumin might be associated with the suppression of PAI-1, MCP-1, TNFα genes (Tyszkowski and Mehrzad, 2023) and augments the synthesis of adipocytes-linked anti-inflammatory influence recognized as adiponectin (Tyszkowski and Mehrzad, 2023). Besides, curcumin decreases the transcript of AP-1 and NF-kB, promotes ROS scavenging, and conquers MAPK (mitogen-activated protein kinases). Lastly, this particle may further decrease differentiation of adipocytes and can boost preventative antioxidant disturbance or imbalance (Aggarwal, 2010).

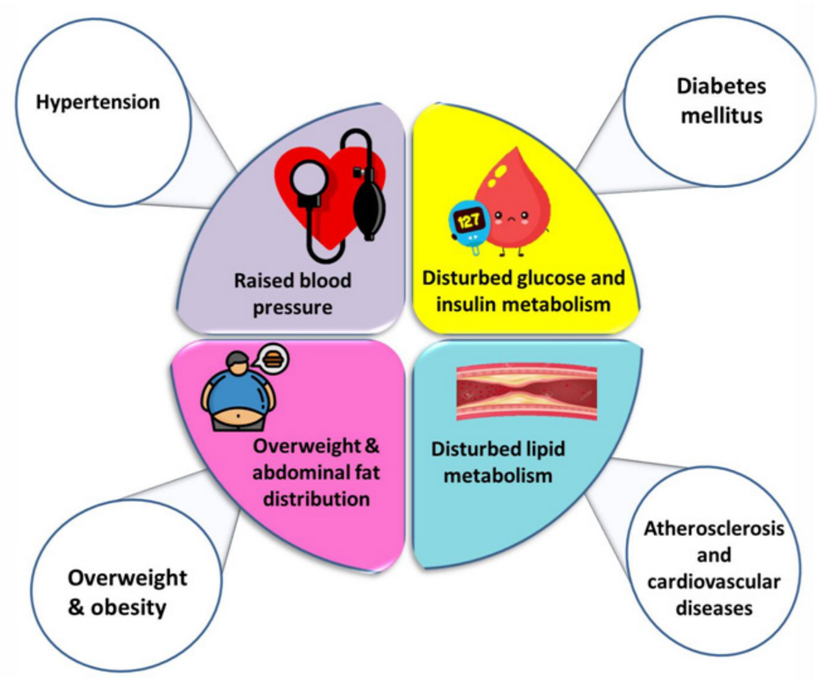

Figure 2. Diseases described as metabolic syndrome

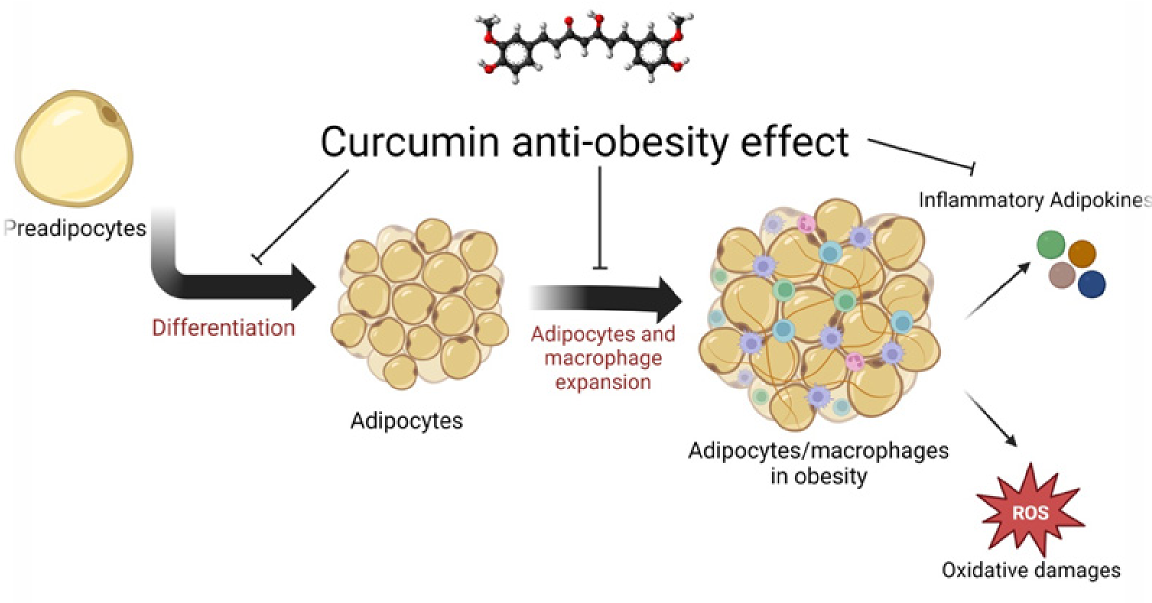

Figure 3. Curcumin effects on adipose tissue in obesity

Obesity-associated instabilities include adipocytokines and cytokines secretions, insulin resistance, transcription mediators, and steroid hormones, which can result in greater risks of malignancy expansion via impeding proliferation-apoptosis cycle (Naghizadeh and Heydari, 2023). Consequently, curcumin can avoid malignancies and obesity via constraining signaling paths connected with leptin, adiponectin, and inflammatory mediators (Casado et al., 2023). Moreover, this machinery could be related to constraining lipid accumulation and fatty acid synthase transcript. Additionally, Shehzad et al. (2012) clarified that the increase in the expression of LDL receptors, bile acid excretion, oxidation blockage LDL, and cholesterol usage in metabolic paths result in lowering cholesterol amounts. Using natural molecules as anti-obesity mediators has received great attention in recent decades with increasing obesity occurrence (Tyszkowski and Mehrzad, 2023). Those molecules may act at various levels in the obesity pathogenesis, for instance, constraining preadipocytes differentiation, conquering adipocytes development, boosting lipolysis, and persuading apoptosis of adipocytes with a resulting decrease of adipose tissue mass (Aggarwal, 2010; Shehzad et al., 2012; Kaleta et al., 2022). Based on the literature, curcumin is considered a powerful anti-obesity mediator via directly or indirectly affecting the above-mentioned pathways (Sajadimajd et al., 2023). In this respect, curcumin has been reported to target numerous molecular signaling, such as cytokines, hormones, enzymes, growth and transcript features (Shehzad et al., 2012), therefore employing antioxidant and anti-inflammatory (Zamani-Garmsiri et al., 2022) upshot on the controlling of lipid metabolism, glucose homeostasis and insulin resistance.

Use of curcumin in the metabolic syndrome treatment

Many researchers and review articles confirmed the important bioactive effects of curcumin to the treatment of metabolic syndrome (Table 2). Using natural supplements for treating prevalent medical ailments is an innovative awareness but still challenging phase in medicine.

These traditional herbals and their derivatives have acknowledged much consideration owing to several motives such as safe, applicable, inferior adverse effect, easy to obtain, and inferior charge related to synthetic medications (Raheem et al., 2021). This phylogenic component, curcumin, is identified to have therapeutic impacts such as the gastroprotective, antiproliferative, anti-inflammatory, neuroprotective and antiarthritic response of both animals and humans (Ahmad et al., 2020; Ibrahim et al., 2020). Dietary supplementation with curcumin 0.2 g/kg diet) significantly enhanced nutrient digestibility and fat metabolism, thus resulting in higher growth performance (Cui et al., 2022; Tian et al., 2022). As mentioned before, this improvement may relate secretions and gastric enzymes for accelerating the increase of bile acid secretions and gastric enzymes for accelerating absorption and digestion (Platel and Srinivasan, 2000). As depicted in Table 2, various reports have shown that curcumin can perfect the signs connected with type 2 diabetes (Tyszkowski and Mehrzad, 2023).

Obesity is a main risk issue for the progress of type 2 diabetes, and both circumstances are now documented to have considerable inflammatory machinery underlying their pathophysiology. As assessed by insulin tolerance, glucose levels, and hemoglobin A1c, curcumin can attenuate diabetes in diets including high lipids-triggered obesity risk and leptin-weakened ob/ob male C57BL/6J mice (Weisberg et al., 2008). Moreover, this experiment illustrated curcumin remediation, likewise considerably decreased macrophage infiltration of white adipocytes (Weisberg et al., 2008). Collectively, this information shows that curcumin administered orally can restore the high inflammatory secretions and metabolic imbalances (Parcha et al., 2022) related to obesity by improving the glycemic in mice models of type 2 diabetes.

Pharmacological curcumin effects on human

The therapeutic effects of curcumin on human health and well-being were scrutinized by utilizing amounts arranged between 0.44 and 2.2 mg/day, comprising 0.36–1.8 mg of curcumin (Sharma et al., 2001). For up to 16 weeks of treatment, 15 patients with progressive colorectal cancer stubborn to normal chemotherapies established *Curcuma* extract daily (Kong et al., 2021). The levels of GST and DNA damage markers were assessed in the circulatory blood cells of patients (Hashem et al., 2021). This study clarified that the oral *Curcuma* extract was well sustained, and no signs of toxicity were distinguished. The amounts of curcumin and its metabolites have been monitored in the urine or blood of patients treated with curcumin (Abadi et al., 2022; Zamani-Garmsiri et al., 2022).

However, only one patient has a level of curcumin sulfate in his circulatory blood. Reports clarified that the uptake of curcumin 0.44 g/day/month of *Curcuma* extract produced 59% lower lymphocytic GST activity than regular one (Dei Cas and Ghidoni, 2019). Moreover, the radiological screening showing a stable ailment was established in 5 patients for 2–4 months of dietary supplementation. Researchers advised that the curcumin extract can be managed carefully for patients with up to 0.180 g of curcumin with inferior oral bioavailability in the intestine of humans and might suffer intestinal digestion (Schiborr et al., 2014). An earlier experiment (Garcea et al., 2005) evaluated whether the therapeutic role of curcumin can be accomplished in the human colorectum as assessed by impacts on DNA damage marker and the transcript of COX-2 protein (Hamed et al., 2022). Oral administration of curcumin (3.6, 1.8, or 0.45 g) in patients with colorectal cancer for one week (Dei Cas and Ghidoni, 2019) induced substantial M1G levels in malignant colorectal tissues. In the other line, the expression of COX-2 was not affected by oral curcumin administration.

Accordingly, this data could reflect the daily level of 3.6 g of curcumin with considerable pharmacologically effective in colorectal cancer in human option and pharmacologically effective in colorectal cancer in humans. In an earlier work by Cruz-Correa et al. (2006), patients with FAP (familial adenomatous polyposis), an autosomal-predominant syndrome categorized by the expansion of hundreds of colorectum cancers, were orally administered with curcumin (0.48 g/3 times/day). Treating with curcumin reduced the size and quantity of polyps from baseline by 50.9 and 60.4%, respectively. Still, curcumin reduces cardiotoxicity, one of the principal lateral impacts of celecoxib. As reported in many papers (Ashraaf et al., 2023; Tyszkowski and Mehrzad, 2023), the potential roles of curcumin were explored against several inflammatory chronic ailments in humans. It was shown that curcumin exhibits considerable beneficial effects against Crohn's disease (Holt et al., 2005).

Additionally, Hanai et al. (2006) explored the efficiency of curcumin as an upkeep remedy in ulcerative colitis (UC) patients (Hanai et al., 2006). The previous authors suggested that the oral administration of curcumin (2 g/day) is a hopeful and safe remedy for preserving reduction in patients with UC disease. In other diseases, patients with tropical pancreatitis (TP) are given oral curcumin for attenuating pain, enhancing the antioxidant status, and reducing inflammation (Durgaprasad et al., 2005).

Table 2. The main outcomes of curcumin administration on metabolic indices

References	Dose, form and time	Results
Bateni et al., 2021	Nano-micelles of curcumin (0.08 g/day) for 12 weeks	– It decreased TG planes assessment of HOMA-ß (ß-cell dysfunction). – No statistical effects on insulin, HOMA-IR, HbA1c (glycosylated hemoglobin), or FBS (fasting blood sugar).
Kheiripour et al., 2021	Curcumin (80 mg/ day) for two months	– Significant decreases in the levels of HOMA-IR and FPG and insulin were observed.
Tabrizi et al., 2018	Curcumin nano-micelles (80 mg/day) for 3 months	– Improvements in LDL and HbA1c amounts and body mass index. – No statistical effects on FPG levels, TC, or HDL-C levels.
Tian et al., 2022	Curcuminoids (1 g/day + piperine 0.01 g/day) for three months	– Reduced weight and BMI in the curcuminoids group. – The lipid profile was reduced significantly, including LDL-C TC, TG, and non-HDL-C in both treated groups. – The curcuminoids group detected a significant reduction in lipoprotein A and an increase in HDL-C levels.

HOMA-ß − homeostasis model assessment of ß-cell dysfunction; BMI − body mass index; HbA1c − glycated hemoglobin A1c; HOMA-IR − homeostasis model calculation measuring insulin resistance; HOMA; TG = triglyceride; HDL = high-density lipoprotein; TC = total cholesterol; LDL = low-density lipoprotein.

Blends of curcumin (0.5 g) and piperine (5 mg) were presented to 20 patients with TP for six months. Results from a prior experiment showed a substantial decrease in MDA in RBCs after supplements therapy compared with the placebo group (Durgaprasad et al., 2005). Therefore, oral piperine and curcumin reduced lipid peroxidation in patients with TP. In another study on pancreatic cancer patients, Dhillon et al. (2008) explored the efficacy of curcumin (8 g/day/2 months), with 21 evaluable for response. Additional work assessed the viability of merging gemcitabine with curcumin in patients (Cardenes et al., 2011) with pancreatic cancer. Cardenes et al. (2011) showed that patients given curcumin (8 g) was the main termination and toxicity outline was the secondary termination. In this regard, abdominal pain was one of the greatest main toxicities that led to a decrease of levels to 4 g/day. A 9% of all evaluable patients (1/11) had an incomplete response for seven months, 36% of patients (4/11) had ailment stabilization for one year and finally, 55% of the majority of patients (6/11) had tumor development. In another medical experiment with asymptomatic manifold myeloma patients, we stated that curcumin could decrease the constitutional transcript of *STAT3* and $NF\text{-}_{k}B$ genes.

Conclusion

Curcumin, a compound present in turmeric (*Curcuma longa*), has been revealed to have anti-inflammatory, antioxidative, antiviral, and immunomodulatory characteristics. Numerous economic revenues (cost-benefit ratio) were described with the administration of curcumin to poultry diets (100–250 mg/kg diet), including enhanced productivity, and blood variables, nutrient absorption, feed efficiency, enhancement of immunity and intestinal health. Moreover, turmeric enrichment in poultry feed has significant health benefits on meat quality. Furthermore, the dietary addition of curcumin may considerably lower cholesterol in chicken meat as required by health-conscious customers. This could be a beneficial topic of curcumin or turmeric in (80–100 mg/day) complementary remedy in some human metabolic disorders and has significant values as a dietary supplement. The obtainable record kinds of curcumin (e.g., nano-curcumin) are applied to acquire the greatest therapeutic outcomes, particularly with hormonal and metabolic syndromes. Curcumin administration reduced abdominal fat and blood lipid profiles in some syndromes. They may aid as catalysts for forthcoming exploration to validate the safety and efficacy of this molecule for the medication of various human syndromes. However, further clinical trials must be done to authorize these possessions and determine the appropriate doses. An additional probable topic of upcoming explorations would be examining the greatest optimal amounts of curcumin additions to create varieties for preventive and therapeutic targets in other diseases.

Conflicts of interest

All authors declare that they have no conflicts of interest that could inappropriately influence this manuscript.

Author contribution

All authors contributed equally to writing this review article. All authors read and approved the final version of this manuscript.

Data availability statement

No data are available.

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