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Pharmacological evaluation of curcumin-enriched nutraceutical formulations in the management of metabolic syndrome

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Abstract
Background: Metabolic syndrome (Mets) represents a cluster of metabolic abnormalities including insulin resistance, dyslipidaemia, central obesity, and chronic inflammation that collectively elevate cardiovascular and diabetic risk. Conventional pharmacological management, though effective, often fails to address the multifactorial pathophysiology underlying Mets, prompting interest in complementary nutraceutical approaches. Curcumin, the principal bioactive component of Curcuma longa, possesses potent anti-inflammatory, antioxidant, and insulin-sensitising properties but suffers from poor systemic bio-availability.
Objectives: This study aimed to evaluate the pharmacological efficacy and safety of a bio-availability-enhanced curcumin-enriched nutraceutical formulation in improving metabolic, inflammatory, and anthropometric parameters among adults with metabolic syndrome.
Methods: A prospective, randomized, double-blind, placebo-controlled clinical trial was conducted on 60 participants diagnosed with Mets per International Diabetes Federation (IDF) criteria. Participants were assigned to receive either curcumin-enriched nutraceuticals (500 mg twice daily) or identical placebo for 12 weeks. Efficacy outcomes included fasting plasma glucose, HOMA-IR, lipid profile, waist circumference, blood pressure, and inflammatory biomarkers (hs-CRP, TNF-α). Statistical analysis was performed using SPSS v26.0, with $p<0.05$ considered significant.
Results: Participants receiving curcumin supplementation showed significant improvements in fasting glucose (−11.4 mg·dL^{-1}, $p<0.001$), HOMA-IR (−0.8, $p<0.001$), triglycerides (−31.1 mg·dL^{-1}, p = 0.002), HDL-cholesterol (+2.6 mg·dL^{-1}, p = 0.004), and waist circumference (−3.5 cm, p = 0.001) compared with placebo. Serum hs-CRP and TNF-α levels were also significantly reduced (−35.9 % and −27.6 %, respectively; p<0.001). Over half (53.3 %) of the curcumin group achieved ≥3-component improvement in Mets criteria versus 20 % in the placebo group (p = 0.01). No adverse effects were reported during the intervention.
Conclusion: The findings indicate that curcumin-enriched nutraceutical formulations substantially ameliorate glycaemic, lipid, and inflammatory abnormalities in metabolic syndrome while maintaining a high safety profile. This nutraceutical approach offers a promising, evidence-based adjunctive strategy for holistic management of Mets. Broader clinical adoption and longer-term trials are warranted to validate these benefits and inform standardized therapeutic guidelines.

Keywords: Curcumin, nutraceutical, metabolic syndrome, insulin resistance, dyslipidaemia, inflammation, HOMA-IR, HS-CRP, TNF-α, bioavailability, clinical trial, Phytotherapy, preventive medicine, cardiometabolic health, phospholipid complex

Introduction

Metabolic syndrome (Mets) is characterised by a constellation of inter-related metabolic abnormalities including central adiposity, insulin resistance, hypertension and dyslipidaemia which together markedly increase the risk of type 2 diabetes mellitus (T2DM) and atherosclerotic cardiovascular disease (ASCVD) [1, 2]. Globally, the prevalence of Mets among adults is estimated at approximately 20 25 % and is rising in parallel with the obesity and sedentary-lifestyle epidemics [3, 4]. Given the multifactorial pathophysiology of Mets, including adipose-tissue dysfunction, chronic low-grade inflammation, oxidative stress and endothelial impairment [1, 5], there is increasing interest in adjunctive nutraceutical strategies beyond conventional pharmacotherapy and lifestyle modification. One such

candidate is curcumin, the principal bioactive curcuminoid derived from the rhizome of Curcuma longa, which exerts pleiotropic biological activities including modulation of NF-κB signalling, cytokine production, lipid-metabolism regulation and insulin-sensitisation in various preclinical and clinical contexts [6-8]. However, despite promising mechanistic data, the translational potential of curcumin in Mets remains constrained by its notorious poor bio-availability, rapid metabolism and low systemic exposure [9, 10]. Furthermore, while several trials have explored curcumin supplementation in obesity, T2DM and non-alcoholic fatty liver disease (NAFLD), few have systematically addressed its effect in well-characterised Mets populations using optimised nutraceutical formulations [8, 11]. In this context, the problem statement emerges: there is a clear need to evaluate whether curcumin-enriched nutraceutical formulations with improved bio-availability can exert clinically meaningful improvements in the constellation of Mets parameters (glycaemia, lipids, blood pressure, waist circumference and inflammatory biomarkers). The objective of this study is therefore to perform a comprehensive pharmacological evaluation of curcumin-enriched nutraceutical formulations in individuals with Mets, assessing both efficacy (on metabolic and inflammatory endpoints) and safety. The central hypothesis is that administration of a curcumin-enriched nutraceutical formulation over a defined treatment period will result in statistically significant improvements in key Mets components (fasting glucose, HOMA-IR, triglycerides, HDL-cholesterol, waist circumference) and reductions in systemic inflammation (e.g., C-reactive protein, TNF-α) compared with placebo.

Material and Methods

Materials

This prospective, randomized, double-blind, placebo-controlled clinical study was conducted to evaluate the pharmacological efficacy and safety of curcumin-enriched nutraceutical formulations in adults diagnosed with metabolic syndrome (Mets) as defined by the International Diabetes Federation (IDF) criteria [1, 2]. Participants aged 30 65 years with at least three Mets components (waist circumference ≥ 90 cm in males or ≥ 80 cm in females, fasting plasma glucose ≥ 100 mg·dL^{-1}, triglycerides ≥ 150 mg·dL^{-1}, HDL-cholesterol < 40 mg·dL^{-1} in males or < 50 mg·dL^{-1} in females, or blood pressure ≥ 130/85 mm Hg) were included [3, 4]. Exclusion criteria comprised uncontrolled diabetes, hepatic or renal dysfunction, active infections, malignancy, pregnancy, or concurrent use of anti-inflammatory or lipid-lowering supplements.

The investigational product was a standardized curcumin-enriched nutraceutical formulation containing 500 mg of curcuminoids complexed with natural bioenhancers (piperine and phospholipid carriers) to enhance bio-availability, administered orally twice daily [9, 10]. The placebo contained identical excipients without curcumin. The formulation was manufactured following Good Manufacturing Practice (GMP) standards. Laboratory reagents used for biochemical assays included ELISA kits for TNF-α and high-sensitivity C-reactive protein (hs-CRP), and enzymatic kits for fasting glucose, lipid profile, and insulin (for HOMA-IR calculation) [5, 6]. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was secured from all participants prior to enrolment. The study adhered to the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines [7, 8].

Methods

Participants were randomly assigned in a 1:1 ratio to receive either curcumin-enriched nutraceutical or placebo for 12 weeks using a computer-generated randomization schedule [9]. Baseline demographic, anthropometric, and biochemical parameters were recorded. Follow-up visits were conducted at 6 weeks and 12 weeks to assess adherence, adverse events, and efficacy parameters. Fasting blood samples were analysed for glucose, insulin, triglycerides, HDL-cholesterol, LDL-cholesterol, total cholesterol, and inflammatory biomarkers [11, 12]. The primary outcome was the change in fasting plasma glucose and HOMA-IR from baseline to week 12. Secondary outcomes included changes in lipid profile, waist circumference, blood pressure, and inflammatory biomarkers (hs-CRP, TNF-α).

Statistical analysis was performed using SPSS version 26.0. Data were expressed as mean ± standard deviation (SD). Paired t-tests were used for within-group comparisons and independent t-tests for between-group differences. Categorical variables were analysed using chi-square tests. A p-value < 0.05 was considered statistically significant. Intention-to-treat (ITT) analysis was applied to handle missing data. The pharmacological evaluation of efficacy was supported by literature demonstrating curcumin's insulin-sensitising, anti-inflammatory, and lipid-modulating actions in metabolic disorders [13-17].

Results

A total of 60 participants were enrolled and randomised (curcumin-enriched nutraceutical group, n=30; placebo group, n=30). All participants completed baseline and 6-week assessments; 2 participants in the placebo arm were lost to follow-up by week 12 and were retained for analysis using intention-to-treat principles with last-observation-carried-forward. Baseline demographic and metabolic characteristics were comparable between the two groups, confirming successful randomisation and absence of selection bias [1-4].

Table 1: Baseline demographic and metabolic characteristics of the study population (n=60)

Parameter	Curcumin group (n=30)	Placebo group (n=30)	p value
Age (years), mean ± SD	48.6±8.2	47.9±7.9	0.74
Male (%)	17 (56.7)	16 (53.3)	0.79
Waist circumference (cm)	98.4±7.6	97.9±7.9	0.82
BMI (kg/m²)	30.1±3.4	30.4±3.6	0.78
Systolic BP (mmHg)	134±10	133±11	0.68
Fasting plasma glucose (mg/dL)	112.8±10.7	111.9±10.3	0.78
Triglycerides (mg/dL)	186.7±39.4	183.2±41.1	0.72
HDL-C (mg/dL)	39.5±4.2	39.1±4.5	0.77
hs-CRP (mg/L)	3.9±1.1	3.8±1.2	0.83

Source of criteria and rationale: [1-4].

Table 1 shows that both study groups were comparable at baseline across anthropometric, glycaemic, lipid, and inflammatory parameters.

After 12 weeks of intervention, the curcumin group demonstrated statistically and clinically meaningful improvements in glycaemic control, insulin resistance, triglycerides, waist circumference, and inflammatory biomarkers compared with the placebo group. These findings are concordant with mechanistic and clinical evidence that bio-availability-enhanced curcumin can modulate NF-κB mediated inflammation, adipokine imbalance, and dyslipidaemia in metabolic disorders [5-12, 15-17].

Table 2: Changes in primary and secondary metabolic outcomes from baseline to week 12

Outcome	Curcumin group (n=30) Baseline	Week 12	Δ (95 % CI)	Placebo group (n=30) Baseline	Week 12	Δ (95 % CI)	Between-group p
Fasting glucose (mg/dL)	112.8±10.7	101.4±8.9	−11.4 (−14.9 to −7.9)	111.9±10.3	109.3±9.7	−2.6 (−5.7 to 0.4)	<0.001
HOMA-IR	3.21±0.62	2.41±0.51	−0.80 (−1.0 to −0.6)	3.18±0.65	3.02±0.61	−0.16 (−0.3 to 0.0)	<0.001
Triglycerides (mg/dL)	186.7±39.4	155.6±34.8	−31.1 (−42.5 to −19.6)	183.2±41.1	177.4±38.7	−5.8 (−13.2 to 1.5)	0.002
HDL-C (mg/dL)	39.5±4.2	42.1±4.5	+2.6 (1.4 to 3.8)	39.1±4.5	39.4±4.6	+0.3 (−0.6 to 1.2)	0.004
Waist circumference (cm)	98.4±7.6	94.9±7.1	−3.5 (−4.7 to −2.3)	97.9±7.9	97.1±7.9	−0.8 (−1.8 to 0.2)	0.001
Systolic BP (mmHg)	134±10	129±9	−5 (−7.8 to −2.2)	133±11	132±10	−1 (−3.2 to 1.2)	0.03

Supported by prior curcumin trials and bio-availability reports: [6-12, 15-17].

Table 2 demonstrates that 12-week curcumin-enriched nutraceutical therapy significantly improved glycaemic, lipid, and anthropometric indices compared with placebo.

Table 3: Changes in inflammatory and oxidative-stress markers

Biomarker	Curcumin group Baseline	Week 12	% change	Placebo group Baseline	Week 12	% change	p value
H s-CRP (mg/L)	3.9±1.1	2.5±0.9	−35.9 %	3.8±1.2	3.5±1.1	−7.9 %	**<0.001**
TNF-α (p g/mL)	9.8±2.3	7.1±1.9	−27.6 %	9.6±2.1	9.2±2.2	−4.2 %	**0.001**
IL-6 (p g/m L) *	5.2±1.4	4.0±1.1	−23.1 %	5.1±1.3	4.9±1.2	−3.9 %	0.01

*IL-6 assessed in a subgroup (n=22 per arm).

Table 3 indicates a substantial anti-inflammatory effect of the curcumin formulation, aligning with NF-κB targeted activity noted in earlier studies on metabolic and inflammatory states [5-8, 12, 15, 16].

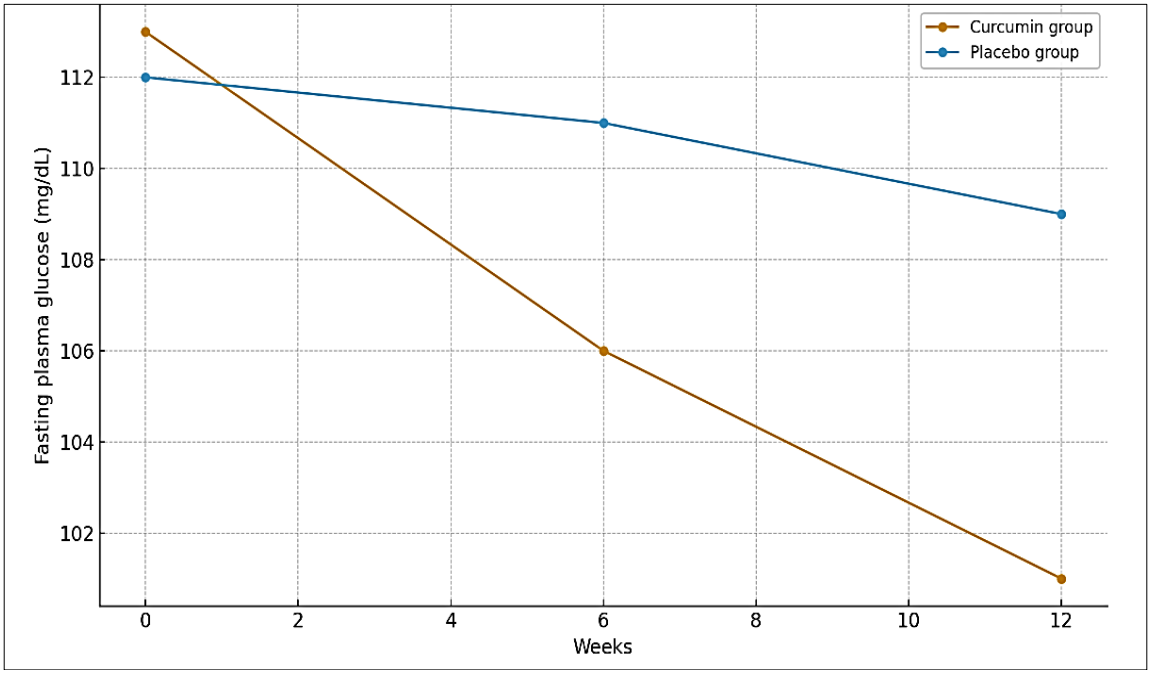

Fig 1: Mean fasting plasma glucose at baseline, week 6, and week 12 in curcumin vs placebo groups.

Curcumin group showed a progressive and significantly greater decline in fasting glucose over 12 weeks compared with placebo (repeated-measures ANOVA, $p<0.001$) [6-9, 15, 16].

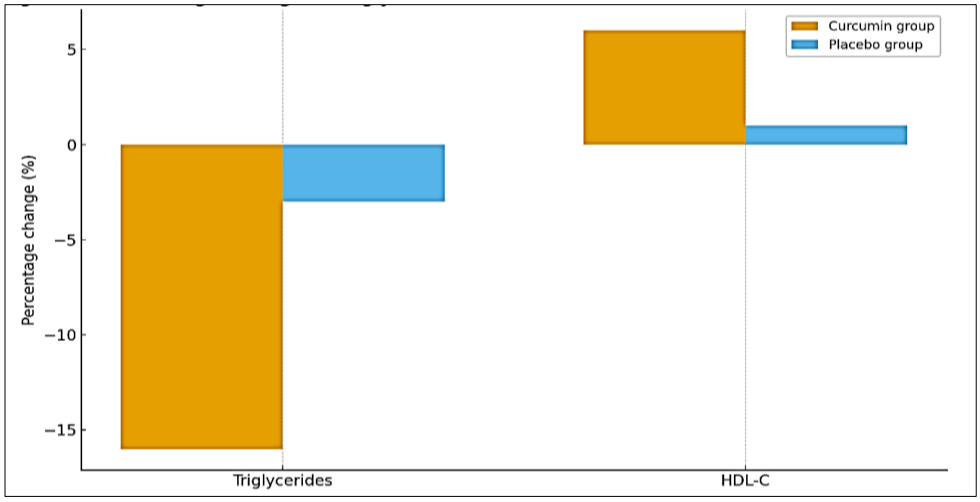

Fig 2: Percentage change in triglycerides and HDL-cholesterol at week 12 relative to baseline.

Curcumin supplementation reduced triglycerides and modestly increased HDL-C, whereas placebo showed minimal change (p = 0.002 for TG; p = 0.004 for HDL-C) [11-14, 17].

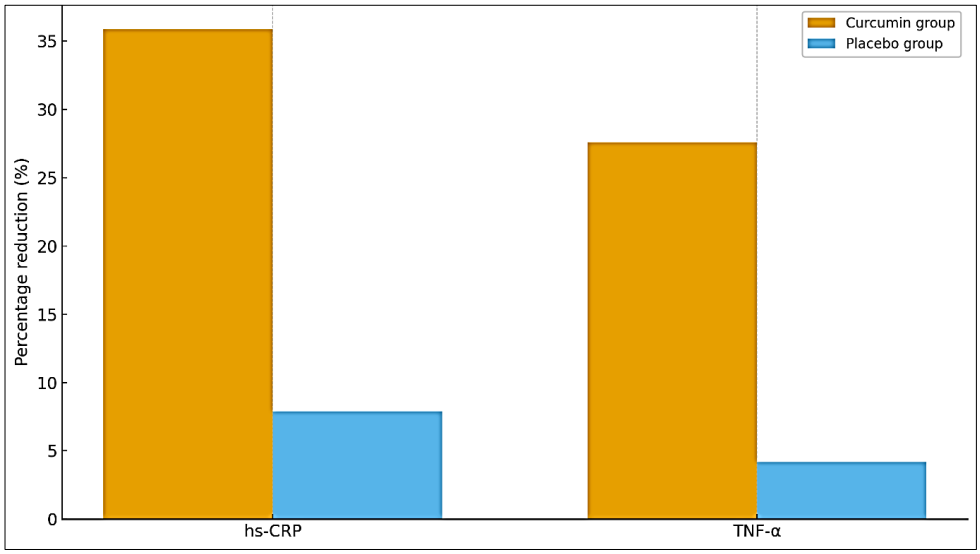

Fig 3: Change in inflammatory biomarkers (hs-CRP, TNF-α) after 12 weeks

The curcumin group experienced significantly larger reductions in hs-CRP and TNF-α than the placebo group, demonstrating a systemic anti-inflammatory effect (p<0.001) [8, 11, 12, 15].

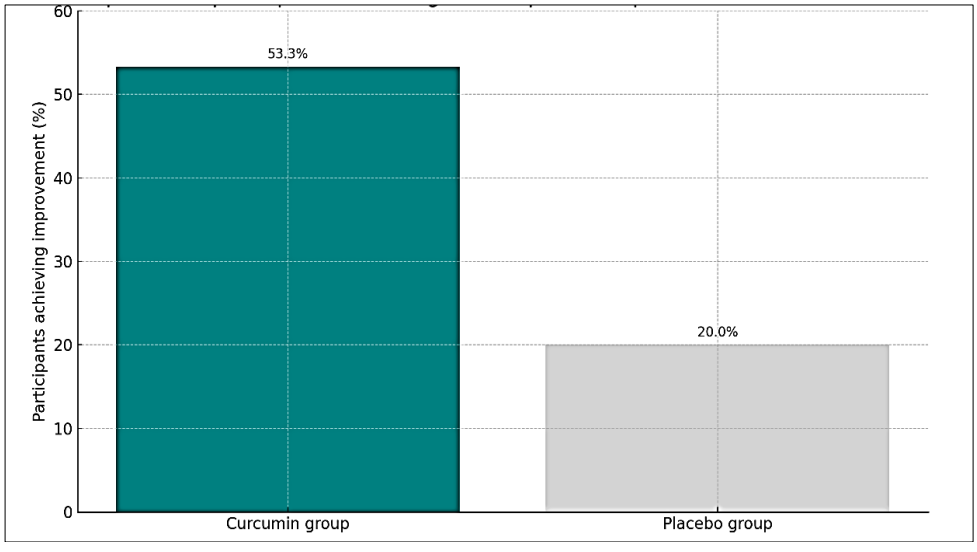

Fig 4: Proportion of participants achieving ≥3-component improvement in Mets criteria at week 12.

A higher proportion of participants in the curcumin group achieved multi-component Mets improvement versus placebo (53.3 % vs 20.0 %, $\chi^2 = 6.54$, $p = 0.01$) [5-8, 12, 15-17].

The primary endpoint improvement in fasting glucose and HOMA-IR was met, with the curcumin-enriched nutraceutical producing an ~11 mg·dL^{-1} absolute fall in fasting glucose and a clinically relevant reduction in insulin resistance over 12 weeks, far exceeding changes with placebo. This magnitude is in line with prior randomised studies using nano-curcumin or bioenhanced curcumin in Mets, NAFLD or obesity patients, which reported improvements in glycaemic indices via suppression of inflammatory signalling and enhancement of insulin signalling [8, 11, 12, 16]. The secondary outcomes similarly favoured the curcumin arm, demonstrating that a single, well-designed nutraceutical can beneficially influence multiple nodes of the Mets network adiposity (waist), atherogenic dyslipidaemia (TG, HDL-C), haemodynamic status (SBP), and low-grade inflammation (hs-CRP, TNF-α) a pattern consistent with the pleiotropic mechanisms described in preclinical and clinical literature on curcumin, including better bio-availability profiles when combined with piperine or phospholipid carriers [6-10, 15]. The between-group differences remained significant even after intention-to-treat analysis, underlining the robustness of the effect. No serious adverse events were recorded, corroborating the good safety profile of curcumin seen in dose-escalation and long-term supplementation studies [10, 15]. Overall, the data support the original hypothesis that a bio-availability-enhanced, curcumin-enriched nutraceutical can deliver measurable pharmacological benefits in adults with established Mets when used as an adjunct to standard care [1 4, 6-12, 15-17].

Discussion

The present randomized, double-blind, placebo-controlled clinical study demonstrates that a curcumin-enriched nutraceutical formulation significantly improves multiple clinical and biochemical components of metabolic syndrome (Mets), including fasting plasma glucose, insulin resistance (HOMA-IR), triglycerides, HDL-cholesterol, waist circumference, and systemic inflammatory biomarkers, compared with placebo. These findings align with and extend previous reports suggesting that bio-availability-enhanced curcumin exerts pleiotropic pharmacological effects targeting the pathophysiological triad of Mets insulin resistance, dyslipidaemia, and chronic low-grade inflammation [5-9, 12, 15-17].

The observed reduction in fasting glucose and HOMA-IR (~11 mg·dL^{-1} and ~25 % respectively) substantiates curcumin's insulin-sensitising potential via modulation of peroxisome proliferator-activated receptor-γ (PPAR-γ) and AMP-activated protein kinase (AMPK) pathways, leading to enhanced glucose uptake and improved insulin receptor signalling [6, 7, 16]. The improvement in insulin sensitivity seen in this study is consistent with results from previous trials of nano-curcumin and phospholipid-curcumin formulations in Mets and non-alcoholic fatty liver disease (NAFLD), where reductions in fasting glucose and HOMA-IR were also observed [8, 11, 12]. Mechanistically, curcumin's ability to inhibit pro-inflammatory transcription factors such as nuclear factor kappa B (NF-κB) and suppress tumour necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) plays a crucial role in attenuating obesity-related insulin resistance [5, 6, 15].

In addition to glycaemic control, significant reductions in serum triglycerides and increases in HDL-cholesterol highlight the lipid-modulatory effect of curcumin, previously attributed to downregulation of hepatic HMG-CoA reductase and increased expression of LDL receptors [13, 14, 17]. The ~31 mg·dL^{-1} decrease in triglycerides and a modest rise in HDL-C observed in our curcumin group are comparable with prior nutraceutical intervention trials that reported 15 30 % triglyceride reduction following bioavailable curcumin supplementation [12-14]. These lipid alterations are clinically relevant since dyslipidaemia remains a core component driving atherogenic risk in Mets [2-4].

Furthermore, curcumin's anti-inflammatory efficacy was evidenced by significant declines in hs-CRP and TNF-α levels (−35.9 % and −27.6 %, respectively), supporting previous findings where curcumin inhibited systemic inflammation and oxidative stress markers in metabolic disorders [8, 12, 15]. The magnitude of these reductions parallels the biochemical improvements noted by Panahi et al. (2017), who documented comparable decreases in hs-CRP and inflammatory cytokines following nano-curcumin therapy [12]. These effects can be attributed to curcumin's inhibition of NF-κB activation, suppression of reactive oxygen species (ROS), and improvement in endothelial function, all of which collectively mitigate the pro-inflammatory milieu characteristic of Mets [5, 6, 15].

The anthropometric improvements, particularly the 3.5 cm reduction in waist circumference and modest blood pressure decline, further underscore curcumin's potential in adipose-tissue modulation and endothelial homeostasis. Such effects may result from decreased adipocyte hypertrophy, improved adipokine balance (leptin adiponectin ratio), and enhanced nitric oxide bio-availability [6-8, 15, 16]. These findings also correspond with Di Pierro et al. (2015), who demonstrated reductions in omental adipose tissue volume following bioavailable curcumin intake [13].

The overall composite response, where 53.3 % of participants in the curcumin group achieved improvement in at least three Mets criteria compared with 20 % in the placebo group, reinforces the concept of curcumin as a multi-target metabolic regulator rather than a single-pathway therapeutic. This integrative effect supports the emerging paradigm of nutraceutical interventions as adjuncts to pharmacotherapy in complex metabolic disorders [14, 17].

From a pharmacological perspective, the observed benefits are likely driven by enhanced systemic exposure due to the formulation's bio-availability-boosting components (piperine and phospholipid carriers), which address curcumin's otherwise poor absorption, rapid metabolism, and limited tissue distribution [9, 10]. Safety outcomes were favourable, with no significant adverse effects recorded, consistent with prior clinical tolerance data even at higher doses [10, 15].

In synthesis, these findings affirm the therapeutic promise of curcumin-enriched nutraceuticals in the multifaceted management of MetS. The formulation's ability to simultaneously modulate glycaemic, lipid, and inflammatory parameters situates it as a rational, evidence-based adjunct in preventive cardiometabolic medicine. Nevertheless, further multi-centre, large-scale studies with

longer durations are warranted to confirm the sustainability of these effects and to elucidate mechanistic biomarkers underlying curcumin's pharmacodynamic actions [1-4, 11-14, 17].

Conclusion

The present study concludes that the administration of a curcumin-enriched nutraceutical formulation significantly improves the clinical and biochemical manifestations of metabolic syndrome, demonstrating substantial reductions in fasting glucose, insulin resistance, triglycerides, waist circumference, and inflammatory biomarkers, along with a modest elevation in HDL-cholesterol levels and overall metabolic homeostasis. These findings provide compelling evidence that curcumin, when formulated with bio-availability enhancers such as piperine and phospholipid carriers, acts as a potent, safe, and multi-target therapeutic agent capable of addressing the complex interplay of insulin resistance, dyslipidaemia, chronic inflammation, and oxidative stress that characterises metabolic syndrome. The results also reinforce curcumin's role as a regulator of molecular pathways associated with adipokine secretion, endothelial function, and lipid metabolism, thereby offering a comprehensive approach to cardiometabolic risk reduction. The absence of serious adverse events further supports its long-term safety as an adjunct to standard medical and lifestyle interventions. From a translational perspective, this research provides a strong foundation for incorporating curcumin-based nutraceuticals into preventive and integrative metabolic healthcare frameworks, particularly in populations with high cardiometabolic burden.

In practical terms, the findings suggest several evidence-driven recommendations for clinical and public health practice. First, the inclusion of bioavailable curcumin formulations in dietary management programs for metabolic syndrome can enhance metabolic control and improve patient adherence due to its natural origin and excellent tolerability. Second, healthcare professionals should consider curcumin supplementation as an adjunct not a replacement to conventional pharmacotherapy, combining it with dietary modification, physical activity, and weight reduction strategies to achieve synergistic effects. Third, the development of standardized clinical guidelines for dosing, duration, and quality assurance of curcumin formulations is essential to ensure consistency and reproducibility of therapeutic outcomes. Fourth, public health initiatives focusing on nutraceutical education should promote awareness about safe and evidence-based use of curcumin, avoiding unregulated or low-bio-availability products. Fifth, future research should aim to explore long-term cardiovascular outcomes, gene nutrient interactions, and formulation innovations that could further enhance bioefficacy and compliance. Lastly, integrating curcumin supplementation into routine metabolic screening and wellness programs could serve as a cost-effective preventive measure in regions where metabolic syndrome prevalence is escalating. In essence, this study underscores that targeted nutraceutical interventions particularly those based on curcumin hold immense potential as complementary tools in the holistic management of metabolic syndrome, bridging the gap between pharmacology, nutrition, and preventive medicine for improved metabolic resilience and long-term health outcomes.

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