J Nepal Health Res Counc 2025 April-June; 23 (67): 216-235

Antidiabetic and Metabolic Effects of Turmeric (*Curcuma Longa*) in Patients with Type 2 Diabetes Mellitus or Hyperglycemia - A Systematic Meta-Review and Meta-Analysis

Kapil Amgain,[1,2] Richa Shah,[3] Siti Munirah Md Noh,[4] Shamsher Shrestha,[5] Bijay Aryal,[6] Lok Raj Joshi,[7] Sujana Neupane,[8] Shamima Abdul Rahman,[1,4,*]

[1]Graduate Research School, University of Cyberjaya (UoC), Persiaran Bestari, Cyberjaya, Selangor, Malaysia·
[2]Department of Clinical Anatomy and Cell Biology, Karnali Academy of Health Sciences (KAHS), Jumla.
[3]Research Wing, Health Action and Research, Kathmandu, Nepal.
[4]Faculty of Pharmacy, University of Cyberjaya, Persiaran bestari, Cyberjaya, Selangor, Malaysia.
[5]Department of Anatomy, BP Koirala Institute of Health Sciences, Dharan, Nepal.
[6]Department of Clinical Pharmacology and Therapeutics, KAHS, Jumla, Nepal,
[7]Department of Physiology, Faculty of Health Sciences, Dadeldhura, Farwestern University, Nepal.
[8]Department of Nursing, Manmohan Cardiothoracic Vascular and Transplant Centre, Kathmandu, Nepal.

ABSTRACT

Background: Curcumin, the primary bioactive compound in turmeric (*Curcuma longa* Linn.), has demonstrated potential benefits in managing type 2 diabetes mellitus (T2DM) and hyperglycemia. This systematic meta-review aimed to evaluate the effectiveness of turmeric in improving glycemic control, lipid profiles, and other metabolic markers in the patients with T2DM or hyperglycemia.

Methods: A comprehensive literature search was conducted across seven electronic databases to identify relevant studies published up to December 2023. Inclusion criteria focused on randomized controlled trials included in systematic reviews or meta-analyses assessing curcumin's effects on metabolic markers. Data were extracted systematically, and the methodological quality of included reviews was assessed using AMSTAR-2. Meta-analyses were performed using STATA 17 to synthesize outcomes for fasting blood glucose (FBG), glycated hemoglobin (HbA1c), lipid profiles, and other markers, employing random-effects models to account for heterogeneity.

Results: Thirteen systematic reviews and meta-analyses of 63 unique randomized controlled trials involving 3706 human participants met the inclusion criteria. The pooled analysis revealed that curcumin significantly reduced FBG (mean difference [MD] = −6.30 mg/dL; 95% CI: −9.33, −3.27), HbA1c (MD = −0.31%; 95% CI: −0.57, −0.05), low-density lipoprotein (LDL) cholesterol (MD = −5.95 mg/dL; 95% CI: −9.43, −2.47), and triglycerides (TG) (MD = −12.88 mg/dL; 95% CI: −20.09, −5.67) while increasing high-density lipoprotein (HDL) cholesterol (MD = 1.46 mg/dL; 95% CI: 0.37, 2.56). No significant effects were observed on total cholesterol, blood pressure, body mass index, blood urea nitrogen, or creatinine levels. Heterogeneity across studies was high but consistent with meta-analytical expectations for diverse populations and interventions.

Conclusions: Curcumin supplementation shows statistically significant improvements in glycemic control and lipid profiles in individuals with T2DM or hyperglycemia, supporting its potential as an adjunct therapy. However, its effects on renal markers, blood pressure, and body weight remain inconclusive. Moreover the efficacy of the crude powder of turmeric remain unexplored. Future trials should address long-term efficacy and safety to optimize the therapeutic role of curcumin and turmeric powder in diabetes management.

Keywords: Antidiabetic potential; curcumin; diabetes; glycemic control; turmeric; type 2 diabetes mellitus.

INTRODUCTION

Diabetes is a chronic metabolic disease caused by either deficient insulin production (type 1 diabetes mellitus [T1DM]) or inefficient insulin utilization (type 2 diabetes mellitus [T2DM]).[1] Owing to the increased consumption of junk food, sedentary lifestyles, and physical inactivity, the incidence and prevalence of diabetes have been rapidly increasing and T2DM has become a global public health concern.[2,3] According

***Correspondence:** Prof. Dr. Shamima Abdul Rahman, Faculty of Pharmacy, University of Cyberjaya. Email: shamima@cyberjaya.edu.my

to a report published by the International Diabetes Federation in 2023, over 537 million adults worldwide were affected by diabetes, with T2DM accounting for the vast majority of cases.[4] T2DM is characterized by elevated blood glucose levels (hyperglycemia), resulting from insulin resistance, pancreatic ß-cell dysfunction, or a combination of both.[1,2] If left unmanaged, T2DM can lead to complications multiple organ systems, retinopathy, neuropathy, etc.[3,5] These long-term complications reduce quality of life and substantially increase healthcare costs.[6,7]

Despite the availability of pharmacological interventions for managing T2DM, their long-term efficacy is often limited by their side effects,[8,9] and many patients fail to achieve optimal glycemic control.[5] This has increased interest in alternative and complementary therapies, particularly those derived from natural ingredients with fewer side effects.[10,11] Curcumin, a major bioactive component of Curcuma longa (turmeric), has been studied extensively worldwide for its potential antidiabetic, anti-inflammatory, and antioxidant properties.[12,13] Preclinical and clinical studies suggest that curcumin may help manage T2DM by improving glucose metabolism, increasing insulin sensitivity, and protecting ß-cells from oxidative stress.[14-17]

While several systematic reviews and meta-analyses (SRMAs) have been conducted on the antidiabetic effects of curcumin in patients with T2DM,[18-24] findings have been inconsistent. Some SRMAs reported significant improvements in glycemic control, whereas others reported minimal or inconsistent effects.[25-28] A meta-review, which involves reviewing and consolidating findings from multiple SRMAs[29], can provide higher-level evidence, offering clearer insights for prevention and management. Hence, this systematic meta-review aimed to evaluate the effectiveness of turmeric in improving glycemic control, lipid profiles, and other metabolic markers in patients with T2DM or hyperglycemia.

METHODS

This meta-review followed a systematic approach to synthesize the evidence and used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a rigorous and transparent process.

Protocol and Search Strategy

Publications were systematically identified by searching seven databases: PubMed/Medline, the Cochrane Library, Web of Science, EMBASE, SCOPUS, CINAHL, and Google Scholar for peer-reviewed research articles. The search employed both MeSH terms and free-text keywords, including "Curcuma longa", "Curcumin", "Curcuminoids", "Turmeric", "Curcuma", "Diabetes", "Type 2 Diabetes", "T2DM", "Antidiabetic", "Antimetabolic", "Metabolic Effects", "Hyperglycemia", "Dysglycemia" and related synonyms. Boolean operators (AND, OR, and NOT) were used to optimize the search results, with specific strategies outlined in Supplementary file 1the reference list of all included studies was manually screened to identify any further relevant reviews. The studies were manually screened to identify any further relevant reviews. This study has been registered in PROSPERO (CRD42024468881).

Eligibility criteria

Population or Participants: Adult patients aged ≥18 years with T2DM or metabolic disorders that are associated with hyperglycemia or hyperlipidemia were included, while studies focusing on patients with type 1 diabetes, prediabetes, or gestational diabetes were excluded.

Interventions: The primary intervention of interest was *Curcuma longa* (turmeric) as a whole or its extract in the form of curcumin or curcuminoids or any other form administered in any form (e.g., capsules, powder, or syrup) and at any dosage. Reviews that included studies where curcumin was combined with other active pharmacological agents were excluded unless the data specifically reported the effects of curcumin alone.

Comparator: The outcomes of the studies were compared with those of the control group, which may have been either placebo, no treatment, standard treatment, or other antidiabetic therapies.

Outcome measures: The primary outcomes included diabetic profile markers, including fasting blood glucose (FBG), fasting insulin (FIL), and glycated hemoglobin (HbA1c) levels. In addition to these primary outcomes, surrogate markers of insulin resistance, the homeostatic model of insulin resistance (HOMA-IR) and the quantitative insulin sensitivity check index (QUICKI) were included. Similarly, the secondary outcomes were lipid profiles, including serum cholesterol levels; total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), blood pressure (BP), and body mass index (BMI); and associated adverse events and safety data.

Study types: This meta-review included only SRMAs from RCTs evaluating the antidiabetic and metabolic effects of curcumin in patients with hyperglycemia, regardless of language. Reviews or meta-analyses that included studies other than RCTs, animal studies, in vitro studies, and RCTs with intervention durations of less than 4 weeks were excluded. Studies published from inception until December 31, 2023, were included.

Study selection process

Two independent reviewers screened the titles and abstracts of all the identified studies. Systematic selection of articles among different reviewers was performed via the Rayyan online software.[30] Full-text articles were retrieved for studies that met the inclusion criteria or when eligibility was unclear. Discrepancies were resolved through discussion or consultation with a third reviewer. PRISMA flow diagram 2020 [31] was used to document the selection process, including the number of studies identified, screened, included, and excluded, along with the reasons for exclusions.

Data Extraction

Data were independently extracted via a standardized spreadsheet by two reviewers, with discrepancies and disagreements resolved through discussion with a third reviewer. The following data were extracted into a Microsoft Excel spreadsheet:

Study characteristics: Title of the study, author(s), publication year, country, study population, intervention, comparator, primary and secondary outcomes, and conclusion of the study.

Participant characteristics: Population, number of randomized controlled trials (RCTs) included in each SRMA, sample size (intervention and control group), and age.

Intervention characteristics: Type (whole turmeric powder, extract, curcumin, or curcuminoids), dosage, duration of intervention/treatment, and form of administration.

Outcome of metabolic profiles: Diabetic profile markers (FBG, HbA1c, FIL, QUICKI, and HOMA-IR), lipid profiles (TC, TG, LDL, and HDL), BMI, and any reported adverse events and safety data.

Assessment of quality of included SRMAs using the AMSTAR-2 tool

The quality of each included SRMA was assessed via the 'A MeaSurement Tool to Assess Systematic Reviews'v (AMSTAR 2) tool, which evaluates criteria across 16 quality domains, such as study selection, risk of bias assessment, data synthesis, and overall review quality [32]. Each domain was rated as Yes (Y), Partially Yes (PY), or No (N). The resulting overall ratings were categorized as high, moderate, or low quality on the basis of the following criteria.

High Quality: No critical flaws and minimal noncritical weaknesses.

Moderate Quality: No critical flaws but more than minimal noncritical weaknesses.

Low Quality: At least one critical flaw, but some strengths in other areas.

Data Synthesis and Statistical Analysis

For the qualitative data, a narrative synthesis was conducted to summarize key findings across the included systematic reviews, providing a comprehensive overview of the various interventions, study populations, and outcomes reported. To ensure accuracy and avoid duplication, all duplicate RCTs were removed from the extraction sheet, eliminating any overlap in studies before performing the meta-analysis.

Meta-analysis for quantitative data was conducted using STATA 17 software. Pooled effect sizes for outcomes were calculated via a random-effects model to account for variability among studies, as the included studies differed in methods, populations, and settings. The effect size of continuous outcomes was calculated with mean differences (MDs) and their 95% confidence intervals (CIs) to summarize the effects across studies. Heterogeneity among studies was assessed via the I^2 statistic; an I^2 value greater than 50% indicated substantial heterogeneity, and a p-value less than 0.05 was assumed to be significant. A forest plot was used to visually present the MD pooled effect sizes and their 95% CIs. All analyses adhered to standard meta-analytic guidelines, and the results were interpreted in the context of the observed heterogeneity and study quality.

RESULTS

The comprehensive literature search resulted in 3534 articles, as described in the PRISMA flow chart in Figure 1. Title and abstract screening were conducted on 2146 articles, with 1388 duplicates removed. Subsequently, 85 full-text articles were reviewed in detail, leading to

the inclusion of 13 articles for this meta-review based on the inclusion and exclusion criteria. The reasons for exclusion during the full-text screening process are provided in Supplementary file 2 and illustrated in Figure 1.

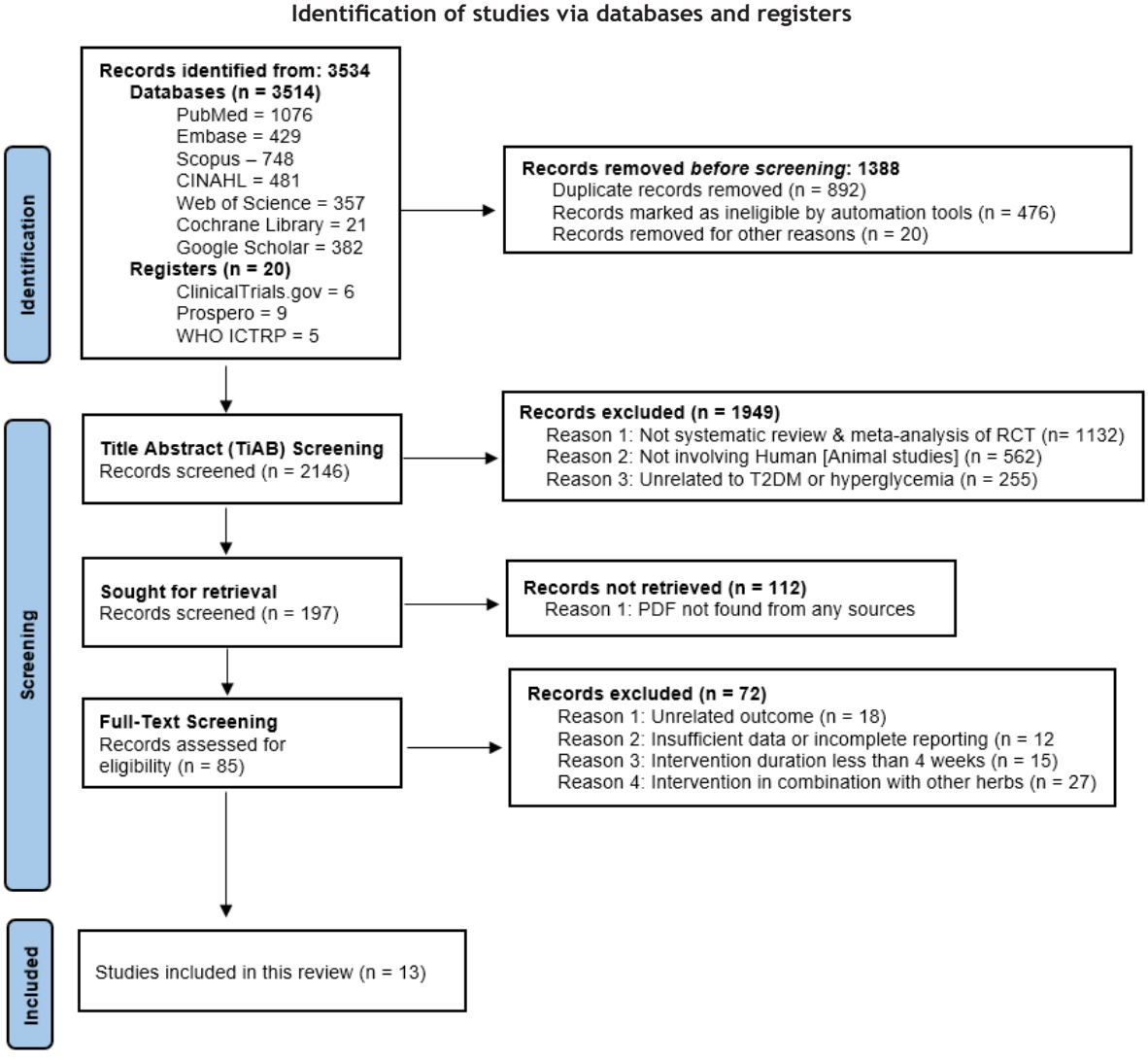


Figure 1. PRISMA 2020 flow diagram for study selection from the literature search, selection, and inclusion/ exclusion process.

Characteristics of the included studies

This meta-review included 13 SRMAs with 191 RCTs investigating the effects of curcumin on glycemic control and related outcomes. The number of RCTs included in each SRMA varied widely, ranging from 3 to 59 per SRMA. Intervention durations ranged from 4 to 48 weeks, reflecting a combination of short- and long-term studies assessing the efficacy of curcumin. The conclusions drawn from the included SRMAs are also noted. (Table 1).

During the data extraction process, it was observed that the same RCT was reported by multiple SRMAs. A detailed examination was conducted to identify duplicates to ensure the accuracy and reliability of pooled analyses, leaving 63 unique RCTs from which data on primary and secondary outcomes were extracted for further analyses. These 63 trials were conducted across diverse countries, with sample sizes ranging from 20-797 individuals, with a combined total of 3706, with 1878 in the intervention groups and 1828 in the control groups. Most RCTs compared curcumin or turmeric to a placebo, with a few studies using active controls (e.g., metformin). Major findings across studies indicated significant improvements in FBG, HbA1c, lipid parameters, and inflammation markers in the intervention

Table 1. General characteristics of the included systematic reviews and meta-analyses (SRMAs) of randomized control trials. (RCTs)

S N	Author Year	Country	Search duration	Total Participants (N)	N (Interv.)	N (control)	Population	Mean age of the participants	Intervention	Outcome	Adverse events	Duration (weeks)	No. of RCT included	Conclusion of the included systematic reviews and meta-analyses (SRMA)
1	de Melo ISV, 2018 [22]	Brazil	inception to July 2017	1,157	775	782	**pre-DM**, **T2DM**, hyperlipidemia, **MetS**, high ALT, NAFLD, Alzheimer	53.02	curcuminoids, isolated curcumin, turmeric extract	FBG, HbA1C, HOMA	Not reported	4-36	11	Isolated curcumin or curcuminoids alone or in combination significantly reduce the FBG and HbA1c in the patient with dysglycemia.
2	Tabrizi R, 2018 [54]	Iran	inception to January 2018	1790	896	894	hyperlipidemia, **T2DM**, ACS, **MetS**, Obese, overweight, diabetic nephropathy, NAFLD, CAD		curcuminoids, curcumin capsule, nanocurcumin, curcuminoids + bioperine, turmeric powder + metformin, turmeric powder	FBG, HbA1C, HDL-C, HOMA- IR, LDL-C, TC, TG	Not reported	4-36	26	Consumption of curcumin significantly reduces FBG, HOMA-IR, HbA1c, TG, and TC levels among patients with MetS and related disorders, however, it does not work for LDL-C and HDL-C levels.
3	Huang J, 2019 [84]	China	inception to June 2018	1296	651	645	**T2DM**, **MetS**, NAFLD, hyperlipidemia, CAD, high ALT	51.29	combined curcuminoids (std. curcumin 70-1890 mg/d), nanomicelle curcumin, turmeric powder (std. curcuminoids 1500-3000 mg/d)	FBG, HbA1C, HOMA	Mild intensity and short duration reported in the intervention group.	4-12	14	Curcumin or combined curcuminoids improves glucose metabolism in patients at risk for cardiovascular disease, and hence it could exert cardioprotective effects
4	Sousa 2020 [50]	Brazil	not indicated	21	11	10	**T2DM**	--	Ethanolic extract	FBG, TC, TG, HDL, LDL, BMI	Not reported	4 - 8	11	Turmeric (Curcuma longa) and Passion Fruit Peel (Passiflora edulis) powder showed significant effects on glycemic control rather than lipid metabolism.
5	Altobelli E, 2021 [55]	Italy	2000 to 20 May 2014	590	296	294	**T2DM**	57.62	curcumin capsule, nanocurcumin, turmeric powder	BMI, HbA1C, HDL-C, HOMA, LDL-C, TC, TG	Not reported	8-24	7	It benefits glucose metabolism more than lipid metabolism. Daily supplement of curcumin could improve glycemic profiles in uncomplicated T2DM patients.

Table 1. General characteristics of the included systematic reviews and meta-analyses (SRMAs) of randomized control trials. (RCTs)

S N	Author Year	Country	Search duration	Total Participants (N)	N (Interv.)	N (control)	Population	Mean age of the participants	Intervention	Outcome	Adverse events	Duration (weeks)	No. of RCT included	Conclusion of the included systematic reviews and meta-analyses (SRMA)
6	Chien 2021 [57]	Taiwan	inception through 28 November 2020.	168	87	81	**PCOS**	26.1	Curcumin (100 - 2000 mg)	BMI, HbA1C, FIL, HDL, HOMA, LDL, TC, TG	Not reported	6-12	3	Curcumin may improve glycemic control and lipid metabolism in the patients with PCOS and metabolic abnormality without significant adverse effects.
7	Jie 2021 [58]	China	inception to July 30, 2021.	290	155	135	**DKD**		Curcumin, Turmeric capsule 1500 mg/day, Nanocurcumin capsule 80 mg/d	SCr, BUN, TC, TG, HDL, LDL, FBG, SBP, DBP	Not reported	4-12	5	Curcumin supplementation provides significant improvements in the SCr, TC, DBP, and FBG levels in patients with DKD, with moderate certainty of evidence.
8	Zhang T, 2022 [60]	China	inception to 3 September 2020	608	303	305	**T2DM**	53.52	curcuminoids, curcumin, curcuminoid-piperine, turmeric	FBG, HbA1C, HDL, HOMA-IR, LDL-C, TC, TG	Mild adverse events reported in both groups.	8-24	12	Curcumin may assist in improving the insulin resistance, glycemic control, and decreased TG and TC in patients with T2DM.
9	Zheng ZH, 2021 [59]	China	inception to December 2020	533	267	266	**T2DM**	53.83	C3 complex + Bioperine, Theracurmin, curcumin supplement, turmeric capsule	BMI, FBG, HbA1C, HDL-C, LDL-C, TC, TG	Not reported	8-24	8	Curcumin can effectively improve multiple biochemical indices in patients with type 2 diabetes and reduce the risk of CVD and risk of T2DM supporting its potential as an adjunct therapy.
10	Ashtary-Larky D, 2021 [85]	Iran	inception to May 2021	510	269	241	NAFLD, **MetS**, **T2DM**, Migraine, T2DM on dialysis	50.52	nanocurcumin	FBG, HDL-C, LDL-C, SBP, TC, TG	Not reported	6-12	9	Nanocurcumin supplementation improves glycemic and lipid profiles hence reduces the risk of cardiovascular diseases.

Table 1. General characteristics of the included systematic reviews and meta-analyses (SRMAs) of randomized control trials. (RCTs)

S N	Author Year	Country	Search duration	Total Participants (N)	N (Interv.)	N (control)	Population	Mean age of the participants	Intervention	Outcome	Adverse events	Duration (weeks)	No. of RCT included	Conclusion of the included systematic reviews and meta-analyses (SRMA)
11	Tian J, 2022 [56]	Iran	inception to March 2022	565	284	281	**T2DM**	41-60.95	turmeric, curcuminoids, and curcumin, nano-curcumin	TG, LDL, HDL, HbA1c, FBG	Not reported	4-12	9	Curcumin has promising effects on improving diabetic and lipid profiles in patients with T2DM, and hence can be used as potential therapeutic options of T2DM.
12	Yuan F, 2022 [86]	China	not indicated	1509	752	757	**T2DM, MetS,** Overweight, Obese, NAFLD, hyperlipidemia, **pre-DM**	50.03	curcuminoids, curcumin, curcuminoid-piperine, nano-curcuminoids, turmeric	FBG, HbA1C	Not reported	4-24	17	Turmeric and curcuminoids decrease FBG, insulin, HbA1c and HOMA-IR significantly and the effect is more pronounced if used for more than 8 weeks.
13	Dehzad 2023 [87]	Iran	inception up to October 2022.	3879	1962	1918	**Patient with disturbed glycemia**	18-65	Curcumin, Turmetic, curcuminoids	FBG, HbA1C, FIL, HOMA-IR	Not reported	4-36	59	Turmeric/curcumin significantly reduces FBG, insulin, HbA1c and HOMA-IR, hence can be use as a complementary therapy for dysglycemia.
		Total no. of participants		**12,917**	**5933**	**5827**			**Total No. RCTs included in 13 included SRMA**				**191**	**Duplicate RCTs = 128 (excluded)** **% Duplication of RCTS = 128/191*100 = 67%** **Include RCTS = 191-128 = 63**

groups (Supplementary file S3).

The types of curcumin used in the intervention groups and their respective dose ranges were as follows: curcuminoid 70 mg/day to 1795 mg/day, curcumin 1000 mg/day to 1500 mg/day, curcuminoid-piperine 500–5 mg/day to 1000–10 mg/day, nanocurcumin 80 mg/day, phospholipidated curcumin 200 mg/day to 330 mg/day, turmeric 1500 mg/day to 2400 mg/day, and unformulated curcumin 1000 mg/day. The control groups in the studies received either a placebo or standard diabetes treatment (e.g., biguanide or sulfonylurea group drugs). Supplementary presents a detailed overview of the 63 included RCTs ((Supplementary file S3).

Supplementary file 4 summarizes the findings from the included SRMAs on the glycemic and metabolic effects of curcumin or turmeric in patients with type 2 diabetes mellitus (T2DM) or related conditions. It highlights outcomes such as FBG, HbA1c, insulin resistance (HOMA-IR), BMI, and lipid profiles (TC, TG, LDL, HDL). The results include mean differences with confidence intervals, heterogeneity (I^2), and analysis models, showing consistent improvements in glycemic and lipid parameters across most SRMAs. Among the 63 included RCTs, approximately half [30 (47.6%)] had an intervention duration of less than 12 weeks, with the minimum duration being 4 weeks [33-36] and the maximum duration being 48 weeks [37]. Similarly, 24 (38%) of the RCTs focused on T2DM patients [33-36,38-53] (Supplementary file S4).

Supplementary file S5 presents a quality assessment of the 13 SRMAs included in the meta-review. Five SRMAs (de Melo 2018 [22], Tabrizi 2018 [54], Altobelli 2021 [55], Tian 2022 [56], and Dehzad 2023 [24]) were rated as high quality owing to strong adherence to the AMSTAR-2 criteria, including rigorous protocol registration, comprehensive literature searches, and appropriate meta-analytic methods. Another six studies (Chien 2021 [57], Jie 2021 [58], Zheng 2021 [59], Ashtary 2021, Yuan 2022, and Huang 2019) were of moderate quality, whereas two studies (Sousa 2020, Zhang 2022) were rated as low quality. Further details of the findings are depicted in Supplementary file S5.

Supplementary file S6 provides a comprehensive PRISMA 2020 checklist detailing the adherence of the meta-review to established guidelines for reporting systematic reviews.

Outcome Measurement

The primary outcomes commonly assessed across these studies included glycemic control (FBG, HbA1c, insulin, HOMA-IR, and QUICKI). In addition to primary outcomes, several reviews also assessed secondary outcomes, including lipid profiles (TG, total cholesterol, HDL, and LDL), renal function indicators (BUN, serum creatinine, and proteinuria), and BMI. The unit of measurement for FBS, TG, TC, HDL, LDL, BUN, and SC is mg/dL. Similarly, the unit of measurement for insulin is micro-IU/dL, HbA1c is expressed as a percentage, and proteinuria is expressed in grams/24 hours. As ratio measures, the HOMA-IR and QUICKI are unitless.

Glycemic profile

Glycated hemoglobin (HbA1C) Level

An analysis of 26 RCTs revealed that supplementation with curcumin/turmeric significantly decreased HbA1c levels in the intervention group (MD = -0.31 mg/dL; 95% CI = −0.57, -0.05; I^2 = 96.27%) (Figure 2a)

Fasting Blood Sugar (FBS) Level

The pooled results from 53 RCTs revealed that, compared with placebo or standard treatment, curcumin significantly reduced FBG levels (MD = −6.30 mg/dL; 95% CI: -9.33, -3.27; I^2 = 96.86%). (Figure 2b)

Fasting Insulin Level (FIL)

An analysis of 28 RCTs revealed that supplementation with curcumin/turmeric did not affect fasting serum insulin levels (MD = -0.58; 95 mIU/L, 95% CI = −1.16, 0.00; I^2 = 91.83%) (Figure 2c).

Quantitative Insulin Sensitivity Check Index (QUICKI)

An analysis of six RCTs revealed that supplementation with curcumin/turmeric did not affect the QUICKI levels in the intervention group (MD = 0.00; 95% CI: -0.00, 0.01; I^2 = 83.45%) (Figure 2d).

Homeostatic Model Assessment of Insulin Resistance (HOMA-IR)

An analysis of 26 RCTs revealed that supplementation with curcumin/turmeric did not affect the HOMA-IR level in the intervention group (MD = -0.17; 95% CI: −0.68, 0.33; I^2 = 99.38% (Figure 2e).

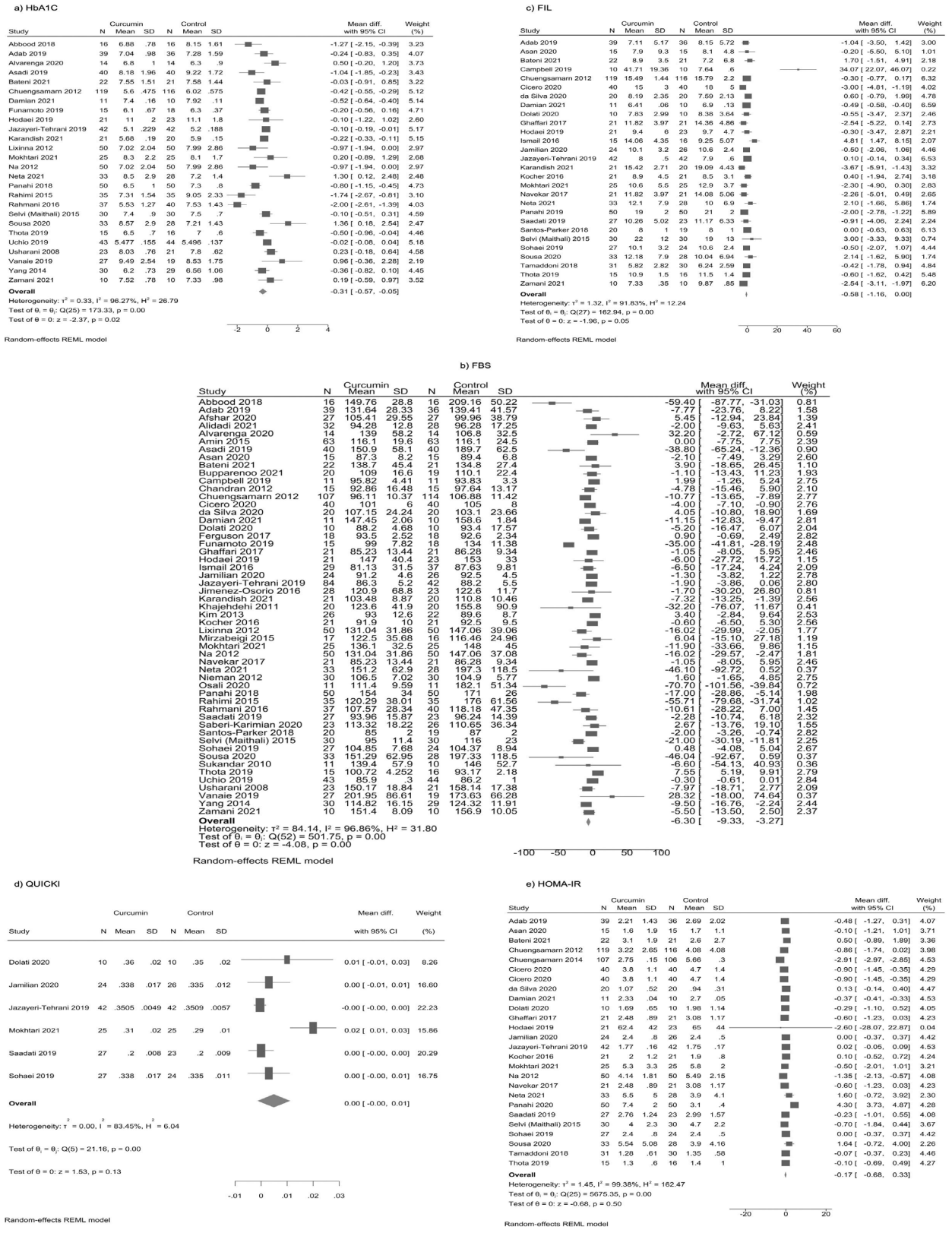


Figure 2. Forest plots showing the mean differences in Glycemic profile a) glycated hemoglobin (HbA1c), b) fasting insulin concentration (FIL), c) fasting blood glucose level (FBG), d) quantitative insulin sensitivity check index (QUICKI), and e) homeostatic model of insulin resistance (HOMA-IR) between the *Curcuma longa* supplementation group and the control group.

Lipid profile:

High Density Lipoprotein (HDL) Level

An analysis of 45 RCTs revealed that supplementation with curcumin/turmeric significantly increased HDL levels (MD = 1.46 mg/dL; 95% CI: 0.37, 2.56; I^2 = 74.28%) in the intervention group (Figure 3a).

Low Density Lipoprotein (LDL) Level

Analysis of 44 RCTs revealed that supplementation with curcumin/turmeric significantly decreased LDL levels in the intervention group (MD = -5.95 mg/dL; 95% CI: −9.43, -2.47; I^2 = 74.61%). (Figure 3b).

Triglyceride (TG) Level

Analysis of 43 RCTs revealed that supplementation with curcumin/turmeric significantly decreased the TG level in the intervention group (MD = -12.88 mg/dL; 95% CI: -20.09, -5.67; I^2 = 93.42%) (Figure 3c).

Total Cholesterol (TC) Level

Analysis of 42 RCTs revealed that supplementation with curcumin/turmeric did not significantly affect TC (MD = -3.87 mg/dL; 95% CI: -11.08, 3.34; I^2 = 93.41%) (Figure 3d).

Renal markers:

Serum Creatinine (SCT) Level

An analysis of five RCTs indicated that supplementation with curcumin/turmeric did not affect the serum creatinine level between the curcumin group and the control group (MD = −0.11 mg/dL; 95% CI: −0.25, 0.03; I2 = 83.57%) (Figure 4a).

Proteinuria

Analysis of three RCTs indicated that supplementation with curcumin/turmeric did not affect DBP levels between the curcumin and control groups (MD = −0.18 gm/24 hours; 95% CI: −0.38, 0.03; I^2 = 0%) (Figure 4b).

Blood Uriea Nitrogen (BUN) Level

Three RCTs reported no difference in BUN between the intervention and control groups (MD = 0.55 mg/dL; 95% CI = −1.02, 2.13; I^2 = 0%) (Figure 4c).

Blood pressure:

Systolic Blood Pressure (SBP)

An analysis of nine RCTs indicated that supplementation with curcumin/turmeric did not affect SBP between the curcumin and control groups (MD = −2.69 mmHg; 95% CI: −6.10, 0.71; I^2 = 84.40%) (Figure 6a).

Diastolic Blood Pressure (DBP)

An analysis of eight RCTs indicated that supplementation with curcumin/turmeric did not affect DBP levels between the curcumin and control groups (MD = −0.28 mmHg; 95% CI: −2.97, 2.40; I^2 = 88.26%) (Figure 6b).

Adverse Events and Safety

Qualitative data synthesis was performed for the adverse events and safety profile analysis. In terms of safety, curcumin was generally well tolerated across all included studies. Adverse events, including gastrointestinal discomfort and nausea, were rare and mostly mild. No serious adverse effects were reported, and curcumin supplementation was considered safe for use at doses of up to 2500 mg per day (Table 1, Supplementary file S3).

Body Mass Index (BMI)

The effect of curcumin/turmeric supplementation on the BMI of participants with T2DM was analyzed across the included SRMAs. The pooled results from 20 RCTs revealed no significant effect of curcumin on BMI (MD = -0.47 kg/m2, 95% CI: -0.99, 0.04, I^2 = 58.42%) (Figure 5).

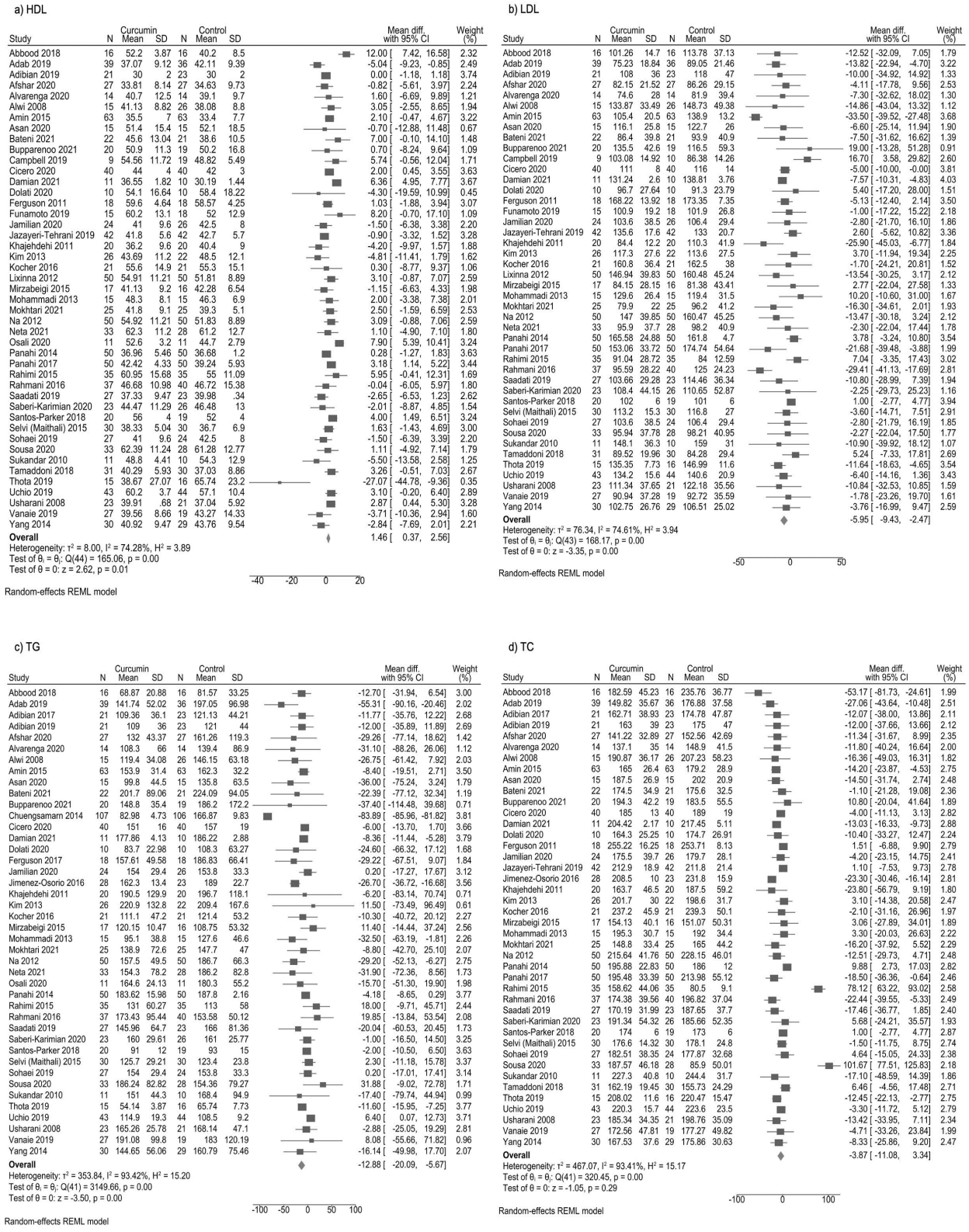
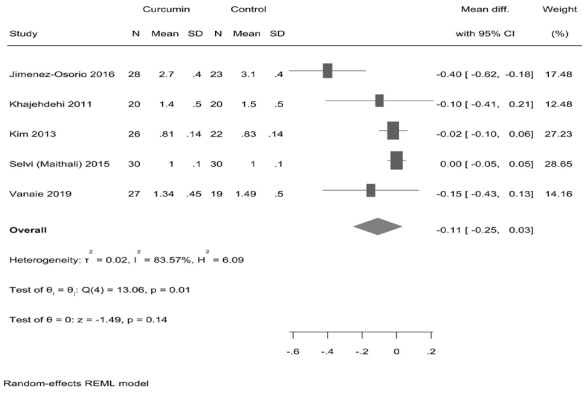
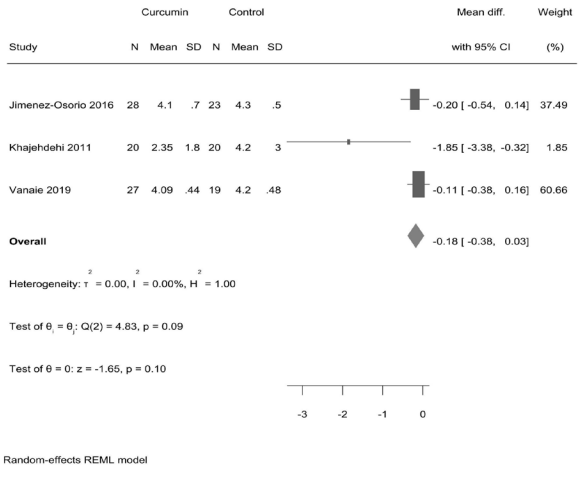


Figure 3. Forest plots showing the mean difference in lipid profile a) high-density lipoprotein (HDL) level, b) low-density lipoprotein (LDL) level, c) triglyceride (TG), and d) total cholesterol (TC) between the *Curcuma longa* supplementation group and the control group.

a. Creatinine



b. Proteinuria



c. BUN

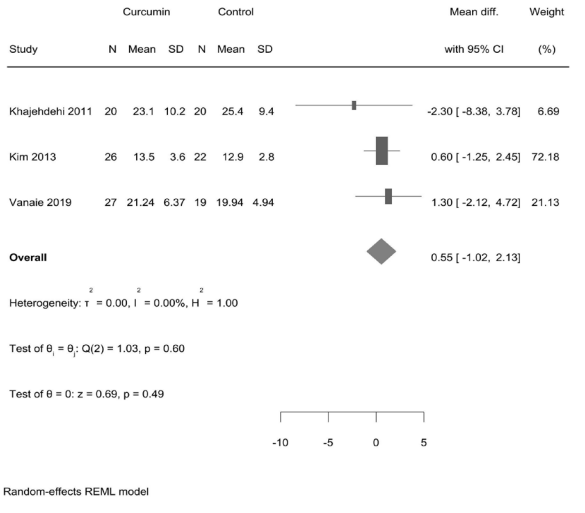


Figure 4. Forest plot showing the mean difference and in renal parameters a) Creatinine, b) Proteinuria c) BUN, between the Curcuma longa supplementation group and the control group.

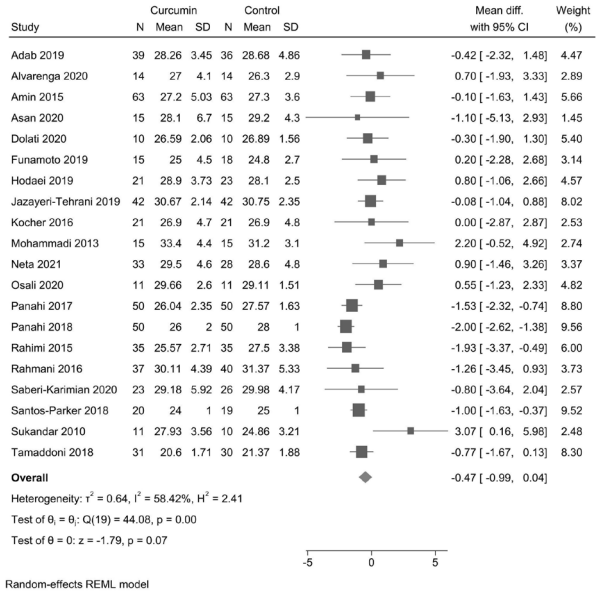


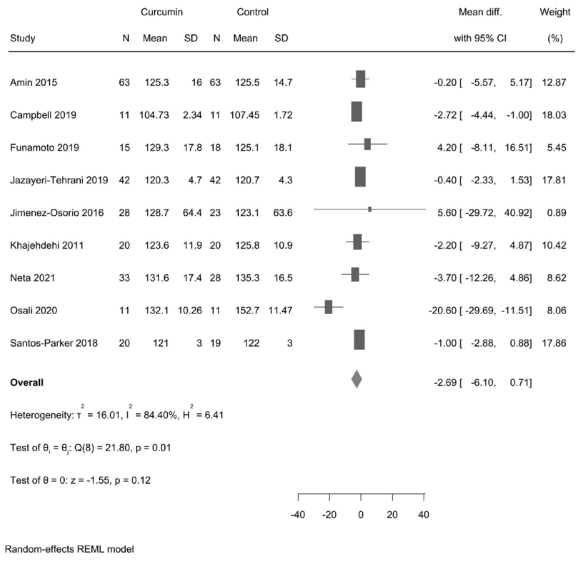
Figure 5. Forest plot showing the mean difference in BMI between the Curcuma longa supplementation group and the control group.

DISCUSSION

This meta-review synthesized data from 13 SRMAs to assess the potential antidiabetic and metabolic effects of curcumin/turmeric in patients with T2DM or hyperglycemia. The analyses revealed a significant effect of curcumin/turmeric supplementation on FBG (decrease), HbA1c (decrease), HDL (increase), LDL (decrease), and TG (decrease) in the intervention groups. However, no significant changes were observed in insulin levels, renal markers, BMI, or blood pressure. These results provide evidence supporting the potential role of curcumin in improving glycemic control and metabolic profiles in T2DM and hyperglycemic patients.

The meta-analysis revealed a significant reduction in FBG levels compared with placebo or standard treatment following curcumin supplementation. This finding aligns with the hypothesis that curcumin enhances insulin sensitivity and modulates glucose metabolism.[60-62] The anti-inflammatory properties of curcumin [63,64] and its ability to downregulate cytokine production[65,66] and improve endothelial function likely contribute to these effects.[3,67,68] However, studies using higher doses of curcumin (≥500 mg/day) formulations with enhanced bioavailability have shown more pronounced reductions in FBG, indicating a potential dose-response relationship.[27,28,69]

a. SBP



b. DBP

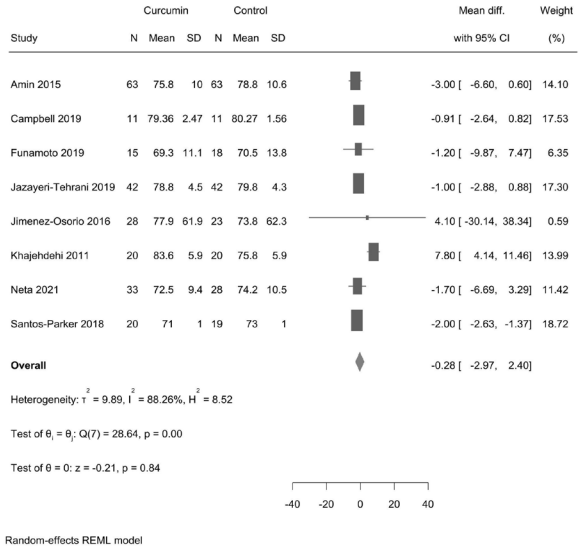


Figure 6. Forest plot showing the mean difference in blood pressure a) SBP and b) DBP between the Curcuma longa supplementation group and the control group.

This study revealed a significant reduction in HbA1c levels associated with curcumin/turmeric supplementation, which aligns with a growing body of literature supporting the role of curcumin in improving glycemic control in patients with T2DM. A systematic review supported our results, demonstrating that curcumin supplementation significantly reduced both FBG and HbA1c levels in multiple studies, highlighting its potential as an effective intervention for glycemic management in T2DM patients.[70] For HbA1c, a marker of long-term glycemic control, curcumin supplementation significantly decreased HbA1c, particularly in studies with longer intervention durations (≥12 weeks), such as the study by Chuengsamarn et al.[40,71] These effects can be attributed to the anti-inflammatory and antioxidant properties of curcumin, which reduce oxidative stress and improve ß-cell function.[5,72] HbA1c reductions are critical in mitigating the long-term complications of diabetes, such as neuropathy, retinopathy, and cardiovascular diseases.[40,73]

Conversely, the effect of curcumin on FIL level was not significant in the pooled analysis. While curcumin may improve insulin sensitivity, its direct effects on insulin secretion may be limited. This result is consistent with the findings of Pathomwichaiwat et al., [28,74] who noted that the primary mechanism of action of curcumin may lie in reducing insulin resistance rather than stimulating insulin production. Similarly, turmeric/curcumin supplementation not only reduces HbA1c levels but also positively impacts fasting insulin levels and homeostatic model assessment of insulin resistance (HOMA-IR) [24,75]. These findings suggest that curcumin may enhance insulin sensitivity and contribute to improved metabolic profiles. addtionally, the anti-inflammatory and antioxidant properties of curcumin play crucial roles in mitigating oxidative stress and inflammation, which are key contributors to the pathophysiology of diabetes.

The effect of curcumin on lipid profiles was mixed. Significant reductions in LDL and improvements in TG and HDL levels were noted. These findings align with those of Kocaadam and Şanlier[26,73], who suggested that the lipid-lowering effects of curcumin are more prominent in LDL reduction, potentially through its role in inhibiting lipid peroxidation and modulating enzymes involved in lipid metabolism. However, variability in outcomes may be attributable to differences in curcumin formulation, dosage, and study populations, with some studies using enhanced curcumin formulations (e.g., nanocurcumin, curcumin-phospholipid complexes), dosage, and duration of treatment.[6]

In terms of renal function markers, curcumin/turmeric supplementation did not affect outcomes such as BUN, creatinine, or proteinuria. While some studies reported slight decreases, others reported no significant effects. Chronic hyperglycemia in T2DM patients can lead to renal damage via increased production of reactive oxygen species (ROS) and other glycation end products.[76,77] The

ability of curcumin to neutralize ROS and downregulate inflammatory pathways may thus play a role in reducing the levels of BUN and creatinine. [66] Curcumin may act as an adjuvant therapy for the treatment of proteinuria in T2DM patients, but effects may take two months or longer.[78]

The impact of curcumin on BMI was not significant in this meta-review. This finding is consistent with those of previous studies suggesting that curcumin may not directly facilitate weight reduction.[20,79] Given that weight loss is a critical factor in managing T2DM, the lack of significant effects on BMI suggests that curcumin should not be relied upon as a standalone treatment for weight management. Its ability to improve metabolic markers may still play a role in improving metabolic health indirectly by enhancing insulin sensitivity and reducing inflammation.[16,79,80]

The included studies reported that curcumin was generally well tolerated, with no serious adverse effects observed. Mild gastrointestinal discomfort was the most common side effect, which is consistent with the findings of previous trials. [12,20] However, long-term safety data, particularly at higher doses, remain limited and warrant further investigation. However, the overall safety profile of curcumin makes it a promising adjunct therapy for T2DM patients, particularly those seeking alternatives to standard pharmacological treatments with a greater risk of side effects.[20,25,81]

Despite the valuable insights into the antidiabetic and metabolic effects of curcumin from this meta-review, several limitations exist. First, there was significant heterogeneity across the included RCTs, particularly in terms of curcumin dosages, formulations (e.g., nanoparticles, phospholipid complexes), and treatment duration. Future research should aim to standardize these factors to better assess their therapeutic potential. Second, some studies included small sample sizes or presented a high risk of bias. This limitation emphasizes the need for more rigorous RCTs with larger sample sizes and standardized methodologies. Finally, most studies have focused only on short-term outcomes, leaving uncertainties regarding the long-term efficacy and safety of curcumin.[78,82-86]

CONCLUSIONS

This meta-review concludes that curcumin, the active compound in turmeric *(Curcuma longa)* supplementation offers significant benefits in improving glycemic control, insulin sensitivity and lipid markers like TG, TC, LDL, HDL. However, its effects on renal makers, BMI, and blood pressure are inconsistent, highlighting the need for further research to confirm these findings and optimize dosing regimens. Moreover the efficacy of the crude powder of turmeric remain to be explored. Given its safety profile and the magnitude of its effects on key diabetic markers, curcumin shows promise as an adjunct therapy for managing T2DM. Nevertheless, the heterogeneity in study designs, curcumin formulations, and patient populations across the included studies . underscores the importance of standardizing future clinical trials to fully elucidate the therapeutic potential of curcumin

COMPETING INTERESTS

The authors declare that they have no conflicts of interest.

FUNDING

This research was funded by the University of Cyberjaya, Research Grant Scheme, grant number URGS/02/05/2022.

ACKNOWLEDGMENTS

This research would not have been feasible without the generous contributions of every participant in the included RCTs. Furthermore, we are sincerely grateful for the high-quality, authoritative work provided by the authors of the Systematic Reviews and Meta-Analyses (SRMAs) whose studies formed the crucial building blocks of this paper.

REFERENCES

1. Lu X, Xie Q, Pan X, Zhang R, Zhang X, Peng G, Zhang Y, Shen S, Tong N. Type 2 diabetes mellitus in adults: pathogenesis, prevention and therapy. Signal Transduct Target Ther 2024;9(1):1-25; doi: 10.1038/s41392-024-01951-9.

2. Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Health Sci Rep 2024;7(3):e2004; doi: 10.1002/hsr2.2004.

3. Kosiborod M, Gomes MB, Nicolucci A, Pocock S, Rathmann W, Shestakova MV, Watada H, Shimomura I, Chen H, Cid-Ruzafa J, Fenici P. Vascular complications in patients with type 2 diabetes: prevalence and associated factors in 38 countries (the DISCOVER study program). Cardiovasc Diabetol 2018;17(1):1-13; doi: 10.1186/s12933-018-0787-8.

4. IDF IDF. Diabetes around the World in 2021. Key Global Findings 2021. Tenth Edition. 2021. Available

from: https://diabetesatlas.org/ [Last accessed: 6/7/2023].

5. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia 2019;62(1):3-16; doi: 10.1007/s00125-018-4711-2.

6. World Health Organization. Global Report on Diabetes. World Health Organization: Geneva; 2016.

7. Esubalew H, Belachew A, Seid Y, Wondmagegn H, Temesgen K, Ayele T. Health-related quality of life among type 2 diabetes mellitus patients using the 36-item short form health survey (SF-36) in Central Ethiopia: a Multicenter Study. Diabetes, Metabolic Syndrome and Obesity. 2024 Dec 31:1039-49. doi: 10.2147/DMSO.S448950.

8. WHO. Key Facts. 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/diabetes [Last accessed: 6/7/2023].

9. Borse SP, Chhipa AS, Sharma V, Singh DP, Nivsarkar M. Management of Type 2 Diabetes: Current Strategies, Unfocussed Aspects, Challenges, and Alternatives. Med Princ Pract 2021;30(2):109–121; doi: 10.1159/000511002.

10. Mortada EM. Evidence-Based Complementary and Alternative Medicine in Current Medical Practice. Cureus n.d.;16(1):e52041; doi: 10.7759/cureus.52041.

11. Islam MS. Natural Products and Disease Prevention, Relief and Treatment. Nutrients 2022;14(12):2396; doi: 10.3390/nu14122396.

12. Sharifi-Rad J, Rayess YE, Rizk AA, Sadaka C, Zgheib R, Zam W, et al. Turmeric and Its Major Compound Curcumin on Health: Bioactive Effects and Safety Profiles for Food, Pharmaceutical, Biotechnological and Medicinal Applications. Front Pharmacol 2020;11:01021; doi: 10.3389/fphar.2020.01021.

13. Liu S, Liu J, He L, Liu L, Cheng B, Zhou F, et al. A Comprehensive Review on the Benefits and Problems of Curcumin with Respect to Human Health. Mol Basel Switz 2022;27(14):4400; doi: 10.3390/molecules27144400.

14. Den Hartogh DJ, Gabriel A, Tsiani E. Antidiabetic Properties of Curcumin I: Evidence from In Vitro Studies. Nutrients 2020;12(1):118; doi: 10.3390/nu12010118.

15. Di Meo F, Filosa S, Madonna M, Giello G, Di Pardo A, Maglione V, et al. Curcumin C3 complex®/Bioperine® has antineoplastic activity in mesothelioma: an in vitro and in vivo analysis. J Exp Clin Cancer Res 2019;38(1):360; doi: 10.1186/s13046-019-1368-8.

16. Rivera-Mancía S, Trujillo J, Chaverri JP. Utility of curcumin for the treatment of diabetes mellitus: Evidence from preclinical and clinical studies. J Nutr Intermed Metab 2018;14:29-41; doi: 10.1016/j.jnim.2018.05.001.

17. Zhang S, Wang J, Liu L, Sun X, Zhou Y, Chen S, et al. Efficacy and safety of curcumin in psoriasis: preclinical and clinical evidence and possible mechanisms. Front Pharmacol 2022;13:903160; doi: 10.3389/fphar.2022.903160.

18. Den Hartogh DJ, Gabriel A, Tsiani E. Antidiabetic Properties of Curcumin II: Evidence from In Vivo Studies. Nutrients 2019;12(1):58; doi: 10.3390/nu12010058.

19. Macena MD, Nunes LF, da Silva AF, Pureza IR, Praxedes DR, Santos JC, et al. Effects of dietary polyphenols in the glycemic, renal, inflammatory, and oxidative stress biomarkers in diabetic nephropathy: a systematic review with meta-analysis of randomized controlled trials. Nutr Rev 2022;80(12):2237–2259; doi: 10.1093/nutrit/nuac035.

20. Panknin TM, Howe CL, Hauer M, Bucchireddigari B, Rossi AM, Funk JL. Curcumin Supplementation and Human Disease: A Scoping Review of Clinical Trials. Int J Mol Sci 2023;24(5):4476; doi: 10.3390/ijms24054476.

21. Zheng X, Zhu J, Haedi AR, Zhou M. The effect of curcumin supplementation on glycemic indices in adults: A meta-analysis of meta-analyses. Prostaglandins Other Lipid Mediat 2024;175:106908; doi: 10.1016/j.prostaglandins.2024.106908.

22. de Melo ISVD, Santos AFD, Bueno NB. Curcumin or combined curcuminoids are effective in lowering the fasting blood glucose concentrations of individuals with dysglycemia: Systematic review

and meta-analysis of randomized controlled trials. Pharmacol Res 2018;128:137-144; doi: 10.1016/j.phrs.2017.09.010.

23. Tamaddoni A, Nasseri E, Mohammadi E, Qujeq D, Zayeri F, Zand H, et al. A Double-blind Randomized Controlled Trial of Curcumin for Improvement in Glycemic Status, Lipid Profile and Systemic Inflammation in ß-Thalassemia Major. J Herb Med 2020;21:100324; doi: 10.1016/j.hermed.2019.100324.

24. Dehzad MJ, Ghalandari H, Nouri M, Askarpour M. Effects of curcumin/turmeric supplementation on glycemic indices in adults: A grade-assessed systematic review and dose-response meta-analysis of randomized controlled trials. Diabetes Metab Syndr Clin Res Rev 2023;17(10):102855; doi: 10.1016/j.dsx.2023.102855.

25. Al-Karbi K, Al-Muhannadi M, Al-Rabeei Y, Al-Kubaisi RJ, Bawazir A, Mahmoud MH. Efficacy of curcumin on inflammatory pain across different disorders: a systematic review and meta-analysis of Randomized controlled trials. WORLD Fam Med 2021;19(8):47-55; doi: 10.5742/MEWFM.2021.94095.

26. Kocaadam B, Şanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Crit Rev Food Sci Nutr 2017;57(13):2889-2895; doi: 10.1080/10408398.2015.1077195.

27. Naghsh N, Musazadeh V, Nikpayam O, Kavyani Z, Moridpour AH, Golandam F, et al. Profiling Inflammatory Biomarkers following Curcumin Supplementation: An Umbrella Meta-Analysis of Randomized Clinical Trials. Evid Based Complement Alternat Med 2023;2023(1):4875636; doi: 10.1155/2023/4875636.

28. Pathomwichaiwat T, Jinatongthai P, Prommasut N, Ampornwong K, Rattanavipanon W, Nathisuwan S, et al. Effects of turmeric (Curcuma longa) supplementation on glucose metabolism in diabetes mellitus and metabolic syndrome: An umbrella review and updated meta-analysis. PLOS ONE 2023;18(7):e0288997; doi: 10.1371/journal.pone.0288997.

29. Belbasis L, Bellou V, Ioannidis JPA. Conducting umbrella reviews. BMJ Med 2022;1(1); doi: 10.1136/bmjmed-2021-000071.

30. Anonymous. Rayyan – Intelligent Systematic Review - Rayyan. 2021. Available from: https://www.rayyan.ai/ [Last accessed: 10/22/2024].

31. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 2021;10(1):89; doi: 10.1186/s13643-021-01626-4.

32. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008; doi: 10.1136/bmj.j4008.

33. Abbood MS. Hypolipidaemic and Anti-inflammatory effects of Curcumin versus Atorvastatin in Type 2 Diabetic Patients. Int J Pharm Sci Rev Res 2018;49(1):1-5.

34. Adab Z, Eghtesadi S, Vafa MR, Heydari I, Shojaii A, Haqqani H, et al. Effect of turmeric on glycemic status, lipid profile, hs-CRP, and total antioxidant capacity in hyperlipidemic type 2 diabetes mellitus patients. Phytother Res 2019;33(4):1173-81.

35. Adibian M, Hodaei H, Nikpayam O, Sohrab G, Hekmatdoost A, Hedayati M. The effects of curcumin supplementation on high-sensitivity C-reactive protein, serum adiponectin, and lipid profile in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial. Phytother Res 2019;33(5):1374-1383; doi: 10.1002/ptr.6328.

36. Vafadar_afshar G, Khadem-Ansari MH, Makhdomii K, Rasooli J. The effects of nano-curcumin supplementation on serum level of hs-CRP, adhesion molecules, and lipid profiles in hemodialysis patients, a randomized controlled clinical trial. Iranian Journal of Kidney Diseases. 2020;14(1):52.

37. Yang YS, Su YF, Yang HW, Lee YH, Chou JI, Ueng KC. Lipid-Lowering Effects of Curcumin in Patients with Metabolic Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial. Phytother Res 2014;28(12):1770-1777; doi: 10.1002/ptr.5197.

38. Alidadi M, Sahebkar A, Eslami S, Vakilian F, Jarahi L, Alinezhad-Namaghi M, et al. The Effect of Curcumin Supplementation on Pulse Wave Velocity in Patients with Metabolic Syndrome: A Randomized, Double-

Blind, Placebo-Controlled Trial. In: Pharmacological Properties of Plant-Derived Natural Products and Implications for Human Health. (Barreto GE, Sahebkar A. eds) Springer International Publishing: Cham; 2021; pp. 1–11; doi: 10.1007/978-3-030-64872-5_1.

39. Asadi S, Gholami MS, Siassi F, Qorbani M, Khamoshian K, Sotoudeh G. Nano curcumin supplementation reduced the severity of diabetic sensorimotor polyneuropathy in patients with type 2 diabetes mellitus: A randomized double-blind placebo-controlled clinical trial. Complement Ther Med 2019;43:253–260; doi: 10.1016/j.ctim.2019.02.014.

40. Chuengsamarn S, Rattanamongkolgul S, Phonrat B, Tungtrongchitr R, Jirawatnotai S. Reduction of atherogenic risk in patients with type 2 diabetes by curcuminoid extract: a randomized controlled trial. J Nutr Biochem 2014;25(2):144–150; doi: 10.1016/j.jnutbio.2013.09.013.

41. Funamoto M, Shimizu K, Sunagawa Y, Katanasaka Y, Miyazaki Y, Kakeya H, et al. Effects of Highly Absorbable Curcumin in Patients with Impaired Glucose Tolerance and Non-Insulin-Dependent Diabetes Mellitus. J Diabetes Res 2019;2019(1):8208237; doi: 10.1155/2019/8208237.

42. Hodaei H, Adibian M, Nikpayam O, Hedayati M, Sohrab G. The effect of curcumin supplementation on anthropometric indices, insulin resistance and oxidative stress in patients with type 2 diabetes: a randomized, double-blind clinical trial. Diabetol Metab Syndr 2019;11(1):41; doi: 10.1186/s13098-019-0437-7.

43. Khajehdehi P, Pakfetrat M, Javidnia K, Azad F, Malekmakan L, Nasab MH, Dehghanzadeh G. Oral supplementation of turmeric attenuates proteinuria, transforming growth factor-ß and interleukin-8 levels in patients with overt type 2 diabetic nephropathy: A randomized, double-blind and placebo-controlled study. Scand J Urol Nephrol 2011;45(5):365–370; doi: 10.3109/00365599.2011.585622.

44. Mokhtari M, Razzaghi R, Momen-Heravi M. The effects of curcumin intake on wound healing and metabolic status in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial. Phytother Res 2021;35(4):2099-2107; doi: 10.1002/ptr.6957.

45. Neta JFDF, Veras VS, Sousa DFD, Neta, JFDF, Veras VS, Sousa DFD, et al. Effectiveness of the piperine-supplemented *Curcuma longa* L. in metabolic control of patients with type 2 diabetes: a randomised double-blind placebo-controlled clinical trial. Int J Food Sci Nutr 2021;72(7):968-977; doi: 10.1080/09637486.2021.1885015.

46. Panahi Y, Khalili N, Sahebi E, Namazi S, Reiner Ž, Majeed M, et al. Curcuminoids modify lipid profile in type 2 diabetes mellitus: A randomized controlled trial. Complement Ther Med 2017;33:1-5; doi: 10.1016/j.ctim.2017.05.006.

47. Panahi Y, Khalili N, Sahebi E, Namazi S, Simental-Mendía LE, et al. Effects of Curcuminoids Plus Piperine on Glycemic, Hepatic and Inflammatory Biomarkers in Patients with Type 2 Diabetes Mellitus: A Randomized Double-Blind Placebo-Controlled Trial. Drug Res 2018;68(07):403–409; doi: 10.1055/s-0044-101752.

48. Panahi Y, Khalili N, Sahebi E, Namazi S, Karimian MS, Majeed M, et al. Antioxidant effects of curcuminoids in patients with type 2 diabetes mellitus: a randomized controlled trial. Inflammopharmacology 2016;25(1):25–31; doi: 10.1007/s10787-016-0301-4.

49. Maithili Karpaga Selvi N, Sridhar MG, Swaminathan RP, Sripradha R. Efficacy of Turmeric as Adjuvant Therapy in Type 2 Diabetic Patients. Indian J Clin Biochem 2015;30(2):180–186; doi: 10.1007/s12291-014-0436-2.

50. Sousa DF, Veras VS, Freire VE, Paula ML, Serra MA, Costa AC, et al. Effectiveness of Passion Fruit Peel Flour (Passiflora edulis L.) versus Turmeric Flour (Curcuma longa L.) on Glycemic Control: Systematic Review and Meta-Analysis. Curr Diabetes Rev 2020;16(5):450–456; doi: 10.2174/1573399815666191026125941.

51. Sukandar EY, Permana H, Adnyana IK, Sigit JI, Ilyas RA, Hasimun P, et al. Clinical Study of Turmeric (Curcuma longa L.) and Garlic (Allium sativum L.) Extracts as Antihyperglycemic and Antihyperlipidemic Agent in Type-2 Diabetes-Dyslipidemia Patients. Int J Pharmacol n.d.;6:456-463.

52. Usharani P, Mateen AA, Naidu MU, Raju YS, Chandra N. Effect of NCB-02, Atorvastatin and Placebo

on Endothelial Function, Oxidative Stress and Inflammatory Markers in Patients with Type 2 Diabetes Mellitus. Drugs R D 2008;9(4):243–250; doi: 10.2165/00126839-200809040-00004.

53. Zamani SK, Rezagholizadeh DM. Effect of eight-week curcumin supplementation with endurance training on glycemic indexes in middle age women with type 2 diabetes in Iran, A preliminary study. Diabetes Metab Syndr Clin Res Rev 2021;15(3):963–967; doi: 10.1016/j.dsx.2021.04.002.

54. Tabrizi R, Vakili S, Lankarani KB, Akbari M, Mirhosseini N, Ghayour-Mobarhan M, et al. The Effects of Curcumin on Glycemic Control and Lipid Profiles Among Patients with Metabolic Syndrome and Related Disorders: A Systematic Review and Metaanalysis of Randomized Controlled Trials. Curr Pharm Des 2018;24(27):3184–3199; doi: 10.2174/1381612824666180828162053.

55. Altobelli E, Angeletti PM, Marziliano C, Mastrodomenico M, Giuliani AR, Petrocelli R. Potential Therapeutic Effects of Curcumin on Glycemic and Lipid Profile in Uncomplicated Type 2 Diabetes-A Meta-Analysis of Randomized Controlled Trial. Nutrients 2021;13(2):404; doi: 10.3390/nu13020404.

56. Tian J, Feng B, Tian Z. The Effect of Curcumin on Lipid Profile and Glycemic Status of Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. Evid Based Complement Alternat Med 2022;2022(1):8278744; doi: 10.1155/2022/8278744.

57. Chien YJ, Chang CY, Wu MY, Chen CH, Horng YS, Wu HC. Effects of Curcumin on Glycemic Control and Lipid Profile in Polycystic Ovary Syndrome: Systematic Review with Meta-Analysis and Trial Sequential Analysis. Nutrients 2021;13(2):684; doi: 10.3390/nu13020684.

58. Jie Z, Chao M, Jun A, Wei S, LiFeng M. Effect of Curcumin on Diabetic Kidney Disease: A Systematic Review and Meta-Analysis of Randomized, Double-Blind, Placebo-Controlled Clinical Trials. Yuan Y. ed. Evid Based Complement Alternat Med 2021;2021:1–14; doi: 10.1155/2021/6109406.

59. Zheng Z-H, Pan H-J, Zhao Z-N, et al. Meta-analysis of Efficacy of Curcumin in the Treatment of Complications of Type Ⅱ Diabetes Mellitus. Chin Pharm J 2021;56(6):489–496; doi: 10.11669/cpj.2021.06.010.

60. Zhang X, Chen X, Tang Y, Guan X, Deng J, Fan J. Effects of medical plants from Zingiberaceae family on cardiovascular risk factors of type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. J FOOD Biochem 2022;46(7); doi: 10.1111/jfbc.14130.

61. Olson LK, Qian J, Poitout V. Glucose Rapidly and Reversibly Decreases INS-1 Cell Insulin Gene Transcription via Decrements in STF-1 and C1 Activator Transcription Factor Activity. Mol Endocrinol 1998;12(2):207–219; doi: 10.1210/mend.12.2.0066.

62. Innocent DC, Innocent RC, Kumar R, Rabaan AA, Emerole CO, Ayando OD, et al. A Systematic Review and Meta-Analysis on the Effect of Curcumin (Turmeric) on Fasting Blood Glucose and Glycated Haemoglobin in Patients with Type 2 Diabetes Mellitus. 2023; doi: 10.1101/2023.10.13.23297012.

63. Emami E, Heidari-Soureshjani S, Sherwin CM. Anti-inflammatory response to curcumin supplementation in chronic kidney disease and hemodialysis patients: A systematic review and meta-analysis. Avicenna J Phytomedicine 2022;12(6):576–588; doi: 10.22038/AJP.2022.20049.

64. Ferguson JJA, Abbott KA, Garg ML. Anti-inflammatory effects of oral supplementation with curcumin: a systematic review and meta-analysis of randomized controlled trials. Nutr Rev 2021;79(9):1043–1066; doi: 10.1093/nutrit/nuaa114.

65. Gorabi AM, Razi B, Aslani S, Abbasifard M, Imani D, Sathyapalan T, et al. Effect of curcumin on proinflammatory cytokines: A meta-analysis of randomized controlled trials. Cytokine 2021;143:155541; doi: 10.1016/j.cyto.2021.155541.

66. He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin, Inflammation, and Chronic Diseases: How Are They Linked? Molecules 2015;20(5):9183; doi: 10.3390/molecules20059183.

67. Hussain Y, Khan H, Alotaibi G, Khan F, Alam W, Aschner M, et al. How Curcumin Targets Inflammatory Mediators in Diabetes: Therapeutic Insights and

Possible Solutions. Molecules 2022;27(13):4058; doi: 10.3390/molecules27134058.

68. Santos-Parker JR, Strahler TR, Bassett CJ, Bispham NZ, Chonchol MB, Seals DR. Curcumin supplementation improves vascular endothelial function in healthy middle-aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress. Aging 2017;9(1):187; doi: 10.18632/aging.101149.

69. Kim HG, Kim JM, Han JM, Lee JS, Choi MK, Lee DS, et al. Chunggan extract, a traditional herbal formula, ameliorated alcohol-induced hepatic injury in rat model. World J Gastroenterol 2014;20(42):15703-15714; doi: 10.3748/wjg.v20.i42.15703.

70. Mahdavi A, Moradi S, Askari G, Iraj B, Sathyapalan T, Guest PC, et al. Effect of Curcumin on Glycemic Control in Patients with Type 2 Diabetes: A Systematic Review of Randomized Clinical Trials. In: Studies on Biomarkers and New Targets in Aging Research in Iran: Focus on Turmeric and Curcumin. (Guest PC. ed) Springer International Publishing: Cham; 2021; pp. 139–149; doi: 10.1007/978-3-030-56153-6_8.

71. Chuengsamarn S, Rattanamongkolgul S, Luechapudiporn R, Phisalaphong C, Jirawatnotai S. Curcumin Extract for Prevention of Type 2 Diabetes. Diabetes Care 2012;35(11):2121–2127; doi: 10.2337/dc12-0116.

72. Cerf ME. Beta Cell Dysfunction and Insulin Resistance. Front Endocrinol 2013;4:37; doi: 10.3389/fendo.2013.00037.

73. Rahimi HR, Mohammadpour AH, Dastani M, Jaafari MR, Abnous K, Mobarhan MG, et al. The effect of nano-curcumin on HbA1c, fasting blood glucose, and lipid profile in diabetic subjects: a randomized clinical trial. Avicenna J Phytomedicine 2016;6(5):567.

74. Ismail NA, Ragab S, El-Baky AN, Hamed M, Ibrahim AA. Effect of Oral Curcumin Administration on Insulin Resistance, Serum Resistin and Fetuin-A in Obese Children: Randomized Placebo-Controlled Study. Res J Pharm Biol Chem Sci 2014;5(5).

75. Marton LT, Pescinini-e-Salzedas LM, Camargo ME, Barbalho SM, Haber JF, Sinatora RV, et al. The Effects of Curcumin on Diabetes Mellitus: A Systematic Review. Front Endocrinol 2021;12; doi: 10.3389/fendo.2021.669448.

76. Nowotny K, Jung T, Höhn A, Weber D, Grune T. Advanced Glycation End Products and Oxidative Stress in Type 2 Diabetes Mellitus. Biomolecules 2015;5(1):194; doi: 10.3390/biom5010194.

77. Ali BH, Al-Salam S, Al Suleimani Y, Al Kalbani J, Al Bahlani S, Ashique M. Curcumin Ameliorates Kidney Function and Oxidative Stress in Experimental Chronic Kidney Disease. Basic Clin Pharmacol Toxicol 2018;122(1):65–73; doi: 10.1111/bcpt.12817.

78. Vanaie A, Shahidi S, Iraj B, Siadat ZD, Kabirzade M, Shakiba F, et al. Curcumin as a major active component of turmeric attenuates proteinuria in patients with overt diabetic nephropathy. J Res Med Sci 2019;24(1):77; doi: 10.4103/jrms.JRMS_1055_18.

79. Baldelli S, Aiello G, Mansilla Di Martino E, Campaci D, Muthanna FM, et al. The Role of Adipose Tissue and Nutrition in the Regulation of Adiponectin. Nutrients 2024;16(15):2436; doi: 10.3390/nu16152436.

80. Abdalla MMI. Therapeutic potential of adiponectin in prediabetes: strategies, challenges, and future directions. Ther Adv Endocrinol Metab 2024;15:20420188231222371; doi: 10.1177/20420188231222371.

81. Hewlings SJ, Kalman DS. Curcumin: A Review of Its' Effects on Human Health. Foods 2017;6(10):92; doi: 10.3390/foods6100092.

82. Ashidi JS, Owagboriaye FO, Yaya FB, Payne DE, Lawal OI, Owa SO. Assessment of reproductive function in male albino rat fed dietary meal supplemented with Mucuna pruriens seed powder. Heliyon 2019;5(10):e02716; doi: 10.1016/j.heliyon.2019.e02716.

83. Amalraj A, Pius A, Gopi S, Gopi S. Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives – A review. J Tradit Complement Med 2017;7(2):205–233; doi: 10.1016/j.jtcme.2016.05.005.

84. Huang J, Qin S, Huang L, Tang Y, Ren H, Hu H. Efficacy and safety of Rhizoma curcumea longae with respect to improving the glucose metabolism

of patients at risk for cardiovascular disease: a meta-analysis of randomised controlled trials. J Hum Nutr Diet Off J Br Diet Assoc 2019;32(5):591-606; doi: 10.1111/jhn.12648.

85. Ashtary-Larky D, Rezaei Kelishadi M, Bagheri R, Moosavian SP, Wong A, Davoodi SH, Khalili P, et al. The Effects of Nano-Curcumin Supplementation on Risk Factors for Cardiovascular Disease: A GRADE-Assessed Systematic Review and Meta-Analysis of Clinical Trials. Antioxid Basel Switz 2021;10(7):1015; doi: 10.3390/antiox10071015.

86. Yuan F, Wu W, Ma L, Wang D, Hu M, Gong J, Fang K, Xu L, et al. Turmeric and curcuminiods ameliorate disorders of glycometabolism among subjects with metabolic diseases: A systematic review and meta-analysis of randomized controlled trials. Pharmacol Res 2022;177:106121; doi: 10.1016/j.phrs.2022.106121.

87. Dehzad MJ, Ghalandari H, Amini MR, Askarpour M. Effects of curcumin/turmeric supplementation on lipid profile: A GRADE-assessed systematic review and dose-response meta-analysis of randomized controlled trials. Complement Ther Med 2023;75:102955; doi: 10.1016/j.ctim.2023.102955.