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ORIGINAL ARTICLE

Efficacy of *Momordica charantia* L. on Blood Glucose, Blood Lipid, and Body Weight: A Meta-analysis of Randomized Controlled Trials

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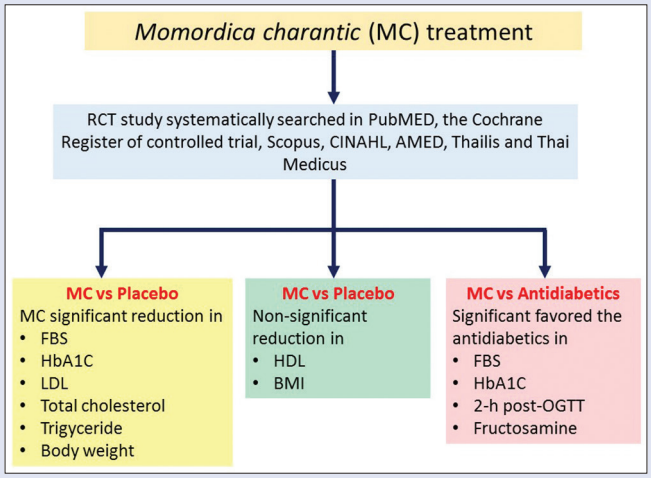
ABSTRACT

Background: Previous studies reported that *Momordica charantia* (MC) improves several metabolic parameters, yet outcomes from numerous trials are contradictory. **Objectives:** This study aimed to assess MC efficacy for improving glycemic status, lipid profile, and body weight. **Materials and Methods:** The databases included PubMed, Cochrane Register of Controlled Trials, Scopus, CINALH, AMED, ThaiLIS, and Thai Medical Index, from inception to June 2016. References from retrieved articles were also evaluated. For this analysis, we selected randomized placebo versus controlled intervention trials conducted in humans dosed with various forms of MC, excluding studies where patients coadministered other medications. We performed a quality assessment of the retrieved studies using Jadad's scoring and Cochrane's risk of bias assessment. **Results:** Eight studies (507 participants) met inclusion criteria, which included six randomized controlled trials (RCTs). Meta-analysis revealed a reduction in fasting blood sugar (FBS) (weight mean difference [WMD] −25.03 mg/dL; 95% confidence interval [CI] −41.17,-8.89) and hemoglobin A1C (HbA1C), favoring MC (WMD −0.20%; 95% CI −0.36, −0.04). Similar results were observed for LDL-C (WMD −5.86 mg/dL; 95% CI: −10.83, −0.89), total cholesterol (WMD −6.29 mg/dL; 95% CI: −10.64, −1.93), and triglyceride (WMD −16.22 mg/dL; 95% CI: −26.40, −6.04). Moreover, patients administering MC experienced a significant reduction in body weight (WMD v3.45 kg; 95% CI −6.73, −0.16). **Conclusions:** MC may improve fasting blood glucose levels, lipid profile, or body weight. A large, well-designed RCT and head-to-head comparison using a standardized preparation of MC will provide definitive data on specific participants.

Key words: Blood glucose, body weight, lipid profile, meta-analysis, *Momordica charantia*

SUMMARY

- The product derived from MC can significantly improve FBS, HbA1C, LDL, total cholesterol, triglyceride level and body weight compared with placebo. MC product was also found to be safe.



Abbreviations used: ACROBAT: A Cochrane risk of bias assessment tool, WMD: Weight mean difference, CI: Confidence interval, SDs: Standard deviations, FBS: Fasting blood sugar, OGTT: Oral glucose tolerance test level; HDL: High-density lipoprotein, TC: Total cholesterol, TG: Triglyceride, BMI: Body mass index.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia. DM is frequently associated with abnormal metabolism of fat, protein, and carbohydrate, which can lead to complications involving the macrovasculature and microvasculature.[1] DM poses a major burden on health care as the prevalence of DM in the year 2030 has been predicted to be as of 366 million worldwide.[2] The progression of the disease has been associated with a number of metabolic abnormalities.[3] Complementary and alternative medicine, which includes herbal medicines, is increasingly utilized as a therapeutic approach to the treatment of DM.[4] To date, more than 400 medicinal plants have been reported to exhibit antihyperglycemic activity.[5] *Momordica charantia* (MC) is one herb that has been identified as effective for glycemic control in diabetes and other metabolic conditions.[6] Earlier studies characterized MC as having significant antidiabetic as well as hypolipidemic activities.[6,7] However, the results of published randomized controlled trials (RCTs) are contradictory,[8-10] with most of these trials being underpowered.[11,12] While a recent meta-analysis suggested that MC improved glycemic control and that its safety profile was positive,[13] this review did not evaluate other metabolic outcomes.

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For this reason, we conducted a systematic review and meta-analysis to assess the efficacy of MC on glycemic control, lipid profiles, and body weight. An analysis of adverse events was also included.

Objectives

The primary objective of our study was to conduct an updated literature review and perform a meta-analysis on the impact of MC on glycemic control, lipid profiles, body weight, and safety.

MATERIALS AND METHODS

Search strategy

In designing this study, we followed the guidelines put forth in the preferred reporting items for systematic review and meta-analysis statement [Table 1].[14] A systematic search of the literature was used to identify the clinical trials used in the current study. The databases that were searched included PubMed, the Cochrane Register of Controlled Trials, Scopus, CINALH, AMED, ThaiLIS, and the Thai Medical Index from inception to June 2016. In addition, we also conducted a hand-search from the reference list of included trials, meta-analyses, systematic reviews, and guidelines. The following MeSH terms were used; MC, MC, hypoglycemic, diabetic mellitus, DM, efficacy, and effectiveness. To increase the sensitivity of the search strategy, we used the wild-card term "*." There were no language restrictions. Uncontrolled trials did not meet the main objective of the review and thus were excluded from the meta-analysis.

Study selection

Two reviewers (WP and BS) selected the eligible studies and differences were resolved by consensus. To qualify for this meta-analysis, a study must have (1) been a controlled trial or RCT utilizing a parallel or cross-over design, (2) investigated the impact of MC on blood glucose and metabolic parameters, and (3) presented sufficient information on blood glucose activities and metabolic parameters in both the control and intervention groups at baseline and the end of the study. It is important to note that studies were excluded if (1) they had an uncontrolled design and were a non-RCT, (2) MC was mixed with other herbs, (3) no numerical values were presented at the end of the study, or (4) the study represented an ongoing trial.

Data extraction and quality assessment

WP and BS extracted data from the recruited studies. The disagreement was resolved by consensus. Eligible studies were thoroughly reviewed and abstracted: the year of publication, location (country), study design, characteristics of included participants, sample sizes of the control and treatment groups, and outcome measurements. The quality of included studies was further assessed using the Jadad scale. Studies possessing a Jadad score of at least 3 out of a total of 5 points were designated as a high-quality study.[15]

ACROBAT was used to screen each of the selected studies for risk of bias. To evaluate the risk of bias, we examined sequence generation, allocation concealment, blinding of participants/personnel and outcome assessors, incomplete outcome data, and selective outcome reporting, as well as other potential sources of bias. Any suspected bias was identified as low, uncertain, or high risk, in accordance with criteria explicitly described in the Cochrane Handbook for Systematic Reviews of Interventions.[16]

Statistical analysis and publication bias

Treatment efficacy for the two groups (MC and control) was statically tested by weight mean difference (WMD) and 95% confidence interval (CI).

The WMD of blood glucose, lipid profile, and body weight were used as primary endpoints to reveal differences between the MC intervention and comparators. The WMD was derived for both the treatment groups and the comparator groups using measurements collected at baseline and the end of the follow-up. SDs of the mean difference were calculated using the following formula.[17]

$$SD = \sqrt{SD_{pre}^2 + SD_{post}^2 - (2R \times SD_{pre} \times SD_{post})}$$

Remark: Pre = pretreatment, post = posttreatment

Data analysis was conducted using Review Manager (Revman® version 5.3 from Cochrane collaboration, Oxford, UK). The Q-statistic was used to examine the heterogeneity of the included studies and was presented as I^2. A value of 50% or higher ($P < 0.10$) was considered as evidence of heterogeneity.[18] Included studies that were determined to be heterogeneous were examined by the random effect model. Alternatively, if homogeneity was found, the fixed effects model was used. A funnel plot was used to evaluate publications biased toward a particular outcome.[19] The safety of MC was also assessed and described. For each study, a sensitivity test for undue influence was conducted by systematically removing one study and recomputing the result of remaining studies.

RESULTS

Summary of included studies

Among the 967 articles found in the initial search, a total of 952 were found to be ineligible following review of the title and abstract. Three articles were retrieved by a hand-search of the evaluated articles [Figure 1]. The full texts of these eight articles were evaluated in detail, and upon meeting the inclusion criteria [Table 2] were qualitatively assessed for risk of bias. Among the six articles that were judged to be of high quality, five were double-blind RCTs[8,11,12,20-22] with the sixth being a single-blind trial.[9,10] The trial by Bunyamahotama[20] was characterized as a crossover study. Overall, 507 participants were included in the meta-analysis (300 participants received MC and 207 received comparator treatment). The majority of participants in the blood glucose outcomes analyses were patients with either type II DM and/or impaired glucose tolerance. Study duration ranged from 1 day to 6 months. Three trials were undertaken in Thailand[11,20,21] and two trials were conducted in India.[9,10] Moreover, other studies were conducted in Pakistan,[12] Germany,[22] and the Philippines.[8] The Fuangchan *et al.*[21] and Rahman *et al.*[12] studies compared MC with oral antidiabetics.

Data quality and risk of bias assessment

The validity of included trials is presented in Table 2. Overall, included trials varied in terms of quality and risk of bias. All recruited RCT studies were verified as utilizing an RCT design. Six trials were double-blinded,[8,11,12,20-22] with blinding and allocation concealment

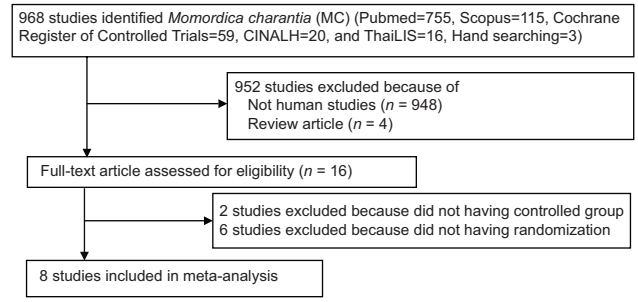

Figure 1: Flow of included studies

Table 1: PRISMA statement

Section/topic	#	Checklist item	Reported on page#
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	351
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	351
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	351
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	352
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	352
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	352
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	352
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	352
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	352
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	352
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	352
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	354
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	354
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	352
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	352
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	354
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	354
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	354
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	354
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	354-356
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	354
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	354
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	356
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	356
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	357
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

PICOS: Participants, interventions, comparisons, outcomes, and study design; N/A: Not available

adequately described in the methods. Only one study earned a Jadad score of 5/5.[21] A majority of studies did not provide any information regarding the issues of blinding, allocation concealment, and participant drop out. Using established criteria to assess randomization and reporting methods, two of the eight studies were identified as having a high risk of bias.[9,10] Most of the recruited RCTs tended to have a high risk of bias associated with random sequence generation, blinding of participants, allocation concealment, and personnel. Selective reporting was described adequately in most of the studies. Overall, we found the studies to be of relatively high quality, according to guidelines published in the Cochrane Handbook for Systematic Reviews of Interventions [Figure 2].[16]

The analysis focused on the ability of MC to reduce levels of glucose, lipid, and body mass index (BMI).

Adverse events related to renal, hepatic functions and the gastrointestinal system were evaluated. The salient features of the included studies have been presented in Table 2.

Effect on blood glucose

Fasting blood sugar

The findings from 10 trial arms comprising 267 participants in the intervention groups and 263 participants in the control groups were pooled. Two separate analyses were conducted to analyze FBS effects: (1) MC versus placebo and (2) MC versus antidiabetic drugs. The results revealed that MC treatment was efficacious for FBS when compared to placebo (WMD, −25.03 mg/dL; 95% CI: −41.17, −8.89; $P = 0.002$). The efficacy of antidiabetic drugs to regulate FBS was significantly

Table 2: Characteristics of included studies

Study (year)	Location	Study design	Participants	Duration of trial	Interventions	Outcomes	Jadad score
John, 2003[9]	India	RCT, single-blind	DM Type II	4 weeks	I: 2 g dried fruit MC tablets x3/day (26) C: Riboflavin (24)	FBS, PPG Fructosamine	2
Bunyamahotama, 2004[20]	Thailand	RCT, double-blind, crossover	Prediabetes	1 week	I: 1.8 g dried fruit MC tablets/day (14) C: Corn starch (14)	OGTT	4
Dans, 2007[8]	The Philippines	RCT, double-blind	DM Type II	3 months	I: 3 g MC/day (20) C: Placebo (20)	FBS, HbA1C, TC, BMI, SCr, AST, ALT, Na, K	4
Fuangchan, 2011[21]	Thailand	RCT, double blind	DM Type II	4 weeks	I1: MC 500 mg/day (33) I2: MC 1000 mg/day (32) I3: MC 2000 mg/day (31) C: Metformin 1000 mg/day (31)	FBS, fructosamine, OGTT, LFTs, BUN, SCr, ADR	5
Hasan, 2012[10]	India	RCT, single-blind	DM Type II	4 weeks	I: 2 g dried fruit MC tablets x3/day (26) C: Riboflavin (24)	FBS	2
Zanker, 2012[22]	Germany	RCT, double-blind	DM Type II	4 weeks	I: MC contain 10% charantin (w/v) x2 (30) C: Placebo (32)	HbA1C, BMI	3
Trakoon-osot, 2013[11]	Thailand	RCT, double-blind	DM Type II	16 weeks	I: MC 6 g/day (19) C: Placebo (19)	FBS, HbA1C, LFT, SCr, weight, BMI, BP	4
Rahman, 2015[12]	Pakistan	RCT, double-blind	DM Type II	2 weeks	I1: MC 2 g/day (30) I2: MC 4 g/day (31) C: Glibenclamide 5 mg/day (29)	FBS, HbA1C, OGTT, TC, LDL, HDL, TG, SBP, weight, ADR	4

I: Intervention group; C: Control group; RCT: Randomized controlled trial; DM: Diabetes mellitus; HDL: High-density lipoprotein, TC: Total cholesterol, TG: Triglyceride, BMI: Body mass index; ADR: Adverse drug reaction; FBS: Fasting blood sugar; PPG: Postprandial plasma glucose, OGTT: Oral glucose tolerance test; HbA1c: Hemoglobin A1C; SCr: Serum creatinine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LFT: Liver function test; BUN: Blood urea nitrogen; SBP: Systolic blood pressure; LDL: Low-density lipoprotein

Figure 2: Risk of bias diagram derived from individual randomized controlled trial studies

Study, year	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
John, 2003	?	?	-	?	-	+
Bunyamahotama, 2004	?	+	+	?	+	?
Dans, 2007	+	+	+	?	-	?
Fuangchan, 2011	+	-	+	?	?	+
Hasan, 2012	-	-	-	?	?	?
Zanker, 2012	-	+	?	?	?	?
Trakoon-osot, 2013	+	+	+	?	?	+
Rahman, 2015	-	+	?	+	+	?

+: Low risk; -: High risk; ?: Unclear

greater than that of MC (WMD, 14.52 mg/dL; 95% CI: 10.47, 18.57; $P < 0.00001$). A statistically significant heterogeneity was detected in the FBS outcome [Figure 3].

Hemoglobin A1C

A comparison of MC treatment to placebo indicated that hemoglobin A1C (HbA1C) levels were significantly reduced in participants who were administered MC (WMD = −0.20%; 95% CI: −0.36, −0.04; $P = 0.02$). Moreover, HbA1C levels were also significantly different in MC-treated participants compared to participants receiving antidiabetic drugs (WMD = 0.54%; 95% CI: 0.31, 0.78; $P < 0.00001$). This analysis did not detect any heterogeneity.

2-h post-oral glucose tolerance test level

The 2-h post-oral glucose tolerance test level (2-h post-OGTT) level was reported in three trials.[12,20,21] The pooled analyses indicated that the WMD of the 2-h post-OGTT levels among participants with MC treatment were not different from the placebo group (WMD −0.39 mg/dL; 95% CI −1.93, 1.16; $P = 0.63$) but the results favored the antidiabetic drugs (WMD 0.58 mg/dL; 95% CI: 0.18, 0.99; $P = 0.005$). Heterogeneity was detected in the overall meta-analysis ($I^2 = 56\%$, $P = 0.03$).

Fructosamine

There were no statistically significant between MC-treated and control group in fructosamine levels (WMD, −14.80; 95% CI: −53.19, 23.59; $P = 0.45$). There was, however, a significant difference when MC treatment was compared to treatment with antidiabetic drugs (WMD, 22.83; 95% CI: 8.07, 37.58; $P = 0.002$). Heterogeneity was not observed for these variables.

Efficacy on lipid profile

The pooled trial report on lipid profiles showed that MC was significantly efficacious with regard to LDL levels (WMD, −5.86 mg/dL; 95% CI: −10.83, −0.89; $P = 0.02$). Pooling of total cholesterol (TC) data indicated benefits from MC treatment ($n = 81$) over comparator treatment ($n = 78$) (WMD, −6.29 mg/dL; 95% CI: −10.64,-1.93; $P = 0.005$). Meta-analysis indicated that MC significantly decreased triglyceride (TG) levels compared to the comparators group (WMD, −16.22 mg/dL; 95% CI: −26.40, −6.04; $P = 0.002$). Moreover, the results showed that HDL levels were significantly increased in the MC group (WMD, 5.77 mg/dL; 95% CI: 3.98, 7.57; $P < 0.00001$) [Figure 4].

Efficacy on body weight and body mass index

Administration of MC produced a statistically significant decrease in body weight (WMD, −3.45 kg; 95% CI: −6.73,-0.16; $P = 0.04$), but no statistically significant differences in BMI (WMD, 0.00; 95% CI −1.62, 1.62; $P = 1.00$) compared to the control group. Heterogeneity was not observed for either variable.

Other laboratory results

In pooled results from five treatment arms,[8,11,21] participants treated with MC did not show significant differences from the control group with regard to their levels of alanine aminotransferase (WMD −0.61; 95% CI: −4.38, 3.15; $P = 0.45$), aspartate aminotransferase (WMD −0.14; 95% CI: −3.15, 2.88; $P = 0.93$) and serum creatinine (WMD −0.04; 95% CI: −0.11, 0.03; $P = 0.26$). Evidence of heterogeneity was observed in the serum creatinine results ($I^2 = 59.0\%$, $P = 0.04$).

Adverse effects

The pooled analysis indicated that participants treated with MC were likely to experience adverse events in the gastrointestinal, central nervous, and dermatologic systems. Back pain was also reported. However, there were no significant differences in adverse events when comparing the MC group with comparators.

Sensitivity analysis

Results of the sensitivity analysis showed an absence of differences for some the evaluated outcomes. For this analysis, the one-study remove approach was applied. Compared with the main analysis, differences were identified only in some outcomes: 2-h post-OGTT level, HDL, TC, TG, weight, and BMI were altered, while other outcomes results remained unchanged.

Publication bias

Funnel plots were applied to analyze outcomes. The plots were visually inspected for publication bias [Appendix 1]. No publication bias was found for the FBS outcome, which was performed using Egger's and Begg's test ($P = 0.334$).

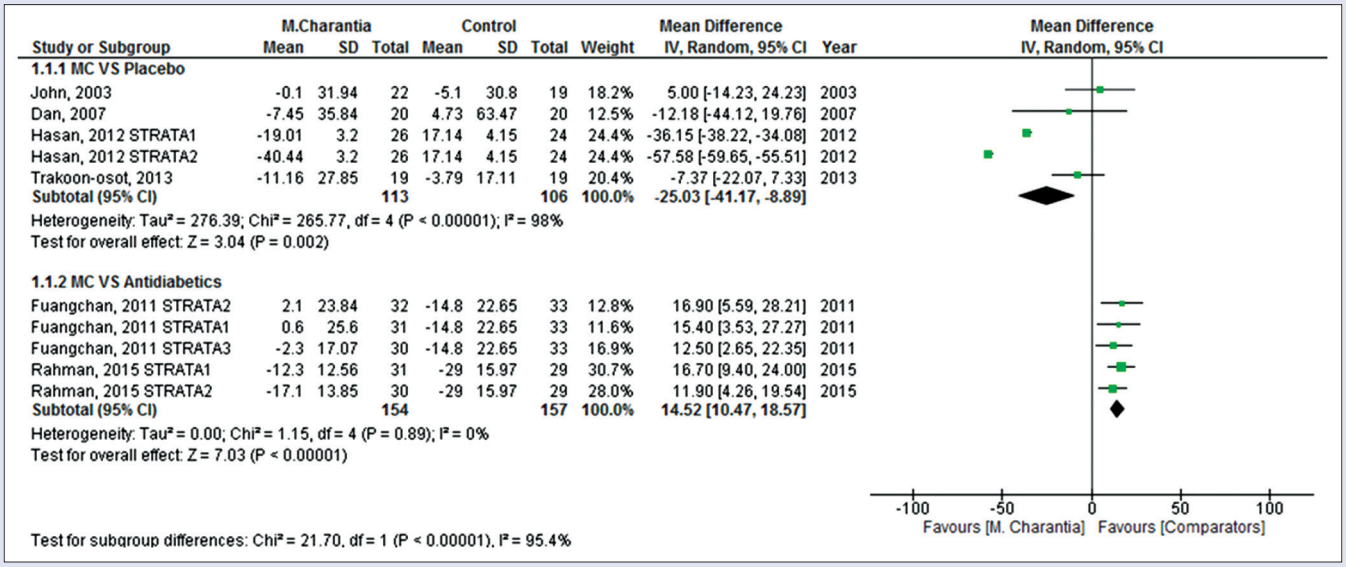

Figure 3: Efficacy of fasting blood sugar reduction in control versus *Momordica charantia* treated groups. The diamond indicates the weight mean difference and 95% confidence interval. The size of the square is proportional to the variance of the studies

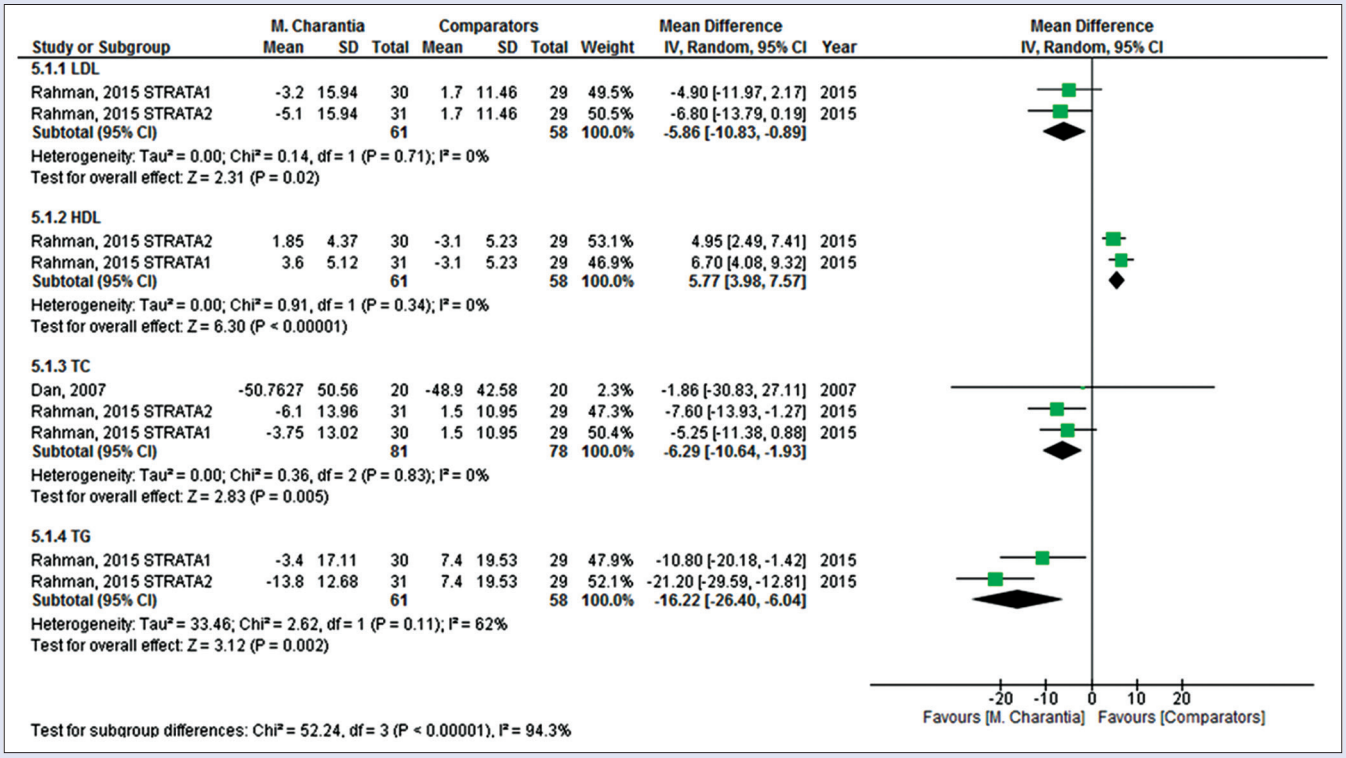

Figure 4: Efficacy of lipid profile reduction in control versus *Momordica charantia* treated groups. The diamond indicates the weight mean difference and 95% confidence interval. The size of the square is proportional to the variance of the studies

DISCUSSION

Our meta-analysis of RCTs aimed to elucidate the beneficial effects of MC on blood glucose, blood lipid, and body weight. Our findings demonstrated that, compared with placebo, MC products have the potential to increase HDL levels and improve FBS, HbA1C, LDL, TC, TG, and weight. This finding is not in agreement with the study by Ooi *et al.*[13] where the authors reported that MC had no beneficial effect on blood glucose levels. However, our findings are consistent with a study by Yin *et al.*[23] in which it was determined that MC had a significant effect on reduction of HbA1C levels compared to placebo. In our meta-analysis, the FBS, HbA1C, and 2-h post-OGTT levels were significantly reduced with antidiabetic drugs. This was not surprising given that these are well-established characteristics of antidiabetic drugs.

Our study is the first meta-analysis that supports MC as an efficacious therapeutic for modifying lipid profiles and body weight. Existing evidence demonstrates that MC does significantly decrease LDL, TC, and TG while increasing HDL levels compared with placebo. Moreover, MC significantly reduced body weight but not BMI.

In a majority of preclinical trials, where testing is typically conducted in mice and rats, investigators have claimed that MC effectively controlled glycemic status[7,24] and hypolipidemic effects.[25] Furthermore, MC has tended to decrease body weight or BMI.[26] It is believed that these physiological effects are mediated by charantin, mormordicin, and momorcharin, the active components in MC extract.[27-31] Previous reports determined that these three substance can increase peroxisome proliferator-activated receptor (PPAR)-α and PPAR-γ expression, which promotes insulin secretion and prevents β-cell damage, inhibits adipocyte hypertrophy, inhibits adipocyte differentiation, and decreases visceral fat mass.[6,32]

Overall, the analysis across all included studies for selected outcomes demonstrated that the difference in findings could be attributed to many factors, such as the characteristics of participants, the MC preparation, the dose of MC extract, and the duration of the study.

Our findings are congruent with the notion that MC products are safe for oral administration. There were no reports of critical adverse or withdrawal effects that affected the gastrointestinal system or CNS, neither did there appear to be serious dermatologic side effects. However, these events were present in both MC and the comparators groups. Moreover, the analysis did not reveal any significant effects between different groups.

The standardization of MC products is essential for quality control before initiation of clinical trials. Our findings revealed that only four studies had standardized the amount of bioactive marker, charantin.[11,20-22] The amount of charantin found in different products may vary depending on the age and part of the plant used, cultivating conditions, and extraction methods.[33,34] Therefore, it is very important that the active ingredient be standardized in all studies to provide more accurate and reliable comparison of results.

In this study, we employed a wide range of accepted international databases to identify relevant studies and quantify relevant outcomes using meta-analysis. In addition, we included the Thai database to increase our chances of identifying all relevant clinical trials of MC published in local databases.

Limitations

It is important to mention some limitations were observed from the included trials. First, patients enrolled in the included studies each had a different status, which included diabetes type II, prediabetes, or overweight participants. Second, two trials[9,10] did not conceal the physical appearance of the intervention used. It is well understood that concealment is an important feature of RCT.

Publication bias is another concern for conducting meta-analysis. Due to the small number of included trials, a rigorous test of publication bias could not be executed on all outcomes. Therefore, the results of our meta-analysis could have been influenced by the small number of studies used for the analysis. Most of the studies we included did not specifically evaluate other metabolic effects of MC. In addition, the range of MC doses used by the included studies (0.04%–10% w/w) may have been too wide. Moreover, the treatment duration (a maximum of 6 months) may have been too short to reveal metabolic profile effects. Further, well-designed RCTs are needed before the effects of MC on metabolic profile can be clearly established. Dosage effects should also be explored.

The results of our meta-analysis support the hypothesis that, compared to placebo, MC may be beneficial for improving blood glucose, lipid profile, and body weight. Given the equivocal results revealed by this meta-analysis of MC efficacy in the treatment of DM, it is suggested that a large-scale randomized prospective, comparative clinical trial be performed in patients with DM, using a standardized formulation.

CONCLUSIONS

The current evidence is consistent with a positive effect of MC on lowering glycemic status, lipid, and body weight. However, the effect on hepatic and renal function was not different between MC and comparators. The adverse events reported by both groups were similar and included gastrointestinal, central nervous system, and dermatologic effects.

Acknowledgment

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Appendix 1: Funnel plot showing publication bias