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Glycemic benefits of a bitter melon-based multi-herbal extract supplement in adults predisposed to metabolic syndrome

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ABSTRACT

Background: Herbal plants are rich in nutrients and bioactive compounds that contribute to health promotion and are associated with a reduced risk of metabolic syndrome. However, evidence from human clinical trials remains limited and inconsistent, particularly regarding the combined effects of multiple herbal species.

Objective: This study aimed to evaluate the effects of consuming a dietary supplement containing extracts from various medicinal herbs on nutritional status, blood pressure, and key biochemical markers in adults predisposed to metabolic syndrome.

Methods: A total of 70 adult participants aged 30-59 years who were at risk of metabolic syndrome were enrolled in a 12-week randomized, double-blind, placebo-controlled trial. Participants were randomly assigned into two groups: the experimental group (n=35), which received a bitter melon–based multi-herbal extract supplement (BMMH), and the placebo group (n=35). Pre-and post-intervention outcomes were compared, including waist circumference, body composition, glucose metabolism, lipid profiles, and inflammatory biomarkers. Dietary intake and physical activity were also assessed.

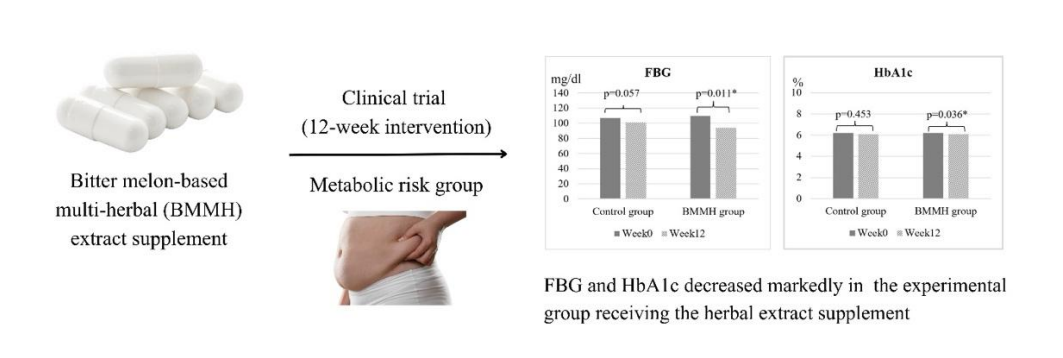
Results: All seventy participants completed the study. After 12 weeks, participants who consumed BMMH extract supplement exhibited significant reductions in fasting blood glucose and HbA1c levels ($p = 0.011$ and $p = 0.036$,

respectively). In addition, a significant decrease in the LDL-C to HDL-C ratio was observed (p = 0.014), whereas no comparable changes occurred in the placebo group. No statistically significant effects were observed for other lipid parameters or inflammatory markers, including IL-6, TNF-α, and hs-CRP.

Conclusion: Bioactive compounds present in medicinal herbs, particularly bitter melon, may support glucose homeostasis by enhancing glucose utilization and thereby reducing blood glucose levels. These compounds may help reduce the risk of cardiovascular disease. Thus, consumption of dietary supplements derived from herbal extracts may serve as a supportive factor in improving metabolic syndrome outcomes and potentially preventing the development of non-communicable diseases.

Trial registration: Thai Clinical Trials Registry TCTR20241122004

Keywords: functional foods, bioactive compounds, bitter melon, fasting blood glucose, metabolic syndrome



Graphical abstract: Glycemic benefits of a bitter melon-based multi-herbal extract supplement in adults predisposed to metabolic syndrome

INTRODUCTION

Metabolic syndrome is a metabolic disorder primarily associated with obesity and insulin resistance. At present, metabolic syndrome has become a major public health concern, as reflected by the high morbidity and mortality associated with non-communicable diseases (NCDs) in Thailand and worldwide [1–2]. Therefore, the prevention and control of NCDs should be emphasized through lifestyle modifications, including increased physical activity and adopting a healthy diet that ensures adequate and balanced nutrient intake.

The concept of healthy eating extends beyond the intake of essential macronutrients required for normal physiological function. Growing attention has focused on bioactive compounds—non-nutrient substances naturally present in foods and medicinal plants—that exert physiological effects beyond basic nutrition [3]. Plant-derived phytochemicals exhibit diverse biological activities that can help regulate or counteract oxidative imbalances, which are closely linked to inflammation, neurodegeneration, cardiovascular dysfunction, immune dysregulation, and metabolic disturbances [4-8]. As a result, herbal extracts are increasingly incorporated into dietary supplements and functional foods across health, medical, and nutritional sectors. A wide variety of medicinal plants have been utilized in dietary

supplements aimed at promoting health, preventing disease, and supporting therapeutic outcomes. These include both Thai and Chinese medicinal herbs, such as *Momordica charantia* (bitter melon), which contains several bioactive compounds that act through multiple mechanisms to prevent hyperglycemia leading to diabetes. These mechanisms include stimulating insulin secretion from the pancreas, reducing hepatic glucose production, enhancing glucose metabolism, improving insulin sensitivity, and increasing glucose tolerance [9-11].

Other medicinal plants also demonstrate complementary metabolic effects. *Ganoderma lucidum* (lingzhi or reishi mushroom), exhibits vasodilatory and anti-inflammatory properties, as well as neuroprotective effects; thus, it is often used as an adjunct in the management of various non-communicable diseases [12-13]. Similarly, *Gynostemma pentaphyllum* (Jiaogulan), a traditional Chinese medicinal herb, demonstrates potent biological activities including anti-inflammatory, anticancer, and cardioprotective effects, along with the ability to regulate lipid metabolism [14-15]. In addition, several Western herbal plants are also recognized for their health-promoting properties, such as *Panax quinquefolius* (American ginseng), a member of the same genus as Asian and Korean ginseng, which has been reported to improve postprandial blood glucose control and reduce blood lipid levels [16-18]. Another notable example is the *Cynara scolymus* (artichoke), a Mediterranean plant whose extracts have been investigated for their lipid-lowering and antihypertensive effects [19-21].

However, previous studies investigating the pharmacological and medical benefits of herbal plant extracts have primarily been conducted in vitro and in animal models. Human clinical trials remain limited, though growing interest in this area has led to an increasing number of such studies in recent years. Moreover, research examining the combined effects of multiple herbal species remains scarce. Therefore, further clinical investigations are needed to elucidate the efficacy of dietary supplements containing herbal extracts on human health. The present study aimed to evaluate the effects of consuming a dietary supplement containing multiple herbal extracts, including bitter melon, Lingzhi mushroom, and Jiaogulan, on health-related outcomes among Thai adults at risk of metabolic syndrome.

MATERIALS AND METHODS

BMMH extract supplement: The extracts (Lot No. 30–31) were formulated into a dietary supplement by Odee Style Co., Ltd. The manufacturing facility is certified under ISO 9001:2015, HACCP, and GHP standards. The product was distributed by Hopeful Co., Ltd. and has been registered with the Thai Food and Drug Administration (FDA) under Food Registration No. 10-1-15662-5-0011.

Study participants: The study participants were recruited between November and December 2024 through social media platforms such as Line and Facebook. Inclusion criteria were adults of both sexes, aged 30–59 years, residing in Bangkok and its metropolitan areas, who were at risk of developing metabolic syndrome with at least one of the following conditions: (1) waist circumference ≥ 80 cm for women and ≥ 90 cm for men; (2) blood pressure ≥ 130/85 mmHg; (3) fasting blood glucose ≥ 100 mg/dL; (4) triglyceride level ≥ 150 mg/dL; or (5) high-density lipoprotein cholesterol (HDL-C) < 50 mg/dL for women and < 40 mg/dL for men.

Exclusion criteria included individuals who were currently undergoing treatment or taking medications for chronic non-communicable diseases, such as cardiovascular disease, cerebrovascular disease, diabetes, liver disease, chronic kidney disease, cancer, or thyroid disorders. Participants with digestive or nutrient absorption disorders, chronic fatigue, or those consuming dietary supplements or herbal products more than twice per week within four weeks prior to

enrollment, or during the study, were excluded. Additionally, individuals with atypical dietary patterns, changes in physical activity within six months prior to the study, smokers consuming more than five cigarettes per day, alcohol consumption exceeding 14 drinks per week, pregnant women or those planning pregnancy within six months, breastfeeding women, and individuals with known allergies to components of the tested dietary supplement were excluded.

Test samples: The test samples, including the BMMH extract supplement and the placebo, were both encapsulated in 1,000 mg hard-shell capsules, manufactured by Odee Style Co., Ltd. The BMMH capsules contained a total of 435 mg of natural herbal extracts, comprising 150 mg of bitter melon extract, 100 mg of American ginseng extract, 70 mg of Lingzhi mushroom extract, 70 mg of artichoke extract, and 45 mg of Jiaogulan extract. In addition, the capsules contained 445 mg of various compounds and minerals, as well as 120 mg of other capsule constituents (Table 1). The placebo capsules were identical in appearance butdid not contain any herbal extracts or added micronutrients; each capsule contained 1,000 mg of cornstarch. Both types of test samples were packaged in identical white capsules labeled as dietary supplements using the letters A and B. Neither the researchers nor the participants were aware of the specific contents of the capsules, ensuring a double-blind design.

Table 1. Composition of the bitter melon–based multi-herbal extract supplement (BMMH).

Composition of BMMH per 1 capsule (1,000 mg)	Amount (mg)
Bitter melon extract	150
American ginseng extract	100
Magnesium	100
Fish oil powder	100
Lingzhi mushroom extract	70
Artichoke extract	70
Propolis	60.5
Chitosan	60
Yeast beta-glucan	60
Gynostemma extract	45
Zinc amino acid chelate	30
Alpha-lipoic acid	24
D-alpha-tocopheryl acetate	10
Chromium picolinate	0.5
Other ingredients	
- Edible gelatin	119.2
- Titanium dioxide	0.8

Study protocol: A randomized, placebo-controlled trial was conducted over a total duration of 12 weeks. A total of 84 individuals were screened for eligibility based on the inclusion and exclusion criteria, resulting in 70 eligible participants. These participants were then randomly assigned to two groups of 35 individuals each using a pair-matching, random-allocation method. Variables used to ensure group comparability included sex, age, and risk level for metabolic syndrome. Participants were first categorized by these variables (female vs. male, age

range, and high, medium, or low risk of metabolic syndrome) and then randomly allocated within each category to either the experimental or control group.

The groups consisted of an experimental group consuming 2 capsules per day of a BMMH extract supplement after meals (1,000 mg per capsule), providing a total of 870 mg of herbal extracts per day, and a control group receiving a placebo capsule of identical appearance and dosage.

The study protocol was approved by the Ethical Review Committee for Human Research, Faculty of Public Health, Mahidol University (Certificate of Approval No. MUPH 2024–121) and was registered with the Thai Clinical Trials Registry (Registration number TCTR20241122004). Written informed consent was obtained from all participants prior to enrollment.

Clinical and Biochemical assessment: Participants' blood pressure was measured using a validated automatic upper-arm cuff device (HEM-7130, OMRON Corporation, Japan). Prior to measurement, participants were seated and rested for at least 5 minutes. Systolic and diastolic blood pressure and pulse rate were recorded twice at 1–2-minute intervals. The average of the two readings was calculated to represent each participant's blood pressure.

Participants underwent laboratory assessments to evaluate their health status at baseline and after the 12-week intervention. Blood samples were collected following a minimum 10-hour fast. Laboratory technicians analyzed fasting blood glucose (FBG), glycated hemoglobin (HbA1c), lipid profiles (total cholesterol, low-density lipoprotein cholesterol: LDL-C, high-density lipoprotein cholesterol: HDL-C, and triglyceride: TG), liver function enzymes (aspartate aminotransferase: AST and alanine aminotransferase: ALT), kidney function indicators (blood urea nitrogen: BUN and uric acid), the acute-phase inflammation marker (high sensitivity-C-reactive protein: hs-CRP), and pro-inflammatory cytokines (interleukin 6: IL-6 and tumor necrosis factor-alpha: TNF-α). All biochemical analyses were performed at Alternate Laboratory Co., Ltd., an accredited laboratory by the Medical Technology Council of Thailand.

Anthropometric assessment: Waist circumference was measured with a non-stretchable tape measure, placed horizontally around the abdomen at the umbilical midpoint, ensuring close contact with the skin. Participants were instructed to breathe normally, and the measurement was recorded at the end of a normal exhalation. Waist circumference was reported in centimeters to one decimal place. Measurements were repeated twice, and the mean value was calculated for each participant. Body weight, body mass index (BMI), total body fat, visceral fat, fat mass, muscle mass, and basal metabolic rate (BMR) were assessed using a bioelectrical impedance analyzer (DC-360, Tanita Corporation, Japan).

Dietary intake and physical activity assessment: Dietary intake was assessed three times per week (two weekdays and one weekend day) using a 3-day food record. To monitor habitual food consumption, participants were instructed to photograph their meals before and after consumption. In addition, a trained nutritionist conducted dietary interviews with each participant at least three times per week. Energy and nutrient intakes were subsequently calculated using the INMUCAL-Nutrient version 2 software.

Physical activity was assessed using the Thai version of the Global Physical Activity Questionnaire (GPAQ), developed by the World Health Organization, as detailed elsewhere [22]. Participants were asked about the duration of activities performed over the past week, using 16 questions grouped into four domains: work activities, travel to and from locations, recreational activities, and sedentary behavior. The reported durations were then used to calculate the total physical activity in terms of metabolic equivalent of task (MET) minutes per week.

Statistical analysis: Data were presented in two formats. Categorical variables were expressed as frequency (n) and percentage (%), while continuous variables were reported as mean ± standard deviation ($\bar{x}$ ± SD). Differences between the two study groups (experimental and control) were analyzed using an independent-samples t-test. Within-group comparisons were performed using a paired-samples t-test. All statistical analyses were conducted using IBM SPSS Statistics version 30.0, with a significance level set at $p < 0.05$.

RESULTS

Baseline characteristics: A total of 84 volunteers were screened, and 70 eligible participants were enrolled and randomly assigned to either a control group (n=35; placebo) or an experimental group (n=35; BMMH extract supplement). All participants completed the 12-week intervention (Figure 1).

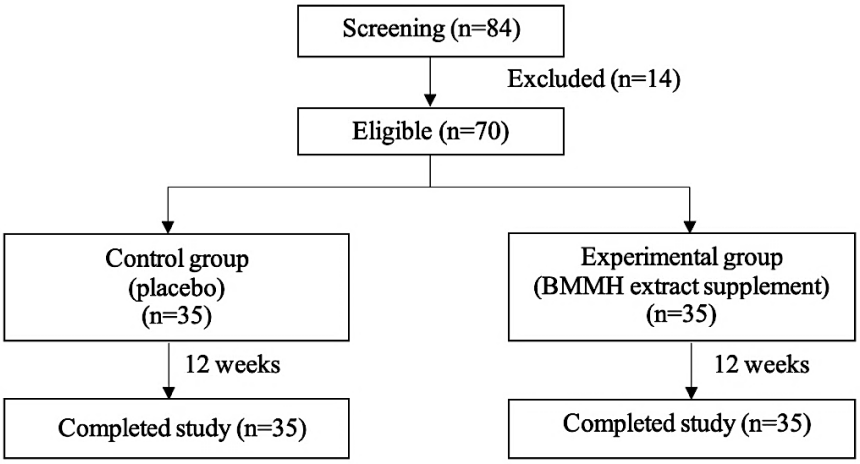


Figure 1. Flowchart of study design

Participants were predominantly female (87.1%), with no significant baseline differences between groups in demographic, anthropometric, or biochemical parameters, or dietary patterns ($p>0.05$ for all), as shown in Table 2.

The mean ages were 44 and 45 years for the control and BMMH group, respectively. Both groups exhibited slightly elevated blood pressure, obesity (BMI > 25 kg/m²), and abdominal obesity (WC > 80 cm in females and > 90 cm in males).

Biochemical profiles indicated a tendency toward increased NCD risk, with elevated FBG and HbA1c, as well as higher total cholesterol and LDL-C concentrations, although TG, HDL-C, and renal and liver function markers were within normal. Notably, both groups exhibited hs-CRP levels exceeding 1 mg/dL, suggesting a heightened inflammatory state and potential health risk, although IL-6 and TNF-α did not differ significantly between groups.

Table 2. Participants' baseline characteristics.

Study parameters	Control (n=35)	BMMH (n=35)	p-value
Sex			0.721*
Male	5 (14.3%)	4 (11.4%)	
Female	30 (85.7%)	31 (88.6%)	
Age	43.8 ± 8.0	45.2 ± 8.4	0.478
Blood pressure			
Systolic blood pressure (mmHg)	125 ± 12	124 ± 11	0.814
Diastolic blood pressure (mmHg)	85 ± 10	84 ± 8	0.587
Anthropometry			
Weight (kg)	73.4 ± 13.1	73.4 ± 11.0	0.991
Body mass index (kg/m^2)	29.0 ± 4.1	28.6 ± 5.2	0.701
Waist circumference (cm)	94.8 ± 10.0	94.0 ±9.5	0.713
Body fat (%)	37.8 ± 10.0	38.4 ± 11.0	0.818
Body fat mass (kg)	28.1 ± 10.6	28.5 ± 10.8	0.854
Visceral fat rating	9.1 ± 3.0	9.1 ±2.9	0.997
Muscle mass (kg)	42.7 ± 9.3	41.9 ± 8.0	0.696
Free fat mass (kg)	45.4 ± 9.8	44.7 ± 8.5	0.775
Basal metabolic rate (kcal)	1355 ± 233	1336 ± 168	0.708
MET (minutes/week)	139.5 ± 133.6	121.7 ± 108.3	0.559
Blood parameters			
Fasting blood glucose (mg/dL)	106.9 ± 47.3	109.6 ± 40.2	0.801
HbA1c (%)	6.2 ± 1.4	6.2 ± 1.0	0.967
Total cholesterol (mg/dL)	226.2 ± 25.6	224.1 ± 34.0	0.770
LDL-C (mg/dL)	155.7 ± 24.1	157.7 ± 32.5	0.774
HDL-C (mg/dL)	54.6 ± 13.2	56.0 ± 10.0	0.619
LDL-C : HDL-C	3.1 ± 0.8	2.8 ± 0.7	0.142
TG (mg/dL)	141.4 ± 75.3	149.5 ± 75.0	0.652
TG : HDL-C	2.9 ± 2.1	2.7 ± 1.3	0.626
Alanine transaminase (U/L)	22.1 ± 21.0	24.3 ± 18.9	0.649
Aspartate aminotransferase (U/L)	23.6 ± 9.0	22.9 ± 10.7	0.768
Blood urea nitrogen (mg/dL)	10.0 ± 2.2	11.2 ± 3.3	0.080
Uric acid (mg/dL)	5.7 ± 1.3	5.7 ± 1.3	0.907
High-sensitivity C-reactive protein (mg/L)	5.8 ± 4.7	4.3 ± 3.8	0.167
Interleukin-6 (pg/mL)	11.2 ± 9.9	8.7 ± 5.6	0.212
Tumor necrosis factor-alpha (pg/mL)	5.5 ± 2.4	5.5 ± 2.3	0.957

Data presented as mean ± standard deviation (SD). *P* values were calculated by chi-square test* and independent samples t-test for the differences between groups

Dietary consumption patterns: Assessment of dietary intake among participants at baseline (week 0) and after the 12-week intervention showed that the control and BMMH groups had comparable mean intakes of macronutrients (carbohydrates, proteins, and fats) and total energy (Table 3). No significant differences were observed between groups.

Within-group comparisons revealed a significant reduction in fat intake in the control group, from 68.1±15.3 g at baseline to 60.1±10.6 g at week 12 (p=0.019), whereas no significant changes in dietary intake were detected in the BMMH groups.

Table 3. Comparison of dialy dietary intake at baseline and after 12-week intervention.

Study parameters	Control (n=35)	BMMH (n=35)	p-value
Energy intake (kcal/day)			
Week0	1727 ± 387	1783 ± 429	0.582
Week12	1627 ± 395	1733 ± 305	0.272
p-value (wk0 vs. wk12)	0.394	0.466	
Mean change (wk0 vs. wk12)	-81 ± 483	-67 ± 452	0.916
Carbohydrate intake (g/day)			
Week0	222.1 ± 55.7	213.6 ± 53.9	0.541
Week12	214.4 ± 34.7	208.0 ± 42.0	0.555
p-value (wk0 vs. wk12)	0.394	0.782	
Mean change (wk0 vs. wk12)	-14.7 ± 79.2	-3.1 ± 54.8	0.567
Protein intake (g/day)			
Week0	77.0 ± 19.4	79.1 ± 19.5	0.674
Week12	71.3 ± 13.3	71.8 ± 16.0	0.915
p-value (wk0 vs. wk12)	0.091	0.167	
Mean change (wk0 vs. wk12)	-7.6 ± 21.5	-7.3 ± 23.9	0.968
Fat intake (g/day)			
Week0	68.1 ± 15.3	70.5 ± 13.9	0.542
Week8	60.1 ± 10.6	65.5 ± 11.7	0.117
p-value (wk0 vs. wk12)	0.019*	0.170	
Mean change (wk0 vs. wk12)	-9.8 ± 16.5	-5.3 ± 16.5	0.401

Data presented as mean ± standard deviation (SD). *P* values were calculated by an independent samples t-test for the differences between groups and a paired sample t-test for the differences within groups.

Effects of BMMH extract supplementation on changes in biochemical markers: Comparison between baseline (week 0) and week 12 revealed significant improvements in the experimental group receiving the BMMH extract supplement. FBG and HbA1c decreased markedly(FBG: 110.29 ± 40.60 mg/dL vs. 93.79 ± 13.87 mg/dL, p=0.011; HbA1c: 6.20 ± 0.99% vs. 6.12 ± 0.89%, p=0.036) , while no changes were observed in the control group (FBG: 106.94 ± 47.35 mg/dL vs. 101.34 ± 58.95 mg/dL, p=0.057: HbA1c: 6.18 ± 1.38% vs. 6.14 ± 1.59%, p=0.453) (Figure 2a and 2b).

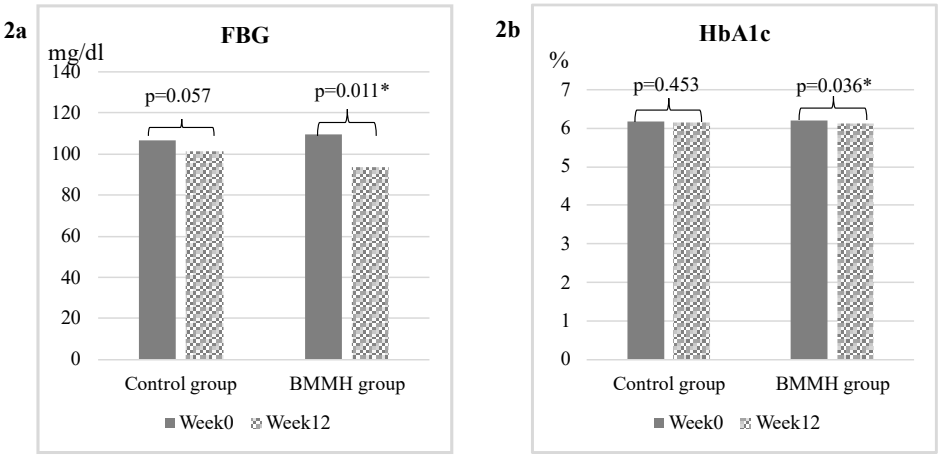


Figure 2. Comparison of changes in blood glucose levels between baseline (week 0) and post-intervention (week 12) for the control and BMMH groups. Figure 2a illustrates changes in FBG. Figure 2b depicts changes in HbA1c.

Both groups showed reductions in total cholesterol and LDL-C ($p<0.01$), and decreases in HDL-C remained within healthy ranges (Table 4). Notably, the LDL-C: HDL-C ratio, a key indicator of cardiovascular risk, improved significantly only in the experimental group ($p=0.014$). Triglycerides, TG: HDL-C ratio, and liver/kidney markers (ALT, BUN, uric acid) trended downward in the BMMH group.

Regarding inflammation, IL-6 decreased significantly in both groups ($p=0.034$ and $p=0.043$), while TNF-α showed a divergent trend with an increase in the BMMH group and a decrease in controls ($p=0.040$). No significant changes were observed in hs-CRP.

These results suggest that 12-week supplementation with BMMH extracts favorably modulates glycemic, lipid, and inflammatory profiles, highlighting its potential for metabolic and cardiovascular health.

Table 4. Comparison of biochemical parameters at baseline and after 12-week intervention.

Study parameters	Control (n=35)	BMMH (n=35)	p-value
FBG (mg/dL)			
Week0	106.9 ± 47.3	109.6 ± 40.2	0.801
Week12	101.3 ± 59.0	93.8 ± 13.9	0.466
p-value (wk0 vs. wk12)	0.057	0.011*	
Mean change (wk0 vs. wk12)	-5.6 ± 16.8	-16.5 ± 35.6	0.112
HbA1c (%)			
Week0	6.2 ± 1.4	6.2 ± 1.0	0.967
Week12	6.1 ± 1.6	6.1 ± 0.9	0.991
p-value (wk0 vs. wk12)	0.453	0.036*	
Mean change (wk0 vs. wk12)	-0.0 ± 0.3	-0.1 ± 0.2	0.535
Total cholesterol (mg/dL)			
Week0	226.2 ± 25.6	224.1 ± 34.0	0.770
Week12	208.2 ± 33.7	203.3 ± 36.8	0.566
p-value (wk0 vs. wk12)	0.000*	0.000*	
Mean change (wk0 vs. wk12)	-21.2 ± 29.0	-19.7 ± 22.9	0.811
LDL-C (mg/dL)			
Week0	155.7 ± 24.1	157.7 ± 32.5	0.774
Week12	140.2 ± 32.0	134.9 ± 37.2	0.529
p-value (wk0 vs. wk12)	0.000*	0.000*	
Mean change (wk0 vs. wk12)	-17.2 ± 20.3	-20.5 ± 19.7	0.501
HDL-C (mg/dL)			
Week0	54.6 ± 13.2	56.0 ± 10.0	0.619
Week12	49.2 ± 10.6	52.5 ± 10.1	0.194
p-value (wk0 vs. wk12)	0.000*	0.000*	
Mean change (wk0 vs. wk12)	-5.4 ± 7.5	-3.6 ± 4.7	0.231
LDL-C : HDL-C			
Week0	3.1 ± 0.8	2.8 ± 0.7	0.142
Week12	2.9 ± 0.7	2.6 ± 0.8	0.096
p-value (wk0 vs. wk12)	0.090	0.014*	
Mean change (wk0 vs. wk12)	-0.1 ± 0.5	-0.2 ± 0.4	0.779
TG (mg/dL)			
Week0	141.4 ± 75.3	149.5 ± 75.0	0.652
Week12	146.1 ± 79.8	126.3 ± 54.9	0.235

Study parameters	Control (n=35)	BMMH (n=35)	p-value
p-value (wk0 vs. wk12)	0.544	0.182	
Mean change (wk0 vs. wk12)	4.7 ± 45.5	-17.4 ± 73.3	0.144
TG : HDL-C			
Week0	2.9 ± 2.1	2.7 ± 1.3	0.626
Week12	3.4 ± 2.7	2.7 ± 1.7	0.238
p-value (wk0 vs. wk12)	0.054	0.992	
Mean change (wk0 vs. wk12)	0.4 ± 1.3	-0.0 ± 1.6	0.206
ALT (U/L)			
Week0	22.1 ± 21.0	24.3 ± 18.9	0.649
Week12	19.0 ± 10.5	21.0 ± 14.6	0.517
p-value (wk0 vs. wk12)	0.208	0.073	
Mean change (wk0 vs. wk12)	-2.9 ± 13.1	-3.1 ± 9.8	0.933
AST (U/L)			
Week0	23.6 ± 9.0	22.9 ± 10.7	0.768
Week12	21.9 ± 4.8	24.2 ± 9.6	0.200
p-value (wk0 vs. wk12)	0.271	0.190	
Mean change (wk0 vs. wk12)	-1.6 ± 8.4	1.3 ± 5.5	0.100
BUN (mg/dL)			
Week0	10.0 ± 2.2	11.2 ± 3.3	0.080
Week12	10.2 ± 2.8	10.8 ± 2.9	0.407
p-value (wk0 vs. wk12)	0.410	0.376	
Mean change (wk0 vs. wk12)	0.3 ± 1.8	-0.5 ± 3.2	0.236
Uric acid (mg/dL)			
Week0	5.7 ± 1.3	5.7 ± 1.3	0.907
Week12	5.6 ± 1.4	5.5 ± 1.2	0.673
p-value (wk0 vs. wk12)	0.672	0.102	
Mean change (wk0 vs. wk12)	-0.0 ± 0.6	-0.2 ± 0.7	0.336
hs-CRP (mg/L)			
Week0	5.8 ± 4.7	4.3 ± 3.8	0.167
Week12	5.0 ± 3.9	4.5 ± 4.2	0.585
p-value (wk0 vs. wk12)	0.214	0.830	
Mean change (wk0 vs. wk12)	-0.7 ± 3.2	0.1 ± 3.6	0.317
IL-6 (pg/mL)			
Week0	11.2 ± 9.9	8.7 ± 5.6	0.212
Week12	7.8 ± 4.1	7.2 ± 2.8	0.465
p-value (wk0 vs. wk12)	0.034*	0.043*	
Mean change (wk0 vs. wk12)	-2.7 ± 6.9	-1.5 ± 4.1	0.399
TNF-α (pg/mL)			
Week0	5.5 ± 2.4	5.5 ± 2.3	0.957
Week12	5.1 ± 1.8	6.2 ± 3.2	0.072
p-value (wk0 vs. wk12)	0.144	0.126	
Mean change (wk0 vs. wk12)	-0.5 ± 1.7	0.8 ± 3.1	0.040*

Data presented as mean ± standard deviation (SD) . *P* values were calculated by independent samples t-test for the differences between groups and paired sample t-test for the differences within group.

Effects of BMMH extract supplement on changes in anthropometric parameters: Changes in blood pressure, body composition, basal metabolic rate, and physical activity between the control and BMMH groups after 12-week intervention showed no statistically significant differences between groups (Table 5).

Both groups maintained slightly elevated systolic and diastolic blood pressure, BMI values within the obese range, and waist circumference indicative of abdominal obesity. Body fat percentage, muscle mass, and basal metabolic rate at week 12 did not differ significantly from baseline (week 0). However, weekly physical activity levels, expressed as MET, tended to decrease in both groups. A significant reduction in MET was observed within the control group between baseline and week 12 (week 0: 139.5±133.6 vs. week 12: 77.1±69.6 minutes/week; p=0.012).

Table 5. Comparison of blood pressure and anthropometric parameters at baseline and after 12-week intervention.

Study parameters	Control (n=35)	BMMH (n=35)	p-value
SBP (mmHg)			
Week0	125 ± 12	124 ± 11	0.814
Week12	125 ± 15	126 ± 13	0.852
p-value (wk0 vs. wk12)	0.658	0.194	
Mean change (wk0 vs. wk12)	-1 ± 12	2 ± 9	0.255
DBP (mmHg)			
Week0	85 ± 10	84 ± 8	0.587
Week12	86 ± 12	83 ± 9	0.357
p-value (wk0 vs. wk12)	0.534	0.810	
Mean change (wk0 vs. wk12)	1 ± 9	0 ± 6	0.705
Weight (kg)			
Week0	73.4 ± 13.1	73.4 ± 11.0	0.991
Week12	73.3 ± 13.2	74.0 ± 11.5	0.803
p-value (wk0 vs. wk12)	0.698	0.083	
Mean change (wk0 vs. wk12)	-0.1 ± 1.9	0.6 ± 2.0	0.120
BMI (kg/m^2)			
Week0	29.0 ± 4.1	28.6 ± 5.2	0.701
Week12	29.0 ± 4.2	28.8 ± 5.4	0.875
p-value (wk0 vs. wk12)	0.695	0.081	
Mean change (wk0 vs. wk12)	-0.0 ± 0.7	0.2 ± 0.7	0.119
WC (cm)			
Week0	94.8 ± 10.0	94.0 ±9.5	0.713
Week12	94.2 ± 9.6	94.7 ± 9.6	0.838
p-value (wk0 vs. wk12)	0.331	0.254	
Mean change (wk0 vs. wk12)	-0.6 ± 3.8	0.7 ± 3.4	0.135
Body fat (%)			
Week0	37.8 ± 10.0	38.4 ± 11.0	0.818
Week12	39.2 ± 7.4	39.0 ± 9.5	0.911
p-value (wk0 vs. wk12)	0.331	0.628	
Mean change (wk0 vs. wk12)	1.4 ± 8.5	0.7 ± 8.1	0.712
Body fat mass (kg)			
Week0	28.1 ± 10.6	28.5 ± 10.8	0.854

Study parameters	Control (n=35)	BMMH (n=35)	p-value
Week12	29.0 ± 9.2	29.4 ± 10.4	0.897
p-value (wk0 vs. wk12)	0.354	0.452	
Mean change (wk0 vs. wk12)	1.0 ± 6.3	0.8 ± 6.5	0.924
Visceral fat rating			
Week0	9.1 ± 3.0	9.1 ±2.9	0.997
Week12	9.6 ± 2.7	9.3 ± 3.0	0.721
p-value (wk0 vs. wk12)	0.155	0.183	
Mean change (wk0 vs. wk12)	0.5 ± 2.0	0.5 ± 2.0	0.999
Muscle mass (kg)			
Week0	42.7 ± 9.3	41.9 ± 8.0	0.696
Week12	41.7 ± 8.4	42.1 ± 6.7	0.837
p-value (wk0 vs. wk12)	0.321	0.921	
Mean change (wk0 vs. wk12)	-1.0 ± 6.0	0.1 ± 6.1	0.443
Free fat mass (kg)			
Week0	45.4 ± 9.8	44.7 ± 8.5	0.775
Week12	44.2 ± 8.8	44.7 ± 7.0	0.822
p-value (wk0 vs. wk12)	0.316	0.914	
Mean change (wk0 vs. wk12)	-1.1 ± 6.5	-0.1 ± 6.5	0.526
BMR (kcal)			
Week0	1355 ± 233	1336 ± 168	0.708
Week12	1323 ± 201	1328 ± 281	0.934
p-value (wk0 vs. wk12)	0.277	0.780	
Mean change (wk0 vs. wk12)	-26 ± 136	-10 ± 203	0.704
MET (minutes/week)			
Week0	139.5 ± 133.6	121.7 ± 108.3	0.559
Week12	77.1 ± 69.6	83.6 ± 64.6	0.691
p-value (wk0 vs. wk12)	0.012*	0.182	
Mean change (wk0 vs. wk12)	-65.1 ± 143.2	-26.4 ± 101.7	0.086

Data presented as mean ± standard deviation (SD). *P* values were calculated by an independent samples t-test for the differences between groups and a paired sample t-test for the differences within groups.

DISCUSSION

Metabolic syndrome, characterized by abdominal obesity, dyslipidemia, hyperglycemia, and hypertension, is a major risk factor for non-communicable diseases (NCDs). These conditions are largely preventable through lifestyle interventions, including regular physical activity and healthy dietary practices [1-2]. In recent years, herbal supplements have been increasingly explored as adjunctive approaches for metabolic risk reduction. Although individual herbs such as bitter melon and lingzhi mushroom have been reported to lower blood glucose, reduce inflammation, and modulate lipid metabolism [23-27], clinical findings from single-herb interventions remain inconsistent. In this context, multi-herbal formulations have been proposed as a strategy to simultaneously target multiple metabolic pathways, potentially offering broader metabolic support than single-herb supplementation. However, robust confirmatory clinical evidence in humans remains inconsistent. Accordingly, this study aimed to evaluate the effects of a multi-herbal extract supplement on metabolic health in individuals at risk of metabolic syndrome, thereby assessing its practical utility and informing preventive health strategies.

A 12-week course of supplementation with a multi-herbal extract containing bitter melon, American ginseng, lingzhi mushroom, artichoke, and jiaogulan resulted in significant reductions in FBG and HbA1c from baseline, whereas the control group showed no significant changes. Although bitter melon is widely recognized for its glucose-lowering effects, the magnitude and consistency of glycemic improvements observed at relatively low per-herb doses suggest that the combined formulation may have contributed additively or synergistically to these effects. Bitter melon contains bioactive compounds such as polypeptide-p (an insulin-like peptide) and cucurbitane-type triterpenoids (e.g., kuguaglycoside K16), which enhance insulin receptor activity and upregulate key proteins involved in insulin signaling pathways, such as AMP-activated protein kinase α1 (AMPKα1) and glucose transport 4 (GLUT4), thereby promoting glucose uptake [23-25]. This insulin-mimetic activity may be further supported by ginsenosides in American ginseng, which have been shown to enhance insulin receptor substrate-1 (IRS-1) phosphorylation, thereby facilitating glucose uptake in peripheral tissues [28-29]. In addition, the combined presence of bitter melon flavonoids and artichoke polyphenols may exert dual-site inhibition of digestive enzymes, including α-glucosidase and pancreatic lipase, thereby slowing carbohydrate absorption and attenuating postprandial glucose spikes more effectively than single-herb interventions [20, 30].

Lipid metabolism was also favorably affected. Participants receiving the multi-herbal supplement exhibited significant reductions in total cholesterol, LDL-C, and the LDL-C: HDL-C ratio, indicating improvements in lipid profiles. While bitter melon has been shown to influence lipid metabolism through reductions in apolipoprotein B (ApoB) secretion and triglyceride synthesis [31-33], the inclusion of artichoke provides a complementary mechanism via inhibition of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase and enhancement of biliary cholesterol excretion [18]. Together, these mechanisms may target both endogenous lipid synthesis and cholesterol handling, supporting a broader lipid-lowering effect. Thus, the formulation may exert a dual-action effect by influencing both lipid synthesis and intestinal cholesterol processing. Liver and kidney function markers, including ALT, BUN, and uric acid, demonstrated decreasing trends in the supplement group, suggesting potential hepatoprotective and renoprotective effects. Bitter melon has been shown to reduce oxidative stress, improve liver function, enhance insulin signaling, and mitigate hepatic steatosis [9, 31, 34-35]. Animal studies also suggest kidney-protective effects via attenuation of oxidative damage, modulation of antioxidant enzymes, and regulation of uric acid metabolism [10, 36]. Other components, including American ginseng, lingzhi mushroom, artichoke, and jiaogulan, possess antioxidant and anti-inflammatory properties that may further support liver and kidney health [12, 16, 37-39], although interindividual variability, dosage, duration, and baseline health status likely influence overall efficacy and safety.

Inflammatory markers responses in this study suggest that the multi-herbal formulation may act as an immunomodulator rather than a purely immunosuppressive agent. The observed stability of TNF-α levels in the herbal supplement group, despite a significant decrease in IL-6 levels, indicates a complex interplay of immune-modulating effects attributable to the components of the supplement, particularly lingzhi and bitter melon. Lingzhi supplementation has been reported to modulate immune responses and may contribute to the stabilization of TNF-α levels [40]. In contrast, bitter melon has been identified for its anti-inflammatory properties, particularly through the modulation of signaling pathways such as transforming growth factor-β activated kinase 1 (TAK1) [41]. These findings suggest that multi-herbal supplementation may improve inflammatory profiles, though the variability in

TNF-α responses and lack of statistically significant changes in some markers highlight the need for long-term and mechanistic studies.

Interestingly, the control group exhibited notable reductions in dietary fat intake, serum cholesterol, and IL-6 levels. These findings warrant careful interpretation. Such improvements in the control arm are frequently observed in clinical trials involving metabolic syndrome and often stem from a combination of factors, including the Hawthorne effect, where participants spontaneously modify their dietary habits due to awareness of being monitored during a clinical trial, and the impact of baseline dietary counseling, which likely sensitized the control group to their nutritional choices. This, in turn, may have led to the observed decrease in fat consumption and subsequent modest reductions in IL-6 and cholesterol levels. The structured nature of study participation and regular monitoring may also have prompted behavioral changes in the placebo group, leading participants to inadvertently adopt healthier dietary patterns.

Moreover, the control group showed a decline in total physical activity, as evidenced by decreased MET values. This trend may be interpreted through the lens of behavioral compensation, whereby a greater focus on dietary improvements, confirmed by reduced fat intake, may have occurred at the expense of regular exercise. Additionally, the administrative demands of trial participation, such as reporting requirements and clinical visits, could have acted as barriers to maintaining baseline activity levels. Taken together, these findings, along with the observed shifts in IL-6 and cholesterol, underscore the complex participation-related effects that can occur in the control arm of metabolic research and highlight the importance of a controlled study design in isolating the specific effects of the multi-herbal supplement. Body composition analysis revealed no significant changes in fat mass or muscle mass in either group. Systematic reviews and meta-analyses of randomized controlled trials indicate no significant reductions in body weight, body mass index, waist circumference, or body fat percentage [42-43]. However, certain clinical studies, such as those involving type 2 diabetes patients supplemented with bitter melon for three months, report significant body composition improvement [44]. Dosage and intervention duration appear critical. Reductions in weight have been observed with bitter melon extract doses of 2,000-4,500 mg, which are 20-30 times higher than those in the present study, potentially explaining the lack of substantial anthropometric changes here [43].

From a translational perspective, this study supports key milestones within the 17-step functional food development model [45], specifically step 9, by providing human clinical evidence for the efficacy of a finalized multi-herbal product intended to deliver health benefits. The strengths of this study include a robust sample size, sufficient intervention duration, and low attrition. Limitations include participants' habitual lifestyle behaviors, which may have introduced confounding factors such as variations in caloric intake, nutrient composition, and daily physical activity. Future research should focus on well-characterized bioactive compounds, including insulin and pancreatic function markers, and assess antioxidant capacity to better understand effects on metabolic health and NCDs risk.

CONCLUSIONS

This 12-week randomized, double-blind, placebo-controlled trial investigated the health effects of a multi-herbal supplement, primarily containing bitter melon and American ginseng extracts, on adults at risk for metabolic syndrome. Participants receiving the supplement exhibited significant reductions in FBG and HbA1c levels, highlighting its potential for glycemic control. Furthermore, the LDL-C:HDL-C ratio decreased significantly, suggesting a promising reduction in cardiovascular risk. These results emphasize the potential of herbal bioactives as a complementary strategy to enhance metabolic health and reduce risk of

NCDs, providing a natural adjunct to traditional lifestyle interventions.

List of abbreviations: NCDs, Non-communicable diseases; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; BMI, Body mass index; WC, Waist circumference; BMR, Basal metabolic rate; MET, Metabolic equivalent for task; FBG, Fasting blood glucose; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; TG, Triglyceride; ALT, Alanine transaminase; AST, Aspartate aminotransferase; BUN, Blood urea nitrogen; hs-CRP, High-sensitivity C-reactive protein; IL6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha.

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Author contributions: J.L.: conceptualization, methodology, resources, sample collection, investigation, validation, writing-original draft, writing-review and editing; C.P.: project administration, conceptualization, methodology, funding acquisition, sample collection, investigation, validation, analysis, data curation, supervision, guarantor, writing-original draft; A.C. and P.Y.: resources, sample collection, analysis.

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REFERENCES

1. Vichitkunakorn P, Bunyanukul W, Apiwan K, Tanasanchonnakul D, Sittisombut M. Prevalence of non-communicable disease risk factors and their association with economic status: findings from the 2021 health behaviour of population survey in Thailand. *Glob Health Action*. 2025;18(1):2485689. DOI: https://doi.org/10.1080/16549716.2025.2485689
2. Taheri Soodejani M. Non-communicable diseases in the world over the past century: a secondary data analysis. Frontiers in Public Health. 2024; 12:1436236. DOI: https://doi.org/10.3389/fpubh.2024.1436236
3. Martirosyan D. Functional Food Science and Bioactive Compounds. *Bioact Compd. Health Dis.* . 2025;8(6):218–229. DOI: https://doi.org/10.31989/bchd.v8i6.1667
4. Febriyanti R.M., Levita J., Diantini A. Immunomodulatory Role of Plants and Their Constituents on the Management of Metabolic Disorders: An Evidence-Based Review. *Drug Des Devel Ther*. 2024;18:513-34. DOI: https://doi.org/10.2147/DDDT.S442566
5. Praveen H, Aparna I, Jagroop S, Amit A, Poulami S, Rashmi P, et al. Phytochemicals, Herbal Extracts, and Dietary Supplements for Metabolic Disease Management. *Endocr Metab Immune Disord Drug Targets*. 2025;25(12):993-1016. DOI: https://doi.org/10.2174/0118715303287911240409055710
6. Djaoudene O., Romano A., Bradai Y.D., Zebiri F., Ouchene A., Yousfi Y., et al. A Global Overview of Dietary Supplements: Regulation, Market Trends, Usage during the COVID-19 Pandemic, and Health Effects. *Nutrients*. 2023;15(15). DOI: https://doi.org/10.3390/nu15153320
7. Alarabei A.A., Abd Aziz N.A.L., Ab Razak N.I., Abas R., Bahari H., Abdullah M.A., et al. Immunomodulating Phytochemicals: An Insight Into Their Potential Use in Cytokine Storm Situations. *Adv Pharm Bull.* 2024;14(1):105-19. DOI: https://doi.org/10.34172/apb.2024.001
8. Zakari A.D., Bashir A., Amoka A.G., Idris E.T., Anoze A.A., Moyosore A.A., et al. Antioxidant and hepatoprotective activities of methanol extract of *Moringa oleifera* leaves in carbon tetrachloride-induced hepatotoxicity in rats: Implications for functional food development. *Agriculture and Food Bioactive Compounds*. 2025;2(7):157–168. DOI: https://doi.org/10.31989/afbc.v2i7.1722
9. Ajaghaku D.L., Chinwuba P. Endocrine disruption and therapeutic potential of *Momordica charantia*: A comprehensive review. *J Complement Altern Med Res*. 2025;26(8):18-34. DOI: https://doi.org/10.9734/jocamr/2025/v26i8688
10. Shawki M., El-Sawi M.R., Aboelnaga A.M. The role of bitter melon extracts in reducing the incidence of some metabolic markers, lipid profile and morphological malformation in diabetic mother rats and their newborn. *Mansoura J Biol*. 2023;67(6):34-42. DOI: https://doi.org/10.21608/mjb.2023.450409

11. Hsu P-K., Pan FF.C., Hsieh C-S. mcIRBP-19 of Bitter Melon Peptide Effectively Regulates Diabetes Mellitus (DM) Patients' Blood Sugar Levels. *Nutrients.* 2020;12(5):1252. DOI: https://doi.org/10.3390/nu12051252
12. Plosca M-P., Chiș M.S., Fărcaș A.C., Păucean A. Ganoderma lucidum-from ancient remedies to modern applications: Chemistry, benefits, and safety. *Antioxidants*. 2025;14(5):513. DOI: https://doi.org/10.3390/antiox14050513
13. Cör Andrejč D, Knez Ž, Knez Marevci M. Antioxidant, antibacterial, antitumor, antifungal, antiviral, anti-inflammatory, and nevro-protective activity of Ganoderma lucidum: An overview. *Front Pharmacol.* 2022;13. DOI: https://doi.org/10.3389/fphar.2022.934982
14. Ahmed A, Saleem MA, Saeed F, Afzaal M, Imran A, Nadeem M, et al. Gynostemma pentaphyllum an immortal herb with promising therapeutic potential: a comprehensive review on its phytochemistry and pharmacological perspective. *Int J Food Prop*. 2023;26(1):808-32. DOI: https://doi.org/10.1080/10942912.2023.2185566
15. Shen Z, Gao X, Huang D, Xu X, Shen J. The potential of Gynostemma pentaphyllum in the treatment of hyperlipidemia and its interaction with the LOX1-PI3K-AKT-eNOS pathway. *Food Sci Nutr*. 2024;12(10):8000-12. DOI: https://doi.org/10.1002/fsn3.4250
16. Yasin M., Khalil M.T., Iftikhar M., Akram M. Medicinal and pharmacological activities of ginseng. *PEHSS*. 2025; 3:28-34. DOI: https://doi.org/10.63163/jpehss.v3i3.552
17. Zhou G, Wang C-Z, Mohammadi S, Sawadogo WR, Ma Q, Yuan C-S. Pharmacological Effects of Ginseng: Multiple Constituents and Multiple Actions on Humans. *Am J Chin Med.* 2023;51(05):1085-104. DOI: https://doi.org/10.1142/S0192415X23500490
18. Liu Z., Qu CY., Li JX., Wang YF., Li W., Wang CZ., et al. Hypoglycemic and hypolipidemic effects of malonyl ginsenosides from American ginseng (Panax quinquefolius L.) on type 2 diabetic mice. *ACS Omega.* 2021;6(49):33652-33664. DOI: https://doi.org/10.1021/acsomega.1c04656
19. Mokhtari I., Shahat A.A., Noman O.M., Milenković D., Amrani S., Harnafi H. Effects of *Cynara scolymus* L. bract extract on lipid metabolism disorders through modulation of HMG-CoA Reductase, Apo A-1, PCSK-9, p-AMPK, SREBP-2, and CYP2E1 expression. *Metabolites*. 2024;14(12):728. DOI: https://doi.org/10.3390/metabo14120728
20. Phimarn W., Sungthong B., Wichiyo K. Effect of *Cynara scolymus* L. on cardiometabolic outcomes: An updated meta-analysis of randomized controlled trials and meta-regression. *Pharmacogn Mag*. 2024;20(2): 372-388. DOI:https://doi.org/10.1177/09731296231217557
21. Moradi M., Sohrabi G., Golbidi M., Yarmohammadi S., Hemati N., Campbell M.S., et al. Effects of artichoke on blood pressure: a systematic review and meta-analysis. *Complement Ther Med.* 2021; 57:102668. DOI: https://doi.org/10.1016/j.ctim.2021.102668
22. Topothai T, Tangcharoensathien V, Suphanchaimat R, Petrunoff NA, Chandrasiri O, Müller-Riemenschneider F. Patterns of Physical Activity and Sedentary Behavior During the COVID-19 Pandemic in the Thai 2021 National Health Survey. Journal of Physical Activity and Health. 2023;20(5):364-73. DOI: https://doi.org/10.1123/jpah.2022-0528
23. Yang Y.S., Wu N.Y., Kornelius E., Huang C.N., Yang N.C. A randomized, double-blind, placebo-controlled trial to evaluate the hypoglycemic efficacy of the mcIRBP-19-containing *Momordica charantia* L. fruit extracts in the type 2 diabetic subjects. *Food Nutr Res*. 2022;66. DOI: https://doi.org/10.29219/fnr.v66.3685
24. Bora A.F.M., Kouame K.J.E., Li X., Liu L., Pan Y. New insights into the bioactive polysaccharides, proteins, and triterpenoids isolated from bitter melon (Momordica charantia) and their relevance for nutraceutical and food application: A review. *Int J Biol Macromol*. 2023; 231:123173. DOI: https://doi.org/10.1016/j.ijbiomac.2023.123173
25. Bara L.V., Budau R., Apahidean A.I., Bara C.M., Iancu C.V., Jude E.T., et al. Momordica charantia L.: Functional Health Benefits and Uses in the Food Industry. *Plants (Basel)*. 2025;14(17):2642. DOI: https://doi.org/10.3390/plants14172642
26. Łysakowska P., Sobota A., Wirkijowska A. Medicinal Mushrooms: Their Bioactive Components, Nutritional Value and Application in Functional Food Production-A Review. *Molecules*. 2023;28(14):5393. DOI: https://doi.org/10.3390/molecules28145393
27. Sharif Swallah M., Bondzie-Quaye P., Wang H., Shao C.S., Hua P., Alrasheed Bashir M., et al. Potentialities of Ganoderma lucidum extracts as functional ingredients in food formulation. *Food Res Int*. 2023 ;172:113161. DOI: https://doi.org/10.1016/j.foodres.2023.113161
28. Zhao Y., Liu Y., Deng J., Zhu C.K., Ma X., Jiang M., et al. Ginsenoside F4 alleviates skeletal muscle insulin resistance by regulating PTP1B in type II diabetes mellitus. *J Agric Food Chem*. 2023;71(39):14263-14275. DOI: https://doi.org/10.1021/acs.jafc.3c01262

29. Kim T.H. Ginsenosides for the treatment of insulin resistance and diabetes: Therapeutic perspectives and mechanistic insights. *J Ginseng Res*. 2024;48(3):276-285. DOI: https://doi.org/10.1016/j.jgr.2024.03.002
30. Li F., Zeng K., Ming J. Lowering glycemic levels via gastrointestinal tract factors: the roles of dietary fiber, polyphenols, and their combination. *Crit Rev Food Sci Nutr*. 2023;65(3):575-611. DOI: https://doi.org/10.1080/10408398.2023.2278169
31. Amini M.R., Rasaei N., Jalalzadeh M., Pourreza S., Hekmatdoost A. The effects of bitter melon (*Mormordica charantia*) on lipid profile: A systematic review and meta-analysis of randomized controlled trials. *Phytother Res*. 2024;38(12):5949-5961. DOI: https://doi.org/10.1002/ptr.8357
32. Bai J., Zhu Y., He L., Zhang J., Li J., Pan R. Saponins from bitter melon reduce lipid accumulation via induction of autophagy in C.elegans and Hep G2 celll line. *Curr Res Food Sci*. 2022;5:1167-1175. DOI: https://doi.org/10.1016/j.crfs.2022.06.011
33. Saeed F., Afzaal M., Niaz B., Arshad M.U., Tufail T., Hussain M.B., et al. Bitter melon (*Momordica charantia*): a natural, healthy vegetable. Inter J Food Prop. 2018: 21(1); 1270-1290. DOI: https://doi.org/10.1080/10942912.2018.1446023
34. Zhang Y., Cao Y., Wang F., Wang L., Xiong L., Shen X., et al. Polysaccharide from *Momordica charantia* L. alleviates type 2 diabetes mellitus in mice by activating the IRS1/PI3K/Akt and AMPK signaling pathways and regulating the gut microbiota. *J Agric Food Chem.* 2025;73:7298-7309. DOI: https://doi.org/10.1021/acs.jafc.4c12660
35. Shahrajabian M.H., Sun W. Multidimensional uses of bitter melon (*Momordica charantia* L.) considering the important functions of its chemical components. *Curr Org Synth*. 2024;22(4):516-530. DOI: https://doi.org/10.2174/0115701794285586240523101245
36. Bini N., Osadolor H.B., Elekofehinti O.O. Protective potential of *Momordica charantia* against CCl4 induced change in liver and kidney serum biomarkers in Wistar rats. *Sokoto J Med Lab Sci*. 2024;9(3):301-307. DOI: https://doi.org/10.4314/sokjmls.v9i3.31
37. Goel R.S. Cynara scolymus in modern medicine: The healing power of phytochemicals and Cynarin's role in cancer therapy. *IJNRPH*. 2025;3(1):226-236. DOI: https://doi.org/10.61554/ijnrph.v3i1.2025.150
38. Hu X., Wang W., Zhang D., Tian X., Zhang A., Xu J., et al. Phytochemistry, bioactivities and application of Gynostemma pentaphyllum polysaccharide: A review. Int J Biol Macromol. 2025;322(Pt1):144964. DOI: https://doi.org/10.1016/j.ijbiomac.2025.144964
39. Vijayakumar N., Kim S. Natural compounds in kidney disease: Therapeutic potential and drug development. *Biomol Ther*. 2025;33(1):39-53. DOI: https://doi.org/10.4062/biomolther.2024.142
40. Iser-Bem P.N., Lobato T.B., Alecrim-Zeza A.L., de Oliveira L.C. dos S., Passos M.E.P., Manuel R., et al. Ganoderma lucidum dry extract supplementation modulates T lymphocyte function in older women. *Br J Nutr*. 2024;132(2):1-27. DOI: https://doi.org/10.1017/s0007114524001144
41. Kao P.F., Cheng C.H., Cheng T.H., Liu J.C., Sung L.C. Therapeutic Potential of Momordicine I from *Momordica charantia*: Cardiovascular Benefits and Mechanisms. *Int J Mol Sci*. 2024;25(19):10518. DOI: https://doi.org/10.3390/ijms251910518
42. Zou Y., Zou W., Jahangir M., Haedi A. The effects of bitter melon (Momordica charantia) on anthropometric indices in adults: A systematic review and meta-analysis of randomized controlled trials. *Prostaglandins & other lipid mediators*. 2024;174:106877. DOI: https://doi.org/10.1016/j.prostaglandins.2024.106877
43. Amini M.R., Pourreza S., Akhgarjand C., Sheikhhossein F., Askari G., Hekmatdoost A. The effects of bitter melon (*Mormordica charantia*) on weight loss and body composition: a systematic review and dose-response meta-analysis of randomized controlled trials. *J Food Biochem.* 2025;2025(1):2921435. DOI: https://doi.org/10.1155/jfbc/2921435
44. Cortez-Navarrete M., Martínez-Abundis E., Pérez-Rubio K.G., González-Ortiz M., Méndez-del Villar M. Momordica charantia administration improves insulin secretion in type 2 diabetes mellitus. *J Med Food.* 2018;21(7):672-677. DOI: https://doi.org/10.1089/jmf.2017.0114
45. Martirosyan D.M., Stratton S. Quantum and tempus theories of functional food science in practice. *Func Food Sci*. 2023; 3(5):55-62. DOI: https://doi.org/10.31989/ffs.v3i5.1122