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Curcumin extract improves beta cell functions in obese patients with type 2 diabetes: a randomized controlled trial

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Abstract

Background Type 2 diabetes mellitus (T2DM) is a chronic condition characterized by insulin resistance and impaired insulin production, leading to elevated blood glucose levels. Curcumin, a polyphenolic compound from Curcuma longa, has shown potential in improving insulin sensitivity and reducing blood glucose levels, which may help mitigate type 2 diabetes progression.

Objective To assess the efficacy of improving type 2 diabetes (T2DM).

Study design This randomized, double-blind, placebo-controlled trial included subjects ($n = 272$) with criteria for type 2 diabetes.

Methods All subjects were randomly assigned to receive curcumin (1500 mg/day) or placebo with blind labels for 12 months. To assess the improvement of T2DM after curcumin treatments body weight and body mass index, fasting plasma glucose, glycosylated hemoglobin A_{1c}, β-cell function (homeostasis model assessment [HOMA-β]), insulin resistance (HOMA-IR), insulin, adiponectin, and leptin were monitored at the baseline and at 3-, 6-, 9-, and 12-month visits during the course of intervention.

Results After 12 months of treatment, the curcumin-treated group showed a significant decrease in fasting blood glucose (115.49 vs.130.71; $P < 0.05$), HbA_{1c} (6.12 vs. 6.47; $P < 0.05$). In addition, the curcumin-treated group showed a better overall function of β-cells, with higher HOMA-β (136.20 vs. 105.19; $P < 0.01$) The curcumin-treated group showed a lower level of HOMA-IR (4.86 vs. 6.04; $P < 0.001$) and higher adiponectin (14.51 vs. 10.36; $P < 0.001$) when compared to the placebo group. The curcumin-treated group also showed a lower level of leptin (9.42 vs. 20.66; $P < 0.001$). Additionally, body mass index was lowered (25.9 4 vs.29.34), with a P value of 0.001.

Conclusions A 12-month curcumin intervention in type 2 diabetes patients shows a significant glucose-lowering effect. Curcumin treatment appeared to improve the overall function of β-cells and reduce both insulin resistance and body weight, with very minor adverse effects. Curcumin intervention in obese patients with type 2 diabetes may be beneficial.

Trial registration Thai clinical trials regentrify no.20140303003.

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Introduction

Diabetes mellitus is a multifactorial chronic metabolic disorder that involves the inability to produce insulin or use it properly, resulting in altered metabolism of carbohydrates, fats, and proteins and long-lasting hyperglycemia [1]. The World Health Organization (WHO) estimated in 2009 that there would be approximately 439 million individual with diabetes worldwide by 2030 [2].

Type 2 diabetes mellitus (T2DM) is the most prevalent form of diabetes mellitus. According to the Global Burden of Disease Study (2016), T2DM and its complications contributed to a 22% rise in disability over the past decade, significantly impacting public health [3]. Acute complications of T2DM include hypoglycemia, diabetic ketoacidosis, and hyperosmolar hyperglycemic state, while chronic complications involve cardiovascular disease, chronic kidney disease, and damage to the retina, nerves, and vascular tissues [4].

Obesity is a key contributor to insulin resistance (IR), often leading to early β-cell dysfunction and the subsequent development of T2DM. Few antidiabetic medications have shown the ability to prevent the progressive decline of β-cell function. However, treatment options for both T2DM and obesity have expanded significantly in recent years. Large-scale clinical trials have demonstrated substantial weight loss and cardiovascular benefits with agents such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2is). Current guidelines from the American Diabetes Association and the European Association for the Study of Diabetes emphasize treating T2DM with a focus on associated comorbidities, particularly obesity [5]. Several antidiabetic medications now offer cardiovascular protection and support weight loss. GLP-1 RAs, SGLT2is, and dipeptidyl peptidase-4 inhibitors (DPP-4is) have demonstrated positive effects on body weight, lipid profiles, blood pressure, and endothelial function. Incretin-based therapies, such as liraglutide, improve glycemic control and reduce cardiometabolic risk in obese patients with T2DM [6–8]. However, the high cost of these medications has sparked interest in alternative treatments, particularly nutritional supplements and medicinal plants.

Nutraceuticals offer a promising alternative for patients at low risk, either as a supplement to existing therapies or as an initial treatment before pharmaceutical intervention in non-high-risk cases [6]. Several plant-based compounds have been explored, including metabolites from Bergamot [7], *Pinus pinaster* [8], *Sophora tonkinensis* [9], and *Curcuma longa* [10].

Turmeric (Curcuma longa), an herb from the Zingiberaceae family, has been a vital component of traditional Indian and Chinese medicine. It grows primarily in tropical and subtropical regions [11]. Curcumin, its active ingredient, possesses a wide range of biological activities, including antioxidant [12], antiproliferative [13] and anti-inflammatory properties [14]. Curcumin also shows therapeutic potential in managing neurodegenerative disorders [15], hepatic damage [16], and diabetes mellitus [10].

Curcumin's potential to reduce insulin resistance has been demonstrated in several in vivo and in vitro models [17, 18]. Our previous studies have shown that curcumin intervention in prediabetic and diabetic populations reduced the progression from prediabetes to T2DM, improved β-cell function, and lowered IR [13, 19]. In an extension of our earlier study [19], we extended the study period from 6 months to 12 months to assess the long-term effects of curcumin, focusing on patients with obesity and T2DM. Additionally, we evaluated curcumin's anti-inflammatory effects on β-cell function, metabolic parameters, and obesity markers in a large, randomized, double-blind, placebo-controlled cohort.

Materials and methods

Study design and participants

This randomized, double-blind, placebo-controlled trial was conducted at the Princess Maha Chakri Sirindhorn Medical Center of Srinakharinwirot University (Nakhon Nayok, Thailand). Consolidated Standards of Reporting Trials (CONSORT) guideline was used for reporting the results (Supplementary Table 1). Two hundred and twenty-nine patients with T2DM were selected to participate in this study according to inclusion and exclusion criteria (for a complete flow chart, see Supplementary Fig. 1). Subjects were enrolled in the 12-month study. We educated all subjects to follow the same diet and exercise protocols for a 3-month period after enrollment (before the randomization). Standard lifestyle recommendations were provided for all subjects in written form. All subjects participated in a 20–30 min one-on-one workshop that emphasized the importance of a healthy lifestyle. Participants were encouraged to follow Medical Nutrition Therapy and physical activity. All subjects received metformin to control hyperglycemia. To avoid any interference with other antidiabetic medications, during the recruitment process, we excluded all type 2 diabetes patients who took any other antidiabetic

drugs except for metformin. Patients with hypertension and dyslipidemia were consistently managed with antihypertensive and antidyslipidemic medications, and no changes to these medication regimens were allowed during the study. The antihypertensive and antidyslipidemic drugs used are listed in Table 1. Furthermore, T2DM medication regimens were not allowed to adjust during the study. Only T2DM patients aged ≥ 35 years with a recent diagnosis of T2DM within 1-year, well-controlled blood glucose (HBA1c < 6.5% and FPG < 110 mg/dl) and body mass index ≥ 23 kg/m^2 were included in this study. T2DM subjects were diagnosed following the 2017 American Diabetes Association (ADA) practice guidelines [20]. Subjects who fit into at least one of these three criteria were included: subjects with a fasting plasma glucose (FPG) ≥ 126 mg/dL, an oral glucose tolerance test (OGGT) plasma glucose at 2 h post glucose load (OGTT at 2 h) ≥ 200 mg/dL and a glycated hemoglobin (HbA$_{1c}$) ≥ 6.5%, and a random plasma glucose ≥ 200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis. This study (Thai clinical trials regentrify no.20140303003) was approved by the Ethics Committee of the Faculty of Medicine of

Srinakharinwirot University, Bangkok, Thailand (serial number SWUECFB-4/2556) in accordance with the Declaration of Helsinki. Participants were informed and gave their consent before enrollment. We excluded patients with type 1 diabetes, impaired glucose tolerance, maturity onset diabetes of youth, and gestational diabetes.

At baseline, each visit follow-up, and the end of the trial (0, 3, 6, 9, and 12 months), all patients were required to fast overnight to allow blood sample collection the next morning. Additionally, if HbA1C ≥ 7.0% or FPG ≥ 130 mg/dl were presented 2 consecutive times during intervention period, the patients were excluded from the study (see Supplementary Fig. 1). Before the study, all subjects were advised of daily food intake and exercise. They were advised to consume low-glycemic index foods, such as legumes and whole grains, increase dietary fiber intake, engage in at least 150 min of moderate-intensity aerobic exercise per week, and maintain consistent physical activity [21, 22]. Subjects were asked to complete a 3-day record (including 2 work days and 1 weekend) record of their food intake, which was analyzed using CDGSS3.0 software to estimate nutrient intake at baseline and at 12 weeks. A questionnaire survey was conducted for each subject at the beginning of the study and contained questions on dietary habits (including how much and how often the participants consumed meat, milk, eggs, and vegetables, etc.). (Supplementary Table 2).

Randomization procedures

After the screening, consenting and diet and lifestyle training steps, all subjects were randomly assigned to the curcumin-treated group (intervention treatment condition) or the placebo-treated group (control condition) using a fixed randomization scheme with assignment based on computer-generated random numbers performed by an independent researcher. The allocation scheme was sealed in opaque envelopes with consecutive numbers. The envelopes were opened sequentially by the independent person. Participants were informed that two types of interventions were being compared.

Blinding procedures

To ensure effective blinding of both participants and healthcare providers, we used placebos that matched the curcumin in appearance, taste, and administration method. We also ensured that participants were not given any information about the nature of the intervention that might reveal their group assignment. Additionally, healthcare providers received training to follow the same procedures for all participants, regardless of group assignment.

Table 1 Baseline characteristics of subjects

Variable	Placebo Mean (S.E.) (*n* = 115)	Curcumin Mean (S.E.) (*n* = 114)	*p*-value*
Sex (M: F ratio)	54/80 (0.67)	62/73 (0.85)	0.87[†]
BMI (kg/m^2)	26.76 (0.38)	27.21 (0.37)	0.41
Weight (kg)	69.50 (1.32)	69.92 (1.24)	0.58
FPG (mg/dl)	125.80 (2.22)	123.65 (1.73)	0.401
Hb A1C (%)	6.26 (0.06)	6.28 (0.07)	0.69
Insulin (uU/ml)	16.96 (0.68)	17.47 (0.67)	0.56
HOMA-IR	5.24 (0.24)	5.38 (0.23)	0.72
HOMA-β	108.44(5.48)	113.26 (5.67)	0.32
Adiponectin (ng/ml)	8.85 (0.11)	8.75 (0.12)	0.82
Leptin(ng/ml)	13.38 (0.36)	13.84 (0.34)	0.20
Creatinine (mg/dl)	0.87 (0.02)	0.86 (0.02)	0.77
AST (U/l)	25.01 (0.87)	25.34 (0.80)	0.58
ALT(U/l)	27.58 (1.56)	30.09 (1.50)	0.08
History of cerebrovascular disease	7 (5.2%)	5 (3.7%)	0.30[†]
History of coronary artery disease	9 (6.7%)	8 (5.9%)	0.80[†]
History of hypertension	82 (61.2%)	76 (51.2%)	0.68[†]
History of dyslipidemia	104 (77.6%)	101 (74.8%)	0.84[†]
Antihypertensive medications[†]			
Angiotensin receptor blockers	80 (70.2)	86 (76.1)	0.39
Calcium channel blockers	26 (22.8)	18 (15.9)	0.25
Beta blockers	21 (18.4)	17 (15.0)	0.61
Antidyslipedemic medications[†]			
Statins	59 (51.8)	55(48.7)	0.74

*P values were evaluated by the samples t-test or Mann-Whitney U test

[†] P values were evaluated by Chi-square test

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The intervention

All participants were instructed to take three capsules with blinded labels of curcumin or placebo twice a day (total of six capsules per day) for 12 months continuously. Each curcumin capsule has a curcuminoid content of 250 mg. The identical placebo capsules and curcumin were manufactured by the Thailand Government Pharmaceutical Organization. Patients were asked to return all capsules at the follow-up visit at 3, 6, 9 and 12 months to assess their compliance. The numbers of capsules taken by the subjects were recorded (Supplementary Table 3).

Preparation of curcuminoids capsules

The dried rhizomes of turmeric (*Curcuma longa* Linn.) grown in Kanchanaburi province, Thailand, were ground into powder. The turmeric powder was extracted with ethanol and evaporated at low pressure to obtain ethanol extract in the form of a semi-solid containing oleoresin and curcuminoids. Oleoresin was removed to produce curcuminoid extract (total curcuminoids content between 75 and 85%). The maximum ratio of curcumin demethoxycurcumin and bisdemethoxycurcumin in the extract was determined by high performance thin-layer chromatography. The extract (calculated for 250 mg of curcuminoids) was filled into capsules according to the Good Manufacturing Procedures standard. The fingerprints of the extract and a detailed analysis of the chemical composition of the preparation in the extract are shown in Supplementary Fig. 3. The appearance of both the curcumin and placebo capsules was indistinguishable; both were white with uniform coloration. They had hard capsule shells, smooth edges, and were tasteless.

Study results

The primary outcome was evaluated by changes of the β-cell functions (homeostasis model assessment: HOMA-β). Secondary outcomes were also measured as follows: fasting plasma glucose, glycated hemoglobin (HbA1C), body weight, and body mass index., insulin, insulin resistance (IR) by HOMA-IR, adiponectin and leptin.

The adverse effects of curcumin were determined by elevated creatinine 1.2 mg/dL and aspartate/alanine aminotransferase (AST / ALT) 3 times the upper limit of the normal value range, and any symptoms of patient complaints were recorded.

Data collection and measurement methods

Measurements were made at baseline (before treatment) and 3, 6, 9 and 12 months after the start of the intervention. We recorded demographic data at baseline; the researchers administered a questionnaire on medical history and medication, and measured body weight, height, and vital signs. The levels of FPG, HbA1c, were measured according to standard procedures. Plasma insulin, leptin, and adiponectin concentrations were determined using the radioimmunoassay kits from Millipore (St. Charles, MO) with a γ scintillation counter, which is calibrated for ^{125}I measurement. HOMA-β, C-peptide, HOMA-IR was calculated to assess change in insulin resistance [23].

Sample size

We estimated the size of the sample for this study based on data from the study by Chuengsamarn et al. [24]. The calculations used a standard deviation of 160. We needed to enroll at least 113 subjects in each treatment group to detect a difference of HOMA-β with 80% power at the 5% level of significance [25].

Statistical analysis

Demographic data at baseline were analyzed and presented as mean±SEM for continuous variables and number with percent for categorical variables. The two-tailed Student t test and χ^2 test were used, respectively, for continuous and categorical variables in the comparisons between the two groups, using $P < 0.05$ for statistically significant difference. We used two-sided significance tests throughout. For the analysis of the outcome variables, the mean SEM values of mean±SEM at 3, 6, and 9 months were presented for both groups. The analyzes were performed on an intention-to-treat basis. All analyses were conducted on an intention-to-treat basis, assessing statistically significant differences between the means of the two groups at 3, 6, 9 and 12 months, separately. All comparisons were performed using paired samples t-test (for normally distributed data) or Wilcoxon signed-ranks test (for non-normally distributed data). Categorical variables were analyzed using chi-square test. The Pearson correlation analysis was conducted to examine the relationship between changes in body weight (Δbody weight) and change in other parameters (Δparameters). $P < 0.05$ was considered statistically significant. All statistical analyzes were performed using R.

Results

A flow chart of the trial is presented (Supplementary Fig. 2). A total of 275 subjects were initially enrolled in the study. The baseline characteristics of 229 subjects who were randomly assigned to the two groups are presented in Table 1. All parameters at baseline between the placebo-treated group and the curcumin-treated group were not statistically different.

Intervention outcomes

β-cell function outcomes

HOMA-β, and insulin were examined as outcomes related to β-cell functions. Table 2 shows that HOMA-β

Table 2 Blood chemistry levels of metabolic, β-cell function and obesity parameters

Outcomes	Follow-up period	Placebo (n = 115)		Curcumin (n = 114)		p value*
		Mean	Minimum-Maximum	Mean	Minimum-Maximum	
BMI (kg/m²)	0 months	26.94	16.45–35.18	27.35	20.40–36.58	NS
	3 months	26.98	16.88–40.37	26.56	19.15–44.81	< 0.05
	6 months	26.96	17.31–40.79	25.90	18.31–43.71	< 0.01
	9 months	27.00	16.88–40.79	25.96	19.14–42.61	< 0.001
	12 months	27.34	17.72–42.11	25.98	17.90–42.24	< 0.001
Body weight (kg)	0 months	69.50	61–112	69.92	71–120	NS
	3 months	69.53	62–113	67.72	70–117	< 0.05
	6 months	69.47	63–119	66.06	69–135	< 0.01
	9 months	69.01	63–117	66.08	68–117	< 0.01
	12 months	69.30	63–140	66.10	68–114	< 0.001
HbA1c (%)	0 months	6.26	4.80–8.90	6.28	4.40–9.50	NS
	3 months	6.44	5–8.90	6.26	4.70–9.20	< 0.01
	6 months	6.46	5.10–9	6.25	4.50–8.30	< 0.01
	9 months	6.47	5–10.40	6.19	4.10–8.20	< 0.05
	12 months	6.47	5–10.50	6.12	4.20–8.40	< 0.05
FPG (mg/dl)	0 months	125.08	91–285	123.65	79–178	NS
	3 months	128.93	100–195	124.40	80–171	NS
	6 months	130.34	77–231	122.82	79–204	< 0.01
	9 months	130.93	97–201	118.67	75–165	< 0.01
	12 months	130.71	98–194	115.49	70–160	< 0.05
Insulin (uU/ml)	0 months	16.96	5.80–51.90	17.47	4.70–39	NS
	3 months	18.51	6.20–52.10	17.06	4.60–37.60	< 0.05
	6 months	18.51	6.20–52.10	16.80	4.60–35.40	< 0.05
	9 months	18.55	6.40–52.30	16.11	4.30–37.10	< 0.05
	12 months	18.54	6.70–52.50	16.05	4–37	< 0.01
HOMA-IR	0 months	5.24	1.70–21.80	5.38	1.20–14.20	NS
	3 months	5.88	2.00–17.00	5.25	1.70–12.80	< 0.05
	6 months	5.93	1.80–17.90	5.17	1.60–16.50	< 0.01
	9 months	6.02	2.20–19.80	5.02	1.30–11.50	< 0.001
	12 months	6.04	2.30–18.00	4.86	1.20–11	< 0.001
HOMA-β	0 months	108.44	13.50–359	113.26	25.60–456.80	NS
	3 months	108.56	30.20–313.80	113.83	19.30–412.90	NS
	6 months	109.19	23.60–408	114.53	20.20–427.50	NS
	9 months	108.32	23.70–310.20	123.73	24.20–546	< 0.01
	12 months	105.19	29.40–275.30	136.20	25.30–915.40	< 0.01
Adiponectin (ug/ml)	0 months	8.85	7.04–10.56	8.75	7.04–10.56	NS
	3 months	8.89	7.04–10.56	8.91	7.04–10.56	NS
	6 months	10.13	3.81–29.28	13.73	5.32–52.05	< 0.01
	9 months	10.38	3.43–27.45	13.74	5.46–53.02	< 0.001
	12 months	10.36	3.21–26.21	14.51	5.78–54.67	< 0.001
Leptin (ug/ml)	0 months	13.38	7.04–19.36	13.84	7.04–19.36	NS
	3 months	13.28	7.04–55.59	13.47	7.04–19.36	NS
	6 months	20.41	3.56– 55.59	10.67	1.11–34.2	< 0.001
	9 months	20.63	3.43–59.32	9.93	1.11–22.87	< 0.001
	12 months	20.66	3.89–59.32	9.42	1.10-21.59	< 0.001

*P values were evaluated by the samples t-test or Mann-Whitney U test

in the curcumin-treated group was increasing and became statistically significant at visits 9 and 12 months. Blood insulin levels (Table 2) were found to be significantly lower in the curcumin-treated group compared to those of the placebo group at 3, 6, 9 and 12 months. The insulin level also showed a lower trend in the curcumin-treated group and became statistically significant at 6, 9 and 12 months. (Table 2).

The glycemic control outcomes

The means of diabetes-related blood chemistries used to assess diabetic progression, such as HbA_{1c}, FPG, were significantly lower in the curcumin-treated group compared to the placebo group at visits at 3,6, 9, and 12 months (Table 2).

Weight measurement results

The means of body weight and body mass index were significantly lower in the curcumin-treated group compared to the placebo group at visits at 3, 6, 9, and 12 months (Table 2).

Insulin resistance and inflammatory cytokine outcomes

The HOMA-IR level is a clinical representative of insulin resistance. HOMA-IR from the placebo and curcumin-treated groups was examined. The HOMA-IR means of the curcumin-treated group were lower than those of the placebo group at all follow-up visits (3, 6, 9 and 12 months) The differences were significant, particularly at the 3-, 6-, 9- and 12-month visits. The levels of adipocytokines such as adiponectin and leptin were examined in both groups. The level of adiponectin in the placebo-treated group increased, while those of the curcumin-treated group increased significantly and became significantly different from that of the placebo-treated group at the 6-,9- and 12-month visits. On the contrary, the leptin level was reduced in the curcumin-treated group at the 6-,9- and 12-month visits. (Table 2).

Effect of changes in body weight on blood chemistry levels, including metabolic and β-cell function markers.

The correlation analysis between changes in body weight and blood chemistry levels, including metabolic and β-cell function markers, revealed no statistically significant correlations for parameters such as FPG, HbA1c, HOMA-IR, HOMA-β, adiponectin, and leptin in either the placebo or curcumin groups. However, a statistically significant positive correlation was observed between changes in body weight and HbA1c within the curcumin group (Supplementary Table 4).

Adverse effects

The mild adverse effects were abdominal pain, diarrhea, and headache. None of the patients were dropped out due to adverse effects (Supplementary Table 5). To monitor the possible adverse effects of curcumin intervention, we determined kidney and liver functions (Supplementary Table 6). We found no significant differences in the mean of AST, ALT and creatinine between the curcumin-treated and placebo-treated group. None of the curcumin-treated groups showed symptoms of hypoglycemia.

Taken together, these results indicated that curcumin extract can be used for intervention, at least for a period of 12 months, without serious adverse effect. At each follow-up visit, we counted the number of remaining capsules brought to us by subjects. Numbers of the capsule consumed by subjects from both groups were very comparable (Supplementary Table 2). Therefore, the effects observed by us were not the result of different levels of compliance between two groups.

Discussion

In an attempt to find safe, well tolerated, and easily available intervention agents for patients with type 2 diabetes, we tested a potential candidate, ethanol-extracted curcumin, due to its known anti-diabetic activity in vivo [26]. In this randomized, double-blind, placebo-controlled clinical trial, we found that curcumin extract was able to significantly and significantly improve hyperglycemic levels in patients with type 2 diabetes. Curcumin extract was capable of inducing weight loss. The effect of curcumin on lowering weight may vary [27–29]. In our study, we observed a greater reduction in weight. However, our understanding of curcumin's effectiveness in weight reduction is still incomplete, and further research is needed for a comprehensive understanding. Additionally, we observed weight gain in the placebo group, may due to unhealthy eating habit, as indicated by excessive weight at the baseline. Moreover, individuals with obesity may experience metabolic adaptations that facilitate weight gain [30]. We also found that curcumin can lower BMI. In line with our results, the study by Rahimi et al. [31] showed that taking nano-curcumin (80 mg/day) for three months led to a reduction in BMI in patients with diabetes. Furthermore, we found that the curcumin intervention improved β-cell functions, indicated by increased HOMA-β. HOMA-β is a straightforward method that is less invasive and more cost-effective compared to other techniques, making it applicable in various research settings and clinical practice [32, 33]. However, the accuracy of HOMA-β depends on several assumptions, such as steady-state conditions of glucose and insulin and a linear relationship between these variables. Deviations from these assumptions can affect the results, and the model's validity can also vary depending on the population studied [34]. Additionally, our findings revealed a significant positive correlation between changes in body weight and HbA1c levels in the curcumin group, indicating that weight loss is associated with improvements in glycated hemoglobin (HbA1c). This association was particularly pronounced among individuals with T2DM [35]. These indicated that curcumin treatment may result in better β-cell function in type 2 diabetes patients. HOMA-IR clinically represents IR. We found that in the curcumin-treated group, HOMA-IR was significantly lower compared to that of the placebo group. In line with our study, Li-Xin Na et al. [36] demonstrated that curcuminoid

treatment (300 mg/day) for three months has a beneficial effect on lowering HOMA-IR in obese patients with type 2 diabetes. Additionally, we found that curcumin reduces FPG and HbA1c levels. Consistent with our findings, the study by Li-Xin Na et al. [36] showed a reduction in fasting blood glucose and HbA1c after three months of curcuminoid treatment (300 mg/day) in obese patients with type 2 diabetes. Furthermore, studies by Rahimi et al. [31] and Asadi et al. [37] demonstrated that nano-curcumin (80 mg/day) can also reduce fasting blood glucose and HbA1c levels in patients with diabetes. From these results, we believe that curcumin intervention in type 2 diabetes patient with obesity can improve the metabolic and obesity parameters by reduced IR level and have anti-inflammatory effect by maintaining healthy β-cell functions. Adiponectin is an anti-inflammatory cytokine produced and secreted by adipose tissue. Adiponectin serum level is reported to have an inverse relationship with insulin resistance and obesity. A higher level of adiponectin has been shown to be associated with a lower risk of T2DM [38]. Moreover, leptin inhibits the orexigenic pathway and stimulates the anorexigenic pathway, underscoring its pivotal role in body weight regulation [39]. Our study showed that the curcumin intervention significantly increases adiponectin and reduces leptin levels. Because inflammation is one of the main causes of β-cell degradation, we hypothesize that the anti-inflammation activity and body weight regulation of curcumin are key factors for the antidiabetic property of curcumin. Curcumin serves as a nutraceutical due to its positive impact on glycemic control and insulin sensitivity [40].

Several randomized clinical trials have shown that curcumin may have potential antidiabetic activity [31, 36, 37]. Although promising, most of these studies could not be easily interpreted, quite often due to a small sample size (range 80–100), or insufficient intervention period (3 months) or lack of safety information and lack of investigation of inflammatory markers. Our study was designed and established specifically to overcome those previous problems by increasing the number of subjects (229 subjects) and extending the follow-up period to 12 months. The findings of our study showed that curcumin extract can effectively improve the β-cell function and reduce IR by anti-inflammatory effects, and these properties of curcumin could affect weight loss in patients with type 2 diabetes. Additionally, we found that the mean daily capsule administration during the first six months exceeds six capsules per day. This is likely due to factors such as non-adherence and variability in adherence to medication regimens, leading to an inflated mean of doses taken compared to the prescribed amount and making the average number of doses over time appear higher than the daily prescribed dose.

We found that a 12-month curcumin treatment was rather safe. We have not found any significant adverse effect caused by curcumin treatment when compared to the placebo treatment. Because of its benefits and safety, we propose that curcumin extract may be used for an intervention therapy in type 2 diabetes mellitus population. Our study has several strengths, including investigating the long-term effect of curcumin in obese patients with type 2 diabetes and having a relatively large sample size. However, it also has several limitations. Firstly, the single-dose design precludes the analysis of potential dose-response relationships. Additionally, being a single-center randomized controlled trial, the generalizability of the findings to other populations or settings may be limited.

Conclusion
Curcumin treatment in type 2 diabetes patients with obesity appeared to improve overall β-cell functions and reduce both of IR and body weight, with very minor adverse effects.

Abbreviations
FPG	Fasting plasma glucose
HbA1c	Glycated hemoglobin
BMI	Body mass index
HOMA-β	Homeostasis Model Assessment of beta-cell function
HOMA-IR	Homeostatic model assessment of insulin resistance
AST	Aspartate transaminase
ALT	Alanine transaminase
T2DM	Type 2 diabetes mellitus

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12937-024-01022-3.

Supplementary Material 1

Author contributions
SC: designed the study, screened and examined all recruited subjects, researched and analyzed data, reviewed and edited the manuscript. MY researched, analyzed data, and wrote the manuscript. LJ researched data. SJ reviewed and edited the manuscript. All authors approved the final version of the manuscript.

Data availability
The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

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Declarations

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