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Effect of Curcumin and Honey on HDL Cholesterol in 4-VCD-Induced Menopausal Wistar Rats

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ABSTRACT

Background and Objective: Menopause in African women is associated with increased health risks, particularly cardiovascular disease, due to a decline in estrogen and subsequent lipid profile alterations. A notable inverse relationship exists between low High-Density Lipoprotein Cholesterol (HDL-C) levels and heightened cardiovascular risk. Phytoestrogens such as curcumin and honey may help mitigate these metabolic disturbances. This study aimed to evaluate the effects of curcumin and honey at varying concentrations on lipid profile and glucose levels in 4-vinylcyclohexene diepoxide (VCD)-induced menopausal Wistar rats. **Materials and Methods:** Female Wistar rats were induced into menopause using VCD. Treatment groups received curcumin and honey supplementation at different concentrations, with one group treated with VCD and 1 µg estrogen serving as a reference. Serum levels of total cholesterol (TC), triglycerides (TG), HDL-C, and glucose were measured using spectrophotometric methods. Low-Density Lipoprotein Cholesterol (LDL-C) was calculated using the Friedewald formula. Data were analyzed using one-way ANOVA, and group differences were compared using post hoc tests at a significance level of $p<0.05$. **Results:** The VCD-induced menopause led to a significant reduction in TC, HDL-C, LDL-C, and glucose levels. Supplementation with curcumin and honey significantly increased HDL-C and decreased LDL-C levels, with some treatment groups surpassing the effects observed in the estrogen-treated group. Glucose levels were also moderately restored. These findings suggest that curcumin and honey modulate lipid metabolism favorably in menopausal conditions. **Conclusion:** Curcumin and honey supplementation improved lipid profiles in VCD-induced menopausal rats, particularly by increasing HDL-C and reducing LDL-C levels, suggesting enhanced cardiovascular protection. These results indicate a potential alternative to estrogen therapy. Future research should investigate long-term effects and mechanisms in clinical settings.

KEYWORDS

Wister rats, female, 4-vinyl-1-cyclohexene dioxide, curcumin, HDL-Cholesterol, honey, menopause

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INTRODUCTION

Menopause in African women is linked to various health issues, such as a heightened risk of cardiovascular disease, osteoporosis, and metabolic syndrome. The decline in estrogen levels during menopause may contribute to an increased risk of cardiovascular disease[1]. This heightened risk is related to alterations in lipid profiles, compromised arterial function, and the activation of the renin-angiotensin system[2].

Coronary heart disease prevalence is greater in postmenopausal women than in their premenopausal counterparts. The primary physiological change that occurs during menopause is a transition towards a more atherogenic lipid profile[3,4]. Following the end of menstruation, studies have shown a rise in plasma triglycerides (TG), total cholesterol (TC), and Low-Density Lipoprotein-Cholesterol (LDL-C), particularly the smaller, denser particles that are more pro-atherogenic[3,5,6]. These alterations appear to be more closely related to increased abdominal fat mass than to age[3].

A crucial aspect of the lipid profile is the concentration of HDL-C and the size of HDL particles. Clinical and epidemiological studies have demonstrated an inverse correlation between low levels of HDL-C and a heightened risk for Cardiovascular Disease (CVD)[7]. The HDL particles play a role not only in mediating reverse cholesterol transport (RCT) but also in exhibiting anti-oxidant, anti-inflammatory, anti-thrombotic, and vasodilatory properties[8-10]. The variations in HDL-C concentration and the composition of HDL particles following menopause have sparked debate. While some authors reported that there is a reduction in HDL-C levels in postmenopausal women[3,4,6], others have observed no changes[11,12] or even an increase in HDL-C levels after menopause[13,14].

Specifically, a decline in estrogen has been consistently linked to adverse alterations in lipid metabolism and glucose homeostasis, predisposing postmenopausal women to higher incidences of cardiovascular disease and type 2 diabetes mellitus[15]. Therefore, understanding and mitigating these metabolic derangements in the context of menopause are paramount for improving long-term health outcomes in women.

To effectively study the complex physiological changes associated with menopause and potential therapeutic interventions, animal models are indispensable. The 4-Vinylcyclohexene Diepoxide (4-VCD) induced rat model has emerged as a well-established and widely accepted experimental paradigm for mimicking ovarian failure and the ensuing menopausal state[16]. The 4-VCD is a chemical ovotoxicant that selectively destroys small pre-antral and primordial follicles in the ovaries, leading to premature ovarian insufficiency and a state analogous to menopause in rodents[17]. This model reliably recapitulates many of the physiological and metabolic alterations observed in natural menopause, including decreased estrogen levels, increased body weight, altered lipid profiles, and impaired glucose tolerance, making it an invaluable tool for investigating menopausal health[18]. The consistent and reproducible nature of 4-VCD-induced ovarian failure allows for controlled experimental conditions to evaluate the efficacy of various interventions aimed at alleviating menopausal symptoms and associated metabolic complications.

Beyond its general anti-inflammatory and antioxidant actions, accumulating evidence suggests that curcumin may exert specific beneficial effects on lipid and glucose metabolism. *In vitro* and *in vivo* studies have revealed that curcumin can enhance insulin sensitivity, ameliorate glucose uptake by cells, and lower hepatic glucose production[19,20]. Its potential to modulate lipid profiles has also been demonstrated in experimental models of dyslipidemia[21,22]. The unique hormonal milieu of menopause, coupled with the systemic effects of estrogen deficiency, may influence the efficacy and mechanisms of action of curcumin. Therefore, this study aimed to explore the impact of curcumin, administered at selected concentrations, on the lipid profile and glucose levels in 4-VCD-induced menopausal Wistar rats.

MATERIALS AND METHODS

Study area and duration: This study was conducted at the Department of Medical Laboratory Science, with contributions from the Faculty of Pharmacy (Laboratory and Animal House), University of Benin, Benin City, between January and November, 2021.

Ethical consideration: The approval for this study was obtained from the Animal Studies Ethics Review Committee of the Faculty of Pharmacy, Department of Pharmacology and Toxicology, University of Benin, Benin City. The approval was given after the experimental protocol was reviewed. The approval with Reference no: (EC/FP/022/19) was issued.

Sample size determination: The sample size for this study was determined using the sample size calculation in Animal studies (Resource Equation Approach). For a study that compares pretreatment with treatment groups, the sample size per group (for seven groups): Any sample size that keeps E between 10 and 20 should be considered adequate. E = total number of animals minus total number of groups. In this study, there are twelve groups E = (12×5)-12 = 48. Since the total animals is more than 20, it is considered adequate. Therefore, 5 animals per group were used. The weight of Wistar rats was between 150-250 g, 60 days of age, and randomly divided into groups.

Curcuminoid powder preparation: In this study, water-soluble curcuminoid powders were prepared. The pulverized dried powder sample was weighed and suspended in 1 L of distilled water with regular agitation for 24 hrs. The solution was filtered, and the resulting filtrate was then concentrated over a water bath at 40°C, and a crude extract was obtained. The dried crude extract was stored in the refrigerator before use. All extraction and preparations of the aqueous extract of various quantities of ground dried turmeric were administered. From literature, turmeric extract (aqueous) and honey have high LD_{50} values (>5 g/kg) as described by Emokpae *et al.*[23].

Experimental animals: The Wistar rats were maintained on a pelleted feed diet from Ewu (Primier Feed Mill Limited, Ewu), Edo, Nigeria. And free access to water *ad libitum*. Before each experiment, the animals were fasted overnight. Because of their ability to mimic the symptoms of perimenopause and post-menopause in humans, such as estrous acyclicity and the fluctuating then undetectable estrogen levels hence Wistar rats were chosen for this study to enable the separation of the impact of hormone levels from that of ageing.

Honey, turmeric purchase and authentication: Pure thick honey was purchased from Pax Herbals, Ewu Monastery, Edo State. The turmeric rhizomes were authenticated at the Department of Plant Biology and Biotechnology (PBB), Faculty of Life Sciences, University of Benin, Benin City, and were given a Voucher number (UBH-C397).

Turmeric extraction procedure: Fresh turmeric roots were cleaned, steamed for 7 min, and sliced into small pieces before drying in a hot air oven at 50°C for about 6 hr. Dried turmeric was collected and ground into fine powder using a high-speed blender. The dried, ground turmeric was packed in a plastic bag, sealed, and kept in the refrigerator (5°C) until used.

Curcuminoid content of dry turmeric: Following the method described by Surojanametakul *et al.*[24], the curcuminoid powder was prepared. Exactly 0.2 g of ground dry turmeric was weighed in a 15 mL screw-cap test tube, and 5 mL of ethanol was added. The mixture was vortexed every 15 min for 2 hrs and centrifuged at 4,500 rpm/min for 10 min at room temperature. The clear supernatant was collected in a 25 mL volumetric flask. The extraction was repeated until a pale-yellow supernatant deposit solution was observed. The deposit solution was adjusted to volume with ethanol. The curcuminoid content in the

extracted solution was investigated using HPLC (Agilent 1100 series) equipped with Synergy 4µ RP 80 A column, mobile phase: acetonitrile: 1% acetic acid (55:45), flow rate 1mL/min, λ: 425 nm, inject volume: 4 µL, and a temperature of 40°C.

Curcuminoid powder preparation: In this study, water-soluble curcuminoid powders with different curcuminoid contents were prepared. The pulverized dried powder sample was weighed and suspended in 1 L of distilled water with regular agitation for 24 hrs. The solution was filtered, and the resulting filtrate was then concentrated over a water bath at 40°C, and a crude extract was obtained. The dried crude extract was stored in the refrigerator before use. All extraction and preparations of the aqueous extract of various quantities of ground dried turmeric were administered.

The safety profile was determined by feeding the animals with different concentrations of honey (10, 20, and 40 g/kg) and *Curcumin* at doses of 250, 50 and 1000 mg/kg body weight. This is an experimental study design of VCD-induced menopause in Wistar rats. The animals were divided into twelve groups of five animals in each group and induced intraperitoneally with a suitable concentration (80 mg/kg) obtained from a previous preliminary study Emokpa *et al*.[23]. The phytoestrogens (turmeric and honey) and estrogen were administered daily for 4 weeks as follows:

- **Group 1:** Normal rats (not induced), negative control
- **Group 2:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide only (positive control)
- **Group 3:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+250 mg/kg of turmeric extract
- **Group 4:** Received 80 mg/kg of 4-vinylcyclohexene+500 mg/kg of turmeric extract
- **Group 5:** Received 80 mg/kg of 4-vinylcyclohexene+1000 mg/kg of turmeric extract
- **Group 6:** Received 80 mg/kg of 4-vinylcyclohexene+10 g/kg honey
- **Group 7:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+20 g/kg honey
- **Group 8:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+40 g/kg honey
- **Group 9:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+250 mg/kg turmeric and 10 g/kg honey
- **Group 10:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+500 mg/kg turmeric and 20 g/kg honey
- **Group 11:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+1000 mg/kg turmeric and 40 g/kg honey
- **Group 12:** Received 80 mg/kg of 4-vinylcyclohexene diepoxide+treatment with 1 µg of Estrogen

Collection of samples: Blood samples were withdrawn directly from the abdominal aorta and the heart chamber with a needle mounted on a 10 mL syringe (Agary Pharmaceutical LTD, Nigeria) into plain sample bottles and fluoride oxalate containers. Biochemical analysis was performed on the sample obtained after centrifugation of whole blood at 2500 rpm for 5 min. The blood glucose was determined immediately after the blood collection, while serum was kept frozen at -20°C until needed for lipid profile.

Biochemical assays: Serum lipid profile (TC, TG, HDL-C, LDL-C) and glucose were assayed by spectrophotometric method using reagents supplied by Randox Laboratories Ltd, UK. The Friedewald formula was used to determine the plasma LDL-C[25].

Statistical analysis: GraphPad Prism version 6.0 was used f or the analysis of all data obtained. The Mann-Whitney non-parametric test was used to compare the means of the groups; the Chi-square test was used to compare qualitative data of the same group.

RESULTS

Table 1 shows the lipid profile and glucose level in female Wistar rats given honey at concentrations of 10 g/kg, 20 g/kg, and 40 g/kg compared with the control. The administration of Honey to Wistar rats resulted in insignificant increase ($p>0.05$) in the levels of total cholesterol in mg/dL (89±4.20, 101.3±5.02,

Table 1: Lipid profile and glucose level in female Wistar rats treated with honey at different concentrations

Parameters	Cholesterol (mg/dL)	Triglyceride (mg/dL)	High density lipoprotein (mg/dL)	Low density lipoprotein (mg/dL)	Glucose (mg/dL)
Control	86.6±8.57	52.4±4.62	29.2±1.77	46.8±6.63	141±9.80
Honey (10 g/kg)	89±4.20	69.25±6.18	32.25±2.32	43±6.01	115.5±14.08
Honey (20 g/kg)	101.3±5.02	70±2.35	30.75±2.56	56.25±7.04	147±6.65
Honey (40 g/kg)	97.25±8.36	68.25±2.32	32±2.16	51.5±10.37	160.5±8.23
F-value	0.9418	4.255	0.4401	0.5453	3.276
ANOVA p-value	0.4487	0.0267	0.7282	0.6599	0.0555
***post hoc* p-value**					
Control vs. honey (10 g/kg)	0.9947	0.0592	0.7454	0.9832	0.3059
Control vs. honey (20 g/kg)	0.4746	0.0473	0.9542	0.806	0.9724
Control vs. honey (40 g/kg)	0.7085	0.0795	0.79	0.9691	0.5236
Honey (10 g/kg) vs. honey (20 g/kg	0.6515	0.9993	0.9639	0.6407	0.1922
Honey (10 g/kg) vs. honey (40 g/kg)	0.8568	0.9985	0.9998	0.8681	0.0404
Honey (20 g/kg) vs. honey (40 g/kg)	0.9799	0.992	0.9784	0.9726	0.7966

Table 2: Lipid profile and glucose level in female Wistar rats treated with curcumin at doses of 250 mg/kg, 500 mg/kg, and 1000 mg/kg compared with controls

Parameters	Cholesterol (mg/dL)	Triglyceride (mg/dL)	High density lipoprotein (mg/dL)	Low density lipoprotein (mg/dL)	Glucose (mg/dL)
Control	86.6±8.56	52.4±4.62	29.2±1.77	46.8±6.63	141±9.79
Control (Gum acacia)	70.75±6.05	52.25±3.47	28.5±1.71	32±3.76	130.8±11.80
Curcumin (250 mg/kg)	86.6±1.78	79.6±1.72	32.2±1.02	38.4±1.94	131.2±7.30
Curcumin (500 mg/kg)	110.2±3.06	72.6±3.54	37±0.44	58.4±3.04	131.8±10.45
Curcumin (1000 mg/kg)	75±1.84	77.8±2.06	31.2±1.71	28.2±1.91	140.4±6.80
F-value	9.53	17.01	5.632	9.825	0.3183
ANOVA p-value	0.0002	<0.0001	0.0037	0.0002	0.8622
***post hoc* p-value**					
Control vs. Control (Gum acacia)	0.2278	>0.9999	0.9969	0.1129	0.9401
Control vs. Curcumin (250 mg/kg)	>0.9999	<0.0001	0.5536	0.5404	0.9371
Control vs. Curcumin (500 mg/kg)	0.02	0.0021	0.0062	0.2404	0.9494
Control vs. Curcumin (1000 mg/kg)	0.4599	0.0002	0.8415	0.02	>0.9999
Control (Gum acacia) vs. Curcumin (250 mg/kg)	0.2278	0.0001	0.4101	0.7949	>0.9999
Control (Gum acacia) vs. Curcumin (500 mg/kg)	0.0003	0.0035	0.0049	0.0016	>0.9999
Control (Gum acacia) vs. (1000 mg/kg)	0.9756	0.0003	0.6929	0.9617	0.9513
Curcumin (250 mg/kg) vs. (500 mg/kg)	0.02	0.544	0.1432	0.0115	>0.9999
Curcumin (250 mg/kg) vs. (1000 mg/kg)	0.4599	0.9942	0.9852	0.3551	0.9494
Curcumin (500 mg/kg) vs. (1000 mg/kg)	0.0005	0.7772	0.0541	0.0002	0.96

97.25±8.36), and HDL-C (mg/dL) 32.25±2.32, 30.75±2.56, 32±2.16), LDL-C (mg/dL) 43.26±6.01, 56.25±7.04, 51.5±10.37) and glucose (mg/dL) (115.5±14.08, 147±6.65, 160.5±8.23) compare with group (86.6±8.57, 29.2±1.7746.8±6.63 and 141±9.80 respectively, except triglyceride (mg/dL) which was markedly increased ($p<0.05$) 69.25±6.18, 70±2.35, 68.25±2.32) when compare with control group (52.4±4.62).

The administration of curcumin to the Wistar rats resulted in a significant increase ($p<0.05$) in the levels of triglyceride (mg/dL) from 52.4±4.62 in the control group to 79.6±1.72, 72.8±3.54, and 77.8±2.06 when curcumin concentrations of 250, 500, and 1000 mg/kg, respectively were administered ($p<0.05$). Total cholesterol levels increased from 86.6±8.56 in the control group to 110.2±3.06 when 500 mg/kg curcumin concentration was administered ($p<0.05$). Similarly, the levels of HDL-C (37.0±0.44), LDL-C (58.4±3.04) increased from 29.2±1.77 and 46.8±6.63, respectively, when 500 mg/kg curcumin was administered to the Wistar rats. However, the level of glucose was not significantly changed (Table 2).

Table 3: Lipid profile and glucose level in 4-VCD induced menopausal Wistar rats treated with curcumin at different concentrations

Parameters	Cholesterol (mg/dL)	Triglyceride (mg/dL)	High density lipoprotein (mg/dL)	Low density lipoprotein (mg/dL)	Glucose (mg/dL)
Control (A)	102.6±5.64	81±4.67	23.2±2.15	63.2±3.69	140.8±12.48
4 VCD (80 mg) (B)	81.25±5.43	84.75±4.48	17±1.23	47.25±4.85	116±17.62
4 VCD (80 mg)+estrogen (1 µg) (C)	60.5±3.86	44±3.94	16.25±2.02	35.5±3.23	161±5.55
Curcumin (250 mg/kg)+ Honey (10 g/kg) (D)	65.5±3.01	74.25±6.49	25±1.47	26±3.34	112.8±5.88
Curcumin (500 mg/kg)+ Honey (20 g/kg) (E)	51.6±1.63 ±3.57	70.4±6.71	22.2±1.28	15.4±1.63	122.8
Curcumin (1000 mg/kg)+ Honey (40 g/kg) (F)	55.67±2.33	79.67±5.33	25.33±2.67	13.33±6.33	125.7±3.93
F-value	23.85	6.857	4.384	28.21	3.2
ANOVA p-value	<0.0001	0.0008	0.008	<0.0001	0.0291
***post hoc* p-value**					
A vs. B	0.0144	0.9958	0.1752	0.0549	0.4861
A vs. C	<0.0001	0.0013	0.1017	0.0004	0.6862
A vs. D	<0.0001	0.9447	0.9765	<0.0001	0.3571
A vs. E	<0.0001	0.6803	0.9979	<0.0001	0.7328
A vs. F	<0.0001	0.9999	0.9662	<0.0001	0.9084
B vs. C	0.0268	0.0008	0.9997	0.2934	0.0556
B vs. D	0.1381	0.7756	0.0619	0.0098	0.9999
B vs. E	0.0006	0.438	0.3324	<0.0001	0.9958
B vs. F	0.0094	0.9907	0.0766	0.0002	0.9883
C vs. D	0.9571	0.0138	0.0347	0.5128	0.0353
C vs. E	0.6288	0.0262	0.2077	0.0101	0.1048
C vs. F	0.9731	0.0065	0.0453	0.0131	0.2584
D vs. E	0.1902	0.9953	0.8645	0.3433	0.9754
D vs. F	0.6567	0.9876	0.9999	0.2953	0.959
E vs. F	0.9846	0.867	0.8509	0.9989	0.99994

-VCD: 4-vinylcyclohexene diepoxide

Table 3 represents values of lipid profile levels in the VCD-induced menopause Wistar rats' model. In the VCD-induced menopause Wistar rats without supplementation with phytoestrogens, there was a significant decrease in the levels of total cholesterol (81.25±5.43 vs 102.6±5.64), HDL-C (17.0±1.23 vs 23.2±2.15), LDL-C (47.25±4.85 vs 63.2±3.69), and glucose (116±17.62±140.8±12.48 compared with the uninduced group. The administration of 1000 mg/kg curcumin + 40 g/kg Honey resulted in the further reduction of the concentration of total cholesterol (55.67±2.23 vs 81.25±5.43), triglyceride (79.67±5.33 vs 84.75±4.48), LDL-C (13.33±6.33 vs 47.25±4.85), but an increase in the concentration of HDL-C (25.33±2.67 vs 17.0±1.23). In the group C, which was given VCD+estrogen (1 µg), there was a significant reduction in the levels of total cholesterol (60.5±3.86 vs 81.25±5.43), triglyceride (44.0±3.44 vs 84.75±4.48), LDL-C (35.5±3.23 vs 47.25±4.85) and increase glucose (161.0±5.55 vs 116.0±17.62) when compare with VCD-induced but untreated (group B).

DISCUSSION

The present study investigated the effects of combined curcumin and honey supplementation on lipid profile and glucose levels in 4-Vinylcyclohexene Dioxide (4-VCD) induced menopausal Wistar rats. The findings revealed an increase in HDL-C levels in VCD-induced menopause Wistar rats, even above the group supplemented with estrogen. Other distinct and varied responses across the different treatment groups were also observed, thus highlighting the complex interplay of these interventions on metabolic parameters.

This baseline effect of 4-VCD on lipid metabolism or the subsequent estrogen intervention sets a context for evaluating the efficacy of the curcumin-honey combination. Both 4-VCD-treated rats and those receiving 4-VCD with estrogen replacement therapy exhibited reductions in cholesterol and LDL-C compared to the control group. This is aligned with previous studies[26,27].

The mechanisms underpinning these reductions may involve curcumin's known ability to inhibit hepatic cholesterol synthesis via HMG-CoA reductase modulation and enhance LDL receptor expression, thereby increasing LDL-C clearance from the bloodstream[28]. Honey's contributions, potentially through its antioxidant and anti-inflammatory properties, could synergistically support these effects[29].

High-Density Lipoprotein Cholesterol (HDL-C) levels showed interesting variations. Both the 250 mg/kg+ 10 g/kg and 1000 mg/kg+40 g/kg curcumin and honey groups significantly increased HDL levels compared to the 4-VCD+estrogen-treated group ($p<0.05$). This is a beneficial outcome, as HDL plays a crucial role in reverse cholesterol transport, removing excess cholesterol from peripheral tissues[30]. The observed increase could be mediated by curcumin's potential to upregulate apolipoprotein A-I, a primary component of HDL, or to enhance cholesterol efflux mechanisms[31]. The lack of a significant increase at the intermediate dose (500 mg/kg+20 g/kg) might suggest a non-linear dose-response or other contributing factors yet to be elucidated.

Conversely, the findings for triglyceride levels presented a more complex picture. While 4-VCD+estrogen-treated rats exhibited significantly lower triglycerides compared to the control, the higher doses of curcumin and honey (500 mg/kg+20 g/kg and 1000 mg/kg+40 g/kg) led to significantly higher triglyceride levels when compared to the 4-VCD+estrogen group ($p<0.05$). This observation warrants further investigation as it contrasts with the beneficial effects on cholesterol and LDL-C. It is plausible that the specific metabolic pathways influenced by the higher concentrations of curcumin and honey, perhaps involving fatty acid synthesis or Very-Low-Density Lipoprotein (VLDL) production, might be differentially regulated, or there could be an interaction effect with the estrogen-deficient state induced by 4-VCD[32] Regarding glucose levels, the results were somewhat heterogeneous. Notably, only the lowest dose of curcumin (250 mg/kg)+honey (10 g/kg) led to a significant reduction in glucose levels compared to the 4-VCD+estrogen-treated group ($p<0.05$). This specific finding suggests that at lower concentrations, the combined treatment might have an insulin-sensitizing or glucose-lowering effect[33]. However, the absence of significant changes in glucose levels in other curcumin and honey supplemented groups relative to controls or the 4-VCD group implies that the glucose-modulating effect might be dose-specific or influenced by other physiological factors not fully captured in this study. Previous research on curcumin's impact on glucose metabolism has shown conflicting results, ranging from significant improvements in insulin sensitivity to no noticeable effect, which aligns with the varied outcomes observed here[34,35]. The duration of treatment and the specific metabolic state of the 4-VCD-induced menopausal model could also contribute to these differential responses.

CONCLUSION

The combined administration of curcumin and honey demonstrates promising improved HDL-C levels, which can be beneficial to post-menopausal women. Furthermore, the glucose-lowering effect appears to be dose-dependent, primarily observed at the lowest tested concentration. These findings underscore the potential therapeutic benefits of curcumin and honey in ameliorating menopause associated dyslipidaemia and cardiovascular events. Additionally, long-term studies and translation to clinical settings are essential to validate these findings and determine their applicability in human menopausal women.

SIGNIFICANCE STATEMENT

Menopause is associated with a heightened risk of several diseases, including cardiovascular diseases, as a result of alterations in lipid profile levels. VCD-induced menopause in Wistar rats resulted in a notable decrease in total cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-C), Low-Density Lipoprotein Cholesterol (LDL-C), and glucose levels. The supplementation with curcumin and honey significantly elevated HDL-C levels while reducing LDL-C levels, with certain treatment groups exceeding the effects

seen in the estrogen-treated group. The supplementation with curcumin and honey positively influenced lipid metabolism in menopausal conditions. Supplementing with curcumin and honey may improve cardiovascular protection during menopause. The results also indicate a possible alternative to estrogen therapy.

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