Trop J Nat Prod Res, May 2025; 9(5): 2323 - 2328 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Effect of a nature-derived combination of *Ananas comosus* and *Bambusa bambos* (L.) in hyperlipidemic experimental animals

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ARTICLE INFO

Article history:
Received 12 February 2025
Revised 23 February 2025
Accepted 22 April 2025
Published online 01 June 2025

ABSTRACT

Hyperlipidemia is an independent modifiable risk factor of cardiovascular diseases which remains the leading cause of disease burden for healthcare systems worldwide. Traditional medicine formulas have a long history of use in Asia for hyperlipidemia treatment. This study aimed to evaluate the potential efficacy of a herbal combination of *Ananas comosus* and *Bambusa bambos* (L.), named "Cao dua tre Lao nha que" (*CDT*), on hyperlipidemic animal models of two pathways. In poloxamer-407 (P-407)-induced model, mice were pre-treated with *CDT* before intraperitoneal injection of P-407; in the dietary model, rats were orally administered a cholesterol mixture and *CDT* for 4 consecutive weeks. Results indicated that *CDT* (0.6 and 1.2 g/kg b.w.) significantly reduced total cholesterol (TC) (from 4.11±0.95 to 3.05±0.60 and 2.93±0.67 mmol/L, respectively) and triglycerides (TG) (from 1.40±0.27 to 1.02±0.20 and 1.13±0.31 mmol/L) in the dietary model; in P-407-induced model, *CDT* significantly reduced TG (from 5.8±1.52 to 4.84±0.95 and 4.76±0.55 mmol/L, respectively) and TC (from 6.09±1.36 to 4.42±1.14 and 4.53±1.15 mmol/L) compared to untreated hyperlipidemic controls. *CDT* improved the serum lactate dehydrogenase (LDH) levels (from 748.50±120.79 to 475.30±109.53 and 534.30±127.74 U/L) and ameliorated the elevated serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in the cholesterol-induced hyperlipidemic rats, suggesting hepatoprotective effects. No dose-dependent relationship was observed. In conclusion, *CDT* demonstrated efficacy in hyperlipidemia treatment by improving lipid profiles and offering hepatoprotection, highlighting its potential to serve as a promising adjunctive therapy for hyperlipidemia and related disorders.

Keywords: *Ananas comosus*, *Bambusa bambos* (L.), cholesterol, experimental models, hyperlipidemia, poloxamer 407.

Introduction

Hyperlipidemias are among the most commonly treated chronic conditions. It is characterized by an imbalance of blood lipid components. The oxidant/antioxidant balance has been suggested as an important factor for its initiation and progression.[1] The most common clinical consequence of hyperlipidemia is an increased risk of cardiovascular diseases due to atherosclerosis associated with increased total cholesterol, low-density lipoprotein (LDL-C), triglycerides (TG), and lipoprotein(a) (Lp(a)), as well as decreased high-density lipoprotein (HDL-C). The management of hyperlipidemia could efficiently prevent the occurrence and progress of cardiovascular diseases (CVDs).[2,3] Currently, the prevalence of hyperlipidemia is increasing in developed and developing countries, including countries in Asia, which is significantly affecting human labor, quality of life, and longevity.[4,5] Management of abnormal lipid profiles is an important component of primary and secondary programs for preventing CVDs.

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Citation: Pham VAT, Pham PX, Tran TT, Dang HTT, Trinh QV, Dau DT. Effect of a nature-derived combination of *Ananas comosus* and *Bambusa bambos* (L.) in hyperlipidemic experimental animals. Trop J Nat Prod Res. 2025; 9(5): 2323 - 2328 https://doi.org/10.26538/tjnpr/v9i5.61

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

The treatment involves dietary changes, lifestyle modifications, and pharmacologic treatment. Lipid-lowering medication including statins, fibric acid derivatives, ezetimibe, and bile acid sequestrants, are effective in controlling blood lipid indices but associated with many adverse effects, such as myositis, rhabdomyolysis, hepatic toxicity, electrocardiographic disorders and gallstones, particularly at high doses for long periods.[3] New drugs, such as monoclonal antibodies targeting proprotein convertase subtilisin/kexin type 9 (PCSK9) that help control hypercholesterolemia; volanesorsen targeting apo C-III that manages familial chylomicrons syndrome; bempedoic acid, evinacumab and inclisira that are approved for indications related to increased LDL-C, are expensive and have limited safety profiles. In addition, the treatment efficacy is not satisfactory and drug resistance has developed in some patients.[6,7]
Traditional herbal medicine and natural products represent a complementary and alternative option for the management of hyperlipidemia because of their various beneficial effects, good tolerance, and commercial value. *Ananas comosus* and *Bambusa bambos* (L.) are popular tropical herbs consumed worldwide, including in Asian countries. They have been reported to have various potential effects, including the efficacy in hyperlipidemia.[8–13] However, to date there has been no systematic experimental study evaluating the effect of the combination of these herbs. This study was carried out to evaluate the potential efficacy of an herbal combination of *Ananas comosus* and *Bambusa bambos* (L.), which is named "Cao dua tre Lao nha que" (*CDT*), on experimental animal models of hyperlipidemia.

Trop J Nat Prod Res, May 2025; 9(5): 2323 - 2328 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Materials and Methods

Plant materials and extraction

The preparation of *CDT* extraction was conducted by the Vi Dieu Nam joint stock company, Hanoi, Vietnam. Fresh plant materials were cultivated from the company farm and identified based on the Vietnamese Pharmacopeia 5th edition. The fresh materials were ground and dried up to a prescribed degree of fragmentation which was controlled by the microbiological safety standards of Vietnamese Pharmacopoeia 5th edition. The materials were extracted two times at 75ºC for 4 hours each with distilled water. These extracts were combined and completely dried under a temperature of 60°C until the humidity had reached under 20% to obtain the final extract. 120 g of *CDT* were prepared and offered in the form of extract, which contained exactly *Bambusa bambos* (L.) 99.7 g and *Ananas comosus* 20 g, preserved at 25°C and under 75% humidity. After the preparation process, the investigational products were subjected to a quality examination confirmed by Vi Dieu Nam Legal Director. The quality examination conformed to the guidelines of Vietnamese Pharmacopeia 5th edition.[14]

Experimental animals

The animals for the experiments were *Wistar* rats (weighed 160–220 g) and *Swiss* mice (weighed 25 – 35 g) provided by the National Institute of Hygiene and Epidemiology. Seven days before the experiments and during the experimental period, the animals were housed under standard conditions (temperature between 23 and 25 °C, humidity of 55 ± 1.5%, a 12 h dark-night cycle, and had free, unlimited, all-time access to water and pellet food) in the Laboratory of the Department of Pharmacology, Hanoi Medical University. This study was approved by the Scientific Board Committee of Hanoi Medical University (ref number: IRB00003121).

Chemicals

Propylthiouracil (Rieserstat®) 50mg, Cholesterol (Lot S107115, Merck, Germany), Acid Cholic (Sigma (Aldrich) Chemicals Pvt. Ltd. USA), Poloxamer 407 (Sigma (Aldrich) Chemicals Pvt. Ltd. USA), Atorvastatin 10mg (Stellapharm J.V. Co., Ltd.), Peanut oil (Vietnam).

Biochemical analyzer ERBA Chem (India) and commercial ERBA diagnostic kits used for serum analysis of total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-C), alanine aminotransaminase (ALT), aspartate transaminase (AST), albumin, bilirubin and LDH (Lactate dehydrogenase). Malondialdehyde (MDA) and glutathione peroxidase (GSH-Px) were measured using an ELISA kit (Cloud-Clone Corp., USA) and a BioTek® ELx808 Reader.

Experimental design and interventions

All methods were carried out following ARRIVE guidelines and the National Institutes of Health guide for the care and use of laboratory animals.

Cholesterol-induced hyperlipidemic model in rats

Hyperlipidemia was induced in male *Wistar* rats by daily oral administration of a cholesterol mixture (cholesterol 10%, cholic acid 1%, PTU 0.5% with peanut oil to 1mL) at a dose of 10 mL/kg b.w. for 4 weeks. This model represents dietary-induced hyperlipidemia through the exogenous pathway of lipid metabolism.[15–18]

Prior to experimental studies, acute and sub-chronic toxicity testing was conducted to determine the safe dosage range for *CDT* extract administration. Based on these results, two doses (0.6 and 1.2 g/kg b.w.) were selected for evaluation.[19]

A total of fifty *Wistar* rats (weighing 160-220 g) of both sexes were randomly divided into five groups of 10 rats each. Group 1 served as the normal control (non-hypercholesterolemic) and received a standard diet with distilled water. Groups 2-5 were administered the cholesterol mixture daily to induce hyperlipidemia. Treatment began simultaneously with hyperlipidemia induction and continued for 4 weeks as follows:

Group 1: Normal control group - Distilled water 10 mL/kg b.w
Group 2: Disease group - Distilled water 10 mL/kg b.w
Group 3: Atorvastatin-treated group - Atorvastatin 10 mg/kg b.w/day
Group 4: 0.6 g/kg-CDT treated group - CDT 0.6 g/kg b.w/day
Group 5: 1.2 g/kg-CDT treated group - CDT 1.2 g/kg b.w/day

Rat body weight was measured at baseline, after 2 weeks and 4 weeks of treatment.

On day 15 and day 29, rats were fasted overnight. Whole blood was collected from each animal into potassium-EDTA tubes and centrifuged at 3000×g and 5°C for 15 mins. Blood samples were used to determine the lipid profile (TG, TC and HDL-C; Non-HDL-cholesterol (non-HDL-C) was estimated by: Non-HDL-C = TC - (HDL-C)., renal function test (creatinine), and liver function tests (ALT, AST, albumin, total bilirubin) and antioxidant markers (LDH, MDA and GSH).

P-407-induced hyperlipidemic model in mice

Poloxamer 407 (P-407) was used to induce hyperlipidemia in mice by primarily affecting endogenous lipid biosynthesis pathways. This model was selected to complement the dietary model as P-407 specifically inhibits lipoprotein lipase activity and increases hepatic cholesterol synthesis, allowing evaluation of *CDT* effects on endogenous lipid metabolism pathways.[15,16,20]

Prior to the main study, preliminary acute toxicity testing was conducted to determine appropriate dosing for mice. Based on these results and accounting for species differences in metabolism, doses of 1.2 and 2.4 g/kg b.w. were selected for the mouse model.[19]

A total of fifty *Swiss* mice (weighing 25-35 g) of both sexes were randomly divided into five groups of ten animals each. Group 1 served as the normal control and received distilled water for 7 days and was injected with 0.9% sodium chloride on day 7. The other four groups (groups 2-5) received their respective treatments for 7 days and were then injected intraperitoneally with 2% P-407 solution at a dose of 200 mg/kg b.w. on day 7.

Group 1: Normal control group - Distilled water 100 mL/kg b.w
Group 2: Disease group - Distilled water 100 mL/kg b.w
Group 3: Atorvastatin-treated group - Atorvastatin 100 mg/kg b.w/day
Group 4: 0.6 g/kg-CDT treated group - CDT 1.2 g/kg b.w/day
Group 5: 1.2 g/kg-CDT treated group - CDT 2.4 g/kg b.w/day

Blood samples were collected 24 h after the injection of P-407 for lipid profile determination including TG, TC and HDL-C. Non-HDL-cholesterol (non-HDL-C) was estimated by: Non-HDL-C = TC - (HDL-C).

Statistical analysis

The data were expressed as the mean ± standard deviation (SD) and statistical analysis was carried out employing T-test using SPSS 26. The p-value < 0.05 was considered to be statistically significant.

Results and Discussion

Hyperlipidemia is a major risk factor for atherosclerosis, hypertension, coronary heart disease, and cerebral vascular diseases. In recent years, natural products have attracted more attention to manage hyperlipidemia. Some herbs have been used as antihyperlipidemic agents in ethnomedicine.[21] Investigating the antihyperlipidemic activity of medicinal plants on experimental models plays a crucial role in developing a natural product for hyperlipidemia treatment. Therefore, it is necessary to develop hyperlipidemia models in experimental animals. In this present study, hyperlipidemia was induced by dietary cholesterol mixture administration and poloxamer 407 injections.

Trop J Nat Prod Res, May 2025; 9(5): 2323 - 2328 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Effects of CDT on lipid levels in the cholesterol-induced hyperlipidemic rat model

After 4 weeks of the experimental period, there were no recorded mortalities. There was no adverse effect observed; no notable change in animal weights, vital signs, skin, fur, and daily behaviors. High cholesterol diet leads to excessive lipid accumulation in the body and is one of the main causes of hyperlipidemia.[22] In our study, rats administered cholesterol mixture for four weeks exhibited a significant increase in serum levels of TG, TC, non-HDL-C, indicating that the cholesterol-induced hyperlipidemic model was established successfully in rats. Similar results were observed in other studies using a dietary hypercholesterolemic model.[23,24]

In this study, the lipid profiles including TC, TG, HDL-C, non-HDL levels are examined. The level of non-HDL, which is the representative of the difference between TC and HDL-C, reflects the contents of low-density lipoprotein cholesterol (LDL-C), very-low-density lipoprotein cholesterol (VLDL-C), remnant chylomicron and Lp(a). This index, reflecting the lipoproteins in atherosclerotic apoB, is demonstrated to be closely associated with the risk of cardiovascular diseases.[24,25]

After 2 weeks of treatment, there was no significant difference in the levels of TC, TG, HDL-C, and non-HDL-C in atorvastatin-treated rats or *CDT*-treated rats compared with the disease group ($p > 0.05$). After 4 weeks of treatment, the levels of TC, TG, and non-HDL-C were significantly decreased in the atorvastatin-treated group and CDT-treated groups compared with the disease group. Whereas there was no significant difference in changes in HDL-C levels between the treated groups versus the normal control group (Table 1). This indicates that *CDT* can interfere with the absorption and metabolism of exogenously administered lipids.

Table 1: Effect of *CDT* on lipid levels in the cholesterol-induced hyperlipidemia

Group	TG (mmol/L)	TC (mmol/L)	HDL-C (mmol/L)	Non-HDL-C (mmol/L)
Lipid levels in the cholesterol-induced hyperlipidemia after 2 weeks of treatment				
Normal control	1.12 ± 0.23	1.25 ± 0.16	0.75 ± 0.16	0.49 ± 0.16
Disease control	1.13 ± 0.23	3.28 ± 0.87***	0.83 ± 0.25	2.45 ± 0.75***
Atorvastatin 10 mg/kg	1.04 ± 0.26	2.81 ± 0.86	0.94 ± 0.14	1.88 ± 0.77
***CDT* 0.6 g/kg**	1.16 ± 0.19	3.45 ± 0.58	0.77 ± 0.06	2.68 ± 0.57
***CDT* 1.2 g/kg**	1.03 ± 0.25	3.22 ± 0.77	0.83 ± 0.10	2.39 ± 0.77
Lipid levels in the cholesterol-induced hyperlipidemia after 4 weeks of treatment				
Normal control	1.08 ± 0.25	1.30 ± 0.13	0.71 ± 0.12	0.59 ± 0.16
Disease control	1.40 ± 0.27*	4.11 ± 0.95***	0.85 ± 0.15*	3.26 ± 0.91***
Atorvastatin 10 mg/kg	1.10 ± 0.28^{+}	2.89 ± 0.68^{++}	0.84 ± 0.20	2.05 ± 0.65^{++}
***CDT* 0.6 g/kg**	1.02 ± 0.20^{++}	3.05 ± 0.60^{++}	0.72 ± 0.21	2.33 ± 0.54^{+}
***CDT* 1.2 g/kg**	1.13 ± 0.31^{+}	2.93 ± 0.67^{++}	0.84 ± 0.22	2.10 ± 0.63^{++}

Values are mean ± SD (n = 10). **, *** compared with normal control group ($p < 0.05$, $p < 0.001$).*
$^{+}$, $^{++}$ *compared with disease group ($p < 0.05$, $p < 0.01$).*

As shown in Table 2, the serum levels of AST and ALT in high cholesterol-administered rats were significantly increased compared with the normal control rats. Elevated serum AST and ALT levels from cholesterol administration suggested that hyperlipidemia could induce hepatotoxicity.[26] It was shown in previous studies that the high-fat diet administration could elevate the serum levels of liver enzymes and damage the liver structure.[27] The degenerative changes were observed in hepatocytes accompanied by lipid deposition and inflammatory cell infiltration.[28] The level of AST in two CDT-treated groups decreased significantly compared with the disease group after 4 weeks of treatment ($p < 0.001$). The level of ALT decreased significantly in CDT at 0.6 g/kg/b.w. (Table 2). Our results showed that while serum levels of AST and ALT in atorvastatin-treated groups were not significantly different from those of the disease group, these biochemical parameters in CDT-treated groups significantly decreased compared with the disease group, indicating that CDT treatment could be hepatoprotective in the cholesterol-induced hepatic injury. Other biochemical parameters, including serum levels of albumin, total bilirubin, and creatinine remained unaffected in all groups (Table 2).

In addition, natural product-derived active compounds that exert antioxidant properties have been demonstrated to lower lipid levels, prevent lipid oxidation, and play an important role in cardiovascular protection.[29] To assess the modulation of oxidative stress-related enzymes in the cholesterol-induced hyperlipidemic rats, LDH, MDA and GSH activities were measured. Compared with the normal control group, LDH and MDA activity was increased, and GSH activity was decreased in the hyperlipidemic rats, indicating oxidative injury in hyperlipidemic rats. LDH level decreased significantly in two *CDT*-treated groups. Glutathione level showed an increasing trend, while MDA level showed a decreasing trend in *CDT*-treated groups, but no significant change was observed (Table 2). A significantly downregulated activity of LDH in two *CDT*-treated groups was shown in this study. LDH, an important enzyme in the anaerobic metabolic pathway, has been demonstrated to be related to the occurrence of cardiovascular diseases.[30] Normally, LDH activity is confined to the heart and is rarely present in the serum. When the heart, muscle, or other tissues are damaged, serum LDH level increases significantly. The extracts decreased the raised serum LDH level in the cholesterol-induced hyperlipidemic rats. This finding indicated the potential of *CDT* in the prevention and treatment of hyperlipidemia's complications, especially cardiovascular events. Our results also showed a trend toward GSH activity increase and MDA activity decrease in CDT-treated rats, but no statistically significant change was observed. *Ananas comosus* and *Bambusa bambos* (L.) contain various antioxidant components, including vitamin C, minerals, and flavonoids. The results of our study indicated that *CDT* did not provide a robust antioxidant activity. This might be due to the extracting process with high temperature for a long time leading to degradation of vitamin C, which has been demonstrated to have antioxidant activity and play a pivotal role in the pathogenesis of cardiovascular diseases.[31] Therefore, the lipid-lowering effects of *CDT* might result from other compounds with different mechanisms of action.

Table 2: Effects of CDT on serum biochemistry parameters

Group	Normal control	Disease control	Atorvastatin 10 mg/kg	*CDT* 0.6 g/kg	*CDT* 1.2 g/kg
Effects of *CDT* on serum biochemistry parameters					
Albumin (g/dL)	3.03 ± 0.32	3.09 ± 0.30	3.05 ± 0.37	3.01 ± 0.22	2.99 ± 0.24

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Total bilirubin (μmol/L)	10.22 ± 0.52	10.42 ± 0.58	10.15 ± 0.78	10.27 ± 1.03	10.20 ± 0.43
Creatinine (μmol/L)	80.90 ± 9.87	81.30 ± 8.10	81.80 ± 5.53	79.50 ± 5.89	80.10 ± 6.23
AST (U/L)	40.30 ± 9.59	108.70 ± 12.73 ***	108.70 ± 12.73 ***	93.60 ± 11.54 $^{+}$, **	93.30 ± 13.28 $^{+}$, **
ALT (U/L)	31.80 ± 4.05	47.20 ± 11.54 **	45.50 ± 13.97 **	37.70 ± 7.60 $^{+}$, *	40.30 ± 9.59 *
Effects of *CDT* on antioxidant activities					
LDH (U/L)	555.10 ± 112.36	748.50 ± 120.79 **	559.60 ± 120.42 $^{++}$	475.30 ± 109.53 $^{+++}$	534.30 ± 127.74 $^{++}$
MDA (nmol/mL)	24.39 ± 6.28	51.00 ± 10.94 ***	38.36 ± 10.13 $^{+}$	45.33 ± 8.79	47.54 ± 13.43
GSH (μg/mL)	87.83 ± 14.90	45.45 ± 11.93 ***	57.60 ± 11.35 $^{+}$	55.32 ± 12.74	51.55 ± 8.75

Values are mean ± SD (n = 10). *, **, *** *compared with normal control group ($p < 0.05$, $p < 0.001$).*
$^{+}$, $^{++}$ *compared with disease group ($p < 0.05$, $p < 0.01$).*

Effects of CDT on lipid profile in Poloxamer 407-induced hyperlipidemic mice

The results showed that all serum lipid parameters were significantly elevated in P-407-induced disease group as compared with control ($p < 0.001$).

There were significant reductions in TC, TG, and non-HDL-C levels and an improvement in HDL-C level in atorvastatin-treated group as compared with the P-407-induced group. In comparison with P-407-induced group, *CDT*-treated groups at both doses significantly decreased two major lipid parameters: TG (from 5.8±1.52 to 4.84±0.95 and 4.76±0.55 mmol/L, respectively), TC (from 6.09±1.36 to 4.42±1.14 and 4.53±1.15 mmol/L) ($p < 0.05$) (Figure 1). P-407 induces hyperlipidemia through the endogenous pathway, which is related to various enzymes in lipid metabolism. The mechanism of P-407-induced hyperlipidemia has been shown to include inhibition of the plasma lipoprotein lipase (LPL), cholesterol 7α-hydroxylase (C7αH); causing an increase in the quantity and activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, and a decrease in the number of LDL receptors (LDLr) in the liver.[32] In this study, P-407-injected mice had a significant increase in serum TC, TG, non-HDL-C while *CDT* at two doses of 0.6 and 1.2 g/kg b.w/day showed a reduction of these parameters. The more pronounced effect of *CDT* in the P-407 model suggests that it may exert its primary hypolipidemic effect by regulating endogenous lipid metabolism enzymes. The two models used in this study represent different pathways of lipid metabolism: the cholesterol mixture induces hyperlipidemia through the exogenous pathway involving chylomicrons and dietary cholesterol absorption, while P-407 affects the endogenous pathway involving very low-density lipoproteins (VLDL) and hepatic cholesterol metabolism.[32,33] The dual model approach allows for a more comprehensive assessment of the hypolipidemic effects of *CDT* extract. Thus, the investigational product showed a significant amelioration of serum lipid profiles in hyperlipidemic animals in both experimental models, suggesting that *CDT* can modulate both exogenous and endogenous lipid metabolism pathways.

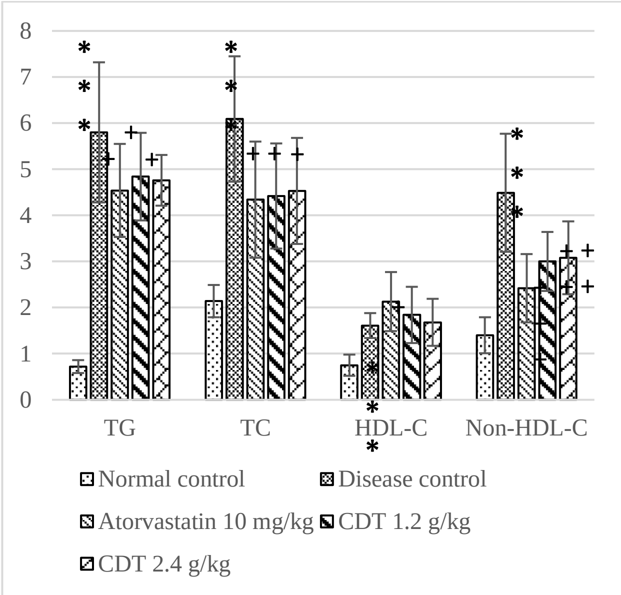

***Figure 1.** Effect of CDT on lipid levels in Poloxamer 407-induced hyperlipidemia mice.*
**** compared with normal control group ($p < 0.001$).*
$^{+}$, $^{++}$, $^{+++}$ *compared with disease group ($p < 0.05$, $p < 0.01$, $p < 0.001$).*

Several studies have demonstrated the lipid-lowering effects of *Ananas comosus* or *Bambusa bambos* (L.) in similar animal models.[8–11] In hyperlipidemic mice induced by high-fat diets, serum total cholesterol reached normal level after *Ananas comosus* treatment. Also, *Ananas comosus* significantly inhibited serum lipids in Triton WR-1339-induced hyperlipidemic mice.[11] Administration of methanol extract of *Bambusa bambos* decreased serum TC, TG, LDL-C in both cholesterol suspension-induced and Poloxamer-407-induced hyperlipidemic rats.[8,9] The active compounds such as flavonoids present in *Ananas comosus* extract have been shown to inhibit the activity of HMG-CoA reductase, the major regulatory enzyme in cholesterol biosynthesis, and accelerate the lipoprotein lipase (LPL), an extracellular enzyme that degrades circulating triglycerides in the blood.[11] Additionally, hypercholesterolemia, associated with oxidative stress, can induce systemic and organ inflammation by overexpressing pro-inflammatory cytokines.[34] *Ananas comosus* was shown to reduce the pro-inflammatory cytokines, including IL-6 and IL-1β levels, indicating its anti-inflammatory activity.[35] These mechanisms may contribute to the synergistic effects of the combination of *Ananas comosus* and *Bambusa bambos* (L.)

Our findings showed that the combination of these two ingredients in one product exhibits lipid-lowering effects. This combination of natural ingredients for hyperlipidemia treatment has advantages including ready availability, low cost, and a favorable safety profile based on their regular and long-standing use in traditional medicine. In addition, because hyperlipidemia is the consequence of multiple factors and is related to various disorders and complications, a multi-component natural product may be able to target various mechanism pathways and biological processes to treat the disease more effectively than single compounds.

The most common drug classes prescribed for hyperlipidemia treatment have been associated with adverse effects of inducing the dysfunction of the liver and/or kidneys, especially when they are indicated for long-term treatment.[3] Natural products that can provide both hypolipidemic and hepatoprotective effects, as observed with *CDT* in our study, may offer advantages for long-term management of hyperlipidemia.

Overall, our findings suggest the potential of *CDT* as a complementary medicine for hyperlipidemia. This naturally-derived treatment offers ease of production and a favorable safety

 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

profile. Further studies are needed to investigate its specific mechanism of action, i.e., its potential activity on inflammation or lipid metabolism-related enzymes, as well as its effects on other experimental models of cardioprotective properties. Future research should also compare the efficacy of the combination versus individual extracts to evaluate potential synergistic effects.

Conclusion

Our results showed that *CDT* extract ameliorates hyperlipidemia by reduced TC, TG and non-HDL-C concentrations in P-407-induced hyperlipidemic mice and cholesterol-induced hyperlipidemic rats. It could be beneficial in ameliorating hepatic damage caused by hyperlipidemia. The effect of *CDT* did not show dose dependents. These findings suggest that *CDT* may hold promise as an effective adjunctive therapy in managing hyperlipidemia and other clinical hyperlipidemia-related disorders.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgments

This study was supported by other departments and faculties at Hanoi Medical University (HMU), Hanoi, Vietnam. The authors, therefore, acknowledge with thanks HMU staff for useful advice and technical support.

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