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IN VIVO LIPID-LOWERING AND ANTI-ATHEROSCLEROTIC EFFECTS OF SCORPION TURMERIC (CURCUMA RANGJUED) EXTRACT

Phung Thi Kim Hue[1,3*], Mai Phuong Thanh[2], Phan Anh Thu[3], Nguyen Nhat Long[3], Le Nhat Minh[1,5], Phan Nu Yen Chi[6], Nguyen Thi Duong[4], Le Dung Sy[1], Le Tri Vien[1]

[1]*Institute of Health Research and Educational Development in Central Highlands - Gia Lai, Vietnam*
[2]*VNU University of Medicine and Pharmacy, Vietnam National University - Hanoi City, Viet Nam*
[3]*Hung Vuong High School for the Gifted - Gia Lai, Vietnam*
[4]*Thao Nguyen Duong Traditional Family Medicine Clinic - Bac Gia Nghia Ward, Lam Dong, Vietnam*
[5]*Foreign Trade University - Hanoi City, Vietnam*
[6]*Soka University of America, Life Sciences Concentration - 1 University Drive, Aliso Viejo City, Orange County, California, USA*

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ABSTRACT

Dyslipidemia represents an independent risk factor for cardiovascular diseases, contributing to high morbidity, mortality and healthcare costs worldwide. Previous studies have indicated that improving lipid profiles can effectively prevent the onset and progression of atherosclerosis and associated CVD events. To explore alternatives to conventional lipid-lowering drugs, which often have adverse effects, this study evaluated the in vivo lipid-lowering and anti-atherogenic effects of Scorpion Turmeric (Curcuma rangjued) extract.

GERC7, a honey-based emulsion prepared from steam-distilled C. rangjued rhizome extract, was administered to mice with Poloxamer-407 (P-407)-induced endogenous dyslipidemia. GERC7 significantly reduced plasma lipid levels at all tested doses compared to the disease control group, with the optimal effect observed at the highest dose (7.2 mL/kg/day), reducing total cholesterol (TC) and low-density lipoprotein (LDL) by 31% and 43%, respectively. The atherogenic index (AI), increased 4.9-fold in the disease control group compared to normal controls, but declined substantially in GERC7- and atorvastatin-treated groups. The lowest AI was observed at the 7.2 mL/kg dose, consistent with maximal lipid reduction.

These findings demonstrate dose-dependent lipid-lowering and anti-atherosclerotic effects of GERC7, indicating its potential utility as a multi-target natural therapeutic option for dyslipidemia and atherosclerosis management.

Keywords: Dyslipidemia, Atherogenic Index, GERC7, Curcuma rangjued, Nghe Bo Cap.

1. INTRODUCTION

Dyslipidemia is recognized as an independent risk factor for cardiovascular disease (Defesche et al., 2017), contributing substantially to global mortality, disability, and healthcare expenditures (Murray et al., 2013). Elevated concentrations of non-high-density lipoprotein cholesterol (non-HDL-C) have been identified as a major cause of ischemic heart disease and stroke, accounting for approximately 3.9 million deaths worldwide (Topor-Madry et al., 2020). Since primary prevention plays a pivotal role in reducing the CVD incidence, advances in the management of dyslipidemia are critical for lowering cardiovascular morbidity and mortality (Murray et al., 2013).

Statins currently remain the first-line lipid-lowering therapy; however, their use is associated with adverse effects such as myalgia, hepatotoxicity and an increased risk of diabetes, particularly at high doses (Lv et al., 2021). Fibrates produce similar side effects, including myopathy, elevated liver enzymes, and cholelithiasis (Murray et al., 2013). Although proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have been developed, their high costs and unresolved safety concerns restrict widespread clinical application (Murray et al., 2013). Additionally, some patients experience suboptimal therapeutic responses or develop drug resistance (Soppert et al., 2020). These limitations

*Corresponding author
Email: whitelily109@gmail.com **Phone**: (+84) 914730099 **DOI:** 10.52163/yhc.v66i8.4075

highlight an urgent need for complementary or alternative therapeutic strategies for dyslipidemia.

Turmeric belongs to a large genus Curcuma within the Zingiberaceae family and is widely cultivated across the Central Highlands of Vietnam. For centuries, preparations from Curcuma longa (yellow turmeric), which contains curcumin, have been used in traditional medicine to treat various ailments. However, Curcuma rangjued, a newly described species (Hue et al., 2024) commonly referred to "Scorpion Turmeric", presents distinctive characteristics. Despite morphological similarities to turmeric species in China, Laos, Cambodia and Vietnam, C. rangjued has distinctive rhizome features, including an intensely bitter taste and a unique chemical composition that confers notable pharmacological properties. In traditional medicine, Scorpion Turmeric is highly valued for its strong anti-inflammatory activity. Unlike C. longa, whose major bioactive constituents are curcumin and its derivatives, C. rangjued primarily contains sesquiterpenes such as curcumenol, germacrone and related compounds (Hue et al., 2025). These metabolites have been shown to exert significant anti-inflammatory and antioxidant activities (Gushiken et al., 2022). Given these properties, C. rangjued represents a promising natural medicinal resource for atherosclerosis management. Its potential lies in the ability to modulate inflammation, regulate dyslipidemia and act on associated biological mechanisms, which suggests a highly promising research direction for future studies.

2. MATERIALS AND METHODS

2.1. Materials

Adult male Swiss albino mice, healthy, weighing 20 ± 2g, were obtained from the National Institute of Hygiene and Epidemiology, Viet Nam. Animals were housed under controlled conditions (at 25 ± 1°C, appropriate humidity and light-dark cycle), with standard laboratory feed and allowed free access to water at the Department of Pharmacology, VNU University of Medicine and Pharmacy, Hanoi. Dyslipidemia was induced by intraperitoneal injection (i.p.) of poloxamer-407 (P-407) at a dose of 200 mg/kg dissolved in physiological saline (0.9%).

Test sample (GERC7) was prepared using 3 kg of cleaned Curcuma rangjued rhizomes. At the beginning, rhizomes were ground in a grinding device. After that, the gound material was transferred to a steam-distillation apparatus and mixed evenly with water at a material-to-water ratio of 2:8. Steam distillation was carried out following the method described by Marcac et al. (2023). The system was maintained at 80°C for the 2 hours, then increased to 90–100°C for an additional 10 hours. Halfway through the distillation process, the essential oil fraction was collected while the aqueous extract was returned to the flask. Temperature was maintained until the end of the time period. After completion, all essential oil and hydrosol were collected and emulsified with "Rừng Sê San" natural honey to obtain GERC7.

2.2. Research Methods

2.2.1. Endogenous dyslipidemia model in mice

The endogenous dyslipidemia was induced according to the method of Leon et al. (2006), using a single intraperitoneal injection of poloxamer 407 (P-407) at a single dose of 200 mg/kg. Mice were randomly divided into 7 groups, 10 animals per group. Groups were injected and given GERC7 orally as follows:

- Group I (Negative control): Saline (0.9% NaCl, 10 mL/kg, i.p.) + distilled water (20 mL/kg/day, oral).

- Group II (Disease control): P-407 (2%, 200 mg/kg, i.p.) + distilled water (20 mL/kg/day, oral).

- Group III (Positive control): P-407 (i.p.) + atorvastatin (100 mg/kg/day, oral).

- Group IV (GE10): P-407 (i.p.) + GERC7 (2.4 mL/kg/day, oral).

- Group V (GE15): P-407 (i.p.) + GERC7 (3.6 mL/kg/day, oral).

- Group VI (GE20): P-407 (i.p.) + GERC7 (4.8 mL/kg/day, oral).

- Group VII (GE30): P-407 (i.p.) + GERC7 (7.2 mL/kg/day, oral).

All treatments were administered once daily for a total of 10 days. On day 10, one hour after oral administration, mice received i.p injection of P-407 at dose 200 mg/kg (injection volume 0.1 mL/10 g body weight). Test mice were later fasted and maintained free access condition to water after P-407 injection. Parameters were determined 24 hours after P-407 administration.

Blood samples were collected from the carotid artery for measurement of lipid parameters (TC, TG, HDL-C) and liver enzymes (AST, ALT). After anesthesia, liver tissue samples were removed and preserved in 10% neutral buffered formalin solution for 24 hours.

VLDL (Very Low-Density Lipoprotein) was calculated as:

$$\text{VLDL} = \text{TG} / 2.2 \text{ (mmol/L)}$$

LDL (Low-Density Lipoprotein) was calculated as:

$$\text{LDL} = \text{TC} - \text{HDL} - \text{VLDL}$$

Atherogenic index (AI) was calculated as:

$$\text{AI} = (\text{TC} - \text{HDL}) / \text{HDL}$$

Where TC: Total cholesterol; TG: Triglyceride; HDL: High-Density Lipoprotein.

2.2.2. Chemicals and Instruments

Poloxamer 407 (Sigma-Aldrich, Singapore); atorvastatin 10 mg tablets (STADA–Vietnam); assay kits for TC, TG, and HDL-C (Erba Lachema s.r.o, Czech Republic); ERBA biochemical analyzer (India).

2.2.3. Statistical Analysis

Data were analyzed using Microsoft Excel 2016 and expressed as mean ± SD. Between-group comparisons were performed using Student's t-test. Statistical significance was set at $p < 0.05$.

3. RESULTS

3.1. Effects of GERC7 on Plasma Lipid Concentrations

In the endogenous dyslipidemia model, P-407 injection markedly elevated lipid concentrations (Table 1). Compared to the normal control, the disease control group exhibited a 4.0-fold increase in TC, 8.9-fold increase in TG, 8.9-fold increase in VLDL, and 3.7-fold increase in LDL. GERC7 at all tested doses significantly reduced plasma lipid levels compared to the disease control. The most pronounced lipid-lowering effect was observed at the highest dose (7.2 mL/kg/day), producing 31% and 43% reductions in TC and LDL-C, respectively.

Table 1. Effects of GERC7 on plasma lipid concentrations

Lot (n=10)	Concentration ($\bar{X}$ ± SD , mmol/L)				
	TC	TG	HDL	VLDL	LDL
Negative control	2.17 ± 0.31	0.88 ± 0.11	0.52 ± 0.03	0.40 ± 0.05	1.25 ± 0.31
Disease control	8.69 ± 0.98***	7.83 ± 1.94***	0.53 ± 0.05	3.56 ± 0.88***	4.60 ± 1.26***
Positive control (atorvastatin)	5.16 ± 0.83###	5.61 ± 1.05##	0.58 ± 0.06	2.55 ± 0.48##	2.03 ± 0.73###
GE10	6.81 ± 1.20###	6.37 ± 0.81#	0.54 ± 0.07	2.89 ± 0.37#	3.38 ± 1.31#
GE15	7.01 ± 0.82###	6.12 ± 0.95#	0.55 ± 0.04	2.78 ± 0.43#	3.68 ± 0.99
GE20	6.72 ± 1.08###	6.36 ± 1.05#	0.53 ± 0.07	2.89 ± 0.48#	3.30 ± 1.34#
GE30	5.99 ± 0.81###[a]	6.16 ± 0.97#	0.56 ± 0.05	2.80 ± 0.44#	2.63 ± 0.99###[a]

Notes: TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very-low-density lipoprotein cholesterol. GE10 (2.4 mL/kg/day); GE15 (3.6 mL/kg/day); GE20 (4.8 mL/kg/day); GE25 (7.2 mL/kg/day). *p < 0.05; **p < 0.01; ***p < 0.001 vs. negative control; #p < 0.05; ##p < 0.01; ###p < 0.001 vs. disease control; ap < 0.05 vs. GE15.

3.2. Effects of GERC7 on the Atherogenic Index

The atherogenic index, determined by non-HDL-C/HDL-C ratio, reflects the balance between atherogenic and anti-atherogenic lipoproteins and is associated with lipid-related disorders such as carotid atherosclerosis, metabolic syndrome, diabetes, and liver disease (Table 2). The disease control group exhibited 4.9-fold higher AI compared to the normal control. AI values decreased significantly in mice treated with atorvastatin and GERC7. Among the GERC7-treated groups, the lowest AI was observed at 7.2 mL/kg, consistent with the best lipid-lowering effect observed at this dose.

Higher AI values indicate greater proportions of "atherogenic" cholesterol and thus a higher risk of atherosclerosis. In this study, the significantly reduced AI in GERC7-treated groups suggests that the sample enhances the availability of HDL to effectively "clear" excess cholesterol, thereby exerting a beneficial anti-atherogenic effect.

Table 2. Effects of the test sample on the Atherogenic Index

Experimental group (n=10)	Atherogenic Index ($\bar{X}$ ± SD)
Negative control (i.p. NaCl 10 mL/kg + distilled water 20 mL/kg/day)	3.18 ± 0.70
Disease control (i.p. P-407 2%, 200 mg/kg + distilled water)	15.58 ± 2.81***
Positive control (i.p. P-407 2% + atorvastatin 100 mg/kg/day)	7.97 ± 1.55###
GE10 (2.4 ml/kg/day)	11.72 ± 2.46##
GE15 (3.6 ml/kg/day)	11.84 ± 1.72##
GE10 (4.8 ml/kg/day)	11.96 ± 3.11###
GE25 (7.2 ml/kg/day)	9.79 ± 1.83###[a]

Notes: AI, atherogenic index; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein. *p < 0.05; **p < 0.01; ***p < 0.001 vs. negative control. #p < 0.05; ##p < 0.01; ###p < 0.001 vs. disease control. [a]p < 0.05 vs. GE15.

4. DISCUSSION

Previous research demonstrated that GERC7, an extract of Curcuma rangjued enriched in curcumenol, germacrone, and isocurcumenol, exhibits strong biological activity (Hue et al., 2025). Among its major constituents, germacrone has been shown to modulate T-lymphocyte balance and slow inflammatory progression (Tan et al., 2022), while curcumenol exerts anti-inflammatory effects (Yang et al., 2021). GERC7 also inhibits HMG-CoA reductase with an IC_{50} of 58.12 ± 2.14 µg/mL ($p < 0.05$ vs. negative control), indicating its potential role in regulating cholesterol biosynthesis.

This study demonstrates that GERC7 has effectively ameliorated dyslipidemia and reduced atherosclerotic risk in the P-407–induced hyperlipidemic mouse model. The marked reduction in total cholesterol (TC), LDL-C, and atherogenic index (AI), particularly at the 7.2 mL/kg dose, suggests that this formulation acts through multiple mechanisms, not only by suppressing cholesterol synthesis but also by improving lipoprotein distribution toward a less atherogenic profile.

Integrating previous findings (Hue et al., 2025) with the obtained results, GERC7 demonstrates clinical potential as a multi-target natural agent for managing dyslipidemia and preventing atherosclerosis. Germacrone, one of its principal components, has been reported to regulate lipid homeostasis and fat metabolism by inhibiting fatty-acid synthesis, enhancing β-oxidation via AMPKα activation, and down-regulating SREBP-1/2 and lipogenic genes in high-fat–diet mice (Guo et al., 2017). Additionally, germacrone provides hepatoprotective effects by reducing hepatic lipid accumulation, lowering LDL-C and TG levels, and increasing HDL-C through inhibition of the Nrf2–Rbp4 pathway and attenuation of hepatic oxidative stress (Xiao et al., 2025). Furthermore, curcumin, structurally related to curcumenol, has been well studied and recognized for its lipid-modulating and antioxidant effects (Bùi et al., 2018). These activities may synergize with those of GERC7, supporting a combined mechanism that simultaneously reduces cholesterol biosynthesis, mitigates inflammation, and limits oxidative injury—all of which are central contributors to atherosclerotic pathogenesis.

The substantial reductions in TC, LDL-C, and AI observed in the P-407 model, especially at the highest dose (7.2 mL/kg), highlight the strong preclinical efficacy of GERC7. These findings suggest that GERC7 may represent more than a mere “supportive supplement,” positioning it as a promising natural pharmaceutical candidate. With further development, GERC7 could become a complementary or alternative therapeutic option for patients with dyslipidemia—particularly those seeking natural products or experiencing intolerance to statins.

Nevertheless, despite its numerous advantages—including combined lipid-lowering and anti-inflammatory effects—GERC7 requires further investigation before clinical application. Detailed phytochemical profiling is needed to quantify germacrone, curcumenol, and other minor constituents. Studies on molecular mechanisms, chronic toxicity, pharmacokinetics, and potential drug interactions, especially with statins or cardiovascular medications, are also essential to support future clinical development.

5. CONCLUSION

GERC7, a honey-based emulsion extracted from Curcuma rangjued rhizomes, significantly reduced total cholesterol, LDL-C, and the atherogenic index, with the maximal effect observed at 7.2 mL/kg, indicating a dose-dependent response. These findings suggest that GERC7 not only suppresses cholesterol biosynthesis, improves lipoprotein distribution and reduces atherosclerotic risk. Overall, GERC7 emerges as a promising natural adjunctive therapy for dyslipidemia and atherosclerosis management. Additional studies on molecular mechanisms, long-term toxicity, and clinical efficacy are required to further validate its therapeutic potential.

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