Postprint: Study on the Inhibition Mechanism of Panax japonicus var. major Leaf Saponins on Lipase and Their Hypolipidemic Effects

Authors: Zheng Huachan, Meng Lingru, He Miao, Huang Wenli, but Lin Wei, Xu Hong, Deng Chong, Zhang Huawei, Jiang Yi, Song Xiaomei

Date: 2023-12-26T00:00:00+00:00

Abstract

The leaves of Panax japonicas var. major are the dried petiolate leaves of Panax japonicas var. major (Araliaceae), a characteristic traditional Chinese medicinal material in the Qinba region. To rationally develop and utilize the leaves of Panax japonicas var. major and elucidate their chemical substance basis, this study employed HPLC to analyze the main chemical constituents of the saponin fraction from the leaves, determined the lipase inhibitory activity and inhibition type of the saponin fraction, and validated the lipase inhibition mechanism and hypolipidemic effects through molecular docking and animal experiments. The results showed that: (1) The main constituents of the saponin fraction from the leaves were 20(S)-ginsenoside Rg2, 20(R)-ginsenoside Rg2, ginsenoside Rb2, ginsenoside Rb3, ginsenoside Rd, and ginsenoside Rh2. (2) The saponin fraction from the leaves and 20(R)-ginsenoside Rg2 exhibited strong inhibitory effects on lipase, with IC50 values of 0.14 and 2.30 mol·L-1, respectively. (3) The inhibition of lipase by the saponin fraction from the leaves, 20(R)-ginsenoside Rg2, and ginsenoside Rb3 was reversible, with a non-competitive inhibition type. (4) Binding of ligands to ARG337B, ASP331B, and ILE248B residues may contribute to enhancing the lipase inhibitory activity of the ligands. (5) The total saponins from the leaves of Panax japonicas var. major could significantly reduce the contents of cholesterol and triglycerides in the serum of hyperlipidemic mice. This study lays a foundation for the further development and utilization of the leaves of Panax japonicas var. major in hypolipidemic applications.

Full Text

Inhibition Mechanism and Hypolipidemic Effects of Saponins from Panax japonicus Leaves on Lipase

ZHENG Huachan[1,2], MENG Lingru[1,2], HE Miao[1,2], HUANG Wenli[1,2], DAN Linwei[1,2], XU Hong[1,2], DENG Chong[1,2], ZHANG Huawei[1,2], JIANG Yi[1,2]*, SONG Xiaomei[1,2]

[1]School of Pharmacy, Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Shaanxi Provincial Key Laboratory of Basic and New Drug Research in Traditional Chinese Medicine, Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

Abstract

Panax japonicus leaves (Zhuzishen Ye), the dried leaves with petioles of *Panax japonicus* var. *major* (Araliaceae), represent a characteristic traditional Chinese medicine in the Qinba region. To rationally develop and utilize this resource and elucidate its chemical basis, this study employed HPLC to analyze the main chemical constituents of the saponin fraction from Panax japonicus leaves, determined its lipase inhibitory activity and inhibition type, and validated the lipase inhibition mechanism and hypolipidemic effects through molecular docking and animal experiments. The results demonstrated: (1) The primary chemical constituents of the saponin fraction were 20(S)-ginsenoside Rg2, 20(R)-ginsenoside Rg2, ginsenoside Rb2, ginsenoside Rb3, ginsenoside Rd, and ginsenoside Rh2. (2) Both the saponin fraction and 20(R)-ginsenoside Rg2 exhibited strong lipase inhibitory effects, with IC_{50} values of 0.14 and 2.30 $mol \cdot L^{-1}$, respectively. (3) The saponin fraction, 20(R)-ginsenoside Rg2, and ginsenoside Rb3 produced reversible, non-competitive inhibition of lipase. (4) Ligand binding to ARG337B, ASP331B, and ILE248B residues may enhance lipase inhibitory activity. (5) The total saponins from Panax japonicus leaves significantly reduced serum cholesterol and triglyceride levels in hyperlipidemic mice. These findings establish a foundation for the further development and utilization of Panax japonicus leaves as a hypolipidemic agent.

Keywords: Panax japonicus leaves, saponins, lipase, enzyme kinetics, molecular docking, in vivo validation

Introduction

Panax japonicus leaves, the dried aerial parts of *Panax japonicus* var. *major*, are characterized by a slightly cold nature and bitter-sweet taste, traditionally used to clear lung heat, relieve cough, generate body fluids, moisten the throat,

prevent heatstroke, and provide tonic effects. In folk practice, they are commonly consumed as tea. The medicinal use of Panax japonicus leaves dates back to the Qing Dynasty, when they served as a cost-effective alternative to ginseng and ginseng leaves as prices for these materials escalated.

Lipase is the key enzyme responsible for hydrolyzing dietary lipids in the gastrointestinal tract, participating in the entire process of fat digestion, absorption, and utilization. Inhibiting lipase activity effectively reduces lipid digestion and absorption, thereby lowering blood lipid levels. Lipase inhibition represents an effective therapeutic strategy for hyperlipidemia, obesity, and non-alcoholic fatty liver disease. Triterpenoid saponins have demonstrated lipase inhibitory activity and represent promising compounds for treating obesity and related metabolic disorders.

As a commonly used medicinal material, Panax japonicus grows slowly with a long maturation period, and wild populations are currently endangered. The aerial parts are typically discarded as non-medicinal waste, resulting in resource inefficiency. Previous investigations by our research group identified the primary chemical constituents of Panax japonicus leaves as triterpenoid compounds, including 20(22)E,24-dammaradiene-3β,6α,12β-triol, ginsenosides Rd, Rb1, Rb2, Rb3, Rc, Rs2, Rl, Rs1, notoginsenoside Fe, Rd2, Gypenoside IX, 20(21),24-dammaradiene-3β,6α,12β-triol, 20(22)Z,24-dammaradiene-3β,6α,12β-triol, zhuzishenoside Z, and 5,7-dihydroxy-8-methoxyflavone. Despite these findings, the lipase inhibition mechanism and hypolipidemic effects of saponins from Panax japonicus leaves remain unreported. This study therefore investigated: (1) the main chemical constituents of the saponin fraction, (2) its lipase inhibitory activity, (3) the inhibition type, (4) which residues contribute to enhanced lipase inhibition, and (5) whether the fraction exhibits hypolipidemic effects.

Materials and Methods

Equipment and Reagents The following equipment was used: analytical balance (EX125ZH, Ohaus Instruments), multi-mode microplate reader (Synergy™ H1, BioTek), high-performance liquid chromatograph (Waters e2695, Waters Corporation), pipettes (Research Plus series, Eppendorf), low-speed centrifuge (TDL-50B, Shanghai Anting Scientific Instrument Factory), and high-speed centrifuge (TG16-WS, Xiangyi Centrifuge Instrument Co.).

Reagents included: orlistat capsules (batch No. 190204, Chongqing Huasen Pharmaceutical), *Candida rugosa* lipase (batch No. S25740), 4-nitrophenyl palmitate (4-NPP, batch No. EC250112), sodium citrate (batch No. 75164) from Sigma-Aldrich; HPLC-grade acetonitrile (AH015, Honeywell); DMSO (batch No. D6370) from Beijing Biotopped Technology; D101 macroporous resin from Nankai University Chemical Plant; 20(S)-ginsenoside Rg2 (No. B21058), 20(R)-ginsenoside Rg2 (No. B21727), ginsenoside Rb2 (No. B21051), ginsenoside

Rb3 (No. B21052), and ginsenoside Rd (No. B21054) from Shanghai Yuanye Biotechnology; ginsenoside Rh2 (No. 111748) from the National Institute for Food and Drug Control; and 50 mM Tris-HCl (pH 7.8, batch No. BB0512) from Shaanxi Zhonghuihecai Biomedical Technology.

Experimental Animals Sixty SPF-grade SD mice (18–22 g) were purchased from Chengdu Dossy Experimental Animals Co., Ltd. (License No. SCXK (Chuan) 2020-030) and acclimated for 5 days.

2.1 HPLC Analysis of Chemical Constituents 2.1.1 Chromatographic Conditions
Column: Agela Technologies Innoval ODS-2 (4.6 mm × 250 mm, 5 m); mobile phase: water (A)–acetonitrile (B) with gradient elution: 0–10 min, 10%$→28→28→31→31→36→39→60^{-1}$.

2.1.2 Preparation of Test Sample Solution
The herbal material was authenticated by Senior Experimentalist Wang Jitao of Shaanxi University of Chinese Medicine as the dried leaves of *Panax japonicus* var. *major*. Following published methods, dried Panax japonicus leaves were extracted. Approximately 0.05 g of the 70% ethanol eluate powder was placed in a 50 mL stoppered conical flask, precisely weighed, and 50 mL methanol was added. After ultrasonic extraction for 10 minutes, cooling, and reweighing, methanol was added to compensate for weight loss. The solution was filtered, and the filtrate was passed through a 0.22 m microporous membrane to obtain the test solution.

2.1.3 Preparation of Reference Standard Solutions
Reference standards of 20(S)-ginsenoside Rg2, 20(R)-ginsenoside Rg2, ginsenoside Rb2, ginsenoside Rb3, ginsenoside Rd, and ginsenoside Rh2 were precisely weighed and dissolved in methanol to prepare solutions at concentrations of 0.10, 0.25, 0.10, 0.25, 0.11, and 0.50 $mg \cdot mL^{-1}$, respectively.

2.2 Lipase Activity Assays 2.2.1 Effects of Different Saponins on Lipase Activity
Lipase inhibitory activity was measured using a modified reported method. Lipase Tris-HCl solution was prepared at 280 $U \cdot mL^{-1}$, 4-NPP DMSO solution at 750 $mol \cdot mL^{-1}$, and orlistat at 250 $mol \cdot mL^{-1}$. The Panax japonicus leaf saponin fraction was dissolved in DMSO at 2.52 $mg \cdot mL^{-1}$, while 20(S)-ginsenoside Rg2, 20(R)-ginsenoside Rg2, ginsenoside Rb2, ginsenoside Rb3, ginsenoside Rd, and ginsenoside Rh2 were prepared in DMSO at 500 $mol \cdot mL^{-1}$ and diluted to various concentrations for subsequent experiments.

In a 96-well plate, 25 L of each saponin sample (final concentrations: saponin fraction 0, 0.625, 6.25, 62.5, 125 $mol \cdot mL^{-1}$; ginsenoside Rb3 0, 5, 12.5, 125, 250 $mol \cdot mL^{-1}$; 20(S)-ginsenoside Rg2 0, 1, 2.5, 5, 12.5 $mol \cdot mL^{-1}$; 20(R)-ginsenoside Rg2 0, 25, 50, 125, 250 $mol \cdot mL^{-1}$; ginsenosides Rb2, Rd, Rh2 0, 12.5, 25, 125, 250 $mol \cdot mL^{-1}$) was incubated with 45 L pancreatic lipase

at 37°C for 30 minutes. Subsequently, 90 L 4-NPP (final concentration 750 mol · mL^{-1}) was added and reacted at 37°C for 20 minutes. The reaction was terminated with sodium citrate, and absorbance was measured at 405 nm.

Pancreatic lipase activity was calculated as:
Lipase activity = (A_{sample} - A_{{{sample}}*{{control}}}) / (*A*{blank} - A_{{{blank}}*{{control}}}) × *100%*
where A{sample} is absorbance with sample and active enzyme; A_{{{sample}}*{{control}}} *is absorbance with sample and inactive enzyme; A*{blank} is absorbance with active enzyme and DMSO; and A_{{{blank}}_{{control}}} is absorbance with inactive enzyme and DMSO. All reactions contained 4-NPP.

2.2.2 Inhibition Mechanism of Different Saponins on Lipase Activity
Following the sample and 4-NPP concentrations described in section 2.2.1 with slight modifications, lipase concentration was varied (final concentrations 0, 70, 140, 280, 560 U · mL^{-1}) to measure absorbance from 4-NPP hydrolysis by different saponin concentrations. After incubating 25 L of various saponin samples with 45 L pancreatic lipase at 37°C for 30 minutes, 90 L 4-NPP (final concentration 750 mol · mL^{-1}) was added and absorbance was measured at 405 nm. Relative enzyme activity was calculated as:
Relative enzyme activity = (A_2 - A_1) / (A_4 - A_3) × 100%
where A_1 and A_2 represent initial and final absorbance with saponins, lipase, and 4-NPP; A_3 and A_4 represent initial and final absorbance with lipase and 4-NPP only.

2.2.3 Inhibition Type and Inhibition Constants of Different Saponins on Lipase Activity
Using the method described in section 2.2.3, lipase concentration was fixed while 4-NPP concentration was varied (final concentrations 0.375, 0.75, 1.5, 3 mmol · mL^{-1}) to measure absorbance from lipase-catalyzed 4-NPP hydrolysis in the presence of different saponin concentrations.

2.3 Molecular Docking Databases and Software Software used included ChemBioDraw3D, AutoDockTools 1.5.6, PyMOL, CADD 1.5.6, and Vision 1.5.6. Two-dimensional structures of compounds were downloaded from the PubChem database, and target protein crystal structures were obtained from the PDB database. PyMOL was used for pretreatment of target proteins (water removal, hydrogen addition). AutoDock Tools 1.5.6 was employed for molecular docking of compounds with target proteins. The target protein and binding site was the A-BOG site of ILPB protein.

2.4 Animal Experiments 2.4.1 Grouping and Administration
Mice were randomly divided into six groups (n=10 each): blank control, hyperlipidemia model, orlistat, and high-, medium-, and low-dose saponin fraction groups. The blank group received standard chow, while all other groups received high-fat diet to establish hyperlipidemia models.

The high-fat diet composition was: 15% lard, 5% egg yolk, 20% sugar, 0.5% salt, and 0.5% sesame oil. After 35 days of high-fat feeding, administration began. The blank and model groups received saline, the orlistat group received 46.8 mg·kg^{-1} orlistat, and the saponin groups received 117.0, 58.5, and 29.3 mg·kg^{-1} saponin fraction (high, medium, low doses, respectively), equivalent to a 70 kg adult consuming 20 g extract daily. All treatments were administered once daily by gavage for 3 weeks. Body weight was measured after final administration. The blank and model groups continued receiving standard chow and high-fat diet, respectively, throughout the treatment period, with ad libitum access to food and water.

2.4.2 Sample Collection and Processing
After final administration, all mice were fasted (water allowed) for 16 hours before orbital blood collection. Whole blood was allowed to clot at 4°C, then centrifuged at 3000 rpm for 15 minutes to separate serum, which was aliquoted by group and stored at -80°C.

2.4.3 Biochemical Index Determination
Serum total cholesterol (TC) and triglyceride (TG) levels were measured using commercial kits according to manufacturer instructions.

2.5 Statistical Analysis All statistical analyses were performed using GraphPad Prism 8.0.1. Data are expressed as mean ± standard deviation (x ± s). Comparisons between two groups used t-tests, while multiple group comparisons employed one-way ANOVA.

Results

3.1 Chromatographic Data The HPLC chromatograms of the saponin fraction and mixed reference standards are shown in [Figure 1: see original paper]. The main constituents were identified as 20(S)-ginsenoside Rg2, 20(R)-ginsenoside Rg2, ginsenoside Rb2, ginsenoside Rb3, ginsenoside Rd, and ginsenoside Rh2.

3.2 Lipase Activity Assay Results Lipase inhibitory activities of various saponins are presented in Table 3 and Figure 3 [Figure 3: see original paper]. The IC_{50} values were 0.14, 28.00, 31.00, 18.00, 8.73, 2.30, and 60.76 mol·L^{-1} for the saponin fraction, ginsenoside Rb2, ginsenoside Rd, ginsenoside Rh2, 20(S)-ginsenoside Rg2, 20(R)-ginsenoside Rg2, and ginsenoside Rb3, respectively.

As shown in Figure 2 [Figure 2: see original paper], absorbance in reaction systems containing the saponin fraction, 20(R)-ginsenoside Rg2, and ginsenoside Rb3 increased gradually over time, with curves passing through the origin, indicating no lag phase. At equivalent time points, increasing saponin concentrations progressively reduced curve slopes, demonstrating decreased lipase-catalyzed 4-NPP hydrolysis rates. During 0–7.5 minutes, the A_{405} nm-time

curves were approximately linear; beyond this period, curves flattened and slopes decreased, indicating reduced reaction velocity. Therefore, the reaction velocity at 7.5 minutes was taken as the initial velocity.

3.3 Inhibition Mechanism of Different Saponins on Lipase Activity Following the method in section 2.2.2, reaction mixtures were incubated at 37°C in a microplate reader with absorbance measured every 20 seconds for 7.5 minutes. The slope of the linear equation fitted to 0–7.5 minute absorbance-time data represented enzyme activity. Plotting relative enzyme activity against enzyme concentration revealed the inhibition mechanism. A series of lines passing through the origin indicated reversible inhibition, while parallel lines indicated irreversible inhibition.

Figure 4 [Figure 4: see original paper] shows the relationships between enzyme concentration, enzyme activity, and saponin concentration. Linear plots passing through the origin were obtained, with slopes decreasing as saponin fraction, 20(R)-ginsenoside Rg2, and ginsenoside Rb3 concentrations increased. This demonstrates that these saponins inhibit lipase activity rather than reducing effective enzyme quantity, confirming reversible inhibition.

3.4 Inhibition Type and Inhibition Constants Using results from section 2.2.3, reaction velocities were calculated as $V = \Delta A_{405}/t$. Lineweaver-Burk plots of 1/V versus 1/[S] were constructed to determine inhibition type and constants.

Figures 5 [Figure 5: see original paper], 6 [Figure 6: see original paper], and 7 [Figure 7: see original paper] present the inhibition types and constants. The Lineweaver-Burk plots for all three samples intersected at a single point on the x-axis, with Km values remaining constant while Vmax decreased with increasing inhibitor concentration, characteristic of non-competitive inhibition. Inhibitor binding constants (KI) were 0.27, 2.53, and 0.17, respectively (Figure 6), while inhibition constants (KIS) were 21.46, 28.00, and 3.80, respectively (Figure 7). The Km values were 1.07, 0.83, and 8.64, respectively.

3.5 Molecular Docking Results Molecular docking was performed to investigate ligand-protein ILPB interactions. 20(R)-ginsenoside Rg2 formed hydrogen bonds with ARG38A, LEU41A, ASP331B, SER333B, ARG337B, and LYS367B, and hydrophobic interactions with HIS30A, ALA40A, and ILE248B (Figure 8A). 20(S)-ginsenoside Rg2 showed similar binding patterns (Figure 8B), with its glycosyl groups forming simultaneous hydrogen bonds with SER333B. Ginsenoside Rb2 formed hydrogen bonds with GLU13A, GLN29A, ASP31A, LEU36A, SER35A, ARG13A, CYS39A, ASP331B, ARG337B, and LYS367B, hydrophobic interactions with GLU13A, and π-cation interactions with LYS367B, embedding in the ILPB active pocket (Figure 8C). Ginsenoside Rb3 formed hydrogen bonds with ASP31A, LEU36A, LEU41A, LYS42A, and CYS61A, and hydrophobic interactions with GLU13A, ARG38A, and ALA40A (Figure 8D). Ginsenoside Rd formed hydrogen bonds with ASP31A,

ARG38A, ALA40A, ALA43A, and ARG44A, and hydrophobic interactions with GLU13A, ALA40A, LEU41A, and ALA43A (Figure 8E). Ginsenoside Rh2 formed hydrogen bonds with GLN29A, LYS42A, GLU48A, and CYS61A, and hydrophobic interactions with GLU13A, ALA40A, LEU41A, ILE248B, and ALA332B (Figure 8F). Orlistat formed hydrogen bonds with ARG337B, ALA332B, and ASP331B, and hydrophobic interactions with ILE248B and LEU41A (Figure 8G).

3.6 Cholesterol and Triglyceride Measurement Results Effects of the saponin fraction on serum TC and TG are shown in Figure 9 [Figure 9: see original paper]. Hyperlipidemia model mice exhibited significantly higher serum TG and TC levels than the blank group ($P < 0.01$), confirming successful model establishment. Low-, medium-, and high-dose saponin groups showed significantly reduced serum TG and TC compared to the model group ($P < 0.01$). The high-dose group's TG-lowering effect was comparable to orlistat, while its TC-lowering effect was superior.

Discussion and Conclusion

Historically, inadequate understanding of rational traditional Chinese medicine resource utilization has led to overexploitation and endangerment of medicinal plants. To protect and develop Panax japonicus resources, systematic chemical and pharmacological investigation of the entire plant is essential to maximize resource utilization. While the underground parts are traditionally used medicinally, the aerial parts' therapeutic value remains underexplored and are typically discarded during harvest, representing resource waste. As a perennial herb, the aerial parts naturally wither annually without utilization.

Previous studies identified triterpenoid saponins as the main constituents of Panax japonicus leaves, and triterpenoid saponins possess lipase inhibitory activity. This study employed HPLC to identify the main saponin monomers and evaluated their in vitro and in vivo lipase inhibitory effects to provide a basis for rational resource development.

Dietary fats are hydrolyzed by pancreatic lipase in the small intestine. Medium-chain triglycerides are hydrolyzed to free fatty acids and glycerol, with medium-chain fatty acids transported to the liver via portal circulation bound to albumin. Long-chain triglycerides are hydrolyzed to free fatty acids, monoacylglycerols, and glycerol, forming chylomicrons that enter the lymphatic system and peripheral tissues for oxidation or re-esterification. Lipase hydrolyzes 50–70% of dietary fat, representing a key target for obesity treatment. Inhibitors reduce dietary fat hydrolysis and absorption, improving metabolic diseases.

Orlistat, the only FDA-approved pancreatic lipase inhibitor, slows gastrointestinal fat hydrolysis, reducing dietary fat absorption by 25–30% and controlling

body weight. *Candida rugosa* lipase and 4-NPP are standard tools for evaluating lipase inhibition. Our results demonstrate that the Panax japonicus leaf saponin fraction and 20(R)-ginsenoside Rg2 exhibit potent lipase inhibition, suggesting potential as lipase inhibitors.

Kinetic analysis revealed that the saponin fraction, 20(R)-ginsenoside Rg2, and ginsenoside Rb3 produce reversible, non-competitive inhibition, binding to both free enzyme and enzyme-substrate complexes. Molecular docking indicated that binding to ARG337B, ASP331B, and ILE248B residues may enhance inhibitory activity. Animal experiments confirmed that the saponin fraction significantly reduced serum TG and TC in hyperlipidemic mice, suggesting lipase inhibition as the mechanism for its hypolipidemic effect.

Traditional Chinese medicines contain multiple active components that often act synergistically. The saponin fraction showed stronger lipase inhibition than individual monomers, possibly due to synergistic interactions among components or the presence of undiscovered high-activity compounds. Future studies will continue isolating and identifying chemical constituents to further elucidate the material basis and biological activities of Panax japonicus leaves.

References

BENET LZ, BROCCATELLI F, OPREA TI, 2011. BDDCS applied to over 900 drugs[J]. AAPS J, 13(4): 519-547.

BUHMAN KK, SMITH SJ, STONE SJ, et al., 2002. DGAT1 is not essential for intestinal triacylglycerol absorption or chylomicron synthesis[J]. J Biol Chem, 277(28): 25474-25479.

CHEN J, WEI JT, PEI D, 2021. Study on the inhibitory effect of oleuropein on tyrosinase[J]. Nat Prod Res Dev, 33(12): 1998-2003.

DE LA GARZA AL, MILAGRO FI, BOQUE N, et al., 2011. Natural inhibitors of pancreatic lipase as new players in obesity treatment[J]. Planta Med, 77(8): 773-785.

DOOLITTLE MH and BEN-ZEEV O, 1999. Immunodetection of lipoprotein lipase: antibody production, immunoprecipitation, and western blotting techniques[J]. Methods Mol Biol, 109: 215-237.

ERCAN P and EL SN, 2016. Inhibitory effects of chickpea and Tribulus terrestris on lipase, α-amylase and α-glucosidase[J]. Food Chem, 205: 163-169.

FENG HY, 2019. Rapid identification, separation and identification of active components inhibiting lipase in Ilex cornuta leaves[D]. Shanghai: Shanghai University of Traditional Chinese Medicine.

HAN LK, ZHENG Y-N, YOSHIKAWA M, et al., 2005. Anti-obesity effects of

chikusetsusaponins isolated from Panax japonicus rhizomes[J]. BMC Complement Altern Med, 5(1): 9.

HE R, LIU Q, LIU YH, et al., 2014. Study on chemical constituents of P. japonicus leaves[J]. Chin J Chin Mat Med, 39(9): 1635-1638.

HOU CB, 2016. Evaluation of lipase inhibition and intestinal absorption in lotus leaves[D]. Beijing: Beijing University of Chinese Medicine.

HUANG GL, WANG YN, MA JJ, et al., 2021. Inhibition of loquat flower polyphenols on lipase[J]. Jiangsu J Agr Sci, 37(1): 5.

JAEGER KE and REETZ MT, 1998. Microbial lipases form versatile tools for biotechnology[J]. Trends Biotechnol, 16(9): 396-403.

JIANG HF, WANG YQ, LIU CG, 2007. Comparison and improvement of three lipase activity determination methods[J]. Chem Bioeng, 24(8): 4.

KANG JG and PARK CY, 2012. Anti-obesity drugs: a review about their effects and safety[J]. Diabetes Metab J, 36(1): 13-25.

LIU R, ZHENG Y, CAI Z, et al., 2017. Saponins and Flavonoids from Adzuki Bean (Vigna angularis L.) Ameliorate High-Fat Diet-Induced Obesity in ICR Mice[J]. Front Pharmacol, 8: 687.

LIU TT, HE XR, XU RX, et al., 2018. Inhibitory mechanism and molecular analysis of furoic acid and oxalic acid on lipase[J]. Int J Biol Macromol, 120: 1925-1934.

LIAO JL, FANG TL, FAN YL, 2022. Inhibitory effect of flavonoids from Lycium barbarum leaves on pancreatic lipase activity[J]. Chin Inst Food Sci Technol, 22(5): 43-53.

LU WC, 2016. Identification of Renseng leaf and Seng leaf[J]. Chin Med Mat, 39(1): 213-215.

MIAO ZG, 2009. Study on the difference of fat metabolism and digestive function between Jinhua and Landrace[D]. Hangzhou: Zhejiang University.

National Pharmacopoeia Committee, 2020. Chinese Pharmacopoeia[S]. Beijing: China Pharmaceutical Science and Technology Press: 283-284.

NAVARRO DEL HIERRO J, CASADO-HIDALGO G, REGLERO G, et al., 2020. The hydrolysis of saponin-rich extracts from fenugreek and quinoa improves their pancreatic lipase inhibitory activity and hypocholesterolemic effect[J]. Food Chem, 338: 128113.

OU HY, YE XP, JI YC, et al., 2021. Based on molecular docking technology to explore the potential material basis and medication rule of traditional Chinese medicine inhibiting human pancreatic lipase activity[J]. Mod Trad Chin Med Mat Med-World Sci Tech, 23(11): 4211-4221.

QIU Y, 2020. Extraction, purification and physiological activity of total saponins from Xanthoceras sorbifolia leaves[D]. Changchun: Jilin Agricultural University.

SIDDIQI SA, MAHAN J, SIDDIQI S, et al., 2006. Vesicle-associated membrane protein 7 is expressed in intestinal ER[J]. J Cell Sci, 119(Pt 5): 943-950.

SONG XM, 2011. Research and application of Taibai Qiyao[M]. Beijing: People's Medical Publishing House: 101-111.

TAKEUCHI H, KASAI M, TAGUCHI N, et al., 2002. Effect of triacylglycerols containing medium- and long-chain fatty acids on serum triacylglycerol levels and body fat in college athletes[J]. J Nutr Sci Vitaminol (Tokyo), 48(2): 109-114.

WANG YF, ZHANG ZX, HE RJ, et al., 2020. Study on the chemical constituents and pancreatic lipase inhibitory activity of the aerial parts of Polygonatum sibiricum[J]. Nat Prod Res Dev, 32(11): 1811-1817.

WANG SW, 2008. 'Molecular Chinese Materia Medica' connotation and modern Chinese medicine[J]. Asia-Pacific Trad Med, 4(3): 9-12.

WANG Z, WANG P, HUANG J, 2013. Application progress of molecular simulation technology in the study of lipase properties and catalytic mechanism[J]. Chem Ind Eng, 32(10): 6.

XI JY, ZHANG DX, NIE HF, et al., 2022. Teaching practice of molecular docking technology in pharmaceutical chemistry experiment[J]. Res Exp Lab, 41(3): 231-234.

XU H, JIANG Y, XU HY, et al., 2007. Study on the extraction technology of total saponins from the leaves of Hanzhong Ginseng[J]. Mod Chin Med, 27(3): 78-79.

YAO XL, NIE K, CHEN Y, et al., 2018. Effect of composite interface on fat digestion in food emulsion[J]. Food Sci, 39(2): 1-7.

YANG Y, ZHANG X, JIANG S, et al., 2019. Research progress on saponins and their pharmacological activities in Panacis Majoris Rhizoma[J]. Sci Tech Food Ind, 40(2): 347-356.

YOSHIZUMI K, HIRANO K, ANDO H, et al., 2006. Lupane-type saponins from leaves of Acanthopanax sessiliflorus and their inhibitory activity on pancreatic lipase[J]. J Agric Food Chem, 54(2): 335-341.

YUN JW, 2010. Possible anti-obesity therapeutics from nature—a review[J]. Phytochemistry, 71(14-15): 1625-1641.

ZHANG HW, JIANG Y, HUANG WL, et al., 2020. A new triterpenoid saponin[J]. Chin Trad Herb Drugs, 51(1): 26-30.

ZHAO DD, SONG XM, TANG HF, et al., 2013. Study on saponins from the leaves of Panacis Majoris Rhizoma[J]. Cent South Pharm, 11(2): 85-88.

ZHAO XM, 1963. Compendium of materia medica[M]. Beijing: People's Medical Publishing House: 61.

ZHI J, MULLIGAN TE, HAUPTMAN JB, 1999. Long-term systemic exposure of orlistat, a lipase inhibitor, and its metabolites in obese patients[J]. J Clin Pharmacol, 39(1): 41-46.

Note: Figure translations are in progress. See original paper for figures.