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In Vitro and In Silico Evaluation of Pancreatic Lipase Inhibition by *Avicennia marina* and *Bruguiera gymnorrhiza* Fruit Flour Extracts

Evaluasi In Vitro dan In Silico Inhibisi Lipase Pankreas oleh Ekstrak Tepung Buah *Avicennia marina* dan *Bruguiera gymnorrhiza*

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ABSTRACT

Indonesia is rich in mangrove species, including *Avicennia marina* (brayo) and *Bruguiera gymnorrhiza* (lindur), whose fruits contain bioactive metabolites with potential anti-obesity activity. This study evaluated pancreatic lipase inhibition by brayo and lindur fruit flour extracts (raw and boiled) using in vitro and in silico approaches. Extracts were prepared by remaceration with 70% ethanol. Lipase inhibition was measured using a multimode microplate reader, while metabolites were identified by LC-HRMS and evaluated by molecular docking. Raw brayo showed the highest inhibition (84.29 ± 4.24%), followed by boiled brayo (83.01 ± 4.59%), raw lindur (75.24 ± 3.02%), and boiled lindur (73.88 ± 4.00%). Docking indicated strong binding of luteolin (−8.23 kcal/mol), 9-oxo-10(E),12(E)-octadecadienoic acid (−6.75 kcal/mol), and methyl eleostearate (−6.59 kcal/mol) to pancreatic lipase. These findings support mangrove fruit flour as a natural source of lipase inhibitors for obesity management.

Kata kunci:
Antiobesitas,
Ekstrak buah mangrove
In silico
In vitro
Lipase pankreas

ABSTRAK

Indonesia memiliki keanekaragaman mangrove yang tinggi, termasuk *Avicennia marina* (brayo) dan *Bruguiera gymnorrhiza* (lindur), yang buahnya mengandung metabolit sekunder bioaktif dengan potensi antiobesitas. Penelitian ini mengevaluasi aktivitas penghambatan lipase pankreas dari ekstrak tepung buah brayo dan lindur pada kondisi mentah dan rebus menggunakan pendekatan in vitro dan in silico. Ekstraksi dilakukan dengan metode remaserasi menggunakan etanol 70%. Aktivitas inhibisi lipase diukur menggunakan microplate reader, sedangkan identifikasi senyawa dilakukan dengan LC-HRMS dan dianalisis menggunakan molecular docking. Ekstrak brayo mentah menunjukkan aktivitas penghambatan tertinggi (84,29 ± 4,24%), diikuti brayo rebus (83,01 ± 4,59%), lindur mentah (75,24 ± 3,02%), dan lindur rebus (73,88 ± 4,00%). Analisis docking menunjukkan afinitas ikatan kuat terhadap lipase pankreas untuk luteolin (−8,23 kkal/mol), asam 9-oxo-10(E),12(E)-oktadekadienoat (−6,75 kkal/mol), dan metil eleostearat (−6,59 kkal/mol).

Hasil ini menunjukkan potensi ekstrak tepung buah mangrove sebagai sumber inhibitor lipase alami untuk pengelolaan obesitas.

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1. INTRODUCTION

According to the World Health Organization (WHO), the prevalence of overweight and obesity has increased substantially worldwide. In 2022, approximately 2.5 billion adults were classified as overweight and 890 million as obese (World Health Organization [WHO], 2024). Obesity is a major risk factor for several metabolic disorders, including type 2 diabetes mellitus, dyslipidemia, hypertension, and cardiovascular diseases. Physiologically, obesity is associated with an imbalance between energy intake and expenditure, particularly through the digestion and absorption of dietary lipids in the gastrointestinal tract. Pancreatic lipase plays a key role in lipid metabolism by hydrolyzing dietary triglycerides into absorbable free fatty acids and monoglycerides; therefore, inhibition of this enzyme has become an important strategy for controlling fat absorption and managing obesity (Birari & Bhutani, 2007).

Orlistat is a well-known synthetic pancreatic lipase inhibitor that has been clinically used to promote weight loss by reducing dietary fat absorption by approximately 30% (Padwal & Majumdar, 2007). However, its use is frequently associated with gastrointestinal side effects, highlighting the need for safer natural alternatives (Henness & Perry, 2006). Mangrove ecosystems represent an important source of coastal biodiversity and contain a wide range of secondary metabolites. Mangrove fruits have been reported to contain bioactive compounds such as flavonoids, phenolics, tannins, saponins, and triterpenoids with diverse biological activities, including antioxidant, antidiabetic, and antihyperlipidemic effects (Bandaranayake, 2002; Kathiresan & Bingham, 2001; Prastiyanto & Wardoyo, 2025). Processing mangrove fruits into flour may enhance material stability, improve storage efficiency, and increase their potential use as functional food ingredients or phytopharmaceutical raw materials.

Previous studies have demonstrated that phenolic and flavonoid compounds can inhibit pancreatic lipase through hydrogen bonding and hydrophobic interactions with amino acid residues in the enzyme's active site (Martínez-González et al., 2017). Plant-derived polyphenols have also been reported to function as natural lipase inhibitors, thereby reducing the absorption of dietary fats (Birari & Bhutani, 2007). Furthermore, flavonoid-rich extracts have shown significant lipase inhibitory activity that correlates with their total phenolic content (McDougall et al., 2008). Various plant sources, including green tea, grape seed, and several tropical fruits, have been reported to exhibit substantial in vitro pancreatic lipase inhibition (Buchholz & Melzig, 2015; Nakai et al., 2005). However, studies investigating the anti-obesity potential of mangrove fruit flour extracts, particularly using an integrated approach combining in vitro enzymatic assays with in silico molecular docking analysis, remain limited.

Therefore, this study aimed to evaluate the pancreatic lipase inhibitory activity of *Avicennia marina* and *Bruguiera gymnorrhiza* fruit flour extracts using integrated in vitro and in silico approaches. The in vitro assay was employed to measure lipase inhibition directly, whereas molecular docking analysis was used to predict the binding affinity and interaction mechanisms of the identified bioactive compounds with the target enzyme (Ferreira et al., 2015).

2. METHODS

2.1. Materials

Mangrove fruit flour samples were obtained from the "Mbak Jamat" product distributed by CV KeMANGI, Indonesia. Brayo fruit flour (*Avicennia marina*) was collected from Kartika Jaya Beach, while lindur fruit flour (*Bruguiera gymnorrhiza*) was obtained from Mangunharjo Beach, Central Java, Indonesia. The extraction solvent used for remaceration was 70% ethanol (Merck, Germany). Reagents used for the pancreatic lipase inhibition assay included crude porcine pancreatic lipase (PPL) (Sigma-Aldrich, USA), *p*-nitrophenyl butyrate (pNPB) (Sigma-Aldrich, USA), phosphate buffer (pH 7.4), dimethyl sulfoxide (DMSO) (Merck, Germany), and orlistat as the positive control (Sigma-Aldrich, USA).

2.2. Sample Preparation and Extraction

Fruit flour samples were extracted using the remaceration method with 70% ethanol at a ratio of 1:5 (w/v) for 3 × 24 h at room temperature. The mixture was filtered using Whatman filter paper, and the filtrate was concentrated using a rotary evaporator at 45 °C. The concentrated extract was subsequently evaporated in a water bath to obtain a viscous crude extract (Rahma et al., 2023).

2.3. Pancreatic Lipase Inhibitory Activity

Pancreatic lipase inhibitory activity was evaluated in vitro using a 96-well microplate assay. The enzyme stock solution was prepared by dissolving 1 mg of porcine pancreatic lipase in 1 mL of phosphate buffer to obtain a final concentration of approximately 0.1 mg/mL. The extract solution was prepared at a concentration of 500 µg/mL.

The substrate *p*-nitrophenyl butyrate (pNPB) was dissolved in 1% DMSO and subsequently diluted with 50 mM phosphate buffer (pH 7.2) to obtain a final concentration of 2.5 mM. The reaction

mixture consisted of enzyme solution, extract solution, and substrate solution, which were incubated at 37 °C for 10 min. Each experiment was performed in triplicate.

Orlistat was used as the positive control, while 1% DMSO without inhibitor served as the negative control. One unit of enzyme activity was defined as the amount of enzyme required to release 1 μmol of *p*-nitrophenol per minute under the assay conditions at 37 °C. Lipase inhibition activity was expressed as the percentage reduction in enzyme activity after incubation with the test samples.

$$\%\ \text{Lipase Inhibitory Activity} = 100 - \left(\frac{B-b}{A-a} \times 100\right)$$

where A is the absorbance of the negative control (enzyme + substrate), a is the negative control blank (without enzyme and substrate), B is the absorbance of the sample (enzyme + substrate), and b is the sample blank (without enzyme and substrate) (Liu et al., 2020; Maharani et al., 2025).

2.4. Structural Elucidation Using LC-HRMS

The extract exhibiting the highest lipase inhibitory activity was further analyzed using liquid chromatography–high-resolution mass spectrometry (LC-HRMS) to identify the constituent compounds. Raw data from the total ion chromatogram (TIC) were processed to determine the metabolite profile of the crude brayo extract.

Chromatographic separation was performed using a Thermo Scientific™ Acclaim™ PepMap™ 100 C18 analytical column (150 mm × 1 mm ID, 3 μm particle size). Mass spectrometry analysis was conducted using full MS/dd-MS^2 acquisition in both positive and negative ionization modes. The sheath gas flow rate was set at 15 AU and the auxiliary gas flow rate at 5 AU. The capillary temperature was maintained at 300 °C with a spray voltage of 4.00 kV. The scanning range was 150–2000 m/z with a resolution of 140,000 for full MS and 17,500 for dd-MS^2.

Compound annotation and data processing were performed using Compound Discoverer® software (Thermo Scientific, USA). Detected compounds were filtered based on relative abundance and spectral matching scores (>98%) against the mzCloud database (Harahap et al., 2025).

2.5. In Silico Molecular Docking

The interactions between identified compounds and pancreatic lipase were evaluated using molecular docking analysis. The crystal structure of pancreatic lipase (PDB ID: 5ZUN) was retrieved from the Protein Data Bank (PDB).

The receptor structure was prepared by removing co-crystallized ligands and water molecules using Biovia Discovery Studio 2021. Polar hydrogen atoms and Kollman charges were subsequently added using AutoDock Tools.

Ligand structures were drawn in two-dimensional form using ChemDraw Professional 15.0. Geometry optimization and energy minimization were performed using the MM2 force field in Chem3D.

The grid box was defined to cover the active binding site residues of the pancreatic lipase enzyme. The grid box coordinates were set at (8.980, 25.120, 50.590) with dimensions of 40 × 40 × 40 Å (Pandey et al., 2019; Ijoma et al., 2024)

2.6. ADMET Prediction

The pharmacokinetic properties and toxicity profiles of the selected compounds were predicted using the pkCSM web server. This platform was used to estimate absorption, distribution, metabolism, excretion, and toxicity (ADMET) parameters of the identified compounds (Rahardhian et al., 2022).

2.7. Data Analysis

All data were expressed as mean ± standard deviation (SD) obtained from triplicate experiments. Statistical analysis was performed using one-way analysis of variance (ANOVA) to determine significant differences among treatment groups. The Brown–Forsythe test was applied to evaluate the homogeneity of variance. A p-value < 0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1. Extraction Yield of Mangrove Fruit Flour Extracts

The extraction yield of mangrove fruit flour extracts varied depending on both species and processing treatment (**Figure 1**). The yields of raw brayo, boiled brayo, raw lindur, and boiled lindur extracts were 63.29 ± 2.57%, 38.42 ± 2.26%, 22.05 ± 1.71%, and 58.19 ± 2.52%, respectively. Statistical analysis showed that the extraction yields differed significantly among treatments ($p < 0.05$). Raw brayo and boiled lindur extracts showed significantly higher yields compared with boiled brayo and raw lindur samples, while raw lindur exhibited the lowest extraction yield. These differences suggest that both mangrove species and the boiling treatment influenced extraction efficiency and the amount of soluble compounds obtained (Harborne, 1998; Sarker & Nahar, 2012). The relatively high yield observed in raw brayo extract may be associated with the presence of abundant water-soluble metabolites such as polysaccharides, simple sugars, and phenolic compounds that remain intact before thermal processing. Boiling treatment can alter plant cell wall structures and may promote the degradation or transformation of certain compounds into volatile or insoluble forms, thereby reducing the extractable fraction in some plant materials (Dai & Mumper, 2010; Wu et al., 2024). In contrast, lindur fruit showed a higher extraction yield after boiling, which may be related to tissue softening and cell wall disruption that facilitate the release of soluble compounds such as hydrolyzed carbohydrates and phenolics (Zhang et al., 2022; Chen et al., 2022). The lower yield observed in raw lindur samples may also be related to the presence of dense tissue structure and high crude fiber content that limit solvent penetration into the cellular matrix (Azmir et al., 2013).

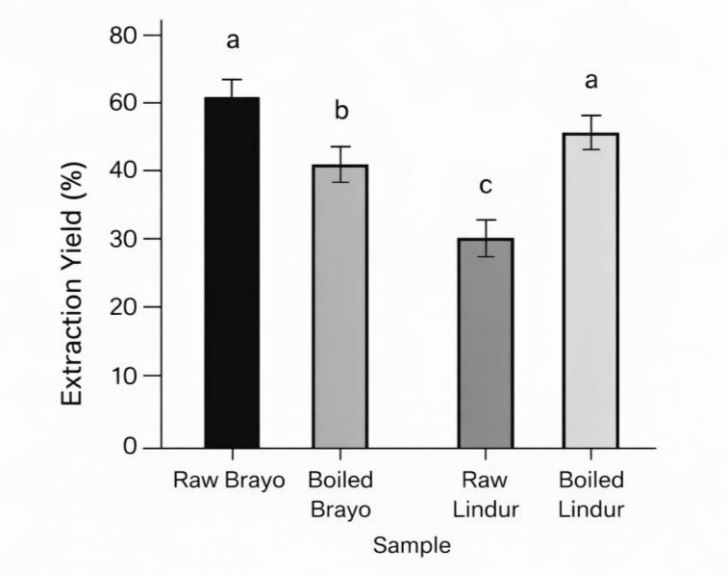


Figure 1. Extraction yield (%) of *Avicennia marina* (brayo) and *Bruguiera gymnorrhiza* (lindur) fruit flour extracts under raw and boiled conditions. Data are presented as mean ± SD (n = 3). Different letters above the bars indicate significant differences among treatments (one-way ANOVA followed by the Brown–Forsythe test, $p < 0.05$).

3.2. Pancreatic Lipase Inhibitory Activity

The pancreatic lipase inhibitory activity of mangrove fruit extracts is presented in **Figure 2**. Among the tested samples, raw brayo extract showed the highest inhibition (84.29 ± 4.24%), followed by boiled brayo (83.01 ± 4.59%), raw lindur (75.24 ± 3.02%), and boiled lindur (73.88 ± 4.00%). Statistical analysis indicated that the inhibitory activities differed significantly among treatments ($p < 0.05$). However, no significant difference was observed between raw and boiled brayo extracts, suggesting that the bioactive compounds in *A. marina* are relatively stable under heat treatment. In contrast, both lindur extracts exhibited lower inhibitory activity compared with brayo extracts. This difference may be associated with variations in the composition and concentration of secondary metabolites between mangrove species. Phenolic and flavonoid compounds are known to inhibit pancreatic lipase through non-covalent interactions with amino acid residues in the enzyme active site, thereby reducing triglyceride hydrolysis into free fatty acids and monoglycerides (Birari & Bhutani, 2007; Buchholz & Melzig, 2015; McDougall et al., 2008). Based on the classification proposed by Ghazali (2013), lipase inhibition values above 80% are categorized as strong, while values between 41–80% are considered moderate. Therefore, both raw and boiled brayo extracts can be classified as strong inhibitors, whereas raw and boiled lindur extracts fall into the moderate inhibitory category.

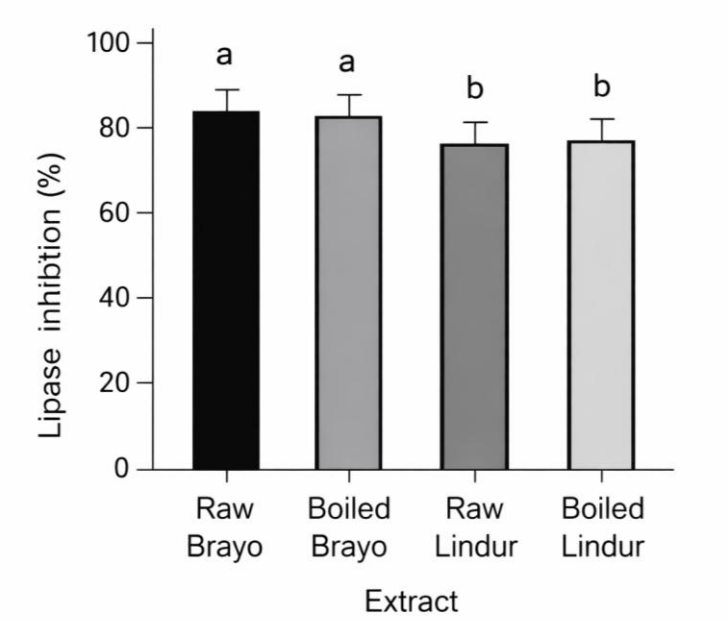


Figure 2. Pancreatic lipase inhibitory activity (%) of *Avicennia marina* (brayo) and *Bruguiera gymnorrhiza* (lindur) fruit flour extracts under raw and boiled conditions. Data are presented as mean ± SD (n = 3). Different letters above the bars indicate significant differences among treatments (one-way ANOVA followed by the Brown–Forsythe test, $p < 0.05$).

3.3. Identification of Bioactive Compounds Using LC-HRMS

The extract showing the highest pancreatic lipase inhibitory activity, namely raw brayo extract, was further analyzed using LC-HRMS to characterize its metabolite profile. Untargeted metabolomic analysis using liquid chromatography–high-resolution mass spectrometry allows comprehensive detection of small-molecule metabolites in complex plant extracts. Reversed-phase liquid chromatography (RPLC) with a C18 column is commonly applied in metabolomics studies because it provides effective separation of non-polar and moderately polar compounds and produces well-defined chromatographic peaks when coupled with mass spectrometry detection (D'Urso et al., 2025). LC-HRMS analysis revealed several metabolites in the raw brayo extract, which were tentatively identified through database matching using Compound Discoverer software integrated with ChemSpider and mzCloud databases.

Seven compounds with similarity scores above 98% were identified, including luteolin, methyl eleostearate, calceolarioside B, caffeic acid, oleamide, 4-indolecarbaldehyde, and 9-oxo-10(E),12(E)-octadecadienoic acid (**Table 1**). These metabolites represent several chemical classes, such as flavonoids, phenolic compounds, phenylpropanoid glycosides, fatty acids and their derivatives, fatty acid amides, and indole alkaloids. The presence of these compound groups indicates that mangrove fruit extracts contain diverse bioactive metabolites that may contribute to their biological activities (Bandaranayake, 2002; Fernandes & Noor'an, 2019).

Among the identified metabolites, luteolin and caffeic acid are phenolic compounds that have been widely reported to exhibit anti-obesity activity through the regulation of lipid metabolism and inhibition of adipogenesis. These compounds can modulate adipogenic transcription factors such as peroxisome proliferator-activated receptor gamma (PPARγ) and CCAAT/enhancer-binding protein alpha (C/EBPα), as well as activate AMP-activated protein kinase (AMPK), which plays an important role in cellular energy homeostasis (Xu et al., 2020). In addition, phenylpropanoid glycosides such as calceolarioside B possess strong antioxidant activity that may help reduce oxidative stress and chronic inflammation associated with obesity (Shahidi & Ambigaipalan, 2015). Fatty acid-derived compounds, including methyl eleostearate and 9-oxo-10(E),12(E)-octadecadienoic acid, have also been reported to influence lipid metabolism and fatty acid oxidation pathways, suggesting that multiple bioactive metabolites may contribute to the observed anti-obesity activity of raw *A. marina* extract (Sun et al., 2016). Based on these findings, molecular docking analysis was subsequently performed to evaluate the potential interaction of the identified compounds with pancreatic lipase.

3.4. Molecular Docking Analysis

Molecular docking analysis was performed to evaluate the potential interactions between the identified compounds and the pancreatic lipase enzyme (PDB ID: 5ZUN). Prior to docking simulations, the docking protocol was validated using a redocking procedure of the native ligand. The validation results showed a root mean square deviation (RMSD) value of 0 Å, which is within the acceptable threshold (≤ 2 Å), indicating that the docking parameters were reliable for predicting ligand–protein interactions (Muttaqin et al., 2019).

The docking results revealed that several compounds identified from the LC-HRMS analysis exhibited favorable binding affinity toward the active site of pancreatic lipase (**Table 2**). Among the tested compounds, luteolin showed the lowest binding affinity (−8.23 kcal/mol), indicating the strongest interaction with the target enzyme. Meanwhile, 9-oxo-10(E),12(E)-octadecadienoic acid (−6.75 kcal/mol) and methyl eleostearate (−6.59 kcal/mol) also demonstrated moderate binding affinity toward the pancreatic lipase binding pocket. In molecular docking studies, lower binding affinity values indicate stronger ligand–protein interactions and greater stability of the ligand within the enzyme active site (Josaphat & Fadlan, 2023; Rao et al., 2007).

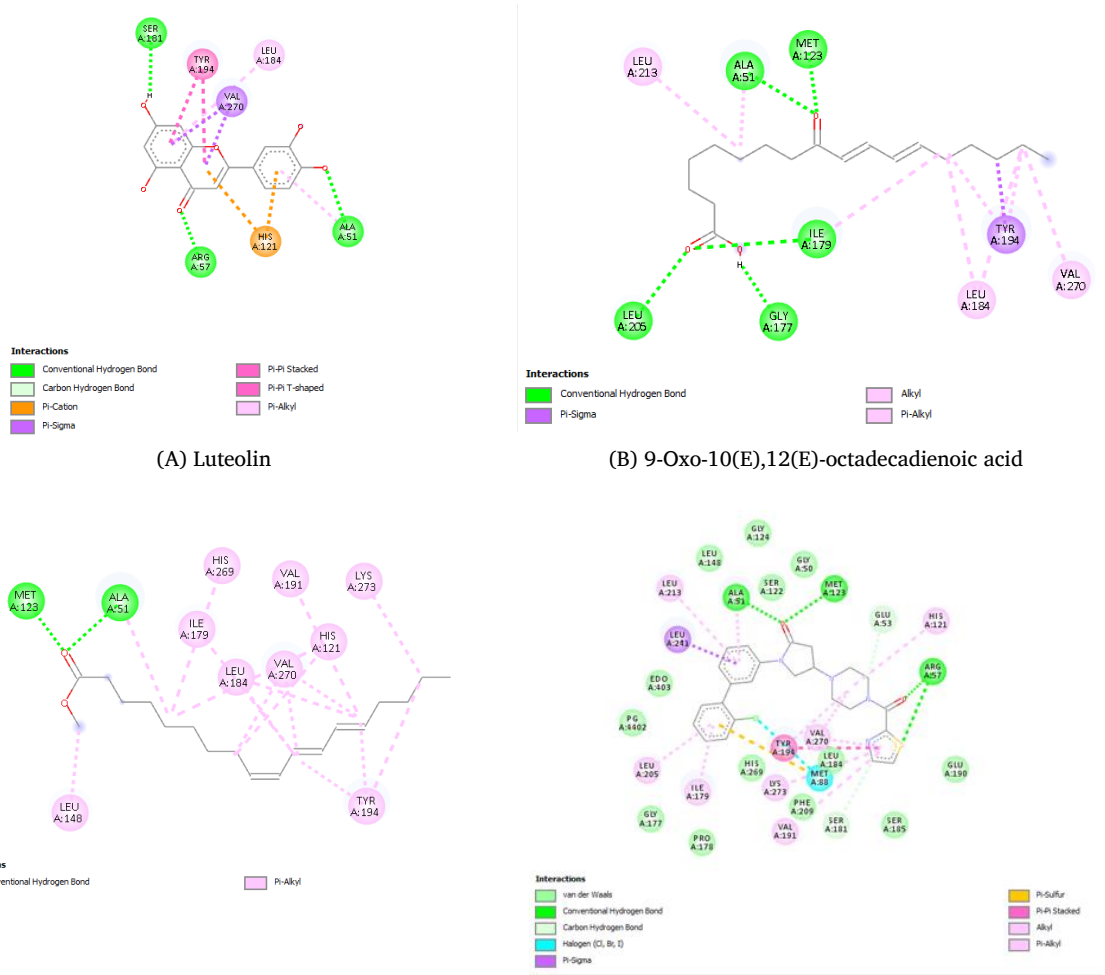
Table 1. Putatively identified metabolites in raw *Avicennia marina* (brayo) fruit extract analyzed by LC-HRMS based on mzCloud database matching (similarity ≥ 98%).

No.	Metabolite	Molecular Formula	Retention Time (min)	Observed m/z	Theoretical m/z	mzCloud Match (%)
1	Caffeic acid	$C_9H_8O_4$	7.26	180.0401	180.16	98.9
2	Calceolarioside B	$C_{23}H_{26}O_{11}$	9.00	478.1424	478.40	99.0
3	4-Indolecarbaldehyde	C_9H_7NO	9.69	145.0514	145.16	98.5
4	Luteolin	$C_{15}H_{10}O_6$	11.01	286.0454	286.24	99.8
5	9-Oxo-10(E),12(E)-octadecadienoic acid	$C_{18}H_{30}O_3$	17.68	294.2166	294.40	98.1
6	Methyl eleostearate	$C_{19}H_{32}O_2$	19.33	292.2373	292.50	99.0
7	Oleamide	$C_{18}H_{35}NO$	19.99	281.2690	281.50	98.8

Table 2. Binding affinity values and interacting amino acid residues of selected compounds from raw *Avicennia marina* extract against pancreatic lipase (PDB ID: 5ZUN) obtained from molecular docking analysis.

Compound	Binding Affinity (kcal/mol)	Hydrogen Bond Interactions	Hydrophobic Interactions
Luteolin	-8.23	SER181, ARG57, ALA51	TYR194, VAL270, LEU187
9-Oxo-10(E),12(E)-octadecadienoic acid	-6.75	ALA51, MET123, ILE179, LEU205, GLY177	TYR194, LEU184, VAL270, LEU213
Methyl eleostearate	-6.59	MET123, ALA51	HIS269, ILE179, VAL191, LYS273, LEU184, VAL270, HIS121, TYR194, LEU148

The interaction patterns between the ligands and the amino acid residues in the pancreatic lipase active site are illustrated in **Figure 3**. The docking visualization shows that these compounds interact with several key residues located within the catalytic region of the enzyme, including ALA51, ARG57, MET123, TYR194, VAL270, and LEU184. Hydrogen bond interactions were mainly observed with residues SER181, ARG57, ALA51, MET123, ILE179, and GLY177, while hydrophobic interactions involved residues such as TYR194, VAL270, LEU184, and LEU213. These interactions suggest that the identified compounds may occupy the enzyme active site and interfere with substrate binding, thereby potentially inhibiting the catalytic activity of pancreatic lipase.



(A) Luteolin

(B) 9-Oxo-10(E),12(E)-octadecadienoic acid

(C) Methyl eleostearate

(D) Native ligand

Figure 3. Two-dimensional ligand–protein interaction diagrams of selected compounds identified in *Avicennia marina* extract with pancreatic lipase (PDB ID: 5ZUN) obtained from molecular docking analysis. (A) Luteolin, (B) 9-oxo-10(E),12(E)-octadecadienoic acid, (C) methyl eleostearate, and (D) native ligand.

The strong binding affinity observed for luteolin is consistent with previous reports indicating that flavonoid compounds can inhibit pancreatic lipase through interactions with catalytic residues and stabilization within the enzyme binding pocket (Birari & Bhutani, 2007; Buchholz & Melzig, 2015). Therefore, the molecular docking results support the experimental findings from the in vitro lipase inhibition assay and suggest that flavonoids and fatty acid derivatives present in raw *Avicennia marina* extract may contribute to its anti-obesity potential.

3.5. ADMET Prediction

The pharmacokinetic and toxicity properties of luteolin were predicted using an in silico ADMET approach (**Table 3**). Luteolin showed a water solubility value of −3.094 log mol/L, indicating moderate solubility that still supports oral absorption (Abdullah et al., 2022). The predicted Caco-2 permeability value (0.096 log Papp in 10^{-6} cm/s) suggests moderate intestinal permeability, which is commonly observed in flavonoid compounds. In addition, the predicted human intestinal absorption reached 81.13%, indicating good absorption potential because compounds with values above 80% are generally classified as having high intestinal absorption (Setyawati et al., 2023).

For distribution parameters, luteolin showed a predicted volume of distribution (VDss) of 1.153 log L/kg and an unbound fraction of 0.168. These values indicate that part of the compound can circulate in its free form and interact with biological targets (Abdullah et al., 2022; Amin & Makia, 2025). The predicted blood–brain barrier permeability (log BB = −0.907) and central nervous system permeability (log PS = −2.251) suggest low penetration into the central nervous system, which may reduce the potential for neurological side effects (Setyawati et al., 2023).

Table 3. Predicted ADMET profile of luteolin.

Category	Parameter	Predicted Value	Unit
Absorption	Water solubility	-3.094	log mol/L
	Caco-2 permeability	0.096	log Papp (10^{-6} cm/s)
	Intestinal absorption (human)	81.13	% absorbed
	Skin permeability	-2.735	log Kp
	P-glycoprotein substrate	Yes	Yes/No
	P-glycoprotein I inhibitor	No	Yes/No
	P-glycoprotein II inhibitor	No	Yes/No
Distribution	VDss (human)	1.153	log L/kg
	Fraction unbound (human)	0.168	Fu
	BBB permeability	-0.907	log BB
	CNS permeability	-2.251	log PS
Metabolism	CYP2D6 substrate	No	Yes/No
	CYP3A4 substrate	No	Yes/No
	CYP1A2 inhibitor	Yes	Yes/No
	CYP2C19 inhibitor	No	Yes/No
	CYP2C9 inhibitor	Yes	Yes/No
	CYP2D6 inhibitor	No	Yes/No
	CYP3A4 inhibitor	No	Yes/No
Excretion	Total clearance	0.49	log mL/min/kg
Toxicity	AMES toxicity	No	Yes/No
	Max. tolerated dose (human)	0.499	log mg/kg/day
	hERG I inhibitor	No	Yes/No
	hERG II inhibitor	No	Yes/No
	Oral rat acute toxicity (LD_{50})	2.455	mol/kg
	Oral rat chronic toxicity (LOAEL)	2.409	log mg/kg bw/day
	Hepatotoxicity	No	Yes/No
	Skin sensitization	No	Yes/No

Note: ADMET parameters were predicted using the pkCSM online server.

Metabolism prediction showed that luteolin is not a substrate of CYP2D6 and CYP3A4 but may inhibit CYP1A2 and CYP2C9. This indicates that possible metabolic interactions should be considered in further studies. The predicted total clearance value (0.49 log ml/min/kg) indicates a moderate elimination rate. Toxicity prediction also showed that luteolin is non-mutagenic (AMES negative), non-hepatotoxic, and not predicted to inhibit hERG channels, suggesting a relatively safe toxicity profile (Pires et al., 2015; Amin & Makia, 2025).

These ADMET results support the potential of luteolin as a bioactive compound with acceptable pharmacokinetic characteristics for further investigation as a natural pancreatic lipase inhibitor.

4. CONCLUSION

This study demonstrates that fruit flour extracts of *A. marina* and *B. gymnorrhiza* possess potential anti-obesity activity through inhibition of pancreatic lipase. Among the tested samples, raw *A. marina* (brayo) extract exhibited the highest lipase inhibitory activity and remained relatively stable after boiling treatment. LC-HRMS analysis identified several bioactive metabolites in the extract, including luteolin, caffeic acid, calceolarioside B, methyl eleostearate, oleamide, and 9-oxo-10(E),12(E)-octadecadienoic acid. Molecular docking analysis showed that luteolin had the strongest binding affinity toward pancreatic lipase, interacting with key amino acid residues within the enzyme active site. In addition, ADMET prediction indicated that luteolin possesses acceptable pharmacokinetic characteristics and a relatively low toxicity risk. These findings suggest that mangrove fruit flour, particularly from *A. marina*, may serve as a promising natural source of pancreatic lipase inhibitors for obesity management. Further studies, including compound isolation and in vivo evaluation, are required to confirm its therapeutic potential.

AUTHOR CONTRIBUTIONS

Conceptualization: LK, MRRR; Methodology and investigation: AC, LK, MRRR; Software and visualization: YDF, AC; Data analysis and curation: AC; Writing—original draft: AC, YDF, LK; Writing—review and editing: LK, MRRR; Resources: RP; Supervision, project administration, and funding acquisition: LK. All authors have read and agreed to the published version of the manuscript.

INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable. This study did not involve human participants or animals.

INFORMED CONSENT STATEMENT

Not applicable.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ROLE OF FUNDERS

The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

DECLARATION OF GENERATIVE ARTIFICIAL INTELLIGENCE (AI) USE

During the preparation of this manuscript, the author(s) used ChatGPT (OpenAI) to assist in improving the clarity, structure, and readability of the text. All generated content was carefully reviewed, edited, and verified by the authors. The authors take full responsibility for the integrity and originality of the published work.

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