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Original Article

Exploring the anti-inflammatory and anti-apoptotic properties of phloroglucinol on pancreatic cells in diabetic models: In silico and in vivo study

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Abstract

Pancreatic cell damage in diabetes mellitus is closely linked to inflammation and apoptosis. This study aimed to investigate the protective effects of phloroglucinol on pancreatic cells in a streptozotocin-induced diabetic model by assessing its anti-inflammatory and anti-apoptotic mechanisms. Phloroglucinol ligand and the structures of Bax, Bcl-2, and caspase-3 proteins were sourced from the PubChem database. Molecular docking was performed using Autodock Tools and docking results were analyzed with PyRx software. In addition, during the in vivo study, the BALB/c mice were grouped into four categories: healthy control, untreated streptozotocin-induced diabetic, and streptozotocin-induced diabetic treated with two doses of oral phloroglucinol at 100 mg/kg and 200 mg/kg body weight. After 28 days, pancreatic tissues were collected for flow cytometric analysis of NF-κB, IL-6, TNF-α, and apoptotic markers (Bax, Bcl-2, and caspase-3). The docking simulations revealed specific binding interactions: phloroglucinol interacted with Bcl-2 via amino acid residues of ALA90 and TYR139, with Bax via ALA42, LEU45, ALA46, LEU47, PRO130, and ILE133, and with caspase-3 through ARG64, SER120, GLN161, CYS163, and ARG207. The binding affinities for Bax, Bcl-2, and caspase-3 were -5.0, -4.7, and -4.9 kcal/mol, respectively. In vivo, results showed that streptozotocin significantly elevated inflammatory cytokines NF-κB, TNF-α, and IL-6, along with apoptotic markers in pancreatic cells (p<0.05) compared to healthy controls. Phloroglucinol administration at 200 mg/kg significantly reduced TNF-α, NF-κB and IL-6 levels. Phloroglucinol also prevented streptozotocin-induced pancreatic cell damage through anti-apoptotic effects by downregulating Bax and caspase-3 and upregulating Bcl-2. These findings suggest that phloroglucinol may offer protective benefits in diabetic conditions by modulating apoptotic and inflammatory pathways.

Keywords: Phloroglucinol, anti-inflammatory, anti-apoptotic, diabetic mice, pancreatic cell damage

Introduction

Diabetes is a metabolic disorder characterized by chronic hyperglycemia due to either inadequate insulin production by pancreatic β-cells or resistance to insulin in target cells [1,2].

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Diabetes is a leading global cause of mortality, impacting multiple organs and associated with complications such as neuropathy, nephropathy, angiopathy, atherosclerosis, periodontitis, and poor wound healing [3]. Elevated blood glucose triggers cascades that enhance oxidative stress, apoptosis, and inflammation [4-6]. Previous studies indicated that oxidative stress and elevated cytokines, particularly tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), play critical roles in initiating apoptosis; therefore, initiate signaling cascades that activate both intrinsic and extrinsic apoptotic mechanisms [6,7].

Streptozotocin, an antibiotic with pancreatic islet β-cell cytotoxicity, is frequently employed in animal models to induce diabetes [8-9]. Streptozotocin has been shown to elevate levels of TNF-α and IL-6, which are critical mediators of apoptosis involved in pancreatic damage progression [10,11]. This process involves caspase-3 pathway activation and reduced levels of the anti-apoptotic protein Bcl-2 [12,13]. Molecular docking, a computational technique predicting ligand-receptor interactions, is essential for virtual screening, particularly to assess ligand interactions with apoptotic proteins such as Bax, Bcl-2, and caspase-3 [14,15].

Previous studies have highlighted active compounds with anti-inflammatory and anti-apoptotic effects, such as fucoidan, curcumin, and quercetin, for potential use in protecting cells in diabetic patients from damage [9,12,16]. Phloroglucinol has also been reported to exhibit anti-inflammatory and anti-apoptotic properties [17-19], with pharmacological activities that include antiviral, antibacterial, diabetes prevention, anti-allergic, antioxidant, and anti-apoptotic effects [20-22]. It has been reported that phloroglucinol possesses anti-inflammatory activities by regulating the AMPK/Nrf2/HO-1 signaling pathway in lipopolysaccharide-stimulated RAW264.7 murine macrophages [18]. Phloroglucinol also attenuated DNA damage and apoptosis induced by oxidative stress by blocking the production of mitochondrial reactive oxygen species (ROS) [18]. However, studies assessing the effect of anti-inflammatory and anti-apoptotic properties of phloroglucinol on pancreatic cells in diabetic models are limited. This study aimed to evaluate phloroglucinol's anti-inflammatory and anti-apoptotic effects in protecting against streptozotocin-induced pancreatic cell damage.

Methods

Study design and setting

In silico was conducted to investigate the anti-inflammatory and anti-apoptotic properties of phloroglucinol. The study was initiated to prepare the ligand (phloroglucinol) and targeted receptors (Bax, Bcl-2, and caspase-3 protein), followed by molecular docking analysis to predict the binding affinity for those three target proteins. To further confirm these findings, an experimental study using male mice strain BALB/c was conducted at the Faculty of Veterinary Medicine, Unversitas Airlangga, Surabaya, Indonesia. After seven days of acclimatization, the mice were divided into four groups and administered varying doses of phloroglucinol for twenty-eight days. The mice were sacrificed on the 29th day, and the pancreases were collected for measurement of cytokines levels (nuclear factor kappa B (NF-κB), IL-6, and TNF-α) and apoptosis analysis via flow cytometry.

In silico analysis of phloroglucinol's anti-apoptotic effects

In the present study, the phloroglucinol compound was downloaded from the PubChem database and used to predict its binding affinity for three target proteins (Bax, Bcl-2, and caspase-3) using in silico molecular docking methods.

Ligand preparation for docking analysis

The structure of the phloroglucinol ligand was drawn using MarvinSketch, based on the SMILES representation obtained from PubChem (https://pubchem.ncbi.nlm.nih.gov/). 3D Geometry optimization of the ligands was performed using ChemDraw Ultra 12.0 software (PerkinElmer, Waltham, United States) and saved in .cdx file format. After structure refinement, the compounds were optimized using Chem3D Pro 12.0 (PerkinElmer, Waltham, United States) and saved in protein data bank (PDB) file format for further analysis.

Preparation of receptor proteins for docking analysis

Structures of Bax, Bcl-2, and caspase-3 proteins were obtained from the PDB using the General Data Protection (GDP) protocol through the RCSB PDB website (https://www.rcsb.org/). These protein structures were subsequently prepared for testing. The protein crystal structures were generated using BIOVIA Discovery Studio 2020 (Dassault Systèmes, Vélizy-Villacoublay, France), which involved the removal of water molecules and separation of native ligands from the Bax, Bcl-2, and caspase-3 protein structures. The processed Bax, Bcl-2, and Caspase-3 receptors, along with their native ligands, were then saved in PDB format.

Molecular docking visualization techniques

Using Autodock Tools 1.5.6 (Scripps Research Institute, La Jolla, United States), the target protein structures and ligand molecular structure (phloroglucinol), were further prepared for docking. To construct the Bax, Bcl-2, and caspase-3 receptor molecules, water molecules were removed, and hydrogen atoms were added along with partial charges. The ligand was separated from the protein to ensure accurate docking, and the derived macromolecular structures were saved in PDBQT format. Molecular docking complexes were then visualized using Discovery Studio Visualizer software (Dassault Systèmes, Vélizy-Villacoublay, France). This visualization enabled the comparison of amino acid residues in the test ligands with corresponding residues in the interacting macromolecules, providing a detailed view of the docking interactions.

Analysis of molecular docking results and interpretations

The docking process of the ligand (phloroglucinol) to the target proteins (Bax, Bcl-2, and caspase-3) was conducted to assess the binding position and grid box size using PyRx software Version 0.8 (Sargis Dallakyan, San Diego, United States). The key parameter evaluated during the docking process was the binding energy value (ΔG binding), which reflects the affinity between the ligand and the receptor.

In vivo study assessing anti-inflammatory and anti-apoptosis of phloroglucinol on diabetic mice pancreas cells

Experimental animals

In the present study, male BALB/c mice aged 10 to 12 weeks and weighing 25 to 30 grams were used. These mice were obtained from the Pusat Veteriner Farma (Pusvetma), Surabaya, Indonesia. All mice were acclimated for 1 week before the study. The mice were housed in plastic cages within air-conditioned rooms maintained at a temperature of 26±2°C, with a 12-hour light-dark cycle. Water was provided *ad libitum* throughout the duration of the experiment.

Diabetic induction

In the present study, the mice received intraperitoneal (i.p.) injection of 150 mg/kg body weight (BW) of streptozotocin mixed with 0.1 M citrate buffer (pH 4.5) following an overnight fast. Blood samples were collected via the lateral tail vein 24 hours after the streptozotocin injection, and blood glucose levels were measured using the Accu-Chek glucometer (Roche Diagnostics, Basel, Switzerland). Mice with glucose levels exceeding 200 mg/dL were used in the study.

Experimental design

Twenty-four mice were divided into four groups: (A) the control group: normal mice received distilled water 10 ml/kg BW orally; (B) the diabetes group: diabetic mice received streptozotocin 150 mg/kg BW intraperitoneally; (C) phloroglucinol group: mice received streptozotocin 150 mg/kg BW intraperitoneally and 100 mg/kg BW of phloroglucinol (Sigma-Aldrich, St. Louis, United States) once a day orally for 28 days; and (D) phloroglucinol group: mice received streptozotocin 150 mg/kg BW intraperitoneally and 200 mg/kg BW of phloroglucinol once a day orally for 28 days. On the 29th day, all groups of mice were administered intraperitoneal injections of ketamine (60 mg/kg BW) and xylazine (7.5 mg/kg BW) to induce anesthesia. Subsequently, the pancreatic tissues were collected and washed 2–3 times with sterile phosphate-buffered saline (PBS) (Thermo Fisher Scientific, Waltham, United States), then cut into 0.5×0.5 cm and mashed. The smooth spleen was added with 5 mL of sterile PBS and filtered with a wire

filter. It was then used to determine the expression of NF-κB, IL-6, TNF-α, and apoptotic markers using flow cytometry.

Sample preparation and pancreatic cell viability assessment

After sacrificing the mice, the pancreas was excised and homogenized using 200-mesh steel filters to create single-cell suspensions under sterile conditions. Following centrifugation at 1,200 rpm for 5 mins, the cells were collected, and red blood cells were lysed. The viability of the collected cells was confirmed using trypan blue staining, with at least 95% of the cells deemed viable.

Cell culture conditions

The collected cells were then resuspended in Roswell Park Memorial Institute (RPMI) 1640 medium supplemented with 10% fetal bovine serum and cultured for two days at 37°C in a 5% carbon dioxide atmosphere. At the end of this period, the cell concentration reached 1×10^9 cells per liter. Supernatants from the pancreatic cultures were collected and stored at -70°C for subsequent assays of apoptosis, IL-6, TNF-α, and NF-κB.

Apoptosis assessment and measurement of IL-6, NF-κB, and TNF-α levels using flow cytometry

The severity of apoptosis was assessed using the annexin/propidium iodide assay, which detects phosphatidylserine externalization in the cell membrane. Briefly, following centrifugation, the collected cells were washed twice with cold PBS and resuspended in 100 µL of binding buffer containing 2 µL of 100 µg/mL propidium iodide (Invitrogen, Carlsbad, United States) and 5 µL of fluorescein isothiocyanate (FITC)-conjugated annexin-V (Sigma-Aldrich, St. Louis, United States). The mixture was incubated at room temperature in the dark for 15 mins. Flow cytometry was performed using the Accuri C6 flow cytometer with the CFlow Plus Analytic software (BD Biosciences, Franklin Lakes, United States), collecting a minimum of 10,000 events. A live pancreatic cell gate was established based on forward scatter and side scatter plots. Pancreatic cells that were double-positive for propidium iodide and annexin-V within the defined gate were quantified to determine the rate of apoptosis.

Inflammatory cytokine expression analysis

A total of 50 µL of the culture supernatant was mixed with 50 µL of capture beads containing NF-κB, TNF-α, and IL-6 in a test tube. The sample was incubated for 20 mins at room temperature in the dark, followed by the addition of 50 µL of fluorescent-tagged antibodies for NF-κB, TNF-α, and IL-6 (Invitrogen, Waltham, United States). After centrifugation for 15 seconds at 200×g, the supernatant was carefully removed, and the cell pellet was resuspended in 300 µL of wash buffer for flow cytometry analysis. The levels of IL-6, NF-κB, and TNF-α were analyzed using a FACS Canto II flow cytometer (BD Biosciences, Franklin Lakes, United States) following the flow cytometry protocol. The guidelines for antibody concentrations provided by the manufacturer were strictly followed. Data evaluation was performed using the FCAP Array software (BD Biosciences, Franklin Lakes, United States).

Statistical analysis

The data were presented as mean values along with their associated standard deviations. The data were then analyzed using the analysis of variance (ANOVA) test, followed by the Duncan multiple comparison test to identify inter-group differences with $p<0.05$. The statistical analyses were conducted using SPSS version 20 (IBM, Armonk, United States).

Results

In silico evaluation of the anti-apoptotic effects of phloroglucinol

In the present study, phloroglucinol was used to predict binding affinity for three target proteins (Bax, Bcl-2, and Caspase-3). To prepare phloroglucinol for ligand docking, geometry optimization of its 3D structure was performed to minimize energy and achieve the most stable conformation. The primary output of the docking was a binding pose, showing the orientation and position of phloroglucinol within the protein's binding site. In 3D visualization, phloroglucinol appears as a

stick model (carbon in gray, oxygen in red, and hydrogen in white) (**Figure 1**). The hydroxyl groups (OH) on the benzene ring, acting as hydrogen bond donors, are presented in **Figure 1**.

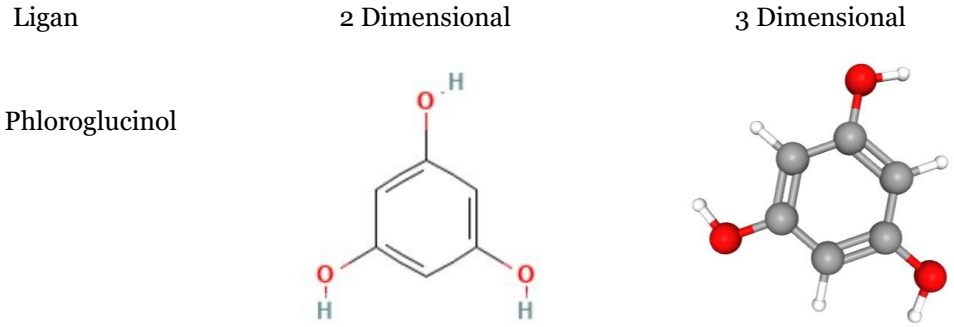

Figure 1. Two-dimensional and three-dimensional structures of phloroglucinol.

Target proteins for ligands Bax, Bcl-2, and caspase-3

The structures of BCl-2, Bax, and caspase-3 proteins are represented as ribbon models highlighting their coiled-coil motifs (**Figure 2**). Redocking was conducted to validate the accuracy of the downloaded PDB files, using the phloroglucinol docking method to ensure valid and accurate results. The primary criterion for redocking validation was the root mean square deviation (RMSD) value. For each protein, the RMSD between the native ligand and the redocked ligand was assessed, with acceptable accuracy indicated by an RMSD value <2.0 Å for BCl-2, Bax, and caspase-3 (**Figure 2**).

Figure 2. Visualization and analysis of molecular docking showing the structure of the BCl-2 (A), Bax (B), and caspase-3 (C) proteins.

Interactions between phloroglucinol molecule and Bcl-2, Bax, and caspase-3 proteins result in ligand-protein linkages (**Figure 3** and **Table 1**). Phloroglucinol forms hydrogen bonds with active Bcl-2 at the amino acid residues ALA90 and TYR139. It interacts with activated Bax at residues ALA42, LEU45, ALA46, LEU47, PRO130, and ILE133, and with the amino acid residues ARG64, SER120, GLN161, CYS163, and ARG207 of caspase-3 (**Figure 3**). Phloroglucinol exhibited the highest affinity for Bax (ΔG affinity =-5 kcal/mol) compared to its interactions with activated Bcl-2 (ΔG affinity =-4.7 kcal/mol) and caspase-3 (ΔG affinity =-4.9 kcal/mol) (**Table 1**).

Table 1. The binding energy of molecular interactions between phloroglucinol with Bcl-2, Bax, and caspase-3

Ligand	Protein molecular	Binding energy (kcal/mol)	H-bound	Amino acid residues
Phloroglucinol	Bcl-2	-4.7	1	ALA90, TYR139
	Bax	-5	2	ALA42, LEU45, ALA46, LEU47, PRO130, ILE133
	caspase-3	-4.9	3	ARG64, SER120, GLN161, CYS163, ARG207

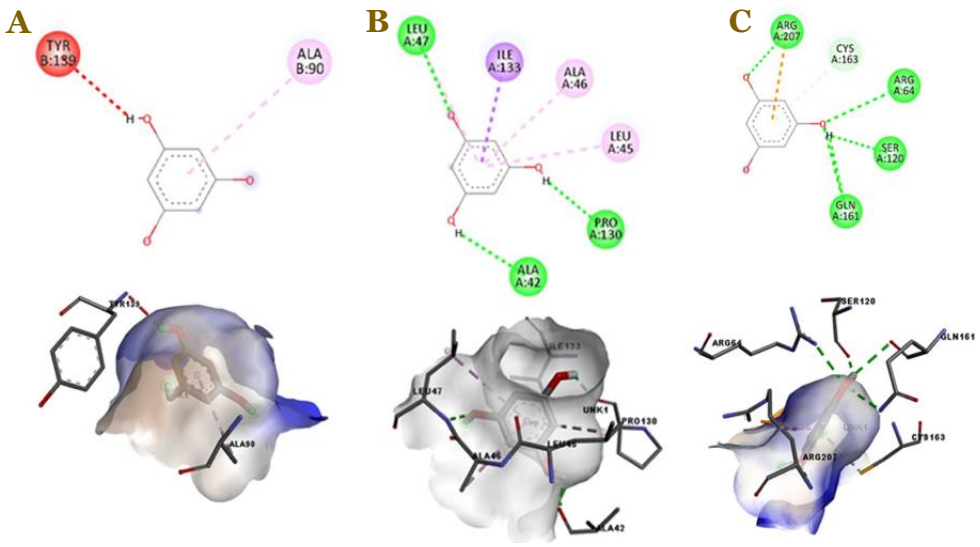

Figure 3. Molecular docking of phloroglucinol (2D and 3D) with the active amino acid sequences as follows: (A) anti-apoptotic protein Bcl-2; (B) apoptotic protein Bax; and (C) apoptotic protein caspase-3.

Effect of phloroglucinol on the expression of NF-κB, IL-6 and TNF-α in streptozotocin-induced diabetic mice model

The expression of NF-κB in pancreatic cells was significantly increased following stimulation with streptozotocin (**Table 2**). However, treatment with phloroglucinol at a dose of 200 mg/kg BW significantly reduced NF-κB expression. These findings underscore the critical role of phloroglucinol treatment in mitigating pancreatic cell inflammation. Our data also indicated that the pro-inflammatory cytokine IL-6 and TNF-α activity significantly increased in diabetic animals (treated or untreated with healthy animals and phloroglucinol) compared to healthy animals. Administration of phloroglucinol at a dose of 200 mg/kg BW significantly suppressed the production of IL-6 compared to the untreated diabetic group (7.54±1.5% vs 4.95±0.3%) (**Table 2**). Administration of phloroglucinol at doses of 100 and 200 mg/kg BW significantly reduced the TNF-α expression compared to the untreated diabetic group (**Table 2**). These findings suggest that phloroglucinol may function as an anti-inflammatory agent by inhibiting the production of pro-inflammatory cytokines.

Table 2. Effect of phloroglucinol on NF-κB, IL-6 and TNF-α expression in streptozotocin-induced diabetic mice model

Study group	Percentage of expression (%)		
	NF-κB	IL-6	TNF-α
	mean±SD	mean±SD	mean±SD
Healthy mice	0.75±0.4[a]	2.04±1.1[a]	0.70±0.4[a]
Untreated diabetic mice	6.45±1.2[b]	7.54±1.5[b]	3.13±0.9[b]
Diabetic mice treated with phloroglucinol 100 mg/kg BW	6.71±2.3[b]	6.04±2.1[b]	1.77±0.6[c]
Diabetic mice treated with phloroglucinol 200 mg/kg BW	4.65±0.5[c]	4.95±0.3[c]	1.46±0.6[c]

IL-6: interleukin-6; NF-κB: nuclear factor kappa B; TNF-α: tumor necrosis factor-alpha.
[a-c] Different letter between groups indicates a significant difference between the groups ($p<0.05$)

Effect of phloroglucinol on streptozotocin-induced pancreatic cell apoptosis

Our data indicated a significant increase in the expression of apoptotic pancreatic cells in the diabetes groups compared to the healthy control group ($p<0.05$) (**Table 3** and **Figure 4**). Administration of phloroglucinol at doses of 100 and 200 mg/kg BW significantly reduced the percentage of apoptotic cells (**Table 3**). These data demonstrated that phloroglucinol could prevent streptozotocin-induced apoptosis in pancreatic cells.

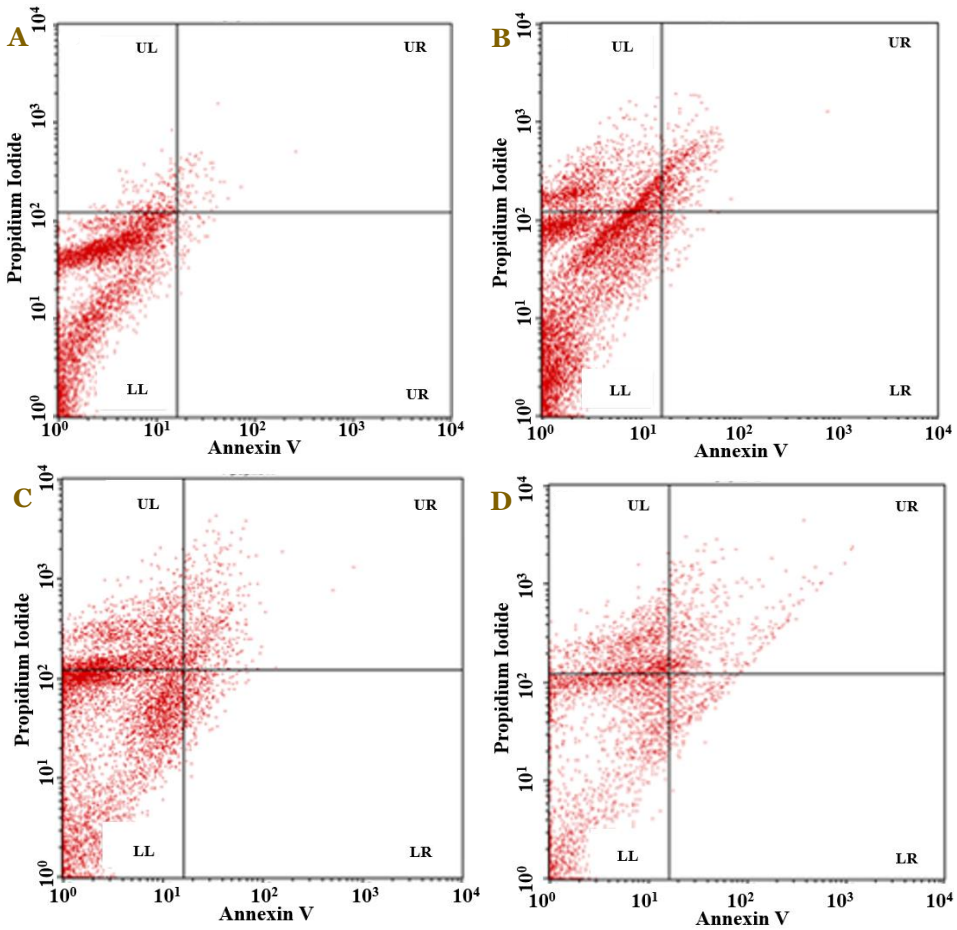

Figure 4. Flow cytometry analysis of phloroglucinol effect on apoptosis expression of pancreatic cells in streptozotocin-induced diabetic mice model: (A) healthy control; (B) diabetic animals (induced by streptozotocin at a dose of 150 mg/kg BW); (C) diabetic animals treated with phloroglucinol at a dose of 100 mg/kg BW; and (D) diabetic animals treated with phloroglucinol at a dose of 200 mg/kg BW. Each group has six animals.

Table 3. Effect of phloroglucinol on apoptotic of pancreatic cells in streptozotocin-induced diabetic mice model

Study group	Apoptosis expression (%) mean±SD
Healthy mice	6.38±1.9[a]
Untreated diabetic mice	34.80±4.4[b]
Diabetic mice treated with phloroglucinol 100 mg/kg BW	12.10±3.7[c]
Diabetic mice treated with phloroglucinol 200 mg/kg BW	11.19±1.8[c]

[a-c] Different letter between groups indicates a significant difference between the groups (p<0.05)

Discussion

The protective effects of phloroglucinol in reducing apoptosis in pancreatic cells suggest its potential as a therapeutic agent for managing diabetic complications. These findings support further exploration of phloroglucinol as part of a comprehensive management strategy aimed at preventing diabetes-related complications, including neuropathy, retinopathy, and nephropathy.

Phloroglucinol protected pancreatic cells from damage in a mouse model of streptozotocin-induced diabetes by exerting anti-apoptotic effects. This was demonstrated by a reduction in the expression of pro-apoptotic markers Bax and caspase-3, along with an increase in the anti-apoptotic protein Bcl-2. Additionally, phloroglucinol exhibited anti-inflammatory properties, as evidenced by decreased production of NF-κB, IL-6, and TNF-α in pancreatic cells. Streptozotocin-induced diabetes serves as a valuable model in diabetes research, providing insights into insulin deficiency and hyperglycemia in animals and enabling investigations into diabetes pathophysiology and potential therapeutic interventions [24-26]. The administration of

streptozotocin induces local pancreatic inflammation due to its cytotoxicity toward β-cells and may also promote systemic inflammation through its toxic effects on various tissues and immune responses [27,28]. This systemic inflammatory response is characterized by elevated levels of cytokines, such as NF-κB, IL-6, and TNF-α, which have intricate interactions with apoptotic pathways [7,10,14]. Moreover, streptozotocin disrupts cellular processes and shifts the balance of apoptotic regulators, including Bcl-2 and Bax, making this regulatory interaction crucial for understanding and treating conditions associated with apoptotic dysregulation, such as diabetes mellitus [10,11,13].

Cytokines associated with inflammation, including TNF-α, IL-6, and NF-κB, can activate apoptotic markers such as Bax, Bcl-2, and caspase-3 in pancreatic cells [6,11]. Sustained inflammation may lead to endoplasmic reticulum stress or mitochondrial dysfunction, both of which can trigger apoptotic pathways [6,7,10]. In this study, phloroglucinol demonstrated significant binding affinities with docking scores of -4.7, -5.0, and -4.9 kcal/mol for Bax, Bcl-2, and caspase-3, respectively. Activated Bax promotes cell death, while Bcl-2 acts as an anti-apoptotic protein that helps cells resist apoptosis and supports cell survival [11,29]. Caspase-3 functions as an effector protein involved in both intrinsic and extrinsic apoptotic pathways [10,13]. Flow cytometry results from this study indicated that phloroglucinol inhibited apoptosis in diabetic pancreatic cells by interacting with apoptotic proteins, such as Bax and caspase-3, as well as anti-apoptotic proteins like Bcl-2. Previous studies have also shown that phloroglucinol could inhibit excessive apoptosis, contributing to tissue protection in models of neurodegenerative diseases and ischemic injury [19,21,23].

The findings from this in vivo study indicated that oral administration of phloroglucinol significantly reduced pro-inflammatory factors, NF-κB, IL-6, and TNF-α, thereby protecting pancreatic cells from damage in diabetic conditions. Chronic inflammation often elevates NF-κB activation, driving the production of inflammatory cytokines such as TNF-α and IL-6, which are key contributors to diabetic complications, including pancreatic cell damage [14,23]. The protective effects of phloroglucinol are likely due to its antioxidant and anti-inflammatory properties [19]. A previous study has shown that phloroglucinol inhibited the production of inflammatory cytokines, including NF-κB, IL-6, TNF-α, and prostaglandins, while also possessing antioxidant capabilities that mitigated inflammation and oxidative stress [20].

Inflammatory cytokines such as TNF-α and IL-6 can induce apoptosis in pancreatic β-cells, a process closely associated with diabetic complications that lead to tissue damage and organ dysfunction [19,23]. Chronic hyperglycemia and metabolic dysregulation in diabetes enhance oxidative stress and inflammation, promoting apoptosis and functional impairment of pancreatic tissue [2,8,9]. Bcl-2 and Bax are pivotal proteins in regulating apoptosis, especially under diabetic conditions [7]. The anti-apoptotic protein Bcl-2, primarily located on the outer mitochondrial membrane, prevents apoptosis by inhibiting cytochrome c release from mitochondria, thus blocking subsequent apoptotic signaling pathways [14]. Elevated Bcl-2 expression supports cell survival by maintaining mitochondrial integrity and delaying apoptosis onset. In contrast, the pro-apoptotic protein Bax facilitates apoptosis by translocating to the mitochondria in response to apoptotic stimuli [11]. When Bax interacts with Bcl-2 and other pro-apoptotic proteins at the mitochondria, it promotes mitochondrial outer membrane permeabilization, releasing cytochrome c and activating apoptotic pathways [6,7,11].

This study demonstrated that phloroglucinol exhibited anti-apoptotic effects in pancreatic cells under diabetic conditions. Phloroglucinol modulates apoptosis by influencing key regulatory proteins, including Bcl-2 and Bax [6,11]. By upregulating anti-apoptotic proteins such as Bcl-2 and downregulating pro-apoptotic proteins like Bax, phloroglucinol helps maintain cellular equilibrium, which is crucial for cell survival in apoptosis-prone conditions such as diabetic complications [19,23]. However, further studies are warranted to assess the expression of Bcl-2, Bax, and caspase-3 using immunohistochemistry, along with histopathological evaluation of pancreatic cell damage.

Conclusion

Phloroglucinol mitigates pancreatic cell damage in streptozotocin-induced diabetic mice through its anti-apoptotic activity, characterized by a decreased expression of Bax and caspase-3, along

with an increased level of Bcl-2. Additionally, phloroglucinol demonstrates anti-inflammatory effects by reducing the production of NF-κB, IL-6, and TNF-α in pancreatic cells.

Ethical Approval

The protocol of the present study was reviewed and approved by the Ethical Committee for Animal Research, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, Indonesia (Approval number: 2.KEH.058.04.2023).

Competing interests

The author declares that we have no competing interests.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

How to cite

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