Lanctos 75™ is A Novel Retino-Protective and Neovascular Inhibitor for Diabetic Retinopathy

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Abstract

Diabetic retinopathy (DR) is a significant neurovascular complication driven by abnormal angiogenesis. This study evaluated the efficacy and safety of Lanctos 75™, a proprietary standardized extract of *Orthosiphon stamineus* leaves (code name C5OSEW5050ESA), as a retinal-protective and anti-neovascular agent in streptozotocin-induced diabetic retinopathy in rats. The safety and neuroprotective properties of Lanctos 75™ were assessed in various in vitro and in vivo models of ischemia-induced neuronal injury. In vitro studies using RGC-5 cells showed that Lanctos 75™ significantly suppressed apoptosis, demonstrating strong cytoprotective effects. In vivo, PanOptic ophthalmoscopic imaging in diabetic rats revealed that Lanctos 75™ protected against retinal damage, inhibiting the development of microaneurysms, hemorrhages, vascular leakage, venous beading, and retinal inflammation. Fluorescence molecular tomography (FMT) imaging further confirmed its protective effect against ischemia-reperfusion injury and related inflammation. Overall, the results suggest that Lanctos 75™, with an effective dose of *O. stamineus*, holds promise as an adjunct therapy for diabetic retinopathy and other neovascular-related eye conditions.

Keywords: Oxidative Stress, Angiogenesis Inhibition, Ocular Drug Delivery Orthosiphon Stamineus, Lanctos 75™ , C5OSEW5050ESA, Neovascularization, Diabetic Retinopathy.

Significance | This study evaluates Lanctos 75™ as a potential therapeutic agent for diabetic retinopathy, targeting angiogenesis, oxidative stress, and inflammation.

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Introduction

Approximately 200 million people worldwide are affected by diabetes mellitus, with about 20 million in the United States alone. Diabetic retinopathy (DR), a microvascular complication of diabetes, is a leading cause of blindness among working-age adults in the U.S. (Chen & Shah, 2011). Nearly all individuals with type 1 diabetes and over 60% of those with type 2 diabetes develop some degree of retinopathy within 20 years of diagnosis.

DR progresses through two stages: non-proliferative and proliferative. The early signs of non-proliferative DR include microaneurysms and retinal hemorrhages. As capillary non-perfusion worsens, additional features like cotton-wool spots, venous beading, and intra-retinal microvascular abnormalities appear (Thomas et al., 2015). Proliferative DR is marked by the growth of new blood vessels on the retina or optic disc, caused by ongoing retinal ischemia (Roberts & Thum, 2021). These abnormal vessels can bleed, leading to vitreous hemorrhage, fibrosis, and tractional retinal detachment.

Diabetic macular edema (DME), a leading cause of vision loss, is characterized by hard exudates in the central retina and impaired

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vascular permeability in diabetics. While treatments such as laser photocoagulation can prevent the progression of diabetic retinopathy (DR) and vision loss, primary interventions like intensive blood pressure and glucose control significantly reduce DR incidence (Yang et al., 2010). Despite numerous new therapies, their effectiveness remains uncertain and requires further evaluation. Hemodynamic changes in diabetics accelerate the formation of advanced glycation end products (AGEs), increase oxidative stress, and activate the renin-angiotensin-aldosterone system (RAAS). Other factors include the polyol pathway, protein kinase C (PKC) activation, elevated growth factors such as vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF-1), as well as subclinical inflammation and capillary damage (Safi et al., 2014).

Orthosiphon stamineus, a plant widely found in Malaysia and Southeast Asia, is traditionally used to treat various conditions like diabetes, hypertension, gout, and kidney stones. Extracts from *O. stamineus* leaves have shown strong antibacterial, anti-inflammatory, and antioxidant properties (Ashraf et al., 2018). A proprietary extract of *O. stamineus*, standardized to rosmarinic acid and known as Lanctos 75™ (C5OSEW5050ESA), has demonstrated anti-inflammatory, antioxidant, anti-angiogenic, and immunomodulatory properties (Al-Suede et al., 2021; Rajasekar et al., 2019). The extract has been found to inhibit VEGF expression and VEGFR phosphorylation (Al-Suede et al., 2014; Almoustafa et al., 2023). Additionally, Lanctos 75™ has shown a strong safety profile at doses up to 5000 mg/kg (Yehya et al., 2019). Recent clinical studies have indicated its ability to reduce F2 isoprostane, a marker of oxidative stress. Given the connection between angiogenesis inhibition, oxidative stress, and diabetic retinopathy, this study aims to assess the efficacy of Lanctos 75™ as both a retinal-protective and neovascular inhibitor in a diabetic retinopathy model. The study also evaluated the extract's physicochemical and pharmacokinetic properties in an in situ gel formulation.

2. Materials and Methods

2.1 Plant Material and Extraction

The proprietary *O. stamineus* extract, Lanctos 75™ (C5OSEW5050ESA), standardized to 6% rosmarinic acid, was produced and supplied by Natureceuticals Sdn. Bhd. (Batch Number: SD0053). The plants were sourced from Natureceuticals' Good Agriculture Certified plantation, using a vertical fertigation technique. The species was authenticated by the Forest Research Institute of Malaysia (FRIM), with voucher specimen number MGF0720.

2.2 In Vitro Studies

2.2.1 Retinal Precursor Cells (R28)

R28 cells, obtained from ATCC, are transformed neural precursor cells with biochemical properties similar to retinal precursor cells. Cultures were maintained at 37°C in a humidified environment with 95% air and 5% CO2. The culture medium consisted of Dulbecco's modified Eagle's medium (DMEM; Sigma-Aldrich), supplemented with 10% fetal bovine serum (FBS; Invitrogen, Paisley, Scotland, UK), 25 mM glucose, 100 U/mL penicillin, and 100 g/mL streptomycin. Cells were routinely passaged at a 1:8 ratio to a density of 4 to 5 x 10^4 cells/mL in 75-cm^2 filter-capped flasks. Cells were seeded at varying densities, including 500 µL onto sterilized borosilicate glass coverslips in 24-well plates and 100 µL in 96-well plates (Seigel, 2014).

2.2.2 Cytotoxicity Assay

The MTT assay was used to assess the cytotoxicity of Lanctos 75™ against R28 cells. R28 cells were seeded in 96-well plates at a density of 3,000 cells per well and allowed to adhere. Media were replaced with medium containing Lanctos 75™ at dilutions ranging from 6.25 to 200 µg/mL for 48 hours, followed by a 4-hour MTT incubation. DMSO was used to dissolve the MTT-transformed crystals, and absorbance was measured at 570 nm with a reference wavelength of 620 nm using a microplate reader (SpectraMax M2, Molecular Devices, Menlo Park, CA).

2.2.3 Serum Deprivation Assay

RGC-5 cells were cultured in 96-well plates for 24 hours and then washed with serum-free media, except for two columns. Cells were then exposed to varying doses of Lanctos 75™. Untreated wells that were not washed with serum-free media served as positive controls. MTT was added 48 hours after treatment, and cells were incubated at 37°C for 4 hours. The medium was then aspirated, and DMSO was used to dissolve the formazan crystals. Absorbance was measured at 570 nm with a reference wavelength of 620 nm (Ibrahim et al., 2016).

2.2.4 Apoptosis Assay

To assess Lanctos 75™'s effects on nuclear morphology, RGC-5 cells were cultured in serum-free media as outlined in the serum deprivation assay. Lanctos 75™ was applied at 10 and 20 µg/mL to cells that were 60–70% confluent. Cells treated with 0.1% DMSO served as negative controls. After the media were removed, cells were washed with phosphate-buffered saline (PBS), fixed in 4% paraformaldehyde for 30 minutes, and stained with 10 mg/mL Hoechst 33342 for 20 minutes. Cells were then rinsed with PBS and photographed at 20X magnification using a fluorescence microscope fitted with a digital camera (Olympus™, Japan).

2.3 In Vivo Efficacy Study

2.3.1 Retinal Vascularization in Rats

In compliance with the guidelines of the Institutional Animal Care and Use Committee and the Association for Research in Vision and Ophthalmology, male Sprague-Dawley rats were acquired from the Universiti Sains Malaysia (USM) Animal House. They were housed in the USM EMAN Laboratory under controlled conditions (22 ± 1°C, 50% humidity, 12-hour light/dark cycle) with unrestricted

access to food and water. The rats weighed 200 ± 10g and were acclimated for 7 days before being randomly divided into three groups. Body weights were recorded at 2-day intervals (Khan et al., 2017).

2.3.2 Rat Model of Diabetic Retinopathy

Type 1-like diabetes was induced in the rats to simulate diabetic retinopathy, following the protocol described by Lai & Lo (2013). Streptozotocin (STZ) was used to disrupt pancreatic cells, inducing diabetes. Six control rats received intraperitoneal (i.p.) injections of physiological saline, while twelve rats were injected with 65 mg/kg STZ. After 7 days, rats with serum glucose levels above 16.5 mmol/L were considered diabetic. These twelve diabetic rats were divided into two groups: one remained untreated, while the other received twice-daily doses of Lanctos 75™ (C5OSEW5050ESA) for 30 days. Blood glucose levels were measured daily via a glucometer, using venous blood from the tail. Eye images were taken using a Welch Allyn PanOptic ophthalmoscope to capture the retinal state of normal, treated, and untreated rats.

2.3.3 In Vivo Study of the Mouse Ischemic Optic Neuropathy Model

To evaluate Lanctos 75™'s effect on inflammation (cathepsin activity) after optic nerve ischemia, an ischemic optic neuropathy model was developed using NCR NuNu mice (Miyake et al., 2007; Khalilpour et al., 2018). The optic nerves were transiently ligated for 30 seconds in both control and treatment groups after anesthetizing the mice with intraperitoneal injections of ketamine (100 mg/kg) and xylazine (20 mg/kg). The treatment group received pre-treatment with Lanctos 75™ (200 mg/kg). Fluorescence Tomography (FMT 1500, PerkinElmer, Waltham, MA, USA) was used to measure anti-inflammatory and anti-angiogenic effects in the eye region. Fluorescent probes (ProSense 750 EX, VisEn Medical) were injected intravenously, and imaging was performed on days 1 and 7. Sedated mice were placed in the FMT Imaging chamber, and fluorescence intensity was measured using WinLight32 software. The three-dimensional regions of interest (ROI) were selected for data collection, which was exported to Microsoft Excel for analysis.

2.4 Corneal Ulcer Healing and Neovascularization in a Rat Model

Twenty-four male Sprague-Dawley rats (200–220g) were purchased from the USM Animal House facility and housed in controlled conditions. They had access to water and a standard diet throughout the experiment. All procedures were approved by the Ethical Committee of Universiti Sains Malaysia and adhered to the guidelines for the Use of Animals in Ophthalmic and Vision Research.

2.5 Quantification of Corneal Neovascularization

According to the method of Cheng et al. (2007), male Sprague-Dawley rats (8–10 weeks old) underwent alkali-induced corneal injury. Under local anesthesia, the rats were randomly assigned to three groups. Group 1 received distilled water, serving as the untreated control. Groups 2 and 3 received 200 mg/kg and 400 mg/kg of Lanctos 75™ extract, respectively. Following anesthesia with xylazine and ketamine, a 2-mm filter paper soaked in NaOH (0.15 mol/L) was applied to the left cornea for 30 seconds. The cornea was then irrigated with sterile saline. Daily examinations of the cornea were conducted using a slit lamp microscope to assess corneal opacity, ulceration, and neovascularization. On day 7, under anesthesia, images were captured using a camera attached to a slit lamp microscope.

3. Results

In Vitro Studies

Cytotoxicity Assay

Experiments were conducted to determine the dose-dependent effects of Lanctos 75™ on R28 cell survival. After 48 hours of treatment, less than 50% inhibition of cell growth was observed at the highest dose of 200 µg/mL (Figure 1).

Serum Deprivation Study on RGC-5 Cells

A 48-hour serum deprivation of RGC-5 cells led to a 50%–60% cell loss compared to serum-free control cells, suggesting that serum deprivation induced apoptosis in these cells (Figure 2).

Measurement of Apoptosis

The effect of various stressors, including 12 hours of serum deprivation, on RGC-5 cells was analyzed using Hoescht 33342 stain. Cells in serum-free media exhibited intensely fluorescent nuclei, indicative of DNA damage, as shown in Figure 3B. However, the nuclear morphology of RGC-5 cells treated with Lanctos 75™ at concentrations of 10 and 20 µg/mL (Figures 3C and 3D) resembled that of control cells in normal serum (Figure 3A). In the serum-deprived condition, cells treated with 10 and 20 µg/mL of Lanctos 75™ showed a significant reduction in apoptotic nuclear signals compared to untreated serum-deprived cells.

In Vivo Efficacy Studies

Imaging of Retinal Vascularization in Rats

Figure 4A shows a healthy, untreated animal's eye as a normal control, displaying typical retinal vasculature without hemorrhagic lesions or inflammation. In contrast, Figure 4B illustrates a streptozotocin-induced diabetic retinopathy model, with arrows marking microaneurysms and circles highlighting hemorrhages. Retinal vascular leakage, indicated by dilated vessels and exudates (arrowhead), suggests inflammation around the blood vessels. Figure 4C shows the eye of an animal treated with Lanctos 75™, where few microaneurysms (arrows) and reduced exudation (arrowhead) are observed, reflecting decreased vascular leakage. The data also confirmed that Lanctos 75™ provided anti-retinopathic benefits, as evidenced by the absence or reduction of hemorrhagic zones.

In Vivo Study of the Ischemic Optic Neuropathy Model

The analysis of FMT images focused on the eye region to quantify the inflammatory response following optic nerve ischemia (Figures 5A, B, and C). In untreated mice, a significant induction of cathepsin expression was observed, marked by strong fluorescent signals in the ocular region (Figures 5D and 5F). However, in mice treated with Lanctos 75™ (200 mg/kg body weight), the fluorescent signal decreased, indicating recovery from transient ischemia (Figures 5B and 5E). Changes in fluorescence volume (cathepsin expression) were quantified and graphically depicted in Figure 6.

Corneal Ulcer Healing and Neovascularization in Rats

Figure 7 highlights the significant differences in neovascularization and corneal opacity between treated and untreated animals using two doses of Lanctos 75™ (200 and 400 mg/kg body weight). Treated rats exhibited less conjunctival redness and edema compared to the untreated group. The untreated animals showed more conjunctival redness, edema, and an increased number of vessels and inflammatory cells in the cornea, while Lanctos 75™-treated rats displayed dose-dependent reductions in redness and edema.

Statistical Analysis

Results of both in vitro and in vivo studies were expressed as mean ± standard error (SEM). Data analysis was performed using SPSS 16.0, with results calculated as the mean ± SD from triplicates of three independent experiments. One-way ANOVA was employed to assess mean differences, followed by Post Hoc-Dunnett's or Tukey's testing. Correlations were determined using bivariate, 2-tailed Pearson's test, and linear regression analysis was performed to evaluate R^2 values. Statistical significance was set at $p < 0.05$, $p < 0.01$, and $p < 0.001$.

4. Discussion

Diabetic retinopathy (DR) is a severe complication of diabetes, leading to retinal blood vessel damage and vision loss. DR is classified into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR), with the latter marked by abnormal blood vessel growth, causing complications like vitreous hemorrhage and retinal detachment. Approximately one-third of diabetics have DR, especially those with type 1 diabetes. Early detection and management are critical for preventing vision loss, especially in regions with limited access to care.

Natural products, including polyphenols, flavonoids, and herbal extracts, exhibit beneficial properties such as antioxidant, anti-inflammatory, and anti-angiogenic activities, which target key pathways in DR pathogenesis (Wang et al., 2020; Zhao et al., 2019). Epidemiological studies have linked antioxidant-rich diets to reduced DR risk and progression (Chen et al., 2021), while experimental studies have demonstrated the efficacy of natural product interventions in animal models (Li & Zhang, 2022).

O. stamineus, a widely found plant in Southeast Asia, possesses strong antioxidant, anti-inflammatory, and antibacterial properties (Ashraf et al., 2018; Al-Suede et al., 2021). Recent studies on **Lanctos 75™**, an extract of O. stamineus, revealed its potent anti-angiogenic activity, attributed to its rosmarinic acid, sinensetin, and eupatorin content (Nazari et al., 2022). The antioxidant and anti-inflammatory properties of Lanctos 75™ make it a promising candidate for DR treatment and ocular damage prevention due to its rich flavonoid and polyphenol content (Sahib et al., 2009).

Flavonoids, known for their anti-inflammatory and antioxidant effects, have been widely studied for their health benefits (Alshehade et al., 2023). These compounds' free radical scavenging properties are influenced by their chemical structure, including hydroxyl group positions (Al-Suede et al., 2014). Previous research has demonstrated that terpenoids, flavonoids, and primary metabolites like polysaccharides and proteins can inhibit angiogenesis (Rajasekar et al., 2019).

In vitro research on R28 cells has led to significant discoveries regarding retinal function and certain disease states. Studies using serum from glaucoma patients, auto-antibodies to minor heat shock proteins in glaucoma, and R28 cells cultured under elevated atmospheric pressure have been employed to simulate the detrimental metabolic effects of glaucoma on retinal cells. As an in vitro model of retinal development, R28 cells have shown enhanced neurite outgrowth in response to mouse acetylcholinesterase and pigment epithelial-derived factor. While R28 cells are not visually sensitive to light, their response to the harmful effects of light has been studied. For instance, blue light (411 nm) caused R28 cells to produce more mitochondrial superoxide radicals and caspase-3 cleavage products upon illumination. Thus, in the current investigation, R28 cells were used as a model for retinal cell function and to assess the safety of Lanctos 75™ extract. At the maximum treatment dose of 200 µg/mL, cell growth suppression was less than 50%, indicating that Lanctos 75™ is not cytotoxic to R28 cells.

To model ischemic conditions seen in diabetic retinopathy (DR) in vitro, serum deprivation was used—a well-established method for studying retinal ganglion cell (RGC) mortality. The current study (Figure 3) showed that serum deprivation significantly reduced RGC-5 cell viability, while Lanctos 75™ promoted RGC-5 cell survival under these neurotrophic-deficient conditions. This suggests that Lanctos 75™ may have protective or proliferative effects on RGC-5 cells, independent of serum-derived factors, possibly by activating cell survival pathways, enhancing cellular metabolism, or inducing the expression of growth-promoting factors.

From a research perspective, compounds that exhibit such activity under serum deprivation conditions are particularly promising for therapeutic use in conditions marked by compromised cell survival or proliferation, such as neurodegenerative diseases or ischemic injuries.

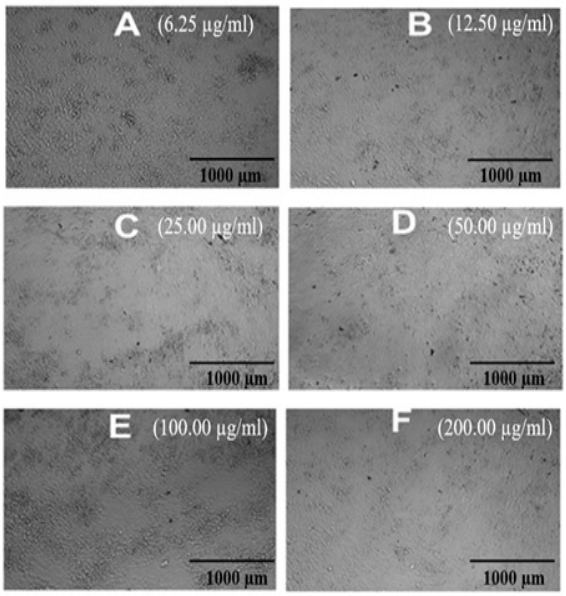

Figure 1. Images of retinal cells (R28) under an inverted phase-contrast microscope with a digital camera at 48 hours after treatment with different concentration of Lanctos 75™ (6.25-200 µg/mL).The suppression of cell growth observed in dos dependent manner with IC_{50} >200µg/ml.

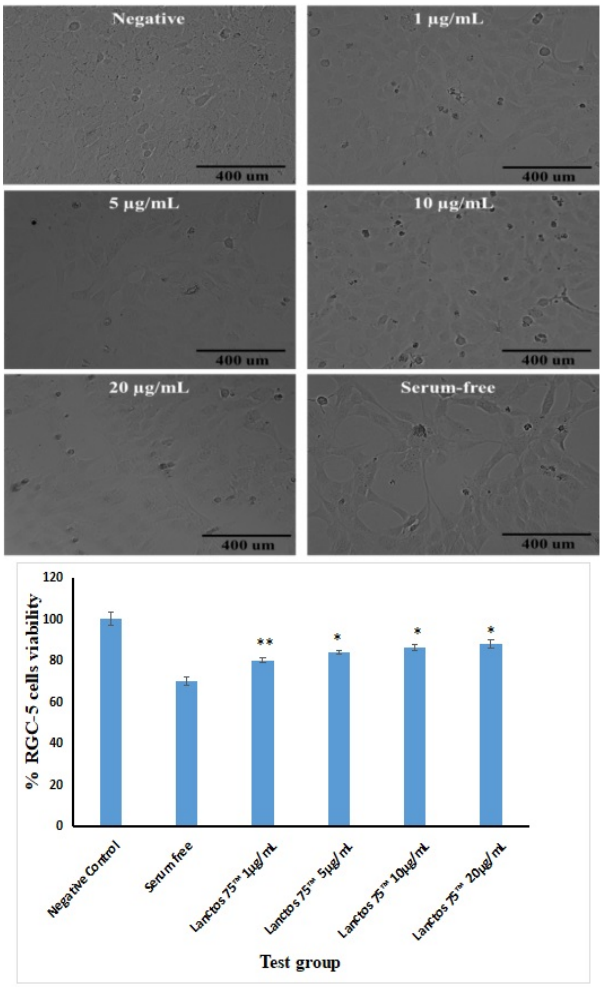

Figure 2. Effect of Lanctos 75™ on 48 hours of serum deprived RGC-5 cells. Cell viability as measured by MTT demonstrates the protective effect of Lanctos 75™ in RGC-5 cells subjected to serum deprivation for 48 h. The results are mean values with error bars indicating ± SEM where (n=3), **P< 0.05 and * P< 0.01 vs. serum free (positive control).

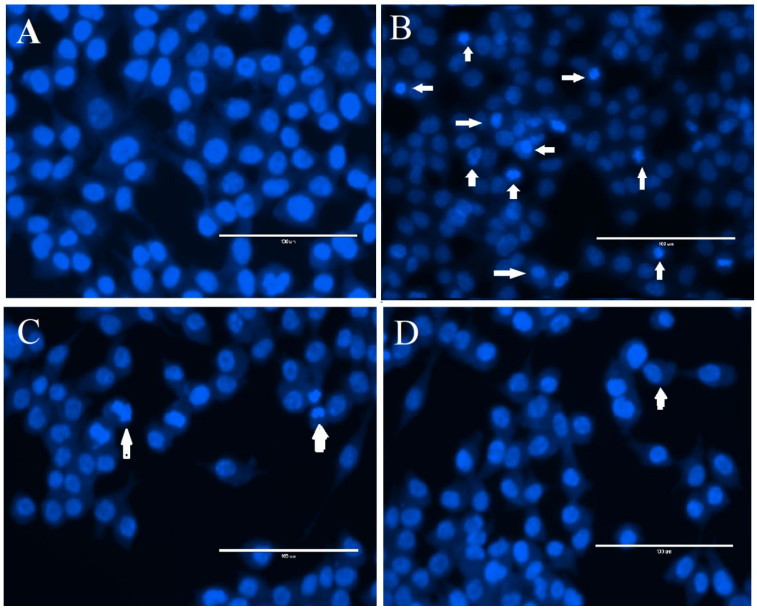

Figure 3. The photomicrographs exhibit images of RGC5 cells stained with Hoechst 33342, taken at 12 hours after treatment with various concentrations of Lanctos 75™ in serum-free conditions. (A)Represents the untreated cells, (B) Shows cells treated with serum-free media, with arrows indicating clear signs of nuclear condensation, including crescent-shaped apoptotic nuclei, chromatin dissolution, breakdown, and fragmentation, (C&D) Show images of cells treated with Lanctos 75™ at concentrations of 10 and 20 µg/mL, respectively.These images demonstrate a decrease in apoptotic cells with an increase in Lanctos 75™ concentration. Cells treated with Lanctos 75™ showed a substantial decrease in apoptosis compared to the serum-free group.

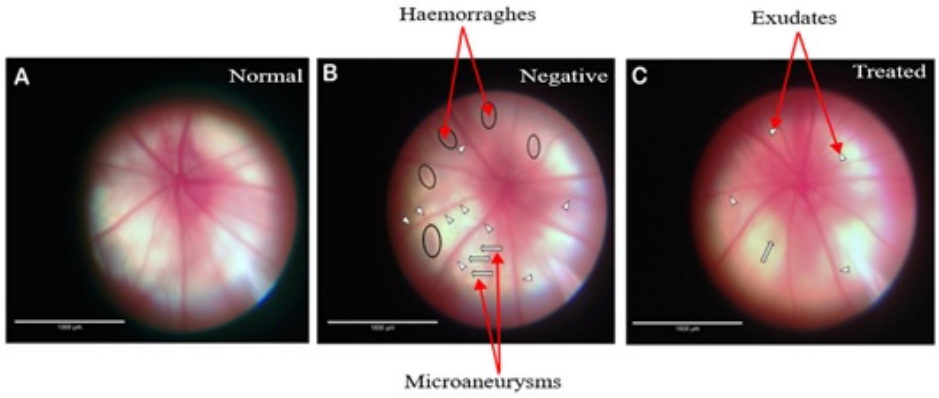

Figure 4. Colour fundus imaging of Sprague-Dawley normal rats. The photos were obtained using Welch Allyn PanOptic ophthalmoscope where **A)** Eye image taken from the healthy animal (normal), **B)** Eye image taken from untreated animal (negative control), **C)** Eye image taken from treated group.

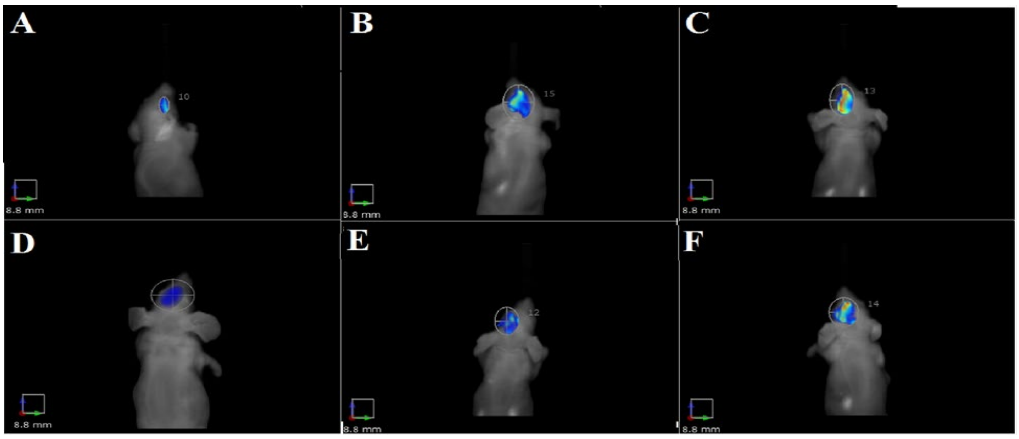

Figure 5. Effect of Lanctos 75™ formulation using FMT imaging system in ischemia induced mice where A = FMT image of normal nude mice, B = FMT image of nude mice after 24 hour treatment with the formulation 200 mg/kg, C = FMT image of untreated nude mice showing the strong fluorescent signal for Cathepsin, D = FMT image of normal nude mice after 7 days, E = FMT image of nude mice after 7 days treatment with the formulation(200 mg/kg) and F = FMT image of untreated nude mice showing the strong fluorescent signal for Cathepsin after 7 days.

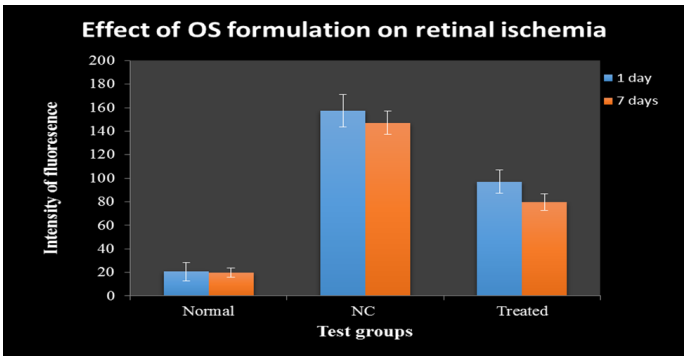

Figure 6. Graphical depiction illustrates the intensity of the fluorescence signal produced following the induction of ischemia. Animals administered with Lanctos 75™ demonstrated a notable decrease in the signal induced by ischemia compared to the untreated control group(NC). Results are presented as mean ± SEM (n = 3), where * indicates a p-value < 0.05 and ** indicates a p-value < 0.01.

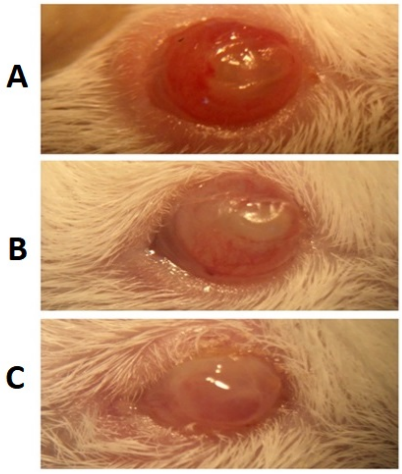

Figure 7. Effect of different treatment doses of Lanctos 75™ formulation on formation of blood vessels in damaged cornea. Alkali burn-induced corneal neovascularization in the rat animal model. Rats received alkali burns on the central cornea of their left eyes where A) Eye image of untreated group , B) Eye image of treated group with 200mg/kg of Lanctos 75™, C) Eye image of treated group with 400mg/kg of Lanctos 75™. Animals treated with Lanctos 75™ exhibited a significant reduction in the eye burn compared to the untreated group.

Retinal ganglion cell (RGC) death in glaucoma and diabetic retinopathy (DR) has been strongly linked to apoptosis, a fundamental process in many biological systems. Apoptosis can be triggered through both intrinsic and extrinsic pathways. The intrinsic pathway involves the release of cytochrome-c from the mitochondria, while the extrinsic pathway relies on the activation of death receptors on the cell surface (Seigel, 2014). In the current investigation, serum deprivation was used to evaluate the signaling pathways involved in retinal ganglion cell (RGC) death in cultured RGC-5 cells. The presence of trophic factors in serum is essential for cell nutrition in culture (Yang et al., 2010). Thus, serum deprivation induces apoptosis in RGCs by disrupting the retrograde trophic factor signaling process, which plays a role in RGC death in both glaucoma and diabetic retinopathy (DR). Serum deprivation in RGC-5 cells has been reported to cause apoptosis-related symptoms such as DNA laddering, caspase-3 and -9 activation, increased Bax levels, decreased Bcl-2 levels, increased NF-κB binding activity, and elevated cellular GSH (Li & Zhang, 2022). Additionally, cytochrome C release and a reduction in mitochondrial membrane potential were observed (Khan et al., 2017). These findings suggest that Lanctos 75™ may have protective effects against retinal nerve fiber damage by exhibiting anti-apoptotic properties in serum deprivation-induced apoptosis in RGC-5 cells.

A key challenge in treating intraocular disorders is the difficulty of drug penetration due to the blood-ocular barrier, which prevents many substances from reaching therapeutic levels in the eye (Cheng et al., 2007). To overcome this, intraocular drug delivery methods such as intracameral and intravitreal injections can bypass the barrier, ensuring adequate drug concentrations (Yehya et al., 2019). In vivo models using NU/NU mice were employed to assess the effects of Lanctos 75™ on the inflammatory response (pan-cathepsin activity) following optic nerve ischemia. The NU/NU nude mouse model has a human-like retinal vascular structure. The optic nerve crush technique was used to induce ischemia, causing axonal injury due to reduced blood supply (Almoustafa et al., 2023).

The in vivo effects of Lanctos 75™ were evaluated using three-dimensional fluorescence molecular tomography (FMT) to measure the inflammatory response at the site of ischemic injury. ProSense 750, a pan-cathepsin fluorescence probe activated by various cathepsins, was used to visualize cathepsin activity. Cathepsins are crucial in apoptosis, neuroinflammation, and angiogenesis. The ischemia-induced group showed an increased fluorescence signal, indicating cathepsin activation linked to neuronal damage. Treatment with Lanctos 75™ significantly reduced signal intensity, suggesting its neuroprotective effects.

5. Conclusion

The study demonstrated that Lanctos 75™ effectively reduced diabetic retinopathy in animal models. Lanctos 75™ exhibited neuroprotective properties, shielding optic nerves from neuronal damage. It successfully prevented the development of microaneurysms, hemorrhages, vascular leakage, and inflammation in the retina in a streptozotocin-induced diabetic retinopathy model. Additionally, Lanctos 75™ provided significant protection against ischemia-reperfusion injury and showed notable anti-angiogenic and anti-retinopathy effects by aiding in corneal ulcer repair. Derived from the standardized extract of *O. stamineus*, Lanctos 75™ demonstrated a strong anti-retinopathy effect by preventing neovascularization and inflammation in rats. These results suggest that Lanctos 75™, made from *O. stamineus* extract, may be an effective treatment for diabetes-related retinopathy.

Author contributions

ASAM and AMSA. supervised this study and designed the experiments. FSRA, GA, MAA and ASAM wrote the manuscript. FSRA, KAB and ASAM designed and performed the experiments. All authors reviewed the manuscript.

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Competing financial interests

The authors have no conflict of interest.

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