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The Protective Effect of Glycine on Retinal Function and Structure in Diabetic Retinopathy

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DIABETIC retinopathy (DR) is a microvascular complication of diabetes mellitus (DM) and is the leading cause of blindness worldwide. It is characterized by the growth of new blood vessels in the retina, a process known as neovascularization. The primary cause of the structural and functional changes associated with DR is the hyperglycemic state that accompanies diabetes.Numerous studies have shown that supplementing with amino acids such as hydroxyproline, lysine, and glycine can protect against proliferative diabetic retinopathy. The purpose of this study was to assess glycine's possible ability to prevent diabetic retinopathy in rats with diabetes produced by streptozotocin (STZ). Method: Eighty-four female Wistar rats, aged 8 to 12 weeks, were used in the study. The rats were divided into four groups: a control group, a glycine group (G), a diabetic retinopathy group (DR), and a diabetic retinopathy group administered glycine (DR+G). Electroretinographic (ERG) and histopathological studies were conducted to assess the protective role of glycine on the retinas of the rats. Results: The electroretinographic and histological findings for the glycine group showed very close values to the control group. In contrast, severe changes were observed in the DR group, leading to decreased ERG parameters and alterations in retinal structure, particularly after four weeks. For the DR+G group, the electroretinographic data indicated no differences from the control retina at both the two-week and four-week marks. The histological cross-sections taken after four weeks showed an intact retina and vitreoretinal interface. Conclusion: This study provides evidence that the administration of glycine can repair the retina's structure and function. Additionally, supplementing the diet of experimental DR rats with glycine demonstrated a protective effect against the retinal damage typically associated with diabetic retinopathy.

Keywords: Glycine, Diabetes, diabetic retinopathy, Electroretinography.

Introduction

The retina is a specialized layer of tissue located in the back of the eye, which is made up of light-sensitive cells in many layers. To enable the perception of visual inputs, these cells are in charge of transforming incoming light into electrical signals, which are then sent to the brain via the optic nerve; these electrical signals can be detected by special electrodes attached to the head and amplified to give what is called the Electroretinography (ERG). [1]

Because of its proactive powers in the early identification and diagnosis of eye problems, ERG is regarded as a groundbreaking diagnostic technique in ophthalmology, and it has even been viewed as providing a window into brain function [2]. ERG offers important insights into retinal function that other diagnostic methods cannot identify. This non-invasive test gauges the retina's electrical reactions to specific light stimuli, giving information about the function and health of the different retinal layers and cells, so it has proactive capabilities in early detection and diagnosis of many eye diseases [1]. ERG is essential for diagnosing inherited or acquired retinal disorders, such as retinitis pigmentosa, macular degeneration, retinoblastoma, retinal detachment, and cone-rod dystrophy [1]. It also can help determine the appropriate treatment strategies for various retinal disorders by differentiating between them [3].

The ERG can also be used to monitor the progression of retinal diseases and evaluate the effectiveness of treatments. Besides, it can detect retinal toxicity due to drugs or other substances, which is essential for patient safety [4].

Diabetic retinopathy (DR) is a microvascular complication of diabetes Mellitus (DM). It is the most common cause of blindness worldwide. It is mainly characterized by the growth of new blood vessels in the retina (neovascularization) [5]. The hyperglycemic state associated with DM is the primary cause of the structural and functional alterations related to DR. Apoptosis, inflammation, and breakdown of the blood-retinal barrier (BRB)

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leading to permeability changes can also be characteristic of DR [5]. Apoptosis of retinal neurons and consequent neurodegeneration were indicated in many studies [6] [7].

Numerous studies were interested in the anti-diabetic activity of amino acids and their potential incorporation into DR treatment and prevention [5] [8] [9]. Glycineis a new trend in treating DR due to its high antioxidant and anti-glycation power [11]. Glycine is a non-essential amino acid synthesized by mammals, microbes, and plants. It can be a flexible component of many proteins due to its small size and absence of a side chain. Glycine serves as an inhibitory neurotransmitter [12].Glycine has been examined in several clinical disorders, including cancer, arthritis, and liver fibrosis, with positive results. Glycine was therefore advised to be used in therapeutic drugs [13].

[14] investigated the preventive effect of glycine against cataractogenesis in STZ-diabetic rats Their study demonstrated the anti-cataract potential of glycine, with the possible mechanism being the suppression of Aldose Reductase (AD) activity. A study by [15] demonstrated the beneficial effects of glycine on alterations in diabetic rats' retinas. They indicated that the mild thinning in most retinal layers due to diabetic retinopathy was improved after sixteen weeks of supplementation of glycine.

Another study by [16] examined the protective effect of glycine on the retinal ultrastructure on Streptozotocin develop diabetes in rats. Histological examination of retinal ultrastructure revealed apoptotic degeneration in the photoreceptor cell layer caused by diabetes; however, supplementing with glycine considerably improved such modifications.

Bovine retinal pericytes (BRPs) were cultured and treated with different amino acids, including glycine and others, and insulin in high glucose conditions. The amino acids hydroxyproline, proline, lysine, glycine, and alanine induced the triglyceride accumulation and expression of adiponectin. Cultured cells treated with glycine or other amino acids had higher levels of antioxidant marker expression. These results suggested that high levels of amino acids, including glycine, could induce adipogenic effects in retinal pericytes. Such transformation is thought to be protective because it increases anti-oxidant potential while decreasing angiogenic markers [8].

The aim of this study was to evaluate the efficacy of amino acids supplements, especially Glycine, in the treatment and/or prevention of some types of ocular complications in streptozotocin (STZ) induced diabetes in rats.

Materials and methods

Experimental animals

Eighty-four female Wistar rats aged 8 to 12 weeks, weighing 200 ± 20 grams, were used in this study. The rats were obtained from the Animal House at the Research Institute of Ophthalmology in Giza, Egypt. Animals were kept in a standard 12 h light-12 h darkcyclewith a balanced diet and free access to water at 25°C ±2°C. The Institutional Animal Care and Use Committee of Cairo University approved the use of laboratory animals in ophthalmic and vision research, which was followed in this study.

Clinical examination and animal groups

All rats' eyes were examined before induction of diabetes by the slit lamp biomicroscope. In all eyes, there were no signs of edema or intraocular inflammation.The rats were divided into four main groups:The control group (C) without streptozotocin injection (STZ) or any treatment (n=21 rats).The Glycine group (G) received glycine130 mM and a concentration of 1% in their drinking waterfor one week, two weeks, and four weeks.The diabetic retinopathy group (DR) in which diabetes was induced by intraperitoneal injection of STZ without receiving any treatment (n=21 rats). The diabetic retinopathy group was administered with glycine (DR+G), in which diabetes was induced by STZ (n=21 rats), andafter the onset of DR, rats received glycine in their free-access drinking water.

Induction of diabetes in the experimental groups

Diabetes was induced in 63 rats using a single intraperitoneal injection of 40 mg/kg streptozotocin (STZ) in 0.1 M freshly prepared sodium citrate buffer (pH = 4.4).After 72 hours of STZ injection, fasting blood glucose levels were measured, and animals with blood glucose levels greater than 240 mg/dl were considered diabetic and used in the study.The retinae of the diabetic rats were monitored for six weeks using a slit lamp bio-microscope (Kowa SL15, Portable slit lamp, Tokyo, Japan) till the onset of DR.

Electroretinogram ERG study

Animal preparation

Before the electrophysiological recording, the animals were dark adapted for one hour. They were generally anesthetized by intramuscular injection with xylazine (21 mg/kg of body weight) and ketamine hydrochloride (45 mg/kg). The animals were placed on a pad of the operating table where their hair around the eye area was

removed, and their body temperature was maintained at 37 °C. Each rat was positioned with its head resting to one side, and Benoxinate eye drops (0.4%) were used for local anesthesia.

Electroretinographic measurements

Topical 1% mydriacyl eye drops was used to dilate the pupil of the recorded eye. All groups were subjected to electroretinographic measurements using the Neuro-ERG system-NeurosoftMedical Diagnostics, Russia. The Neurosoft ERG system comprises a computer interface, light stimulus generator, electrodes, and software for data acquisition and analysis. The system is equipped with various stimulus modalities, including flash and pattern stimuli, allowing for comprehensive evaluation of retinal function.

Extracellular ERG was recorded by using three electrodes; the active electrode was placed on the eyelid; the reference and earth electrodes were placed ipsilaterally and contralaterally on the two ears respectively.To record the effect of ultrasound on all retinal layers, we used full-field ERG stimulation (using the system mini ganzfeld light stimulus), with a frequency of 1 flash/second and no background intensity. Amplitudes were measured from baseline to the lowest point of the negative peak for the a-wave and from the latter to the positive peak for the b-wave.

Histological examination

All rat groups were euthanized according to their estimated periods using four times the dose used for anesthesia. Eyeballs were enucleated carefullyand injected with 4% glutaraldehyde in 0.1 M PBS (pH 7.4) at 4°C at the corneoscleral junction of the rats' eyes. The posterior chamber of the eye containing the retina was immersed in a freshly prepared glutaraldehyde-buffered solution. After half an hour, the retina was dissected into sections (about 1.0 mm^3) and then further fixed for 8.0 h with fresh glutaraldehyde buffered solution (pH 7.4). The sections were washed for 1.0 h with several changes of PBS at 4°C, fixed in 1.33% osmium tetroxide, dehydrated in cold ethanol grads (50%, 70%, 80%, 90%, and 96%), and then embedded in freshly prepared Araldite CY212 mixtures. Semi-thin sections were cut (about 1.0 μm) by ultratome (L.K.B. Produkter, Sweden), fitted on glass slides, and stained with toluidine blue for light microscope examination.

Statistical evaluation

The results were calculated as a mean and standard deviation (Mean ± SD) for all experimental groups. A one-way analysis of variance and the student t-test was employed to contrast groups [17]. The results were considered statistically significant at $p < 0.05$.

Results:

The electroretinogram (ERG) response was obtained for the glycine, DR, and DR+G groups after 1 week, 2 weeks, and 4 weeks and compared to the control group's response. To investigate the function of distinct retinal cell types, two major ERG parameters were examined: (i) the a-wave emanating from photoreceptor cells, and (ii) the b-wave produced by ON- and OFF-type bipolar cells and Müller cells. The amplitude of the a-wave is measured from the baseline to the a-wave trough, and the amplitude of the b-wave is measured from the a-wave trough to the b-wave peak [18].

Table 1. Mean ± SD of the amplitude of a-wave, the amplitude of b-wave, and the b/a ratio for the Control, Glycine, DR, and DR+G groups after periods of 1 week, 2 weeks, and 4 weeks.

Parameter	Amplitude of a-wave (μV)			Amplitude of b-wave (μV)			b/a ratio		
Period Groups	1 week	2 weeks	4 weeks	1 week	2 weeks	4 weeks	1 week	2weeks	4weeks
Control	11.5 ± 0.15			33.7 ± 0.29			2.93		
Glycine	11.7±0.3	11.1±0.1	11.24±0.6	32.9±0.12	34.2±0.18	32.9±0.2	2.81	3.08	2.92
DR	6.1±0.7	5.17±0.8	4.19±0.2	23.3±0.23	20.8±0.4	19.7±0.19	3.81	4.02	4.70
DR+G	7.12±0.2	8.02±0.5	9.98±0.3	24.15±0.13	27.31±0.6	29.88±0.24	3.39	3.4	2.99

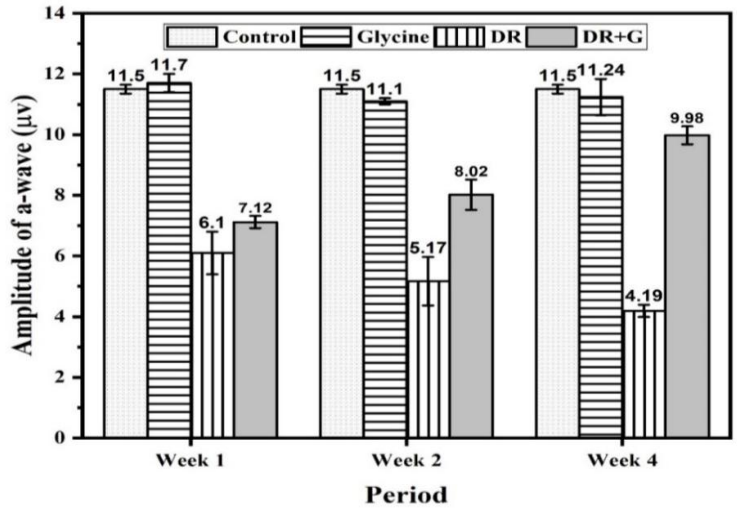

Fig. 1. The amplitude of a-wave for the Control, Glycine, diabetic retinopathy DR, and diabetic retinopathy administered glycine DR+G groups after 1 week, 2 weeks, and 4 weeks.

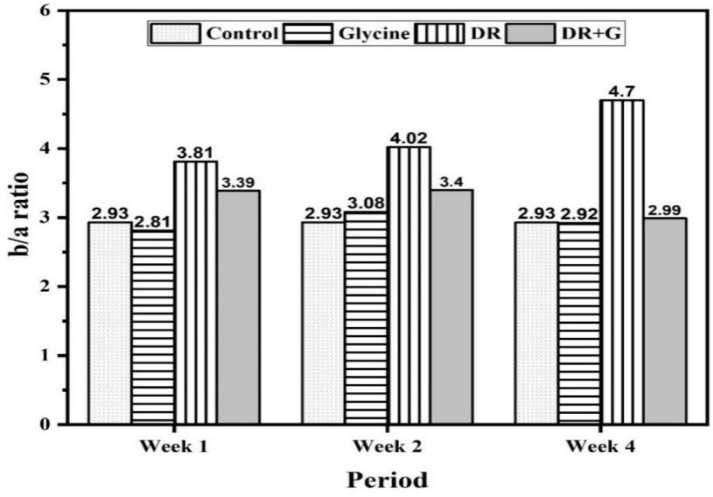

Fig. 2. The amplitude of b-wave for the Control, Glycine, diabetic retinopathy DR and diabetic retinopathy administered glycine DR+G groups after 1 week, 2 weeks and 4 weeks.

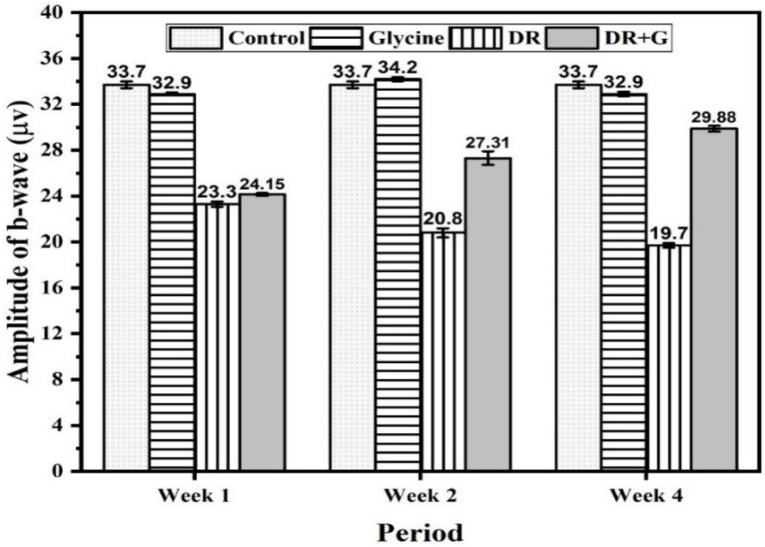

Fig. 3. The b/a ratio for the Control, Glycine, diabetic retinopathy DR, and diabetic retinopathy administered glycine DR+G groups after 1 week, 2 weeks, and 4 weeks.

Table 2. The percentage of changes of amplitudes of a-wave and of b-wave for the Glycine, DR and DR+G groups after 1 week,2 weeks and 4 weeks compared with the control group.

	Percentage change of a-wave (%)			Percentage change of b-wave (%)		
Period Groups	1 week	2 weeks	4 weeks	1 week	2 weeks	4 weeks
Glycine	1.73	3.40	2.26	2.30	1.40	2.37
DR	46.95	55.04	63.56	30.86	38.27	41.54
DR+G	38.08	30.26	13.21	28.33	18.96	11.33

The glycine groups showed negligible changes in the observed ERG parameters even after four weeks of treatment compared to the control group, as shown in Table (2). The percentage changes in a-wave amplitudes were 1.73%, 3.4%, and 2.26% after one, two, and four weeks, respectively. The percentage changes in b-wave amplitudes were 2.3%, 1.4%, and 2.37% after one, two, and four weeks, respectively. These minor differences in glycine groups were not significant, confirming that glycine had no negative effect on retinal cells, as suggested by the comet assay results.

In the DR groups, there was a marked reduction in the amplitude of a-wave, which became more significant with the progression of the DR. The amplitude of a-wave was reduced to 6.10±0.7 µv, 5.17±0.8 µv, and 4.19±0.2 µv with percentage changes of 46.95%, 55.04%, and 63.56% compared to the control group after 1 week, 2 weeks and 4 weeks respectively. In addition, the amplitude of b-wave showed a gradual reduction with values of 23.30±0.23 µv, 20.80±0.4 µv and 19.70±0.19µv and percentage changes of 30.86%, 38.27%, and 41.54% compared to the control group after 1 week, 2 weeks and 4 weeks respectively. This work agrees with many studies that reported STZ-induced ERG alterations aftersix weeks of injection [19], [20], [21].

The early involvement of photoreceptors and bipolar cells in DR was corroborated by these alterations in the a- and b-waves in the DR groups. They offered proof that vascular anomalies in DR don't manifest clinically until after brain deterioration has taken place.

Such a decrease in ERG parameters raises the death of retinal neurons and indicates vascular and neuronal damage across the retina [18]. Reduced function of photoreceptors (a-wave) and bipolar or Müller cells (b-wave) may be indicated by lower ERG amplitudes or delayed (longer) ERG implicit times [22]. Lower quantal absorption, or the mechanism by which light is absorbed by the photopigments in the cone cells of the retina, may be the cause of lower a-wave amplitude, indicative of cone sensitivity loss [22] and photoreceptor degeneration are reported previously in DR [9].

The middle retinal layer, which receives its primary supply from the retinal circulation, produces the b-wave. Accordingly, changes in the retinal circulation, hypoxia, and ischemia are thought to be the cause of the decrease in the b-wave [23]. On the other hand, it was discovered that these modifications in ERG parameters were connected with the BRB function alteration [24]. Additionally, a link was observed between the concentration of retinal GSH and decreased neuronal signals [22]. According to [25], the b/a ratio is a measure of retinal hypoxia and ischemia, and changes in its value correspond to a worsening of the retinal blood supply and its effects.

Furthermore, it is thought that the b-wave and the b/a ratio represent the retina's overall function and can serve as a strong basis for diagnosing visual function [26]. The photoreceptor layer and inner nuclear layer, as well as changes in the blood supply to the retina with an a-wave that changed more dramatically than the b-wave, are all responsible for the change in the b/a ratio in DR groups. Glycine treatment enhanced the ERG response in the DR+G groups at both the a- and b-wave amplitude levels.

After one week, two weeks, and four weeks, respectively, the amplitude of the a-wave was increased to 7.12±0.2 µv, 8.02±0.5 µv, and 9.98±0.3 µv with an enhanced percentage change of 38.08%, 30.26%, and 13.21% in comparison to the control group. After one week, two weeks, and four weeks, respectively, glycine increased the amplitude of the b-wave to 24.15±0.13 µv, 27.31±0.6 µv, and 29.88±0.24µv (as in Table 1), with an enhanced percentage change of 28.33%, 18.96%, and 11.33% (as in Table 2) relative to the control group. Values improved over untreated DR even though they did not recover to control group levels.

Glycine's antioxidant properties are responsible for the enhancement of the ERG response that was obtained with its administration. Glycine's antioxidant qualities allow it to counteract the effects of Reactive Oxygen Species (ROS), free radicals, and increased oxidative stress, which are the main causes of retinal cell death [9] Furthermore, it was shown that glycine functions as a retinal neurotransmitter via glycine receptors (GlyRs), which are primarily found in bipolar cells [27]. As a result, glycine enhances the amplitude and implicit time of the b-wave while also supporting the visual signals pathway.

The improvement in both a-wave and b-wave amplitudes is what causes the b/a ratio to decrease after glycine is administered. The observed enhancement could be ascribed to the established cytoprotective function of Glycine in hypoxic and ischemic circumstances [28]. Glycine has recently been investigated for its potentially important function in regulating microcirculation. According to [9], this endogenous metabolite has the ability to widen blood microvessels, such as spasmodic arterioles, and increase microcirculatory flow.

Histological examination

The Control retina (Fig. 4) with ten retinal layers identified as (1) Pigmented epithelium (PE), (2) Photoreceptors (PR), (3) Outer limiting membrane (OLM), (4) Outer nuclear layer (ONL), (5) Outer plexiform layer (OPL) (6) Inner nuclear layer (INL), (7) Inner plexiform layer (IPL), (8) Ganglion cell layer (GCL), (9) Nerve fiber layer (NFL) and, (10) Inner limiting membrane (ILM).

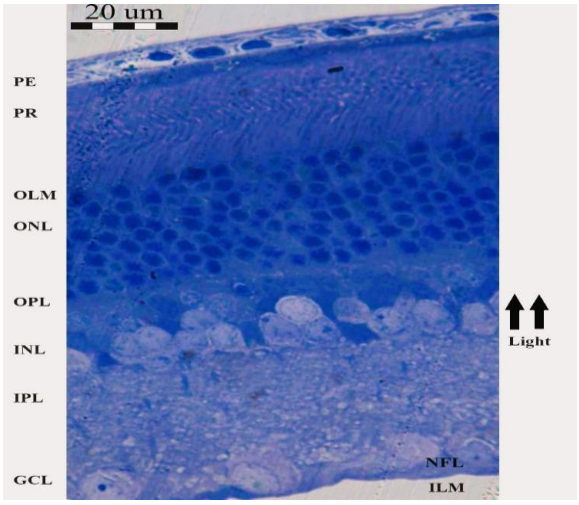

Fig. 4. Cross section of thecontrol retina.

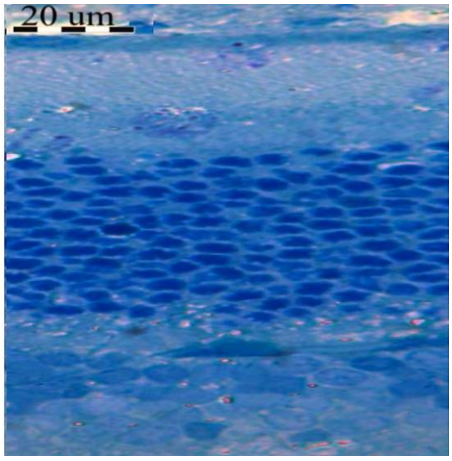

Fig. 5. Cross-sections for retina samples from theGlycine groups showed no deviation from theControl group after 1 week, 2 weeks, and 4 weeks.

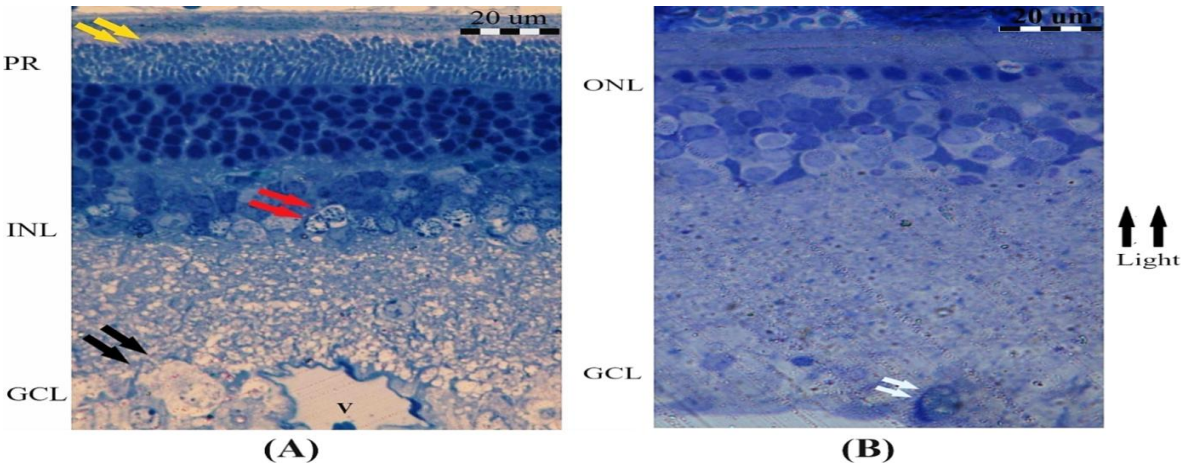

Fig. 6. Cross sections from retinal samples of DR groups (A) After 1 week, showing fragmentation of outer segments of PR (yellow arrows), accumulation of chromatin of the cells of INL (red arrows) with faintly stained nuclei of the GCL (black arrows) and thickened, dilated blood vessels (V). (B)After 2 weeks, the ONL was thinned out to one layer and an occluded blood vessel (white arrows).

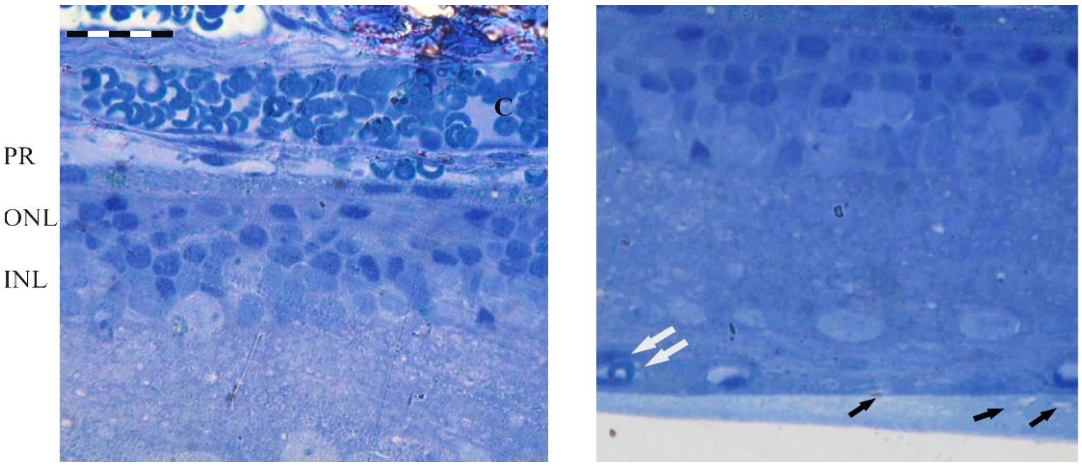

Fig. 7. Cross section from retinal samples of the DR group after 4 weeks showing severe congestion of the choroid layer (C), the ONL was reduced in thickness and intermingled with the INL, partially occluded blood vessel (white arrows), and partial separation of the vitreous from the retina (black arrows).

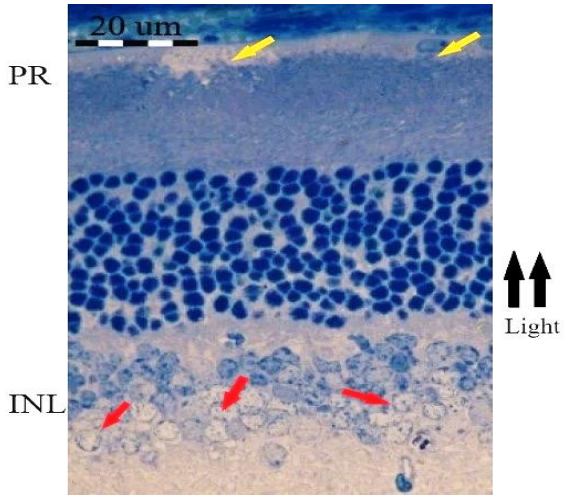

Fig. 8. Cross sections from retinal samples of the DR+G group after 1 week showing fragmentation of outer segments of PR (yellow arrows) and accumulation of chromatin of the cells of INL (red arrows).

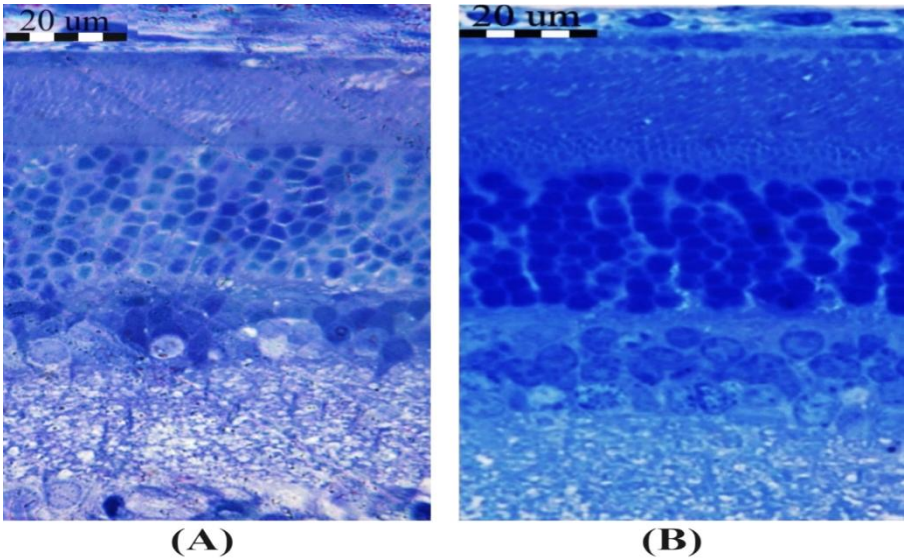

Fig. 9. Cross sections from retinal samples of the DR+G groups (A) After 2 weeks and (B) After 4 weeks. Both groups showed no deviation from the Control group.

Discussion

As shown in Fig. (5), cross-sections of retinal samples from all glycine groups showed no deviation from the control retina (Fig. 4), which indicated that glycine has no harmful effects on the histological arrangement of the retina architecture. This result agrees with the ERG response results recorded from all glycine groups (Table 1) and (Table 2).

In the DR groups, the changes were observed early after one week and two weeks of DR onset. These include fragmentation of PR outer segments, dilation of blood vessels, occlusion of other blood vessels, and thinning of some layers, which may be related to apoptosis, as shown in Fig. (6).All previous alterations are per the literature work by [10]. With the progression of the DR for 4 weeks, the samples showed severe congestion of the choroid layer and partial separation of the vitreous from the retina, Fig. (7).

The fragmentation of PR outer segments, Fig. (6 A) can be interpreted by the fact that the outer segments of PR lose the ability to renew themselves in DR [11]. This was attributed to hypoinsulinemia associated with DR. Moreover, the neuronal cells of INL were seriously affected after 1 week, and the ONL was affected after 2 weeks (Fig. 6 A&B) of DR. In addition, regional variation in blood vessel diameters is observed where dilated blood vessel is shown in Fig. (6A) and occluded blood vessels in Fig. (6 B), and Fig. (7). This regional variation in blood vessel diameters was previously reported in the work of [29]. In the macular area, the predominant finding is vasodilation and impaired pressure autoregulation as hyper-perfusiontransmits arterial blood pressure to the capillary bed and, in turn, contributes to macular edema by the formation of microaneurysms, hemorrhage, and BRB breakdown [30], [29], [31]. Meanwhile, the capillaries occlude in the retinal periphery, resulting in ischemia and hypoxia [29]. These histological changes, along with changes in ERG parameters of DR groups, confirmed the early involvement of photoreceptors and bipolar cells in DR and provided evidence supporting the fact that neural degeneration in DR may precede clinically apparent vascular abnormalities.

The dilatation of the retina's blood vessels may be due to disturbances in neurovascular coupling (the mechanism by which neural activity affects the blood flow). However, it may also be a physiological reaction to changes in retinal metabolism with excessive release of vasodilating compounds [29]. In addition, nonenzymatic glycation and oxidative stress contribute to retinal vascularbasement membrane (BM) stiffening and `irreversible thickening in diabetes [32]. The occlusion of the retina's blood vessels is expected in STZ-induced models of DR in rats and affects the blood supply to the retina, causing hypoxia and ischemia [33]. Retinal ischemia leads to neuronal damage and eventual death, and the retinal non-perfusion likewise triggers the release of growth factors, including VEGF, which promote angiogenesis, proliferation of new vessels (neovascularization), the defining characteristic of proliferative DR [34].

In hyperglycemic conditions, two events act together and contribute to capillary occlusion.First,capillary endothelial cells (ECs) are stressed and liable to damage and apoptosis. This effect could be due to the direct effects of the high glucose level or to ROS and nitrous oxide species (NOS). Second, circulating leukocytes are activated and then adhere to the vessel wall, a process termed leukostasis. It is implied that increased circulating ROS directly damages the vascular endothelial surface, which depolymerizes and thins, eventually exposing the plasma cell membrane to direct contact with activated leukocytes [35]. Increased levels of adhesion molecules were reported and related to the severity of DR. Moreover, they were found to be related to the level ofglycated hemoglobin (HbA1c) and were considered measures of endothelial cell (EC) damage [36].

The choroidal changes observed after 4 weeks of DR, as shown in Fig. (7) may be related to the outcome of hyperglycemic conditions that affect the vascularity of the choroid as well as the retina [37]. Systemic inflammation seems responsible for the choroidal damage, which plays a role in the progression of DR [38]. Since the vascular tissue of the choroid supplies blood to the outer retina, photoreceptors, and retinal pigment epithelium, changes in choroidal capillary flow (CCF) may be associated with greater damage to photoreceptors and thus affecting visual function. The reduction in CCF may cause retinal dysfunction and lead to ERG impairment [39]. This is in accordance with the present work that reported the depression of ERG parameters, especially after four weeks of DR.

In the DR+G group, after 1 week, there was no significant improvement in the retina's histological structure, which can be attributed to a short administration period, Fig. (8). Meanwhile,the DR+G groups showed no deviation from the control retina after 2 weeks and 4 weeks (Fig. 9 A&B). Glycine enabled PR to renew its outer segments and protect them from fragmentation due to itsinsulin-enhancing effect, as reported previously [40], [8], [9]. In addition, glycine protected the retina from the neural changes related to the DR group, including accumulation of chromatin of the cells of INL and faintly stained nuclei of GCL (Fig. 6 A) and reduced thickness of neural layers (Fig. 6 B and Fig. 7). This can be attributed to the protective role of glycine against apoptosis due to the antioxidant effect. Moreover, glycine protects retina vasculature through its protective role against angiogenesis and inflammation. A treatment using glycine significantly decreased the amount of serum glucose, serum AGEs, and glycated hemoglobin (HbA1c) in diabetic rats [41]. Another study found that glycine reduced the expression of RAGE and VEGF and reduced inducible nitric oxide synthase (iNOS) expression [5]. Glycine competitively inhibits the binding of glucose to proteins such as actin and collagen, whose glycation plays a role in reducing leukocytes deformability and promotes capillary occlusion [10]; [42]. Inhibition of

iNOS, which reduces retinal NO levels, restores neurovascular coupling in diabetic retinas [43]. Also, glycine reduces intracellular levels of ROS through its antioxidant effect [11].

During DR progression, the metabolic and functional modifications of the retinal tissue and systemic responses that occur can result in structural and molecular alterations of the vitreous. This, in turn, can result in the separation of the vitreous from the retina, known as vitreoschisis [44]. The retina sample from the DR group after 4 weeks showed partial separation of the vitreous from the retina, Fig. (7). Noticeably, the vitreous is composed mainly of collagen and hyaluronic acid (HA) that interact in the normal vitreous, forming a supramolecular three-dimensional complex. Elevated glucose levels in the diabetic vitreous increase the probability of collagen glycation and cross-linking of collagen fibrils with other structural proteins. In addition, the accumulation of AGEs in the vitreous accelerates the degradation of HA. The cross-linking of vitreous collagen and degradation of HA may contribute to diabetes-related vitreoschisis and early posterior vitreous detachment PVD [45].

In the DR+G group, the cross-section obtained after 4 weeks showed an intact vitreoretinal interface, which ensures the protective effect of glycine against DR (Fig. (9 B). Glycine was proven protective against the glycation of proteins and other macromolecules through competition with glucose and blocking initial nonenzymatic glycation reactions [42]. So, glycine is strongly thought to prevent the glycation of collagen and HA, a major step in preserving vitreous architecture.

Conclusion

Glycine's ability to act as an antioxidant and as a cytoprotectant in hypoxic and/or ischemic environments is responsible for the improvement of ERG readings.

Since glycine functions as a neurotransmitter, it is postulated that it will improve the implicit timing and amplitude of particular ERG components. The injection of glycine prevented the fragmentation of photoreceptors (PR) in diabetic retinopathy (DR) and facilitated PR renewal mostly due to its insulin-enhancing action.

The groups who received glycine treatment showed no vascular alterations that are typical of DR. This is likely because glycine has a preventive effect against inflammation and angiogenesis. Glycine repairs the structure and function of the retina, maintains an intact vitreoretinal interface, and prevents the vitreous and retina from separating, which is a characteristic of the late stages of diabetic retinal degeneration.

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Declaration of Conflict of Interest
The authors declare that there is no conflict of interest.
Ethical of approval
This study follows the ethical guidelines of the Institutional Animal Care & Use Committee (IACUC) of Cairo University regarding the use of sentient animals for scientific purposes.

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التأثير الوقائي للجلايسين ضد تلف الشبكية في اعتلال الشبكية السكري

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الخلفية والهدف: اعتلال الشبكية السكري هو أحد المضاعفات الوعائية الدقيقة لمرض السكري وهو السبب الرئيسي للعمى في جميع أنحاء العالم. ويتميز بنمو أوعية دموية جديدة في شبكية العين، وهي عملية تُعرف باسم توسع الأوعية الدموية الجديدة. السبب الرئيسي للتغيرات الهيكلية والوظيفية المرتبطة باعتلال الشبكية السكري هو حالة ارتفاع السكر في الدم المصاحبة لمرض السكري، وقد أظهرت العديد من الدراسات أن تناول مكملات الأحماض الأمينية مثل الهيدروكسي برولين والليسين والجليسين يمكن أن توفر فوائد وقائية ضد اعتلال الشبكية السكري التكاثري. هدفت هذه الدراسة إلى تقييم التأثير الوقائي المحتمل للجلايسين ضد اعتلال الشبكية السكري في الفئران المصابة بداء السكري STZ. الطرق والأدوات المستخدمة: استخدمت في الدراسة أربع وثمانون أنثى من فئران ويستار تتراوح أعمارها بين 8 إلى 12 أسبوعًا. قُسمت الفئران إلى أربع مجموعات: مجموعة ضابطة، ومجموعة الجلايسين (G)، ومجموعة اعتلال الشبكية السكري (DR)، ومجموعة اعتلال الشبكية السكري التي أُعطيت الجلايسين (DR+G). أُجريت دراسات تخطيط كهربية الشبكية (ERG) ودراسات مرضية نسيجية لتقييم الدور الوقائي للجلايسين على شبكية العين لدى الفئران.

النتائج: لم تظهر نتائج تخطيط كهربية الشبكية والنسيجية لمجموعة الجلايسين أي اختلافات كبيرة عن شبكية العين الخاضعة للمراقبة. في المقابل، لوحظت تغيرات حادة في مجموعة DR، مما أدى إلى انخفاض في بارامترات تخطيط كهربية الشبكية وتغييرات في بنية الشبكية، خاصة بعد أربعة أسابيع. بالنسبة لمجموعة (DR+G) و G، لم تُظهر بيانات تخطيط كهربية الشبكية أي اختلافات عن شبكية العين في كل من الأسبوعين والأربعة أسابيع. أظهرت المقاطع العرضية النسيجية المأخوذة بعد أربعة أسابيع وجود شبكية سليمة وواجهة شبكية مع الجسم الزجاجي سليمة. الخلاصة: تقدم هذه الدراسة دليلاً على أن إعطاء الجلايسين يمكن أن يصلح كلاً من بنية الشبكية ووظيفتها. بالإضافة إلى ذلك، أظهرت إضافة الجلايسين إلى النظام الغذائي لفئران التجارب المصابة باعتلال الشبكية السكري تأثيرًا وقائيًا ضد تلف الشبكية المرتبط عادةً باعتلال الشبكية السكري.

الكلمات الدالة: الجلايسين، داء السكري، اعتلال الشبكية السكري، تخطيط الشبكية الكهربائي.