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DIABETIC RETINOPATHY FOR THE TREATMENT OF DIABETIC COMPLICATIONS

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ABSTRACT:

The aim of this investigation is to address the existing evidence on antidiabetic effects of the selected plants (coccinia indica, basella rubra, hemidesmus indica, pterocarpus marsupium and swertia chirayita). The plants selected depending upon the literature available. The selected plant parts collected and authenticated, the plant parts were extracted using maceration method using methanol and ethanol as solvents, the prepared extracts screened for preliminary phytochemical screening and then the doses decided by performing acute toxicity studies. Diabetic retinopathy is a serious sight-threatening complication of diabetes. Diabetes interferes with the body's ability to use and store sugar (glucose). The disease is characterized by too much sugar in the blood, which can cause damage throughout the body, including the eyes. Over time, diabetes damages small blood vessels throughout the body, including the retina. Diabetic retinopathy occurs when these tiny blood vessels leak blood and other fluids. This causes the retinal tissue to swell, resulting in cloudy or blurred vision.

Keywords: Diabetic, antidiabetic, Plants, retinopathy etc.

[1] INTRODUCTION

1.1. DIABETIS

Diabetes mellitus is one of the most common endocrine diseases in all populations and all age groups. It is a syndrome of disturb ed intermediary metabolism caused by inadequate insulin secretion or impaired insulin action, or both. Diabetes mellitus comprises of heterogeneous group of disorders characterized by hyperglycemia, altered metabolism of carbohydrates, lipids and proteins. Diabetes mellitus is associated with complications such as nephropathy, retinopathy, neuropathy and cardiovascular disease.1

Diabetes is mainly classified into three types as: Type-I (Insulin-Dependent Diabetes Mellitus, IDDM) and Type-II (Non- Insulin-Dependent Diabetes Mellitus, NIDDM), Type-III(Gestational diabetes. Both these types are associated with excessive morbidity and mortality. Type I diabetes accounts for 5% to 10% of diabetes, usually occurs in children or young adults. This disease is caused by autoimmune destruction of the pancreatic β-cells that secrete insulin. The process involves a smoldering destructive

process that can persist for several years and ultimately leading to failure of insulin secretion. Patients with type I diabetes require insulin therapy for survival and most patients ultimately develop devastating complications of this disease.

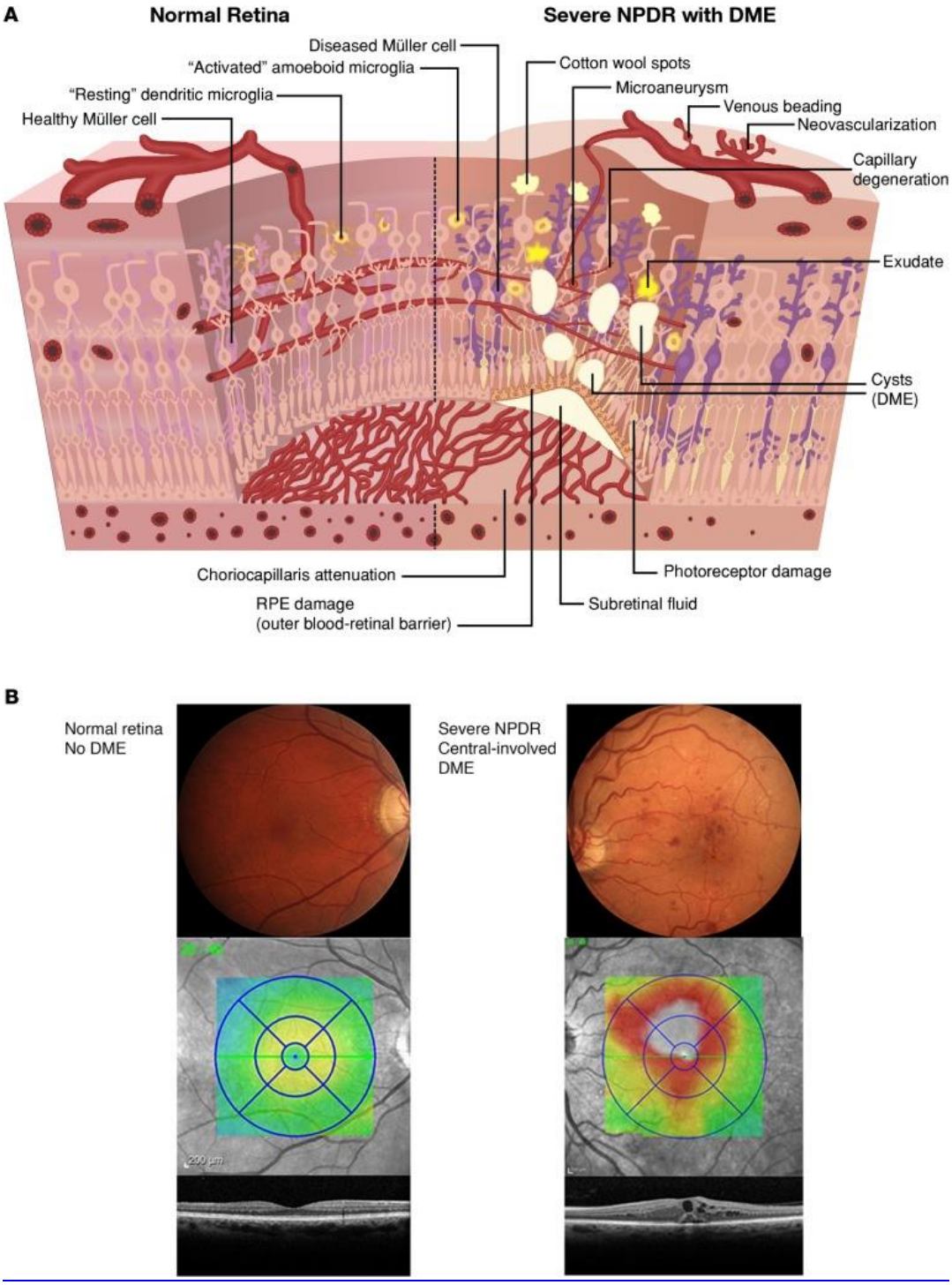
Type II diabetes accounts for 90% to 95% of all patients with diabetes and is increasing in prevalence. Some of the known environmental factors that contribute to development of type–II diabetes are obesity, a sedentary lifestyle, and aging. Insulin resistance is a characteristic metabolic defect in the great majority of patients with type II diabetes. As a consequence of insulin resistance, the β-cell produces increased amounts of insulin, and, if sufficient, the compensatory hyperinsulinemia maintains glucose levels within the normal range.

DIABETIC RETINOPATHY

The global prevalence of diabetes mellitus is predicted to increase dramatically in the coming decades, from an estimated 382 million in 2013 to 592 million by 2035. Type 2 diabetes (T2D) in particular has already attained epidemic levels, while type 1 diabetes (T1D) is increasing in incidence. Patients with diabetes suffer many life-limiting and life-threatening complications, including macrovascular-related stroke, ischemic heart disease, and peripheral artery disease and/or microvascular-related retinopathy, neuropathy, and nephropathy. Diabetic retinopathy (DR) is the most common microvascular complication of diabetes. Although some reports suggest that the incidence of visual impairment from DR has decreased in recent years in the US largely due to improvements in systemic control, DR is a burgeoning problem globally. DR currently affects almost 100 million people worldwide and is set to become an ever-increasing health burden, with estimates between 1990 and 2010 showing that DR-related visual impairment and blindness increased by 64% and 27%, respectively.

DR classification and risk factors

Based on their obvious manifestations during DR progression, microvascular lesions have been utilized as the major criteria for evaluating and classifying the retina in DR. However, diabetes-induced changes also occur in nonvascular cell types that play an important role in the development and progression of DR, albeit in unison with the vasculature. DR falls into 2 broad categories: the earlier stage of nonproliferative diabetic retinopathy (NPDR) and the advanced stage of PDR. Classification of NPDR is based on clinical findings manifested by visible features, including microaneurysms, retinal hemorrhages, intraretinal microvascular abnormalities (IRMA), and venous caliber changes (Figure 1), while PDR is characterized by the hallmark feature of pathologicpreretinal neovascularization. While these visible features of DR provide useful measures for detection and diagnosis, improving technology has enabled the detection of more subtle pathologies such as retinal function deficits and neural layer abnormalities in patients. An important additional categorization in DR is diabetic macular edema (DME), which is an important manifestation of DR that occurs across all DR severity levels of both NPDR and PDR and represents the most common cause of vision loss in patients with DR. DME arises from diabetes-induced breakdown of the blood-retinal barrier (BRB), with consequent vascular leakage of fluid and circulating proteins into the neural retina. The extravasation of fluid into the neural retina leads to abnormal retinal thickening and often cystoid edema of the macula.



Pathological lesions of diabetic retinopathy.

(**A**) An illustrated schematic of normal retina compared with nonproliferative diabetic retinopathy (NPDR) with diabetic macular edema (DME). The normal healthy retina includes healthy retinal blood vessels, glial elements including Müller cells, neuronal elements including photoreceptors, and resting microglia. The inner and outer blood-retinal barriers are intact. In contrast, the retina in diabetic retinopathy exhibits multiple abnormalities, including vascular changes (microaneurysms, venous

beading, capillary degeneration, and neovascularization), lesions associated with vascular damage (cotton wool spots and exudate), glial dysfunction including Müller cell swelling, neuronal damage, activated microglia, retinal pigment epithelium (RPE) damage, and thinning of the choriocapillaris. There is dysfunction of the inner and outer blood-retinal barrier, with resulting accumulation of fluid in the retina, which can be manifested by thickening of retinal layers, cysts, and subretinal fluid. (**B**) Color fundus photograph and OCT images of a normal healthy retina and retina with severe NPDR with central-involved DME are shown. Illustrated by Rachel Davidowitz.

Many systemic features of diabetes influence DR. For example, hyperglycemia isinextricably linked to DR as evidenced by seminal large-scale clinical trials. The Diabetes Control and Complications Trial (DCCT) for T1D and the United Kingdom Prospective Diabetes Trial (UKPDS) for T2D support intensive glycemic control, as assessed by hemoglobin A1c (HbA1c), to delay initiation and progression of this complication, although the need to avoid hypoglycemia can make intensive control challenging for many patients. The importance of glycemia management as early as possible during the course of diabetes is emphasized by robust preclinical and clinical evidence that indicate the long-term impact of intensive glycemic control. The Epidemiology of Diabetes Intervention and Complications (EDIC) study was an observational follow-up of the DCCT cohort of individuals that had initially received either intensive glycemic control or conventional therapy. Although both groups subsequently underwent intensive glycemic control in the subsequent years encompassed by the EDIC study, the group receiving intensive control during DCCT continued to exhibit a significantly lower incidence of further progression of their diabetic retinopathy severity stage. This durable impact of initial intensive control has been termed metabolic (or, sometimes, glycemic) memory, and in DCCT/EDIC patients, there is associative evidence of accumulation of certain advanced glycation endproduct (AGE) adducts in long-lived proteins that correlate with retinopathy risk. Whether hyperglycemia alone accounts for the persistent effects of poorly controlled diabetes remains an important question, but nevertheless, the concept of metabolic memory remains an area of intensive investigation. The memory phenomenon has support from studies using animal models of diabetic retinopathy that are returned to normoglycemia (achieved using insulin therapy). For example, hyperglycemia-mediated oxidative damage impaired function of key transcription factors, and changes to enzymes controlling the electron transport chain are sustained in the retinas of animals even following several months normoglycemia. Many of these pathways can become dysregulated following DNA and histone methylation, and there is now convincing preclinical evidence that such epigenetic modifications are associated with the metabolic memory phenomenon for not only retinopathy, but also other complications. Interestingly, a recent transcriptomics study in the retinas of diabetic mice receiving insulin-producing islet cell transplants has suggested that gene changes relating to metabolic memory may be particularly associated with the neurovascular unit.

Dyslipidemia and hypertension may also influence DR, although in the context of individual patients, the associations between plasma lipids, lipoproteins, and DR are not sufficiently strong to define retinopathy risk. Likewise, hypertension has been linked to increased risk of DR, and some data indicate that patients may benefit from the use of antihypertensive agents. However, recent studies have demonstrated that more intensive blood pressure control does not confer additional benefits on retinopathy progression compared with standard control. Taken together, optimization of systemic risk factors is clearly important; however, even hyperglycemia (as measured by HbA1c) may only account for around 10% of DR risk, and hypertension and dyslipidemia combined may carry <10% risk in some cohorts. Such data strongly suggest that additional unidentified factors also play critical roles in DR initiation and progression.

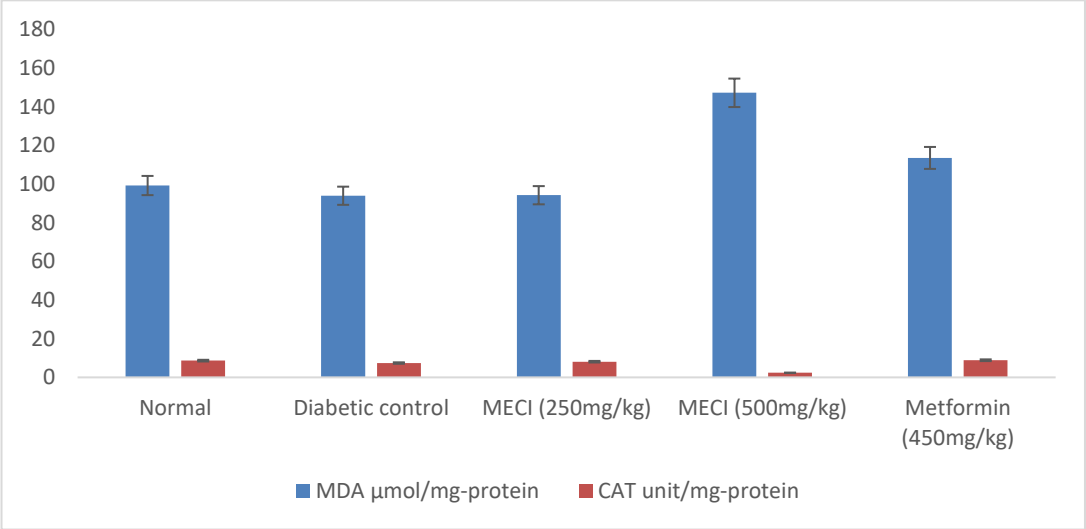
[2] AIM AND OBJECTIVES

The present study is to conduct Preliminary Screening of plant extracts, pharmacological studies of selected medicinal plants for treating Diabetic complications.
Evaluation of some medicinal plant extracts activity for the treatment of following Diabetic retinopathy.

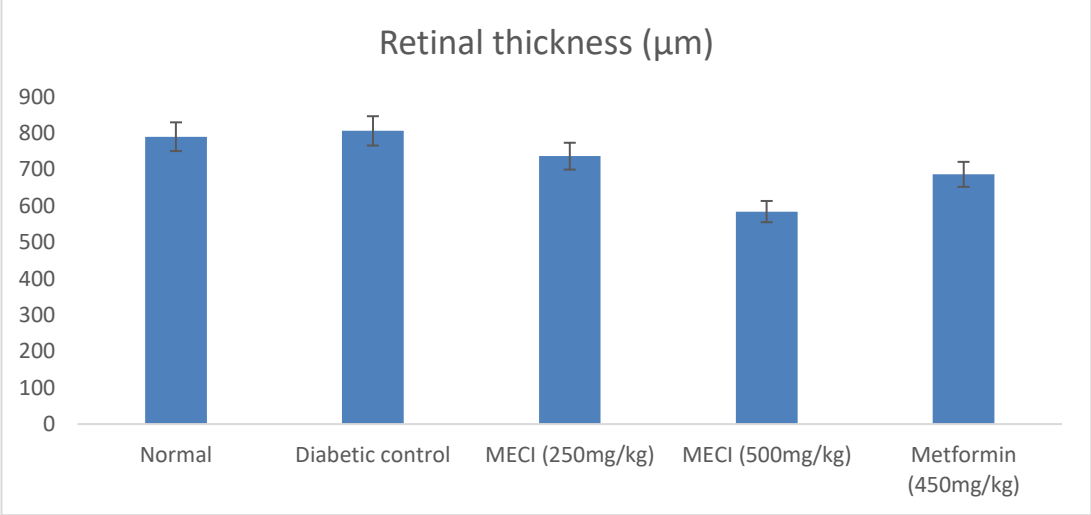
[3] RESULTS & DISCUSSION

DIABETIC RETINOPATHY

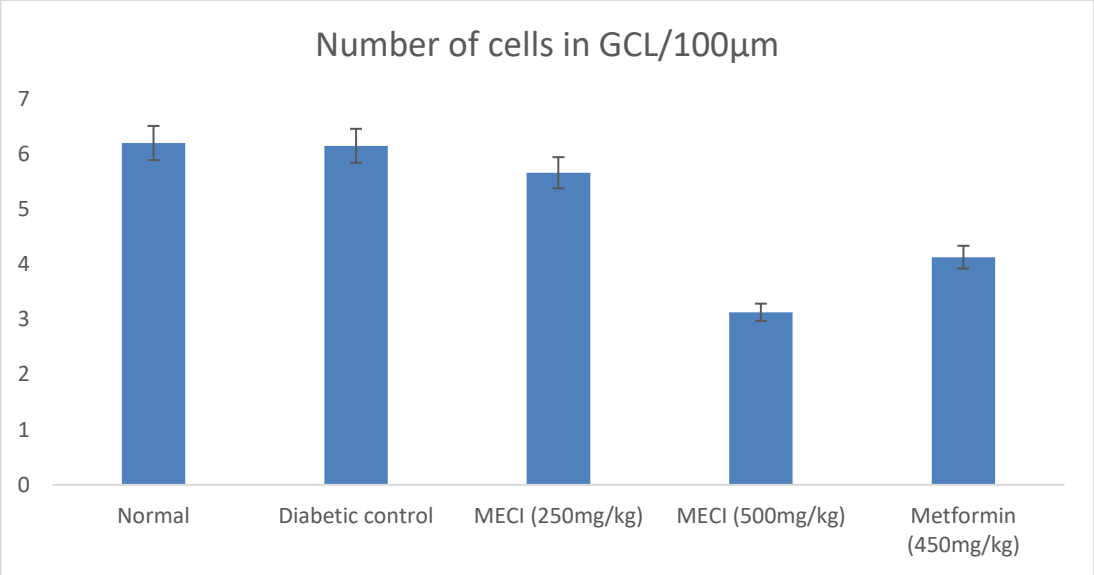
Coccinia indica



Effect of the leaf extract on biochemical markers of rat retina affected by STZ-induced diabetic retinopathy

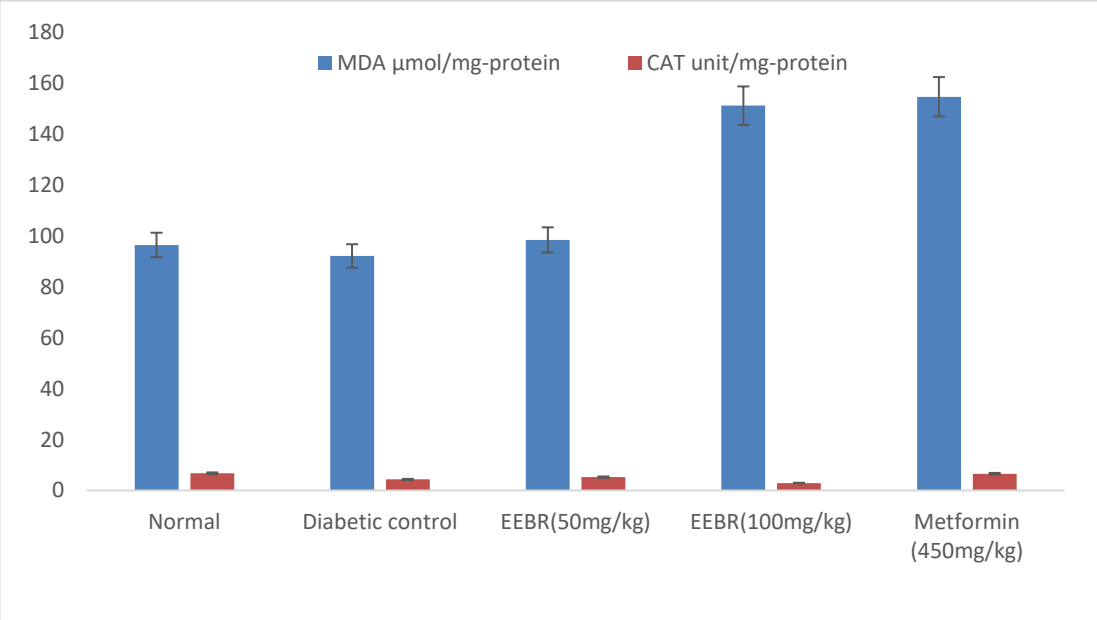


Effect of the leaf extract on morphometric analysis of the diabetic Retinal thickness

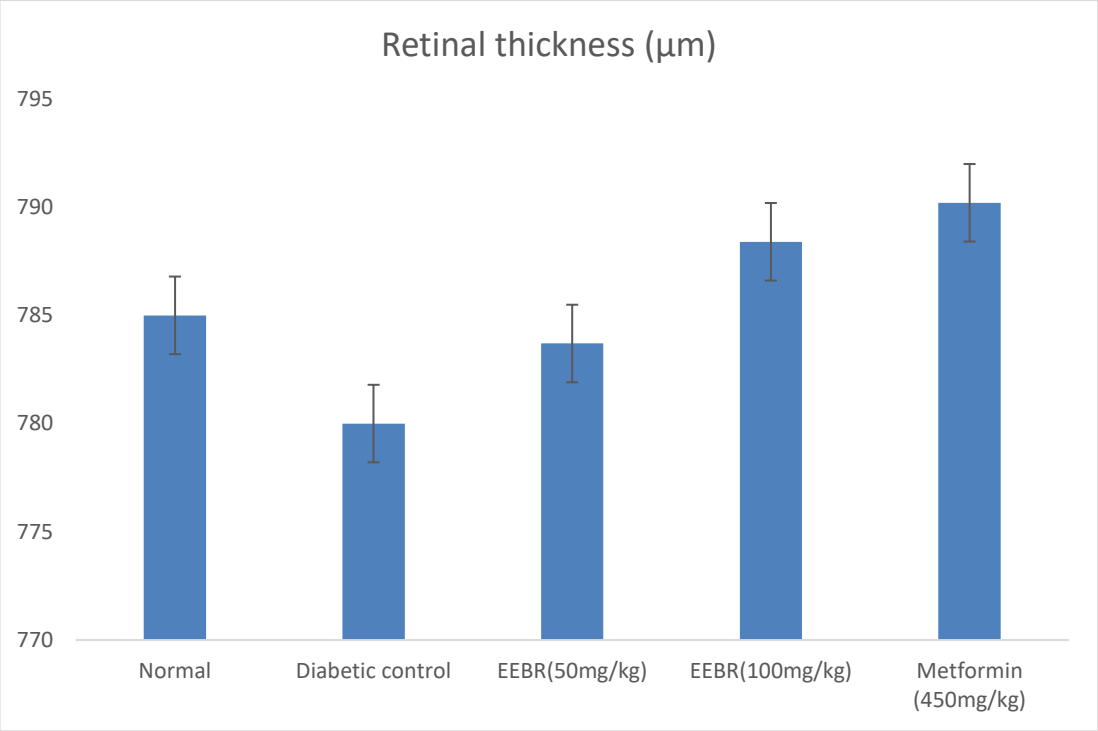


Effect of the leaf extract on morphometric analysis of the Number of cells in GCL/100µm

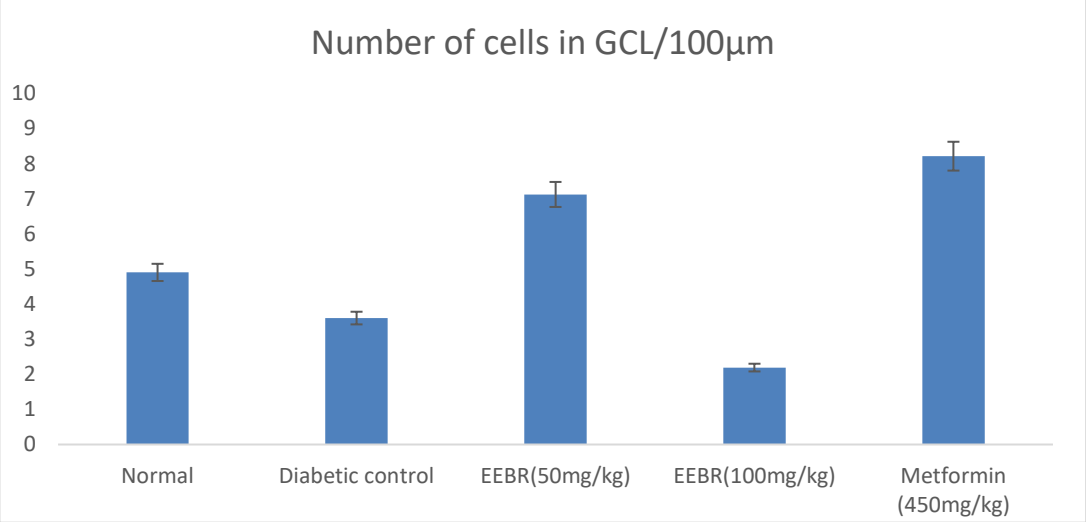
Basella rubra



Effect of the leaf extract on biochemical markers of rat retina affected by STZ-induced diabetic retinopathy



Effect of the leaf extract on morphometric analysis of the diabetic retina



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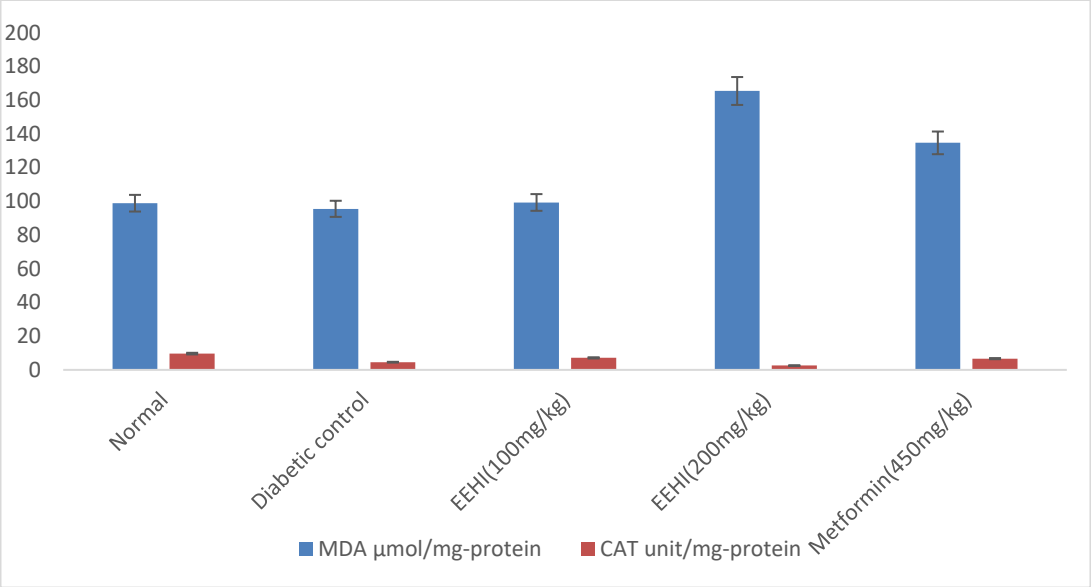
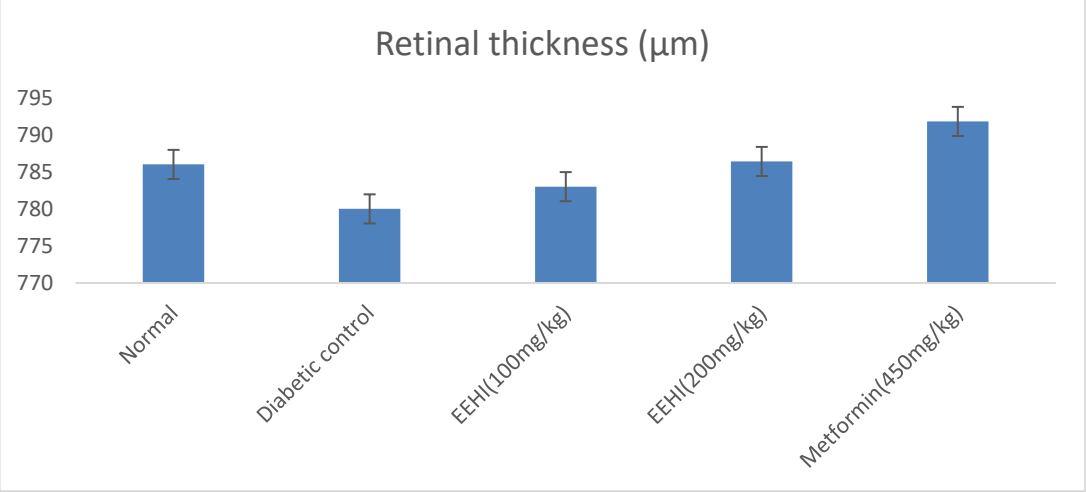
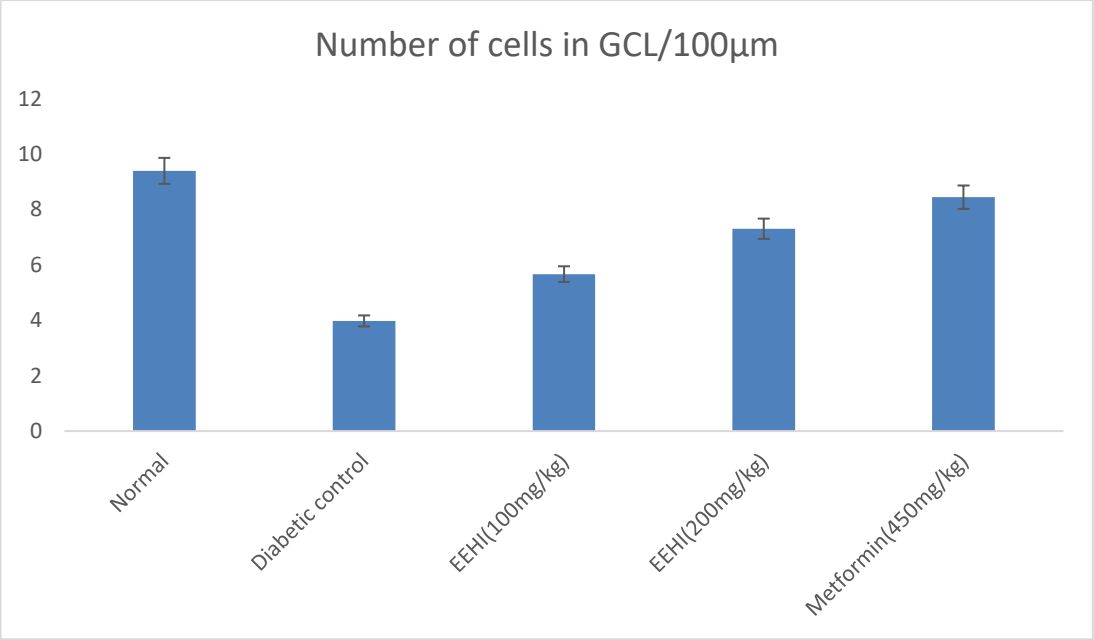


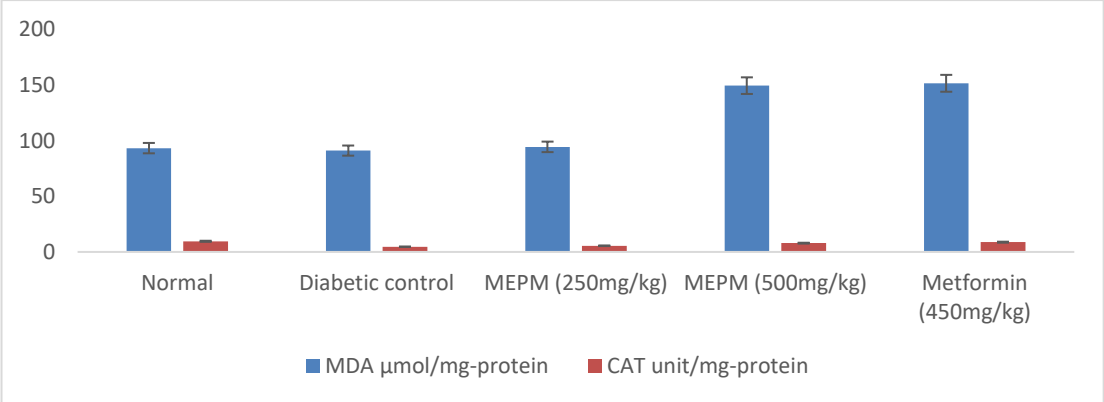
Effect of the leaf extract on biochemical markers of rat retina affected by STZ-induced diabetic retinopathy



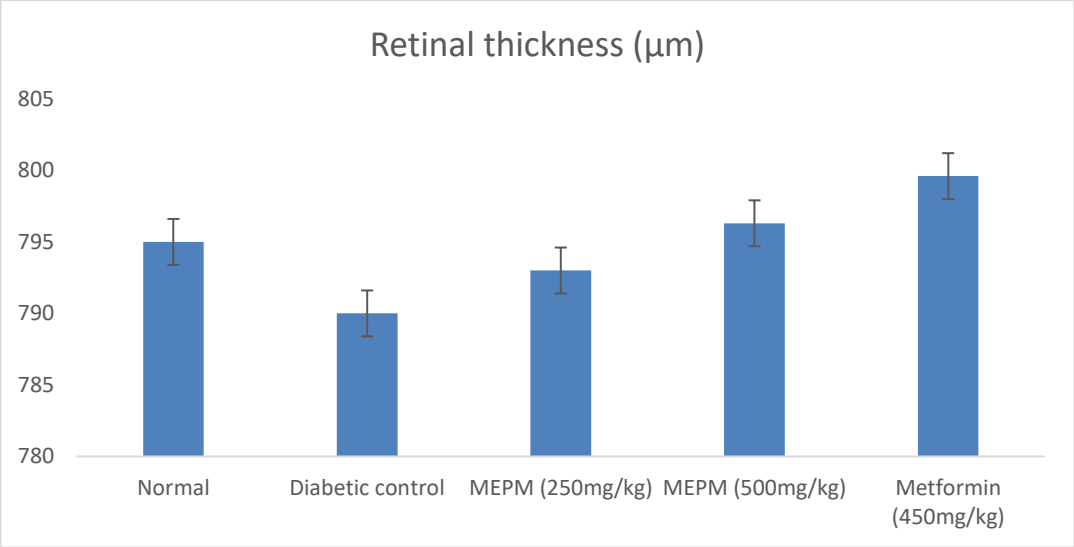
Effect of the leaf extract on morphometric analysis of the diabetic retina



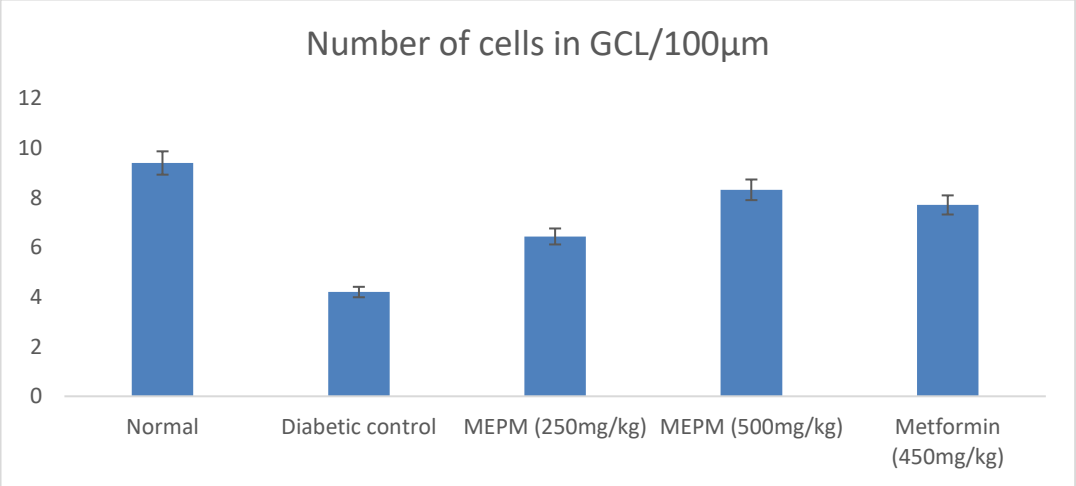
Effect of the leaf extract on morphometric analysis of the diabetic retina



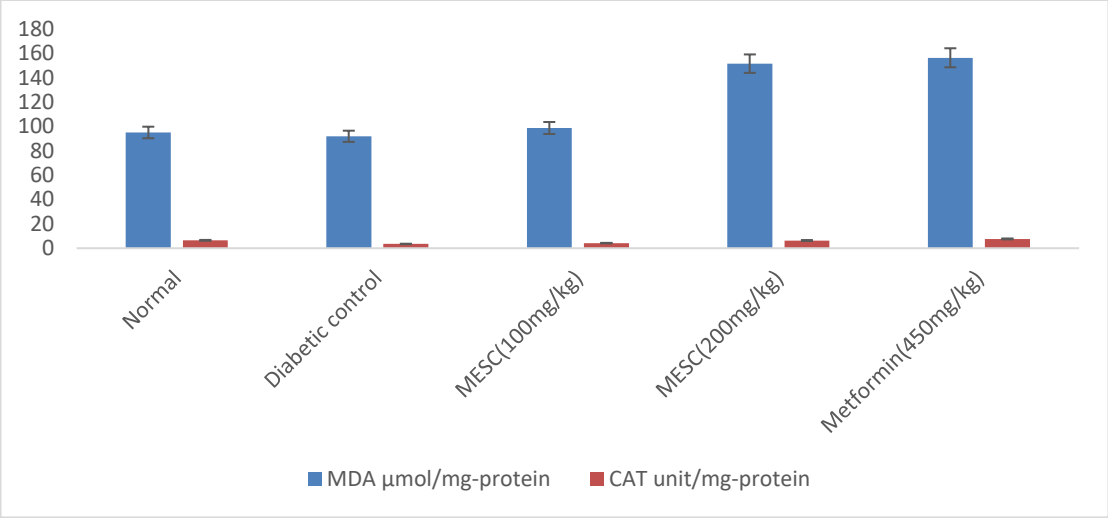
Effect of the leaf extract on biochemical markers of rat retina affected by STZ-induced diabetic retinopathy



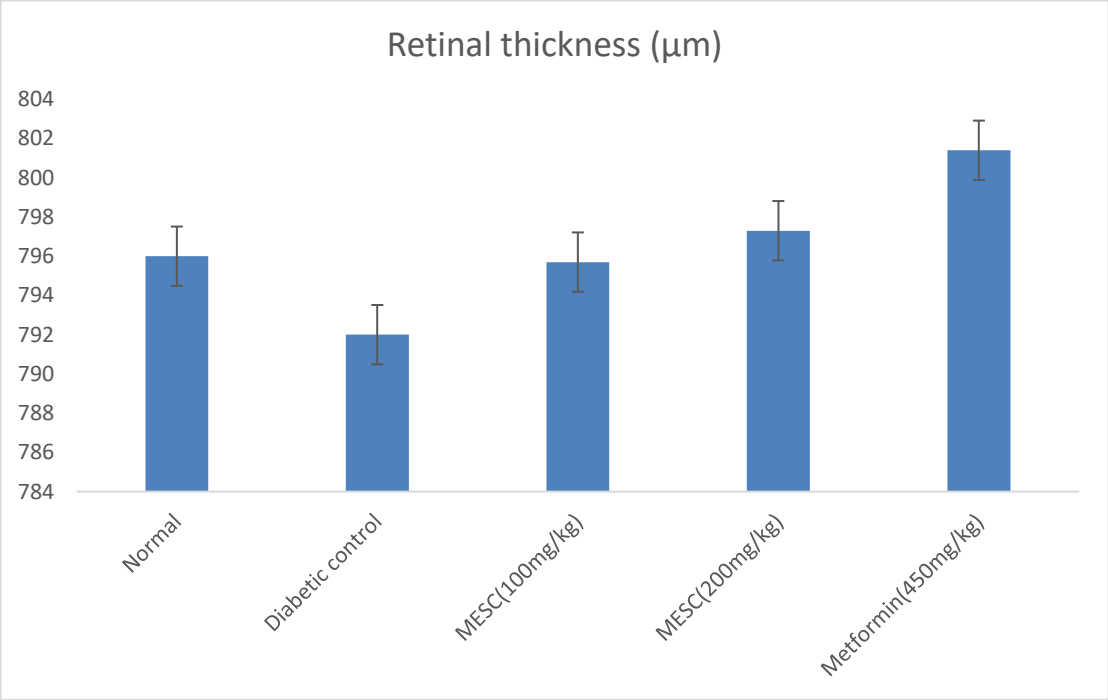
Effect of the leaf extract on morphometric analysis of the diabetic retina



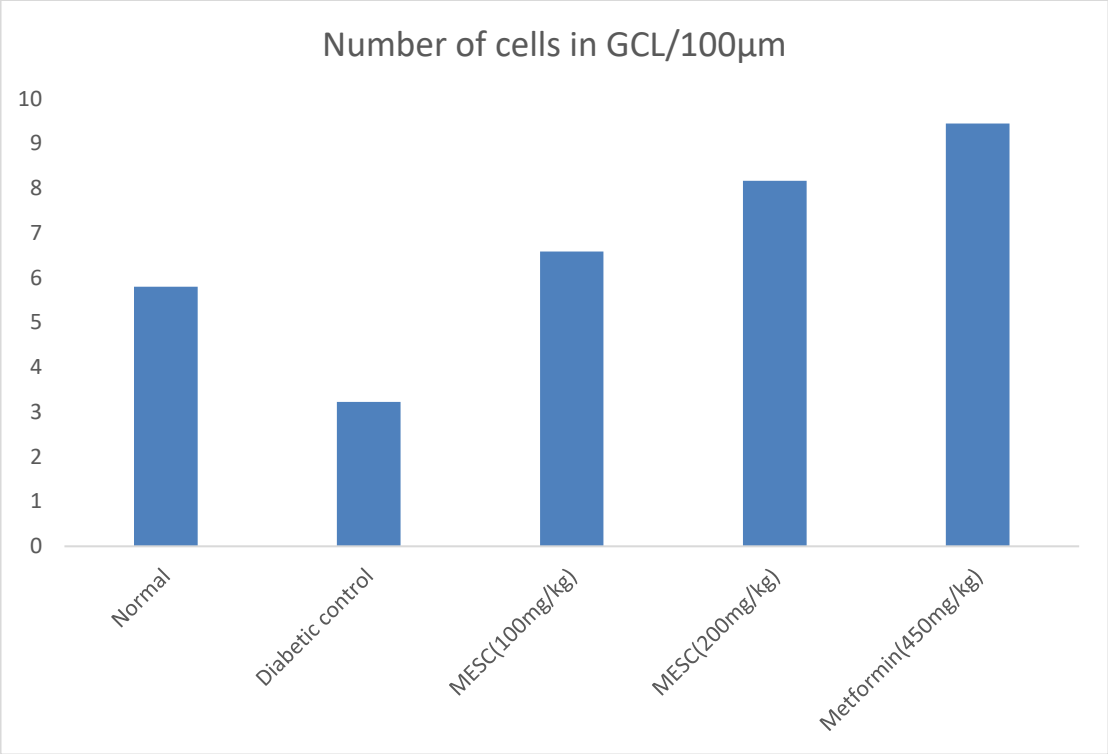
Effect of the leaf extract on morphometric analysis of the diabetic retina



Effect of the leaf extract on biochemical markers of rat retina affected by STZ-induced diabetic retinopathy



Effect of the leaf extract on morphometric analysis of the diabetic retina



Effect of the leaf extract on morphometric analysis of the diabetic retina

Inference: in the presant work the plan extracts were investigated for anti diabetic retinopathy and by following the results represented in above section it is confirmed that the plant extracts posses anti diabetic retinopathy properties and the plant extract showed similar results to that of a standard treatment.

[4] CONCLUSION

In the presant investigation is to address the existing evidence on antidiabetic effects of the selected plants (*coccinia indica, basella rubra, hemidesmus indica, pterocarpus marsupium and swertia chirayita*) were evaluated.

- The plants selected depending upon the literature available. The selected plant parts collected and authenticated, the plant parts were extracted using maceration method using methanol and ethanol as solvents.
- The prepared extracts screened for preliminary phytochemical screening and then the doses decided by performing acute toxicity studies. The animals are pre treated with extracts for 28 days, and then diabetis in animals induced by a single shot of streptozocin injection.
- Later the animals checked for anti diabetic properties by checking the blood glucose levels.
- And diabetic complications like diabetic neuropathy, diabetic nephropathy, and diabetic retinopathy are investigated. And the results obtained found to be very relative to the standard drug used.

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