African Journal of Sciences and Traditional Medicine

ISSN : 3434-6031

Index: Harvard, Boston, Sydney University, Dimensions, Lens, ResearchGet Scilit, Semantic, Google Scholar, Base etc

https://doi.org/10.58578/AJSTM.v2i1.4590

Anti-intra Ocular Pressure of *Stachytarpheta jamaicensis* Leaf Aqueous Extract on Prednisolone-Induced intra Ocular Pressure in Rabbits

Stella E. Odjimogho[1], MacDonald Idu[2], Sunny E. Odjimogho[3], Benjamin O. Gabriel[4]
University of Benin, Edo state, Nigeria
Stella.odjimogho@gmail.com

Article Info:

Submitted:	Revised:	Accepted:	Published:
Dec 1, 2024	Dec 18, 2024	Dec 30, 2024	Jan 6, 2025

Abstract

Intraocular pressure is generated by the dynamics of secretion and outflow of aqueous humour, a transparent colorless fluid (secretion) that fills the complex space in the front part of the eye. This study is aimed at investigating the effect of *Stachytarpheta jamaicensi* leaf aqueous extract on induced intraocular pressure (IOP) in rabbits to validate its ocular potential. The experiment involved twenty five (25) healthy adult rabbits (n=5), divided into negative positive and positive control (0.5% timolol), and the treatment groups (SJ) at graded concentrations (0.00351, 0.00702 and 0.0143 mg/ml).The baseline IOP value of all rabbits were measured with Perkins hand-held applanation tonometer before the commencement of the study. Thereafter, the IOP of the experimental and treatment groups were induced with daily instillation of 1% prednisolone suspension for one week until IOP reading was 5 mm. Hg above the baseline level. The treatment groups were administered with varying concentrations of the aqueous extract of *Stachytarpheta jamaicensis*. The IOP was also measured at intervals before each application of aqueous extract until the IOP returned to baseline level**.** The result showed the distribution of the mean IOP before, and after instillation with 1% Prednisolone suspension and the treatment with varying concentrations of *S. jamaicensis* extract. The observed mean IOP before and after the treatment with prednisolone was 8.77±0.5

mmHg, and 14.2±0.51 mmHg respectively. After oral application of *S. jamaicensis* extract had a significant mean IOP decrease across the days when compared with the controls. The decrease in mean IOP was observed with a significant increase at higher concentrations of the extract, hence the plant caused a reduction in IOP level. Inconclusion, the plants have been implicated in reducing intraocular pressure in rabbits, thus may be helpful in the management of intraocular pressure (IOP), thereby, required further study to validate the efficacy of the extract.

Keyword: *Stachytarpheta jamaicensis,* Leaf Aqueous Extract, Intra Ocular Pressure, Rabbits

INTRODUCTION

Intra Ocular Pressure (IOP) is an expression of the degree to which the pressure within the eye (corneoscleral coat) exceeds atmospheric pressure (Mel Flagg and Melissa, 2012). It is the highest pressure within the body except for the arterial system and its unit of measurement is expressed in mmHg. Generally, in the healthy human eye, the normal IOP range is 10-21 mmHg with an average of 15 mmHg above atmospheric pressure. A range of 22 to 25 mmHg is considered suspiciously high though not necessarily abnormal or glaucomatous, because its effect depends on the response of the individual's ocular tissues to the raised ocular pressure. In rabbit the normal IOP range is 5-10 mmHg IOP with an ave0rage of 8 mmHg above atmospheric pressure (Guyton and Hall, 2006; Kanski, 2007; Wang, Cull and Fortune, 2015). Intraocular pressure is generated by the dynamics of secretion and outflow of aqueous humour, a transparent colorless fluid (secretion) that fills the complex space (anterior chamber) in the front part of the eye. It is bounded in front by the cornea and at the rare by the lens, and it nourishes both structures (lens and cornea) because they are avascular i.e. devoid of blood vessels. Aqueous humour is a medium of refraction with refractive index 1.3333 which makes it an important component of the eye's optical system. The eye as an optical device which obey's the law of optics and this makes it imperative for eye to maintain a specific size and shape, to enable it properly focus rays on the retina and produce quality image (Kanski,1997; Bron et al., 2017; Riordan-Eva and Augsburger, 2018).

The relationship between blood pressure (BP) and intraocular pressure (IOP) is based on the influence of the variations in the hydrostatic pressure within the capillaries. Blood pressure is not generated in the main artery (larger vessel) but within the arterioles and

capillaries (smaller vessels), and this is because of arteriolar constriction that causes resistance to blood flow (Klein et al., 2005; Mitchell et al., 2005). It is worthy to note that in the eye if there is arteriolar dilatation more blood will be allowed to enter the capillary bed at a higher pressure, and this creates a higher ocular tension provided the capillaries maintain their status quo. Clinically a sudden change in the general BP will break through to the capillaries and the same change will be reflected in the IOP (stimulation of vasomotor centre, sympathetic nerves, injection of adrenalin, nicotine) (Stahl et al., 2012; Tiambeng et al., 2022). Thus, it is generally said that if capillary dilatation occurs as a separate phenomenon without alteration in the feeding arteries (main artery), a low hydrostatic pressure will result in the widely dissipated capillary bed, thereby causing a volumetric change which is readily compensated for in the normal eye. This is usually through the drainage channels if both arteriolar and capillary dilatation occurs and the resultant change will depend on which of the two (arteriole or capillary) predominates. If, however, obstruction occurs in the venous system, the rise in pressure therein will readily become effective in the capillaries and a rise in IOP will result (Klein et al., 2005; Mitchell et al., 2005; Liang, et al., 2007).

Stachytarpheta jamaicensis locally termed "Blue Porter Weed" or "Brazilian Tea", is a small weedy perennial herb of the family "Verbenaceae". It is indigenous to most of the Caribbean Island but has been found all over the tropics as a stubborn road side weed. The plant is perennial and has a dimension of 1-3 feet wide and about 1-1.5 m tall. It has reticulated leafing with tiny bluish-purple flowers from where it derives its name and this makes it very attractive to the butterfly. Its growth rate is fast and it requires full sun, light shade and it flowers all through the year though less in July and December through to February. The soil tolerance for salt is high and the leaf is persistently evergreen. *S. jamaicensis* originated from South Florida and it is found throughout the Caribbean, Bahamas, southern Mexico, Brazil and Ecuador (Alvares et al., 2004; Sulaiman et al., 2009). *S. jamaicensis* has some medicinal potentials because of its phytochemical properties. Some studies have shown that it has inhibitory effects on cardiovascular system, influences systemic and intraocular pressure, exhibits antibacterial and antimicrobial actions (Alvares et al., 2004; Ataman et al., 2006; Idu et al., 2006; Idu et al., 2007)

MATERIALS AND METHODS

Plant Collection

Stachytarpheta jamaicensis fresh leaves was obtained from Gelegele village in Edo state. The plant was identify and authentical by Dr. O. Timothy a plant taxonomist in the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin. A voucher number UBH-S316 was issued for a proper plant identification

Plant Preparation

Stachytarpheta jamaicensis leaves was obtained from Gelegele village in Edo state. The leaves were plucked from the stem, dried in an electric oven for two days after which they were crushed into powdered form with use of electric grinding machine. Thereafter, some quantities of the powder substances were measured with a sensitive electrical balance of *S. jamaicensis* powder. The grinded sample was then weighed in 1litre of hot water each for twenty-four (24 hrs) to obtain varying concentrations needed for the work. The soaked sample was then filtered using a sieve, and the residues were discarded while the filtrate was concentrated and stored in a clean bottle.

Experimental Animals

Forty-five (45) healthy New Zealand rabbits of about six to seven months old were bought from "Aduwawa" cattle market in Benin-city Edo-state were used for the experiment. On arrival each rabbit was weighed with a Camry scale and their mean weight was 1.35±0.14 kg. They were then kept in fifteen wooden cages in the animal house of the Department of Microbiology. The rabbits were left for two weeks to enable them acclimatize to their new environment. Their care was in conformity with the rules and the guidelines of the Animal Right Committee of the University of Benin. During this period the animals were well fed with pellets, elephant grass, potato leaves and their health maintained by a Veterinary doctor. The drugs used include: 1% Ivermectin (antihelminth),1% Oxytetracycline (antibiotics) and were administered for one week by oral ingestion and intramuscularly for prophylactic purpose to prevent infection. Other drugs such as keproceryl (vitamin K), and oral rehydrating therapy ORT (each satche dissolved in 1litre of water) and were also given at intervals to help the rabbits stay alive and healthy. The environment was kept clean by the daily emptying of the animal droppings and the sweeping and mopping of the floor with disinfectant (Izal). The rabbits were kept warm by lightening the environment with

100-watt bulb to protect them from cold. Ethical committee in the Faculty of Life Science grant the use of animals for this study with an ethical number of LS20154.

Experimental Procedure

The experiment involved twenty five (25) healthy adult rabbits, divided into six groups (n=5); standard drug (0.5% timolol), untreated control (1% prednisolone acetate suspension) and graded concentration of the treatment groups (0.00351, 0.00702 and 0.0143 mg/ml). Physical assessment of the tissues of the eyes of each rabbit was carried out. The external tissue was examined with the aid of the penlight/ hand magnifier, while the internal tissues were examined with the direct ophthalmoscope for detection of abnormalities. Thereafter the baseline IOP measurements were taken with the Perkins hand held applanation tonometer. This measurement was done by first instilling a drop of local anesthetic (xylocaine preparation) to desensitize the cornea, thereafter the cornea was stained with fluorescein dye. The probe of the tonometer was placed on the central portion of the cornea and the mires observed through the peep hole of the tonometer was seen as two semi-circular arcs. The tips of the inner point of the semi-circular arcs were adjusted to touch one another, and the reading in mm noted. The value obtained is then multiplied by a factor of 10 mmHg to get the IOP readings. Thereafter the rabbits in the experimental and the treatment groups were administered topically with 1% prednisolone suspension two times daily for a period of 1 week (bdx1/52) to induce intraocular pressure in the rabbits. The treatment groups were thereafter treated with varying concentrations of the aqueous extract.

Data Analysis

The statistical software package for social sciences (SPSS), was used to analyze the means, standard deviation and standard error for all the variables collected. For comparism of these variables, tables and line graphs were used. The significant difference in intraocular (IOP) before and after treatment was analyze using the student paired T-test, while the significant difference between the different concentrations of treatments was determined using the one way analysis of variance (ANOVA).

RESULTS

The result in Figure 1-7 showed the distribution of the mean IOP before, and after the treatment with 1% Prednisolone suspension and varying concentrations of *S. jamaicensis* extract. The result showed that the observed mean IOP before and after the treatment with

prednisolone was 8.77±0.5 mmHg, and 14.2±0.51 mmHg respectively. The result also showed that with the oral application of *S. jamaicensis* extract which was administered daily; the mean IOP decreased gradually each day until the 7th day. The decrease in mean IOP was observed to increase with the application of higher concentration of *S. jamaicensis* SJ1, SJ2, and SJ3 extract.

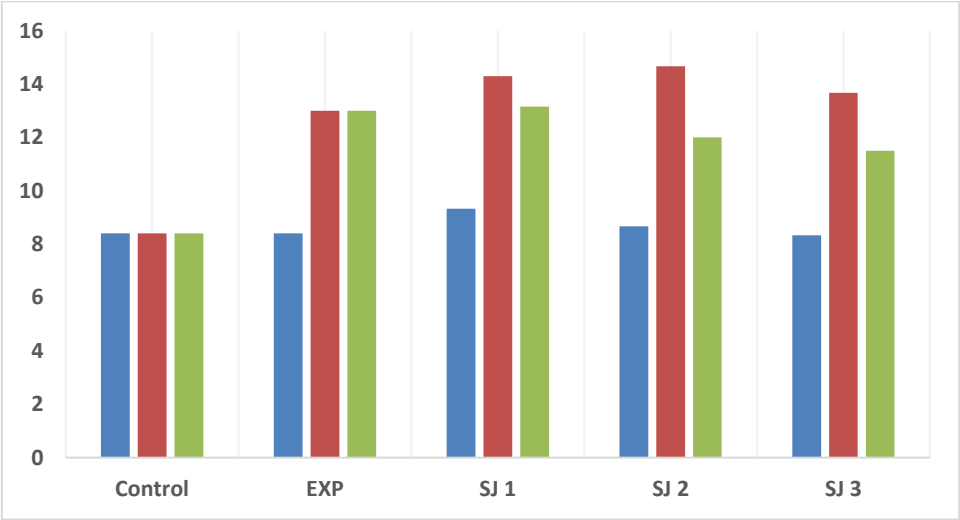

Figure 1: Distribution of mean IOP (mmHg) before and 1 day after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

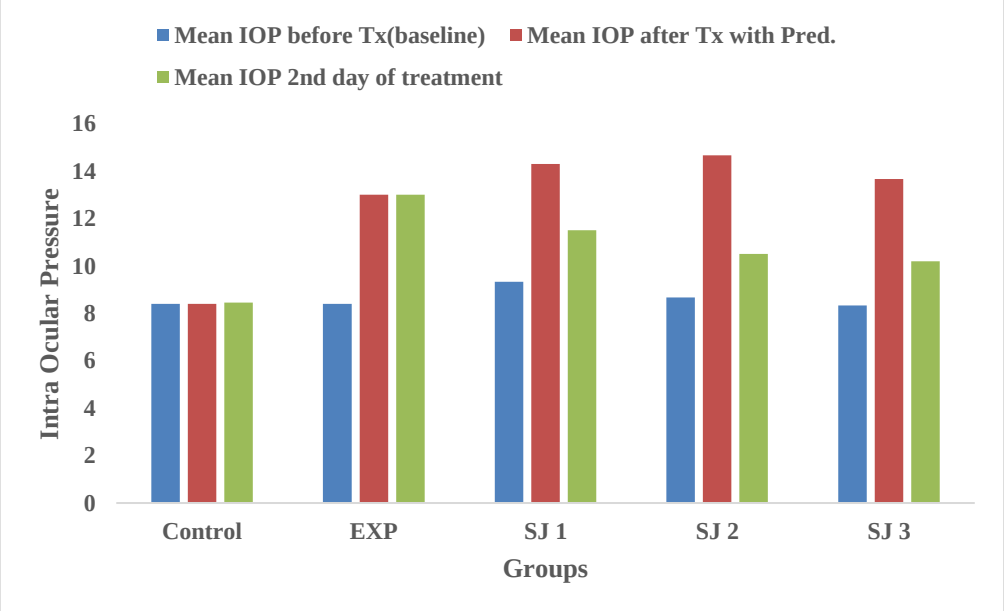

Figure 2: Distribution of mean IOP (mmHg) before and 2 days after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

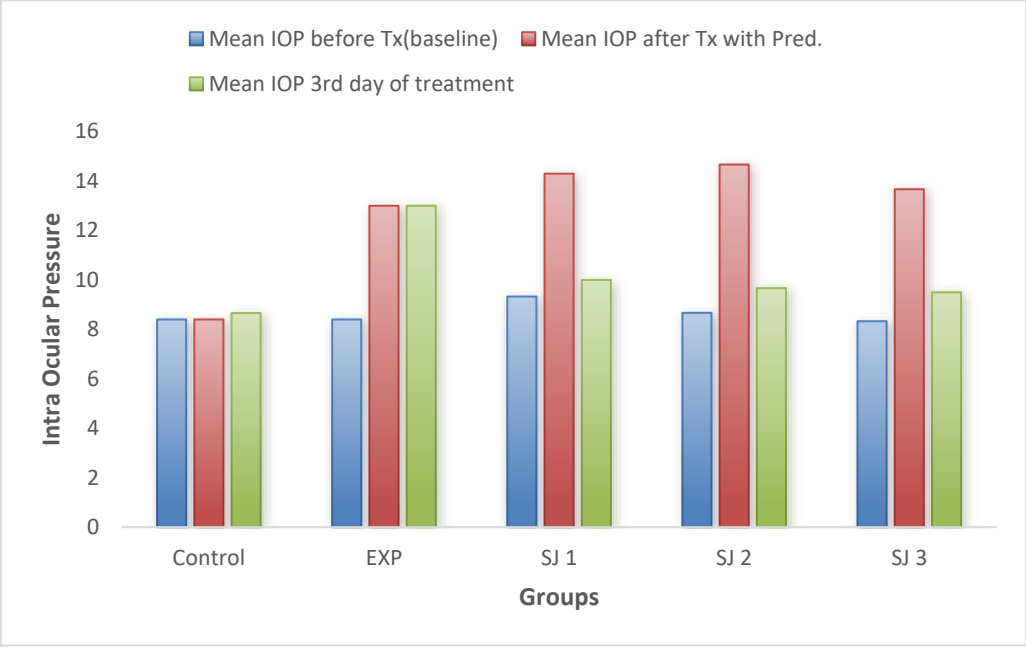

Figure 3: Distribution of mean IOP (mmHg) before and 3 days after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

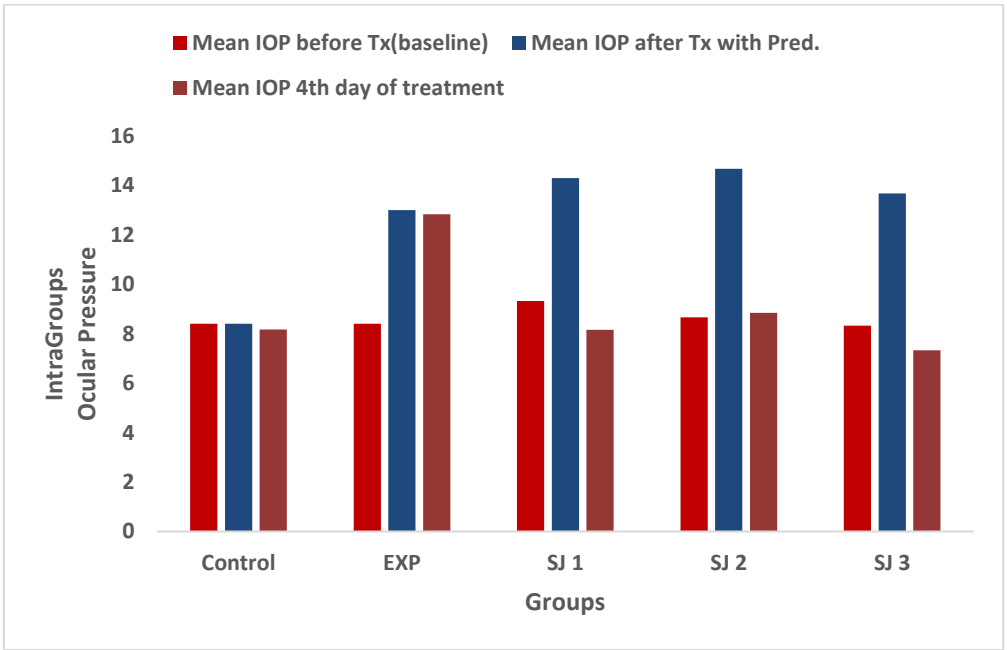

Figure 4: Distribution of mean IOP (mmHg) before and 4 days after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

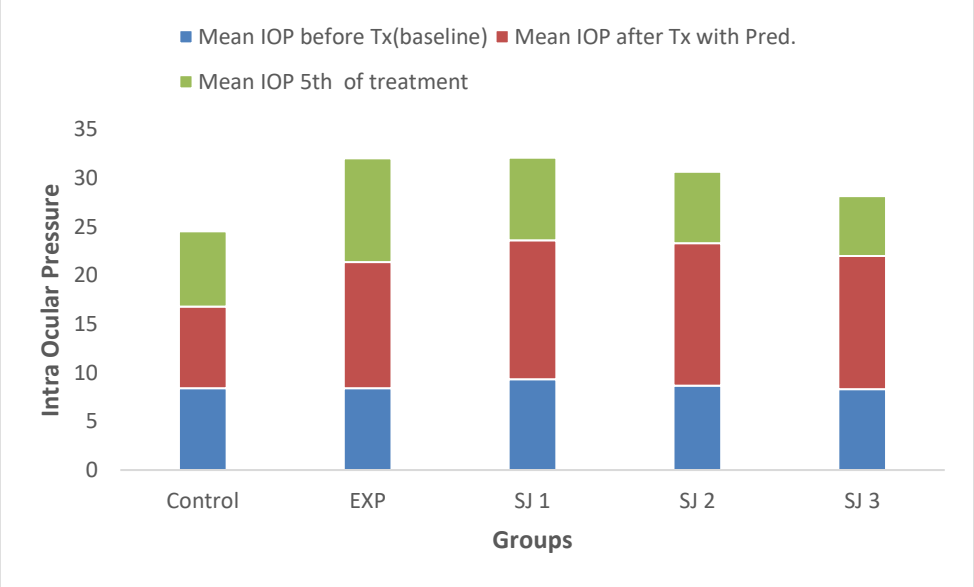

Figure 5: Distribution of mean IOP (mmHg) before and 5 days after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

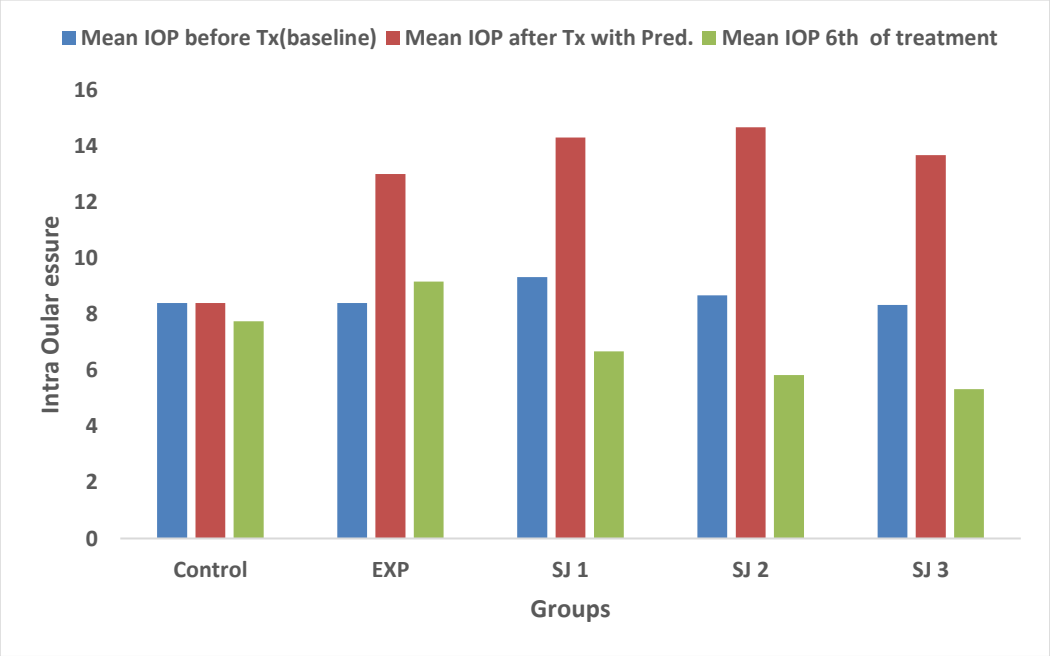

Figure 6: Distribution of mean IOP (mmHg) before and 6 days after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

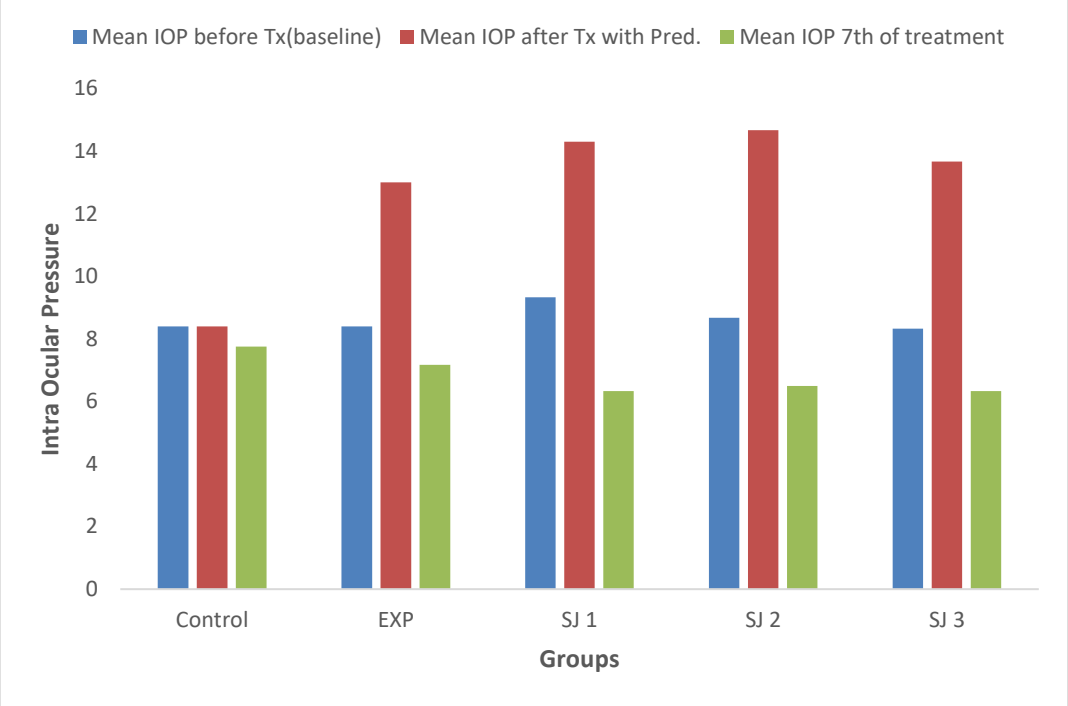

Figure 7: Distribution of mean IOP (mmHg) before and 7 days after treatment with *Starchytapheta Jamenciensis*

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

Table 1 Showed that when the treatment was discontinued after 7days, a slight increase in mean IOP was observed till the effect of the treatment wore off. The mean IOP before treatment with SJ was 10.08±7.78 mmHg and after the treatment was 9.11±2.62 mmHg and the effect was statistically significant using the paired t-test ($t=1.805$ $p < 0.05(0.099)$. Also, the mean IOP after treatment with the three concentrations (0.00351 kg/litre: 0.00702 kg/litre; 0.0143 kg/litre) sample A (SJ1, SJ2, and SJ3*)* were 1.90±3.69, 1.15±3.37, and 1.35±3.62 respectively. However, the effect of the varying concentrations of SJ on IOP when compared is not statistically significant using the one-way analysis of variance ANOVA ($F= 0.982$: $p > 0.05$) thus, it could be said that the effect of the extract is not dose dependent.

TABLE 1: Relapse Distribution of mean IOP (mmHg) after stoppage of treatment with "*Starchytapheta Jamenciensis*"

Group	Mean IOP at the end of treatment	Mean IOP 1st day after stoppage of treatment	Mean IOP 2nd day after stoppage of treatment	Means 3rd after stoppage of treatment
Control	7.75±1.84	7.58±1.28	7.33±0.61	8.17±1.25
Exp	7.17±0.76	6.67±0.58	6.83±0.29	7.17±.0.76
SJ 1	6.33±0.58	6.33±0.29	6.50±0.87	8.50±3.12
SJ 2	6.50±0.50	6.50±1.00	6.67±1.16	7.33±0.58
SJ 3	6.33±0.58	6.50±0.00	7.67±0.58	7.17±0.76

Key: control (0.5% timolol); Exp (1% prednisolone) SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml)

DISCUSSION

The function of the human body is regulated by two major controlled systems from neural and hormonal or endocrine systems. The hormonal system is concerned principally with the control of different cellular and metabolic functions of the body, chemical reactions in the cells and the transport of substances through cell membranes. The production of cortisone is stimulated by its low level in the blood. This causes the hypothalamus to release corticotrophin releasing factor (CRF). This is carried to the Anterior Pituitary gland which further releases Adrenocorticotropin stimulating hormone (ACTH), which is a growth factor which is transported to the adrenal gland to stimulate the adrenal cortex to produce corticosteroid and release it into the blood stream. The production of Although glucocorticoid receptors have been identified in the cells of the outflow pathways, the biochemical and consequent physical processes causing the facility decrease are unclear. However, the mechanism may be consequent to modulation of macromolecular metabolism, or prostaglandin/adrenergic interactions involving the outflow system (Sit, Gong and Ritter, 1997). These macromolecules are presumably produced by meshwork endothelial cells, and their synthesis and turnover may be one means by which outflow resistance is modulated (Massoudi, 2022). Though the control mechanisms are largely unknown, new evidence have suggested that modulation of TIGR gene expression and TIGR protein production also plays a role (Lindsay *et al.*, 1997; Pflugfelder and Stern ,

2020). Fluid movement across the endothelium of the inner canal wall appears to be predominantly through passive pressure-dependent transcellular pathways, and the flow is between the cells, (Bill, 2003; Kanski, 2007).

Prednisolone is a synthetic steroidal drug which mimics the actions of natural steroid (cortisol). Its topical application into the conjunctival sac caused an increase in mean IOP in the rabbit; this could be that as a lipid soluble drug there was good intraocular penetration of the drug through the bipolar lipid cell membrane. The process is by the binding of the drug to the cells of the pectinate membrane, and its active transportation across the cell membrane into the cytoplasm of the cell where it binds to specific protein to form specific protein/hormone complex. This could be transported across the nuclear membrane into the cell nucleus again to form complexes that lyses and initiates a number of cellular activities. The activity could be inhibition of the activities of the receptors innervating the blood vessel thereby resulting in vasoconstriction, decrease in perfusion pressure (intra-ciliary capillaries) and consequent increase in intraocular pressure (Jones and Douglas, 2006). Another reason could be that the presence of the steroidal drug (prednisolone) could have activated the secretion of the enzyme Na^+ K^- ATPase within the cell that is responsible for increase in aqueous humour formation, thereby resulting in increased IOP. Other reason could be that prednisolone increased vascular permeability of the cell, thereby allowing transportation of ions (Na^+&Cl^-) across the aqueous -blood barrier into the posterior chamber. This increased the osmolality of the aqueous resulting in increased water inflow from the surrounding stroma of the ciliary processes. This led to the accumulation of fluid within the eye, resulting in increased intraocular pressure. Also, the administration of prednisolone may have led to increased plasma free cortisol, thereby making the aqueous to become more plasmoid and less able to leave the eye (Vaughan and Asbury, 2004; Jones and Douglas, 2006). Another reason could be that the presence of cortisol in the aqueous could have led to the breakdown of blood-aqueous barrier leading to the leaking of protein molecules and blood cells through the capillary pores into the anterior chamber. The protein molecules could block the openings in the trabecular mesh work and narrow the anterior chamber angle thereby causing greater resistance to aqueous outflow and consequent increase in intraocular pressure, (Civa and Macknight, 2004; Jones and Douglas, 2006).

Another reason could be as a result of the modulation of macromolecular metabolism or prostaglandin/adrenergic interaction involving the outflow systems. This could lead to the

inhibition of sympathetic stimulation and the inhibition of beta receptors thereby causing muscular relaxation of the ligament. This closes the opening and reduces the diameter of the perforations (openings) thereby resulting in resistance to aqueous outflow and consequent increase in IOP. Prednisolone could also act on the extracellular matrix of the ciliary smooth muscles metabolism thereby inhibiting uveoscleral outflow and causing a reduction in intraocular pressure (Johnson, McLaren and Overby, 2017; Tamn, Braunger and Funchofer, 2015). The mean IOP after repeated administration of 1% Prednisolone suspension increased in all the rabbits as shown in Figure 1 - 7 The reason for this was because the repeated application of the drug led to increase intraocular penetration with consequent increased concentration in the cell cytoplasm, and nucleus thereby producing greater effect. (Jones and Jones and Douglas, 2006).

The result in Figure 1-7 showed that the mean IOP after treatment with SJ decreased and the difference in the effect was significant different when compared with the control groups. The reason could be as a result of dopamine component present in *S. jamaicensis* which binds to special dopamine beta receptors in the drainage system (pectinate ligament) and penetrates it through the protein cell membrane layer. This caused the stimulation of the sympathetic nerve innervating the smooth muscles of the blood vessel resulting in vasodilation of the ciliary capillaries, and decrease in perfusion pressure within the capillary (Idu et al., 2006a; Idu et al., 2006b) . This causes resistance to blood flow, thereby allowing increased volume of blood flow, and consequently decrease the intraocular pressure. As precursor to epinephrine and norepinephrine, dopamine can bind to the cells of the pectinate ligament, and stimulate the contraction of the ligament resulting in the opening of the perforations in the ligament thereby, enhancing the rate of aqueous outflow with consequent reduction in IOP. (Aleksie et al., 1999; Reitsamer et al., 2002; Idu et al., 2007). The result in table 2b also showed that the reduction in the observed mean IOP decreased each day as the treatment continued and the mean IOP in the rabbits treated with the highest concentration of extract (14.30 gm/litre) had the highest decrease in mean IOP. However significant decreased in the effect of the extract at different concentrations SJ1 (0.00351 mg/ml), SJ2 (0.00702 mg/ml) and SJ3 (0.0143 mg/ml) lowers the IOP level. The reason for this is because dopamine stimulates ciliary vasodilation, changes in ciliary blood flow, and aqueous production at the lowest infusion rate and stimulates vasoconstriction and secretory inhibition at higher infusion rate. This effect however, started decreasing gradually after the stoppage of the treatment. This is because with repeated application

greater quantity of treatment penetrated the cell thereby increasing the dopamine blood plasma level. This however started wearing off because the drug was being excreted through the trabecular mesh work, canal of Schlemm, aqueous vein to join the main venous circulation. It was observed that the effect of the extract on the degeneration improved best with the effect from the aqueous extract having a competitive effect as timolol. This may e as a result of the inhibition derived from the activity of the metabolizing enzymes thereby affecting the metabolism of the drug resulting in cell excito-toxicity and consequent breakdown of cells a condition termed degeneration. It could also be as a result of the increased pressure which compresses on the retinal cell fibre and the optic nerve thereby blocking the axoplasmic flow to the fibre and consequently cause ischemia and break down of cell (degeneration).

CONCLUSION

The studies conducted with *S. jamaicensis* showed that the extract had a systematic decrease in intraocular pressure. The additive effect of *S. Jamaicensis* had reduction in IOP level. Thus, the plants have been found to be capable of reducing intraocular pressure in rabbits, thus can be used to reduce the intraocular pressure (IOP). hence, required further study to validate the efficacy of the extract.

Acknowledgement

We the authors are thankful to the department of optometry and biochemistry, Faculty of Life Sciences, University of Benin for their support and access to the equipment required for this study

REFERENCES

Alvarez, E., Leiro, J.M., Rodriguez, M., Orallo, F. (2004). Inhibitory effects of leaf extracts of *S. jamaicensis* (verbenaceae) on the respiratory burst of rat macrophages. Phythotherapy Research, 18(6):451-62..

Ataman, J.E., Idu, M., Odia, E.A., Omogbai, E.K.I., Amaechina, F., Akhigbe, A.O., Ebite, L.E. (2006). Histopathologic effects of *S. jamaicensis* (L.) Vahl. On Wistar rats. Pakistan Journal of Biological Sciences, 9:26-28.

Asrani, S., Zeimer, R., Wilensky, J. (2000). Large diurnal flunctuation in intraocular pressure is independent risk factor in patients with glaucoma. Journal of Glaucoma, 9: 132-42.

Bill, A. (2003). Some thoughts on the pressure dependence of ultrafiltration flow. Journal of Glaucoma,12 (1): 88-93.

Carreon, T., van der Merwe, E., Fellmam, R.L., Johnson. M., Bhattacharya, S.K. (2017). Aqueous outflow- A continuum from trabecular meshwork to episcleral veins, Progress Retin Eye Research, 57: 108-133

Civan, M. M., Macknight, A.D. (2004). the ins and out of aqueoue humoiur secretion, Experimental Eye Research, 78 (3): 625-31

Guyton, A.C., Hall, J.E. (2006). *Textbook of Medical Physiology* 11th ed., Philadelphia: Elsevier-Saunders.

Idu, M., Omogbai, E.K.I., Aghimien, G.E., Amaechina, F., Timothy, O., Omonigho, S.E. (2007). Preliminary phytochemistry, antimicrobial properties and acute toxicity of *S. jamaicensis* (L.)Vahl. Leaves. Trends in Medical Research, 2(4):193-98.

Idu, M., Omogbai E.K.I., Amaechina F., and Ataman, J.E. (2006)a. Some cardiovascular effects of the aqueous extract of the leaves of *S. jamaicensis* L.Vahl. International Journal of Pharmacology, 2(2):163-65.

Idu, M., Ataman, J.E., Akhigbe, A.O., Omogbai, E.K.I., Amaechina, F., Odia, E.A. (2006)b. Effect of *S. jamaicensis* (Vahl.) on Wistar rats: Serum biochemistry and Ultrasonography. *Journal of Medical Sciences,* 6(4):646-49.

Johnson, M., McLaren, J.W., Overby, D.R. (2017). Unconventional aqueous humor outflow *A review*. Experimental Eye Research, 158 94-111.

Jones, R., Douglas, J. (2006). Corticorsteriod-induced ocular hypertension and glaucoma. Current Opinion in Opthalmology, 17 (2): 163-167

Kanski, J.J. (2007). Physiology and anatomy of Aquoeus Secretion *Clinical Opthalmology. A systemic approach* 6th edi. Butterworth Heinemann. pp 382-383.

Klein, B.E.K., Klein, R., Knudtson, M.D, (2005): "Intraocular pressure and systemic blood pressure: longitudinal perspective: the Beaver Dam eye study". Bristish Journal of Ophthalmology, 89(3):284-87.

Liang, X., Wang, H., Jonas, J.B. (2007). Intraocular pressure correlated with arterial blood pressure: The Beijing eye study. American Journal of Ophthalmology, 144(3):461-62.

Lindsay, J.D., Kashiwagi, K., Kashiwagi, F., Weinreb, R.N. (1997). Prostaglandin action on ciliary muscles extracellular matrix metabolism: implication for uveoscleral outflow, Survey Ophthalmology, 42 (2): S53-S59

Masoudi, S. (2022). Biochemistry of Human Tear Film, A review Experimental Eye Research, 220: 109-110.

Mel-Flagg, O, S., Melissa, C. (2012). The Definition of Intraocular Pressure.

Mitchell, P., Franzo-Lee, A.J., Wang, J.J., Rochtchina, E. (2005). Intraocular pressure over the clinical range of blood pressure: Blue mountain eye study findings.American Journal of Ophthalmology, 140(1):131-32.

Okoye, T.N., Akah, P.A., Okoli ,C.O., Ezike, A.C., Mbaoji, F.N.(2010). Antimicrobial and antispasmodic activity of leave extracts and fractions of "*S. jamaicensis"*. Asian journal of Tropical Medicine, 3(3):189-92.

Pillunat, L.E.,Anderson, D,R., Knighton, R.W., Joos, K.M., Feuer, W.J.(1997). Auto regulation of optic nerve head circulation in response to intraocular pressure. Experimental Eye Research., 64 :737-747

Pflugfelder. S.C., Stern, M.E. (2020). Biological functions of tearfilm. Experimental Eye research, 197:108-115.

Reitsamer, H. A., Kiel, J.W. (2002). Effect of dopamine on ciliary body flow. Aqueous production and intraocular pressure in rabbits. Investment Ophthalmology Vision Science, 43: 2697-2703

Riordan-Eva, P., Augsburger, J.J. (2018). Vaunghan and Asbur's General Ophthalmology, 19th edition. New York.: McGraw-Hill Education LLC.

Sasidharan, S., Latha, L.Y., Zuraini, Z., Suryani, S., Sangetha, S., Shirley, L. (2007). Antidiarrheal and antimicrobial activities of *Stachytarpheta jamaicensis.* Indian Journal of Pharmacology, 39(5):245-48

Sit, A.J., Gong, H., Ritter, N. (1997). The role of soluble proteis in generating aqueous outflow resistance in the bovine and human eye. Experimental Eye Research*.,* 64 :813

Stahl, U., Willcox, M., Stapleton, F. (2012). Osmolarity and tear film dynamics. Clinical Experimental Biology, 95 (1):3-11

Sulaiman, M.R., Zakaria, Z.A., Chiong, H.S., Lais, S.K., Israf, D.A., Azam Shah, T.M, (2009). Antioceptive and Anti-inflammatory effects of *S. jamaicensis* (Verbenaceae) i. experimental animal models. Medical Principle of Practical, 18(4):272-79.

Tamn, E.R., Braunger, B.M., Funchofer, R. (2015). Intraocular Pressure Mechanism Involved in Resistance of Aqueous Humour Flow in Trabecular Meshwork Outflow Pathway, Progress Molecular Biology and Translational Science, 134: 301-314

Tiambeng, C., Batur, A., Dikmetas, O., Aksu, N.M. (2022). The acute effect of systemic blood pressure reduction on intraocular pressure in hypertensive patients. Turkish Journal of Emergency Medicine, 22 (3): 131

Vaughan, D., Asbury, T. (2004). General Ophthalmology. Apple and Lange. 19th ed. pp166-183.

Wang, L., Cull, G., Fortuna, B. (2915). Optic nerve head blood flow response to decrease ocular perfusion pressure by alteration of either the blood pressure or the intraocular pressure, Current Eye Research, 21:359-393