

EFFECT OF MORINGA OLEIFERA LEAF AQUEOUS EXTRACT ON INTRAOCULAR AND BLOOD PRESSURE OF NORMOTENSIVE ADULTS IN EDO STATE, NIGERIA

George, G. O.¹, Ajayi, O.B.¹ and Oyemike, A.A.¹

1. Department of Optometry, Faculty of Life Sciences, University of Benin, Benin City, Edo State, Nigeria.

Corresponding Author: George, G.O | Email: gladys.george@uniben.edu | Tel: +234 08144393468

Abstract

For centuries, *Moringa Oleifera* leaf is used in traditional medicine for common ailments in many countries of the world. Traditionally it is used in the treatment of systemic hypertension but there are very limited literature on its effect on ocular hypertension. Therefore this clinic based-observational study investigated the effect of graded doses of *Moringa oleifera* leaf aqueous extract on intraocular and blood pressure of thirty normotensive adults, male and female aged 18 to 35 (mean age of 28.93 ±1.62) years. They were divided into three groups of ten participants in each group. Another group of ten normotensive adults, aged matched were used as a control group. Baseline intraocular pressure (IOP) and blood pressure (BP) of each participant were measured. Three different masked doses of *Moringa oleifera* aqueous leaf extract labelled 'E', 'F', and 'G' were orally administered to groups 1, 2, and 3 respectively by a laboratory technician, while group 4 participants drank water only. Thereafter IOP and BP were measured at 30 minutes interval for the four groups until values returned to baseline. Results showed that *Moringa oleifera* leaf aqueous extract when administered orally has statistically significant ($p < 0.05$) hypotensive effect on IOP and BP of the three experimental groups. The effect was dose-dependent and the maximum reduction in BP was at 60 minutes. This preceded the maximum reduction in IOP which occurred at 90 minutes, thereafter IOP and BP rose toward baseline values. Therefore *Moringa oleifera* leaf aqueous extract may be effective in the control of systemic and ocular hypertension.

Keywords: intraocular pressure, blood pressure, *Moringa oleifera* leaf aqueous extract, normotensive adults.

Introduction

Intraocular pressure (IOP) refers to the pressure exerted by intraocular contents on the coats of the eyeball. The normal level of IOP is essentially maintained by a dynamic equilibrium between the aqueous humour formation, aqueous humour outflow and episcleral venous pressure¹. Normal IOP has been defined as the average pressure, which the normal eye can tolerate over a period of time without compromise to the integrity of the eye, or without glaucomatous damage². The range of normal human intraocular pressure is 11-21 mmHg³. Elevated intra ocular pressure is often associated with optic disk cupping and visual field loss- a condition called Glaucoma⁴. Due to the positive correlation

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between IOP and systemic blood pressure, it was observed from the study of Bulpitt *et al.*,⁵ in 1975, that the higher the blood pressure (BP), the greater the IOP, the greater IOP was not related to sex, age, height or haemoglobin. An elevated IOP will cause visual field loss only if the systemic blood pressure is high that the BP/IOP ratio is beyond a certain critical value⁶.

Hypertension is a worldwide common problem occurring mostly in the middle age and also as a hereditary or genetic condition. Systemic Hypertension can be defined as a sustained rise in blood pressure. A person is said to have hypertension when the diastolic pressure is greater than 90mmHg and systolic pressure is greater than 135mmHg⁷. Blood pressure is the pressure exerted by the blood on the walls of the blood vessels. It is understood to mean arterial blood pressure, that is, the pressure in the large arteries, such as the brachial artery (in the arm). Pressure values are universally stated in millimeters of mercury (mmHg). Blood pressure measurement consists of two values. The first value is the systolic pressure; which is the peak or maximum pressure in the arteries during the cardiac cycle; that is, when the ventricles contract. Normal systolic pressure is 120mmHg. It ranges between 110 and 135mmHg. Diastolic pressure is the second number and it is defined as the lowest pressure in the arteries at the resting phase of the cardiac cycle that is, when the ventricles of the heart relax. Normal diastolic pressure is 80mmHg. It varies between 60 and 80mmHg⁸.

Medicinal plants constitute a major source of therapeutic agents for lowering ocular and systemic hypertension. *Moringa oleifera* is a highly valued medicinal plant, distributed in many countries of the tropics and subtropics. It has an impressive range of medicinal

uses with high nutritional value. *Moringa oleifera* (MO) belongs to *Moringaceae* family with about fourteen species and it is widely distributed in the tropics. MO has anti-cancer⁹, anti-inflammatory¹⁰ and thyroid status regulator efficacies¹¹, and some researchers have reported its hypoglycemic and its hypotensive effect¹². Omolaso *et al.*, (2016) conducted a study on the effects of *Moringa oleifera* aqueous leaf extract on systemic blood pressure and blood glucose level in healthy humans and found that *Moringa oleifera* reduced blood pressure significantly ($p < 0.05$) after 2 hours and blood glucose decreased significantly after 4 hours of oral administration of 75mg/kg body weight of *Moringa oleifera* dissolved in 250mls of water. Various parts of this plant such as the leaf, root, seed, bark, fruit, flower and immature pod act as cardiac and circulatory stimulants, anti-inflammatory, antihypertensive, cholesterol lowering, hypoglycemic and antioxidant⁹⁻¹³ but we have not seen any reported studies of its effect on intraocular pressure therefore we investigated the effect of graded doses of *Moringa oleifera* leaf aqueous extract (MOLAE) on intraocular pressure and blood pressure of normotensive adults.

METHODS

This was a clinic based experimental study in which thirty normotensive adults comprising fifteen males and fifteen females with age ranging from 18-35 (mean age of 25.3 ± 5.1) years were selected for experimental groups while ten normotensive adults comprising five males and five females aged matched were selected for the control group from the screening exercise using a purposive sampling method, at the University of Benin Optometry Clinic in Benin City, Edo State Nigeria. During the screening exercise, the case history of each participant was taken. External and internal examination of the anterior and posterior segments of the eyes of each participant

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were carried out using Haag-streit slit lamp model 900 and keeler Ophthalmoscope respectively to rule out abnormalities. The central corneal thickness was assessed with SW-1000P ultrasound pachymeter. Intraocular pressure was measured with the CT-20-non-contact tonometer. Blood pressure was measured with U-MEC mercurial sphygmomanometer and Sprague stethoscope (Model No 112).

Inclusion criteria include normotensive adults who were newly selected from screening and were not on any treatment. They had IOP less than 21mmHg in three consecutive measurements; at 9am, 3pm and 6pm. Three readings were taken in order to observe the diurnal variations in IOP before selection. Each participant's IOP was adjusted and corrected for CCT using the Ehler's formula. Similarly three measurements were taken for the blood pressure (BP); systolic BP less than 120mmHg and diastolic BP less than 90mmHg were included in the study. The selected participants had no history of hypertension; they had no visual field defect, no loss of neural disc tissue from the assessment of the thickness, symmetry and color of the neuro-retinal rim of the optic disc. The participants in the three groups had their visual field assessed using Octopus 900 manufactured in USA. They all had no remarkable ocular or medical history. All the participants were non-alcoholics and non-smokers. Exclusion criteria include participants who were on topical and / or systemic medications and those with ocular or systemic disease.

The first thirty participants selected were divided into three groups 1, 2, and 3; with ten participants in each group. A detailed explanation of the research procedure was given to them and Informed consent was obtained from each volunteer. Approval for the study was granted by the Ethics and Research Committee of the Department of Optometry, University of Benin, and was performed in accordance with the guidelines of the Declaration of Helsinki. Selected participants were instructed to abstain from all medication a

week before and during the period of the experiments. Each participant was weighed and body weight recorded before the experiment. Experiments commenced at 9am in the morning. The participants were served with the same light meal in the morning before they drank aqueous extract of *Moringa oleifera* leaf. Three different concentrations of the aqueous extract of *Moringa oleifera* leaf (28.5mg/kg body weight, 57.0mg/kg body weight and 85.7mg/kg body weight) were administered to groups 1, 2, and 3 participants respectively. The last ten participants formed the group 4 which was the control group and 250ml of distilled water without *Moringa oleifera* leaf was administered orally to each participant in this control group.

Description of Procedure

The methodology of Moussa et al.,(2007)¹⁴ was adopted in the preparation of *Moringa oleifera* leaf aqueous extract (MOLAE). *Moringa oleifera* leaves of the same species were harvested from different trees in the University of Benin, Faculty of Agriculture wild Forest reserve, in Benin City, Nigeria. The leaves were air-dried at room temperature (36.0±10 OC) for 120 hours, thereafter pounded to powdered form. Extracts were prepared by laboratory technicians in the Department of Pharmacognosy University of Benin, using the standardized method of Moussa et al.,¹⁴. This is by dissolving 2g, 4g and 6g of dried powdered *Moringa oleifera* leaf weighed with an electronic scale in 250ml of distilled water respectively to obtain different concentration. 250 ml was the standard volume administered orally based on body weight of each participant in groups 1, 2, and 3. Group 1 participants were administered orally with 250ml of 28.5 mg/kg body weight of MOLAE. Group 2 participants were administered orally with 250ml of 57.0 mg/kg body weight of MOLAE. Group 3 participants were administered orally with 250ml of 85.7 mg/kg body weight of MOLAE while group 4 participants were administered orally with 250ml of water only.

14 Moussa N, Mariko U, Shin-ichi K, Kazuharu S. Effects of Oral Administration of *Moringa oleifera* Lam on Glucose Tolerance in Goto-Kakizaki and Wistar Rats. Journal of Clinical Biochemistry and Nutrition. 2007; 40(3): 229–233.

The calcium and potassium electrolytes in the *Moringa oleifera* leaf powder administered to the participants were analyzed in Marlet environmental research laboratory, Benin City using AAS model-solar 969 unicam series (acetylene flame). The following were obtained for calcium and potassium electrolytes in mg/100g of the *Moringa oleifera* leaf powder:

Electrolytes in	Moringa oleifera leaf powder/100g	Distilled water
Potassium.....	1324.0mg.....	0.6
Calcium	2003.0mg.....	2.9

Statistical analysis

All the data in this study were analyzed with SPSS version 20. A one way Analysis of Variance (ANOVA) was used to determine if *Moringa oleifera* leaf aqueous extract had significant effect on IOP and BP. *Post-hoc* Least Significant Difference (LSD) was used to determine at what minute is the difference most significant. Significance was declared when probabilities values were $p < 0.05$.

RESULTS

The results are summarized in Tables. Tables 1-3

Table 1
Mean of intraocular pressure and blood pressure across different time of assessment in Group 1 participants before and after oral administration of 28.5mg/kg body weight of *Moringa oleifera* leaf aqueous extract.

TIME INTERVAL MINUTES	MEAN IOP ± SD (mmHg)	MEAN IOP ± SD (mmHg)	MEAN SBP ± SD (mmHg)	MEAN DBP ± SD (mmHg)
	OD	OS		
Baseline	12.90 ± 2.42	13.50 ± 2.45	117.10 ± 8.55	80.00 ± 4.97
30	12.90 ± 2.42	13.30 ± 2.35	114.50 ± 7.61	77.60 ± 5.40
60	11.60 ± 2.41	12.80 ± 2.25	111.30 ± 8.18	75.50 ± 4.08
90	10.70 ± 2.22	11.40 ± 2.20	113.50 ± 7.42	77.50 ± 3.20
120	11.80 ± 2.32	12.00 ± 2.41	115.70 ± 9.84	76.50 ± 4.74
150	12.60 ± 2.38	13.20 ± 2.39	116.50 ± 8.36	81.20 ± 6.05

showed that after oral administration of 250ml of 28.5mg/kg, 57.0 mg/kg and 85.7mg/kg body weight of MOLAE to the three experimental groups, there were significant changes ($p < 0.05$) in intraocular pressure and blood pressure at 30, 60 and 90 minutes compared to the baseline values, thereafter IOP and BP returned to baseline values after 150 minutes in the normotensive participants. Tables 4 showed that after oral administration of 250ml of water only, to group 4 participants which was the control group, there was no significant change ($p > 0.05$) in the intraocular pressure and blood pressure at 30, 60, 90, 120 and 150 minutes compared to the baseline values in the normotensive adults, Tables 5 and 6 showed that the maximum mean difference in BP and IOP occurred at 60 and 90 minutes respectively in the experimental groups after oral administration of the three doses of MOLAE and the difference was statistically significant ($p < 0.05$) in the three experimental groups of normotensive participants. After the peak of fall in IOP and BP at 90 and 60 minutes respectively, the IOP and BP rose toward baseline values. The fall in intraocular pressure and blood pressure was also observed to be dose-dependent. The higher the dose of the aqueous extract of *Moringa oleifera* leaf, the greater the fall in IOP and BP.

Table 2
Mean of intraocular pressure and blood pressure across different time of assessment in Group 2 participants before and after oral administration of 57.0mg/kg body weight of *Moringa oleifera* leaf aqueous extract.

TIME INTERVAL MINUTES	MEAN IOP ± SD (mmHg)	MEAN IOP ± SD (mmHg)	MEAN SBP ± SD (mmHg)	MEAN DBP ± SD (mmHg)
	OD	OS		
0	15.90 ± 2.83	16.80 ± 2.27	118.80 ± 8.09	75.00 ± 7.07
30	15.80 ± 2.48	16.30 ± 2.31	117.60 ± 7.45	74.50 ± 6.43
60	14.20 ± 2.61	14.10 ± 2.13	112.70 ± 7.11	70.00 ± 6.23
90	13.00 ± 2.48	14.00 ± 1.91	114.80 ± 6.94	73.00 ± 7.52
120	14.50 ± 2.67	15.20 ± 2.04	115.00 ± 7.81	71.00 ± 6.14
150	15.30 ± 2.79	16.30 ± 2.16	118.50 ± 8.18	74.50 ± 5.98

Table 3
 Mean of intraocular pressure and blood pressure across different time of assessment in Group 3 participants before and after oral administration of 85.7mg/kg body weight of *Moringa oleifera* leaf aqueous extract

TIME INTERVAL MINUTES	MEAN IOP ± SD (mmHg)	MEAN IOP ± SD (mmHg)	MEAN SBP ± SD (mmHg)	MEAN DBP ± SD (mmHg)
	OD	OS		
Baseline	13.90±2.80	14.80±2.83	117.10±8.55	79.80 ±4.83
30	12.40±2.59	14.50±2.95	116.10±8.10	79.50 ±4.37
60	10.70±2.49	12.00±2.74	110.50±8.31	73.00 ±4.13
90	10.20±2.49	11.30±2.65	112.00±8.23	76.50 ±5.79
120	11.60±2.45	12.70±2.71	113.00±8.20	74.00 ±4.59
150	12.90±2.51	13.10±2.92	116.50±8.18	78.50±4.74

Table 4
 Mean of intraocular pressure and blood pressure across different time of assessment in Group 4 participants (control group) before and after oral administration of 250mls of distilled water only

TIME INTERVAL MINUTES	MEAN IOP ± SD (mmHg)	MEAN IOP ± SD (mmHg)	MEAN SBP ± SD (mmHg)	MEAN DBP ± SD (mmHg)
	OD	OS		
Baseline	14.50±1.60	14.65±1.52	120.60±9.60	85.90 ±6.54
30	14.40±1.59	14.60±1.45	120.40±9.50	85.80 ±6.52
60	14.40±1.59	14.55±1.42	119.20±9.45	84.85 ±5.86
90	14.20±1.49	14.50±1.40	120.00±9.52	85.64 ±6.50
120	14.30±1.45	14.60±1.45	120.00±9.52	85.75 ±6.54
150	14.50±1.60	14.60±1.45	120.80±9.80	85.85±6.54

Table 5
 Maximum Mean Difference in intraocular pressure of right and left eye with their p-values after oral administration of 28.5mg/kg, 57.0mg/kg and 85.7mg/kg body weight of *Moringa oleifera* leaf aqueous extract to the three experimental groups

Dosage administered to groups	Maximum Mean Diff in IOP (mmHg) ± SD (OD)	p-values for OD	Maximum Mean Diff in IOP (mmHg) ± SD (OS)	p-values for OS
28.5mg/kg BW (Grp.1)	2.20±0.20	(p=0.000)***	2.10±0.25	(p=0.000)***
57.0mg/kg BW (Grp.2)	2.90±0.35	(p=0.000)***	2.80±0.36	(p=0.000)***
85.7mg/kg BW (Grp.3)	3.70±0.31	(p=0.000)***	3.50±0.18	(p=0.000)***

Table 6
 Maximum Mean Difference in systolic (SBP) and Diastolic blood pressure (DBP) with their p-values after oral administration of 28.5mg/kg, 57.0mg/kg and 85.7mg/kg body weight of *Moringa oleifera* leaf aqueous extract to the three experimental groups

Dosage administered to groups	SBP Maximum Mean Diff ± SD (mmHg)	p-values for SBP	DBP Maximum Mean Diff ± SD (mmHg)	p-values for DBP
28.5mg/kg BW (Grp.1)	5.80±0.37	(p=0.000)***	4.50±0.89	(p=0.000)***
57.0mg/kg BW (Grp.2)	6.10±0.98	(p=0.000)***	5.00±0.84	(p=0.000)***
85.7mg/kg BW (Grp.3)	6.60±0.24	(p=0.000)***	6.80±0.70	(p=0.000)***

DISCUSSION

The fall in intraocular pressure and blood pressure observed in the three normotensive groups of participants showed that the aqueous extract of *Moringa oleifera* leaf has hypotensive property. The mechanisms responsible have not been identified, but numerous possibilities have been proposed. Many of the proposals have attempted to relate dietary calcium to calcium metabolism in vascular smooth muscle and altered vascular tone¹⁵. Potassium supplements have modest blood pressure-lowering effect in persons with low dietary intake. The study by Frank et al.,¹⁶ further showed the importance of potassium for blood pressure regulation in the general population. Therefore the high potassium and calcium content in the aqueous extract of *Moringa oleifera* leaf may have played a role in lowering blood pressure. The main cause of hypertension is believed to be the increased level of sodium in the blood. When the level of potassium in the blood decreases, the absorption of sodium naturally increases leading to hypertension or High Blood Pressure. *Moringa oleifera* leaf is one of the richest sources of potassium. From the phytochemical and electrolytes analysis carried out in Marlet environmental research laboratory, Benin City using AAS model-solar 969 unicam series (acetylene flame), it was observed that *Moringa oleifera* leaf has high content of potassium and potassium is known to prevent the excessive absorption of sodium thereby decreasing the blood pressure. Clinical studies suggest that potassium is an important regulator of blood pressure. Potassium supplementation lowers

blood pressure in hypertensive patients. Blacks appear to be more sensitive to the hypotensive effects of potassium^{17,18}. Potassium chloride lowers blood pressure and increases sodium excretion in patients with hypertension. The blood pressure effect may be due to potassium-induced natriuresis^{19,20}.

The results of this study agrees with the study of Faizi et al.,²¹ they conducted a study on effect of the crude extract of *Moringa oleifera* leaves on systolic, diastolic as well as mean blood pressure of anaesthetized rats. They concluded that the crude extract of the leaves of *M. oleifera* caused a fall in systolic, diastolic, and mean BP in a dose-dependent manner. They also analyzed that thiocarbamate and isothiocyanate in the crude extract were responsible for the antihypertensive activity. Anwar et al.,²² showed that *Moringa oleifera* had 3 major compounds which are capable of lowering systemic blood pressure. The compounds included nitrile, mustard oil glycosides and thiocarbamate glycosides.

There are significant direct correlations between changes in systemic blood pressure and changes in intraocular pressure in humans and animals studies²³⁻²⁹. The peak of fall for blood pressure preceded the peak of fall for IOP in this study, because a decrease in episcleral venous pressure may have resulted in an increased outflow of aqueous causing a fall in intraocular pressure⁶. Therefore the fall in blood pressure is believed to cause a resultant fall in intraocular pressure but further researches are needed in this area in order to determine the exact mechanism by which this occur.

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CONCLUSION

The use of 28.5mg/kg, 57.0 mg/kg and 85.7mg/kg body weight of MOLAE have significant hypotensive effect on intraocular pressure and blood pressure when administered orally to normotensive adults. The lowering effect on intraocular pressure may have resulted from the fall in blood pressure which may have resulted from the high content of potassium and calcium in aqueous extract of *Moringa oleifera* leaf. *Moringa oleifera* leaf is innocuous because toxicological studies of oral administration on rats demonstrated good tolerability without mutagenic or genotoxic effects. Therefore it may be consumed as a form of adjunct therapy in controlling blood pressure and intraocular pressure in systemic and ocular hypertensive humans but further investigations may be required to determine the therapeutic dose of *Moringa oleifera* leaf in the management of ocular and systemic hypertension.