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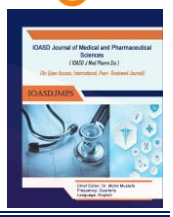

Effect of *Gongronema Latifolium* (Utazi) Leaves on Intraocular Pressure

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ABSTRACT

Intraocular pressure (IOP) is an important physiological measure in ocular health and chronic increase is a major risk factor for glaucomatous optic nerve damage. There is a growing interest in the possible benefits of medicinal plants on the eye including Gongronema latifolium, a plant commonly used in traditional medicine. The effect of Gongronema latifolium leaf extract (GLLE) on intraocular pressure among apparently healthy volunteers was evaluated in this study. The study population consisted of 20 apparently healthy male and female participants. The participants were separated into two groups, 10 in the control group and 10 in the experimental group. The duration of the trial was 7 days. Baseline IOP was recorded, followed by recordings at 30, 60 and 90 minutes. The experimental group was administered Gongronema latifolium leaf extract while the control group was without the administration of the extract. IOP was measured in mmHg and variations in IOP were evaluated for the observation periods.In the control group, IOP showed very moderate changes over the seven-day observation period and no consistent progressive decline after measurements at 30, 60 and 90 minutes. The control group had a baseline mean IOP between 12.57 and 21.14 mmHg and showed relatively small fluctuations in subsequent examinations. In contrast, there was an overall decrease in IOP following administration of the extract in all subjects receiving GLLE. At 60 and 90 min the decline was progressively more noticeable. The individual mean baseline IOP readings in the experimental group ranged from 12.86 to 19.71 mmHg with decreases at 60 and 90 minutes. The observed trend supports a potential time-dependent IOP-lowering impact of GLLE. The results suggest that Gongronema latifolium leaf extract may possess IOP-lowering effect in apparently healthy persons and that the impact may become more pronounced at 60-90min after treatment. The lack of a similar gradual decline in the control group suggests a potential connection between the delivery of GLLE and the alterations noted in IOP. However, the generalisability of the findings is limited by the small sample size and short observation duration. Further research with bigger sample sizes, varied doses, longer follow-up periods and proper statistical testing are recommended to establish the efficacy, safety and mechanism of action of Gongronema latifolium on IOP.

Keywords: Gongronema latifolium, glaucoma, intraocular pressure, ocular health, leaf extract, medicinal plant.

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INTRODUCTION

Gongronema latifolium Benth is an edible and medicinal plant originating from West Africa. It is widely spread in Nigeria and other tropical countries including Guinea-Bissau, western Cameroon and Sierra Leone [1]. The plant is quite widespread in the rain forest areas of south-eastern Nigeria where it is historically eaten as a vegetable and utilised for numerous therapeutic purposes. It is one of the fragrant plants with high nutritional and therapeutic values in Nigeria [2]. Gongronema latifolium is a member of the family Asclepiadaceae and the genus Gongronema [3]. It is known by numerous local names in different parts of Nigeria. It is termed "Utazi" by the Igbo people of southeastern Nigeria, "Utasi" by the Ibibio, Qua and Efik groups and "Arokeke" by the Yoruba of southwestern Nigeria. In English it is generally known as bushbuck. The plant has green leaves, yellow flowers, and a stem that produces a milky latex when cut. Its leaves, particularly when eaten fresh, have a characteristic harsh, bitter and faintly sweet taste. G. latifolium is a perennial

climbing shrub that can grow to around 5 m long; It rises by twining around supporting vegetation but can also trail along the ground, developing adventitious roots. The stem is soft, hollow, hairy at first and woody at the base, with a peculiar milky latex.

The leaves are simple, green and opposite, although may rarely be whorled. They are normally without stipules and have virtually complete edges. The petiole is 3 cm long. The leaf blade is broadly ovate to virtually round, with a deeply cordate base, acuminate apex and pronounced three-veined venation [4]. The blooms of G. latifolium are yellow, fragrant, tiny, regular and bisexual. They are carried in terminal and axillary cymose panicles up to about 13 cm long. Pedicels 2–4 mm long; calyx lobes elliptical to rounded, hairy. The flower is about 5 mm long, tubular, with a campanulate apex and five lobes which are triangular to oval. The corona is made up of 5 fleshy lobes, cream coloured with brown bases, shorter than the staminal column. The five stamens have small appendages, the filaments coherent in a tube. The anthers are erect and have membrane apical appendages. The ovary is superior and the pollinarium has two pollinia [5]. The fruit is a dehiscent follicle, oblong-lanceolate in form. The hue varies from green in the immature fruit to dark brown and finally black in the ripe fruit. At maturity the follicle separates lengthwise along the suture to release the seeds. The seeds are compressed and flattened, about 0.5cm long. The seed is connected to a white silky tuft or pappus which aids wind dissemination [6]. G. latifolium is of great importance nutritionally and medicinally. It is rich in proteins, lipids, fibre, minerals, vitamins and vital amino acids, hence its leaves are of high value as a source of food [7]. The leaves are extensively used in traditional Nigerian cuisine, especially as a vegetable in soups, but they can also be dried and pounded into a powder for use as a spice. Its tender leaves are also consumed and used in several salad recipes [8]. Beyond its nutritional value, G. latifolium has a long history of usage as a traditional medicine. Different portions of the plant are used traditionally for the management of digestive diseases such loss of appetite, dyspepsia, constipation and dysentery. It has also been traditionally used in the treating of malaria, cough, wheezing and asthmatic symptoms. The herb is utilised in some communities for the management of high blood glucose and blood pressure. For example, in Sierra Leone roots and stems have traditionally been used as chewing sticks and for production of herbal beverages Some preparations have also been used traditionally as purgatives in colic, stomach discomfort and suspected worm infections [9]. Pharmacological activities of G. latifolium have been attributed to many bioactive compounds. Constituents reported are flavonoids, tannins, alkaloids and phytosterols such as β-sitosterol.

The leaves are also a source of important quantities of crude protein, lipids, ash, fibre, nitrogen and vital amino acids. The plant reportedly has the necessary amino acids leucine, valine and phenylalanine. Some of the biological activity traditionally attributed to this plant may be due to these phytochemical and nutritional components. The hypotensive and antihypertensive potential of G. latifolium is of special interest to the present study. Some studies have revealed that elements of plants may modulate cardiovascular function and blood pressure. This could be attributed to the presence of minerals such as potassium and other bioactive substances. Systemic blood pressure and intra-ocular pressure are biologically connected. Substances that might influence vascular and systemic haemodynamic parameters may potentially alter intra-ocular pressure as well. The pressure inside the eye due to the aqueous humour is known as the intraocular pressure (IOP). The equilibrium between formation of aqueous humour and its drainage through the trabecular meshwork and uveoscleral channels is maintained. Maintenance of IOP within the normal physiological range is crucial to preserve the anatomical and functional integrity of the eye. High IOP over the normal level is one of the most important modifiable risk factors for the onset and progression of glaucoma, particularly in those persons who are predisposed [10].

Globally, glaucoma is a leading cause of irreversible vision impairment and blindness. higher IOP is not synonymous with glaucoma. However, prolonged or pathologically higher IOP can cause mechanical and circulatory stress to the optic nerve head, and may lead to progressive optic nerve injury. Therefore, adequate management of IOP is a crucial factor in eye health and the prevention of glaucoma. Medicinal plants and chemicals from plants have been historically significant for the discovery and development of therapeutic treatments. Plant medicines have been widely used in traditional medicine for the prevention and treatment of several ailments [11]. One such medicinal plant with reported antihypertensive and other pharmacological effects is G. latifolium. Considering the possible impacts on cardiovascular function and the known physiological link between systemic blood pressure and IOP, there is a reason to investigate the possibility to alter IOP by intake of G. latifolium leaves. G. latifolium is widely consumed and used in traditional medicine; nevertheless, little is known about its direct influence on intraocular pressure. The question of whether the plant influences IOP may give valuable information on its ocular safety and therapeutic significance, particularly in persons who use it regularly or as a traditional cure. Therefore, this study was aimed at establishing the influence of Gongronema latifolium (Utazi) leaves on intraocular pressure in normotensive individuals and quantifying the amount and direction of any observed changes in IOP after ingestion of the plant preparation.

MATERIALS AND METHODS

Research Design

The study adopted an experimental research design to determine the acute effect of oral consumption

of *Gongronema latifolium* leaf extract on intraocular pressure (IOP) among normotensive adults. The study employed a controlled experimental approach in which participants were allocated into an experimental group that received *G. latifolium* leaf extract and a control group that did not receive the extract. Intraocular pressure was assessed at baseline and at specified intervals following administration of the extract.

Research Setting

The study was conducted at the Optometry Clinic, Imo State University, Owerri, Imo State, Nigeria. The clinic provided an appropriate setting for the ocular examination and measurement of intraocular pressure using standard clinical procedures.

Study Population

The study population comprised healthy normotensive adult volunteers aged 20–30 years who met the specified inclusion criteria and consented to participate in the study.

Sampling Technique

A randomized controlled study approach was adopted. A total of 20 eligible participants were recruited and randomly allocated into two groups: an experimental group and a control group. The experimental group received *Gongronema latifolium* leaf extract, while the control group did not receive the extract. The intraocular pressure of participants in both groups was assessed under standardized conditions.

Research Materials and Procedures

Research Materials

The following materials and instruments were used for the study:

- Twenty (20) eligible adult participants.
- *Gongronema latifolium* fresh leaves.
- *Gongronema latifolium* leaf extract.
- Perkins applanation tonometer.
- Proparacaine ophthalmic anaesthetic.
- Fluorescein dye strips.
- Methylated spirit for disinfection.
- Cotton wool.
- Weighing scale.
- Clean storage container for the leaf extract.
- Basic examination and data collection sheet.

Research Procedure

The study was conducted over a period of seven days. All participants underwent an initial ocular examination and baseline measurement of intraocular pressure. Before each tonometric examination, the tonometer was appropriately disinfected using cotton wool moistened with methylated spirit and allowed to dry. The participant was comfortably positioned for the examination. A drop of topical proparacaine was instilled into each eye, followed by application of fluorescein dye. Baseline intraocular pressure was then measured in both eyes using a Perkins applanation tonometer.

Following baseline measurements, participants were randomly assigned to either the experimental or control group. The experimental group received the prescribed dose of *Gongronema latifolium* leaf extract orally. Intraocular pressure was subsequently measured at 30, 60 and 90 minutes after administration of the extract. Participants in the control group underwent the same measurement procedures and were monitored over the same time intervals but did not receive the *G. latifolium* leaf extract. This allowed changes in IOP in the experimental group to be compared with those observed in the control group.

Validation and Reliability of the Instruments

The Perkins applanation tonometer was used according to standard clinical procedures for measuring intraocular pressure. The tonometer was appropriately disinfected before and after use, and measurements were repeated until a consistent and stable reading was obtained. The tonometer readings were converted to intraocular pressure values in millimetres of mercury (mmHg) according to the manufacturer's calibration procedure. To improve measurement reliability, all IOP measurements were performed under similar environmental conditions and, as much as practicable, by the same examiner. The procedure was standardized for all participants to minimize inter-observer and procedural variations.

Method of Data Collection

A structured examination and data collection sheet (Appendix) was used to record participants' demographic characteristics, baseline measurements and subsequent IOP readings. Baseline intraocular pressure was measured before administration of the *Gongronema latifolium* leaf extract. The extract was administered immediately after the baseline measurement to participants in the experimental group.

Subsequent IOP measurements were obtained at 30, 60 and 90 minutes following administration of the extract. Corresponding measurements were obtained from the control group at the same time intervals. All measurements were recorded in mmHg for subsequent statistical analysis.

Precautions Taken During Tonometry

The following precautions were observed throughout the study:

1. Participants were adequately informed and allowed to relax before and during tonometric examination to minimize anxiety-related changes in IOP.
2. The body weight of each participant was measured before administration of the extract, and the calculated dose was administered

according to the predetermined weight-based dosage.
3. All tonometric measurements were performed in the morning, as far as practicable, to minimize the potential influence of diurnal variation in intraocular pressure.
4. The Perkins tonometer probe was disinfected appropriately before and after examination of each participant.
5. The fluorescein and ophthalmic dropper tips were handled carefully and positioned to avoid contact with the eyelashes, eyelids or ocular surface.
6. The same standardized procedure was followed for all participants and at all measurement intervals.
7. Participants were instructed to remain relaxed and avoid unnecessary physical activity immediately before IOP measurements.

Preparation of *Gongronema latifolium* Leaf Extract

Fresh *Gongronema latifolium* leaves weighing 50 g were carefully selected and thoroughly washed with clean water to remove dirt and other contaminants. The washed leaves were mechanically crushed and squeezed to obtain the fresh leaf extract. The extract was collected in a clean, appropriately labelled container and stored under refrigeration until use to minimize deterioration.

A dose of 50 mg/kg body weight of the freshly prepared extract was administered orally to each participant in the experimental group. The dose administered to each participant was determined according to the individual's body weight.

Inclusion and Exclusion Criteria

Inclusion Criteria

Participants were eligible for inclusion if they:

1. Were healthy male or female volunteers aged 20–30 years.
2. Were normotensive.
3. Had no known ocular disease that could affect intraocular pressure.
4. Were not receiving treatment likely to influence IOP.
5. Were willing to participate in the study and provided informed consent.

Exclusion Criteria

Participants were excluded if they:

1. Had any significant systemic illness or were receiving treatment that could affect intraocular pressure.
2. Were glaucoma suspects or had a known history of glaucoma.
3. Had a history of ocular disease or surgery that could influence IOP.
4. Were unwilling to participate or unable to complete the study procedures.

Data Analysis Techniques

The data obtained from the study were coded, tabulated and analyzed using the IBM Statistical Package for the Social Sciences (IBM SPSS), version 25.0. Descriptive statistics were used to summarize the data and were presented using appropriate tables, means and standard deviations. Baseline and post-intervention IOP measurements were compared within and between the experimental and control groups. An appropriate inferential statistical test, such as repeated-measures analysis of variance (ANOVA) for within-group changes and an independent-samples *t*-test for between-group comparisons, was used depending on the distribution and structure of the data. Statistical significance was set at a *p*-value of less than 0.05, with a 95% confidence interval.

Ethical Considerations

Ethical approval for the study was obtained from the Ethics and Thesis Committee of the Department of Optometry, Imo State University, Owerri. The purpose, procedures, potential benefits and possible risks associated with the study were explained to all prospective participants before enrolment. Written informed consent was obtained from each participant. Participation was voluntary, and participants were informed of their right to withdraw from the study at any time without penalty. Confidentiality of participants' information was maintained throughout the study, and data were used strictly for academic and research purposes. The study procedures were conducted in accordance with accepted ethical principles and standard requirements for human research.

RESULTS

4.0 Results

Data were obtained from twenty (20) apparently healthy volunteers comprising both males and females. Ten (10) participants were assigned to the control group, while the remaining ten (10) participants constituted the experimental group. The study was conducted over a period of seven (7) days. Intraocular pressure (IOP) was measured at baseline and subsequently at 30, 60, and 90 minutes.

For clarity and consistency, the following abbreviations were used throughout the presentation and interpretation of the results:

- **GLLE** – *Gongronema latifolium* Leaf Extract
- **IOP** – Intraocular Pressure (mmHg)

4.1 Baseline and Post-Intervention IOP Measurements

Table 1: IOP Measurements of Control Group Subjects on Day 1

S/N	Baseline (mmHg)	30 min (mmHg)	60 min (mmHg)	90 min (mmHg)
1	14.00	14.00	14.00	16.00
2	12.00	12.00	10.00	12.00
3	20.00	18.00	20.00	20.00
4	18.00	18.00	18.00	18.00
5	12.00	10.00	10.00	12.00
6	22.00	22.00	22.00	22.00
7	18.00	20.00	18.00	18.00
8	18.00	18.00	20.00	18.00
9	14.00	14.00	16.00	16.00
10	14.00	14.00	14.00	14.00

Analysis

Table 1 presents the IOP measurements of participants in the control group on Day 1. The baseline IOP values ranged from 12.00 to 22.00 mmHg. There were minor fluctuations in IOP at 30, 60, and 90 minutes, with no consistent pattern of increase or decrease across the participants.

Control Group Measurements on Days 2–7

The Day 2 to Day 7 measurements followed the same format as Day 1. Across the seven-day observation period, the control group demonstrated relatively small fluctuations in IOP measurements at the different time points. No consistent progressive reduction in IOP was observed in the absence of GLLE administration.

Table 2: Mean IOP Measurements of Control Group Subjects Across the Seven-Day Period

S/N	Baseline (mmHg)	30 min (mmHg)	60 min (mmHg)	90 min (mmHg)
1	13.71	14.00	15.14	15.43
2	12.57	12.57	12.57	13.14
3	19.43	18.57	18.86	19.43
4	18.57	18.29	18.29	19.14
5	12.57	12.57	11.71	12.86
6	21.14	22.00	20.86	21.71
7	18.86	19.71	18.00	18.57
8	18.00	18.29	18.86	17.71
9	13.71	13.71	14.29	15.43
10	13.14	14.00	13.71	14.29

Analysis:

Table 2 shows the mean IOP measurements of the control group across the seven-day study period. The mean baseline IOP ranged from 12.57 to 21.14 mmHg among the participants. Measurements at 30, 60, and 90 minutes showed only modest variations from baseline. Overall, the control group did not demonstrate a consistent reduction in IOP over the observation period.

4.2 IOP Measurements of the Experimental Group

Experimental Group IOP Measurements from Day 1 to Day 7

The experimental group received *Gongronema latifolium* leaf extract following baseline IOP measurement. IOP was subsequently measured at 30, 60, and 90 minutes after administration. Across the seven-day period, the experimental group generally demonstrated a progressive reduction in IOP following administration of GLLE, particularly at 60 and 90 minutes. The magnitude of reduction varied among participants and across study days.

Table 3: Mean IOP Measurements of Experimental Group Subjects Across the Seven-Day Period

S/N	Baseline (mmHg)	30 min (mmHg)	60 min (mmHg)	90 min (mmHg)
1	14.57	13.71	11.71	11.43
2	13.43	12.29	11.43	10.29
3	19.71	18.00	16.29	15.14
4	18.29	17.71	15.43	13.43
5	17.71	16.57	13.43	12.57
6	16.29	14.29	13.71	12.29
7	12.86	13.14	11.71	10.86
8	17.14	15.14	14.00	12.86
9	14.29	12.86	10.29	10.00
10	14.57	13.71	11.71	10.57

Analysis:

Table 3 presents the mean IOP measurements of participants who received GLLE. A general reduction in IOP was observed following administration of the extract. The reduction became more pronounced at 60 and 90 minutes compared with baseline measurements. This pattern suggests a possible time-dependent effect of GLLE on IOP among the experimental participants.

DISCUSSION

The present study studied the effect of oral administration of Gongronema latifolium leaf extract on intraocular pressure (IOP) among healthy normotensive persons. For the study, twenty volunteers were recruited. Ten people were in the control group and ten in the experimental group. Intraocular pressure was measured at baseline and at 30, 60 and 90 min after administration of the extract. The data revealed an overall decrease in IOP after oral ingestion of Gongronema latifolium leaf extract. The mean IOP in the experimental group was 15.89 mm Hg at baseline, 14.74 mm Hg at 30 minutes, 12.97 mm Hg at 60 minutes, and 13.20 mm Hg at 90 minutes. The mean decrease in IOP was around 1.15 mmHg at 30 minutes, 2.92 mmHg at 60 minutes and 2.69 mmHg at 90 minutes compared with baseline. The biggest decrease was after 60 minutes, but the IOP was still lower than baseline at 90 minutes. The reduction observed may reflect an immediate IOP reducing action of G. latifolium leaf extract in healthy normotensive subjects.

This study is potentially of relevance as management of IOP is critical for the maintenance of ocular health, and elevated IOP sustained over time is an important modifiable risk factor for glaucomatous optic neuropathy [12]. However, the current results should be regarded with caution as the study was carried out in healthy normotensive subjects and with a very small sample size. The statistical results provide additional evidence for the observed alterations [13]. There was no statistical difference in IOP at baseline between the control and experimental groups ($p = 1.000$) indicating that the groups were equivalent before extract delivery. There was no statistically significant difference between the groups at 30 minutes ($p = 0.225$). However, statistically significant changes were identified at 60 minutes ($p=0.019$) and 90 minutes ($p<0.001$). The greater amplitude of the between-group difference with time shows the effect of the extract may become more apparent in the latter post administration interval. The possible IOP-lowering action of G. latifolium could be related to the bioactive ingredients of the plant [15]. Earlier research have reported the existence of numerous phytochemicals such as flavonoids, tannins, alkaloids and other phenolic compounds in the leaves. Flavonoids are of special relevance due to their antioxidant and vascular properties [16]. Certain flavonoid compounds have also been related with improvements in vascular function and reductions in systemic blood pressure. For instance, it was described positive cardiovascular benefits related with dietary components rich in flavonoids [17]. Such effects may be important because systemic haemodynamic variables may influence ocular perfusion and may be a contributing reason to IOP fluctuations. The physiological effects of G. latifolium may possibly be related to its mineral content. Potassium, calcium and other minerals in the plant may affect vascular smooth muscle function and fluid and electrolyte balance.

Moreover, the biological activity of the plant may be due to the presence of antioxidant ingredients like as vitamin C and phenolic compounds, which may reduce oxidative stress [18]. Oxidative stress has been proposed to be involved in numerous ocular disease processes including glaucoma. However, these phytochemical, vascular or biochemical pathways were not directly measured in the present investigation and, therefore, their contribution to the observed drop in IOP remains hypothetical [19]. The results of the present investigation are also biologically feasible given the known traditional therapeutic usage of G. latifolium. It has been used in traditional dishes in parts of West Africa and eaten for a long time as a vegetable. It has antihypertensive and other pharmacologic characteristics that have spurred attention in possible therapeutic uses. However, the traditional use and evidence of systemic blood-pressure lowering activity should not be seen as direct evidence of ocular hypotensive impact. The present study provides preliminary evidence of a relationship between oral G. latifolium ingestion and short-term IOP reduction but further investigations are required to establish the mechanism responsible [20]. The decrease in IOP in the experimental group was not the same for all subjects or in all the measurement times. This variability could be due to normal physiologic changes in IOP, individual variability in reaction to the extract, variability related to the testing process, or differences in absorption and metabolism of the active ingredients. IOP also has a diurnal change which was taken into account in the design of the study by measuring in the morning. Residual biological variance, however, cannot be entirely ruled out. A major point is that only 20 healthy normotensive subjects were recruited in this study. Therefore, the results cannot be immediately extrapolated to patients with glaucoma or ocular hypertension. A decrease in IOP in healthy subjects may not necessarily translate to a clinically relevant decrease in subjects with elevated IOP or developed glaucomatous visual neuropathy. In addition, the study assessed the short-term response up to 90 minutes post-administration and so does not give data on the long-term efficacy or safety of G. latifolium. The findings should, therefore, be considered as a preliminary indication for further exploration of G. latifolium as a potential source of ocular hypotensive chemicals [21]. In future investigations, greater sample size, standardisation of extraction processes, well defined doses, longer follow-up duration and inclusion of patients with ocular hypertension or glaucoma should

be considered. It would also be of interest to determine which phytochemical constituents are responsible for the effect observed and whether the reduction in IOP is mediated via changes in aqueous humour production, aqueous outflow facility, episcleral venous pressure, systemic blood pressure or other physiological pathways [22].

CONCLUSION

The outcomes from this study revealed that oral administration of Gongronema latifolium leaf extract at a concentration of 50 mg/kg reduced intra ocular pressure among healthy normotensive subjects. Reduction was not statistically significant at 30 minutes but was statistically significant at 60 minutes and more dramatic at 90 minutes compared with control group. The mean drop from baseline was greatest at 60 minutes, and the IOP was below baseline after 90 minutes. Thus, G. latifolium leaf extract may have potential for short term ocular hypotensive action. However, this was a trial of a limited number of healthy normotensive participants and the findings are preliminary and should not be regarded as evidence that the extract is an established treatment for glaucoma or ocular hypertension.

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