

**THE EFFECT OF *Dennettia tripetala* (PEPPER FRUIT) AQUEOUS EXTRACT ON
INTRA OCULAR PRESSURE AND BLOOD PRESSURE OF NORMOTENSIVE
SUBJECTS**

BY

EBHOHON EGHOSA GRACE (Miss)

LSC1806906

DEPARTMENT OF OPTOMETRY

FACULTY OF LIFE SCIENCES

UNIVERSITY OF BENIN

BENIN CITY

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**A THESIS SUBMITTED TO THE DEPARTMENT OF OPTOMETRY,
FACULTY OF LIFE SCIENCES, UNIVERSITY OF BENIN, BENIN CITY,
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD DOCTOR
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DEDICATION

I dedicate this project work to God first and then to my parents, Mr. and Mrs. EBHOHON, and to myself for remaining courageous, steadfast, committed, diligent and determined during these past rigorous six years.

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The successful completion of this project would not have been possible without the immense contributions of many people, too numerous to mention.

First and foremost, I give all glory to the Almighty God for guiding me through this journey. It was not an easy feat, but He carried me every step of the way, and for that, I am truly grateful.

I would also like to express my deepest appreciation to my parents, Mr. and Mrs. Ebhohon—my greatest sponsors, my guide, and my shield. Having you in my life is a blessing beyond measure, and I am forever thankful. To my one and only sibling, thank you for your unwavering support; your presence means the world to me.

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To my amazing aunties, your contributions in various ways have been instrumental to the success of this project, and I sincerely appreciate you all. Aunty Makua, the sweetest person I have ever met, your encouragement and kind words meant so much to me. Thank you for helping me choose this topic—it made all the difference.

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ABSTRACT

Over the years, studies has been carried out on the effects of various plants on intraocular pressure and blood pressure. However, the numerous benefits *Dennettia tripetala* on the eye are still unfolding. The work below is the effect of graded doses of pepper fruit extract on intraocular pressure and blood pressure. The purpose of this study is to determine the effect of pepper fruit aqueous extract on intraocular pressure and blood pressure using normotensive patients. 60 subjects was be used within the age of 18 – 35years, for the experiment. Intraocular pressure and blood pressure was measured using the Perkins tonometer and Mercury sphygmomanometer before ingestion and at 30 minutes interval for 180 minutes for group A, B and C. The measurement was carried out three times and the average is taken. 50mg/kg, 75mg/kg and 100mg/kg body weight of *Dennettia tripetala* doses was given to group A, B and C respectively, while group D will be given 500ml of pure water, intraocular pressure and blood pressure was measured at 30 minutes interval for 180 minutes. The data obtained from this study was analysed using repeated measures Analysis of Variance (ANOVA) as processed by the statistical package for social sciences (SPSS), version 22.0. The result obtained from this study will enlighten optometrist on the effect of *Dennettia tripetala* on intraocular pressure and blood pressure

Keywords: Pepper fruit (*Dennettia tripetala*), , intraocular pressure

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background of the Study

In recent years, there has been a growing interest in exploring the therapeutic potential of medicinal plants, particularly in the treatment of conditions such as hypertension and ocular diseases. One such plant that has attracted attention in traditional medicine is *Dennettia tripetala*, commonly known as African pepper fruit. This plant, indigenous to West Africa, particularly Nigeria, is widely used for both culinary and medicinal purposes. Its pungent fruits and seeds are commonly consumed, and various parts of the plant have been traditionally used in managing health conditions like gastrointestinal disorders, fevers, and inflammatory conditions. The use of natural products in managing health conditions is increasingly being recognized for its potential benefits, including fewer side effects and accessibility to diverse populations. While the antihypertensive potential of *Dennettia tripetala* has been suggested in preliminary studies, there is limited scientific research on its effect on intraocular pressure. Since elevated IOP and hypertension are interrelated in the pathogenesis of glaucoma and other cardiovascular diseases, it is critical to investigate whether *Dennettia tripetala* could serve a dual role in managing both conditions.

This study seeks to examine the effect of *Dennettia tripetala* on intraocular pressure and blood pressure, offering potential insights into its broader therapeutic applications. By understanding its impact on these physiological parameters, this research could provide a basis for further investigation into the development of plant-based treatments for glaucoma and hypertension.



Source: Researchgate.net

1.1.2 CLASSIFICATION

Dennettia tripetala belongs to specie tripetala which is classified as follows:

Taxonomy of *Dennettia tripetala*

Kingdom: Plantae,

Phylum: Magnoliophyta,

Class: Magnolidae;

Order: Magnoliales;

Family: Annonaceae;

Genus: Denettia;

Species: *Dennettia tripetala*.

Nutritional Differences and similarities between the fruit and leaves.

The fruit differs from the leaves in that it contains sterols (subgroup of steroids) and balsam(a resinous, oily, aromatic substance), while both of them contains carbohydrates, tannins, alkaloids, terpenes, flavonoids and phenols.(Omoregie et al, 2015).

1.1.3 DESCRIPTION

Pepper fruit usually grows as a small woody shrub that grows to a height of 12-15m and have a width of 0.6m. The wood of pepper fruit is white in colour, soft and can be used as fuel. The wood is also not durable. The trees usually has a characteristic scent. The bark usually has a strong pungent smell. The fruit are usually green when unripe but turns red as it ripens. It is grown during the rainy season. It's moisture content also increases on ripening. It also has a pungent strong smell. The leaves are 3-6 inches long and 1.5-2.5 inches broad. They are elliptic in shape. The seeds can be eaten and are spicy in nature. The plants can be grown using the seeds which is why traders and farmer stores the seeds till the next planting season.

1.1.4 NUTRIENT COMPOSITION

The nutritional benefits of Pepper fruit by Okwu and Morah (2004) has been shown to contain 0.42% magnesium. 1.8% Calcium, 2.50% potassium, 9.84% Crude fibers, 15.31% Crude protein, 8.0% Moisture, 62% carbohydrate, 3.47% crude lipids, 0.33% phosphorus, trace elements such as cadmium, iron. Zinc and copper, it was also said to contain water soluble vitamins such as niacin, ascorbic acid, riboflavin and thamine.

Pepper fruit is an excellent source of essential vitamins, minerals, and antioxidants. It is rich in vitamins A and C, potassium, magnesium, and iron (Simonne et al., 2010). The antioxidants present in pepper fruit have been shown to reduce inflammation, improve cardiovascular health,

and enhance immune function (Lee et al., 2012; Liu et al., 2013). Additionally, pepper fruit's anti-cancer properties and neuroprotective effects make it a valuable addition to a healthy diet (Surh & Lee, 1996; Kim *et al.*, 2017).

Variations in temperature and precipitation can affect the nutrient levels in *Dennettia tripetala*. For instance, studies on chestnut fruits indicate that mean annual temperature and precipitation correlate with nutrient concentrations, suggesting similar patterns may exist for *Dennettia tripetala* (Turfan *et al.*, 2024).

Research comparing *D. tripetala* with other plants like *Aframomum melegueta* highlights differences in mineral and phytochemical content, suggesting that local growing conditions play a significant role (Evuen & Kpomah, 2023).

1.1.5 BIOCHEMISTRY

Research utilized sophisticated methods such as Fourier Transform Infrared Spectroscopy (FT-IR) and Gas Chromatography with Flame Ionization Detection (GC-FID) to examine the essential oil. This analysis uncovered a wide variety of compounds, including linalool and benzyl nitrile, among others, which are recognized for their biological properties Moses *et al.*, (2024).

Natural products are widely used in African communities to treat diseases caused by microbes and oxidative stress. This study evaluated the bioactive compounds, antimicrobial, and antioxidant properties of *Dennettia tripetala* fruit using in vitro and in vivo models.

Phytochemical screening of hexane and ethanol extracts revealed saponins, tannins, flavonoids, steroids, phenols, and terpenoids. GC-MS analysis identified various bioactive compounds. Both extracts exhibited strong antioxidant activity in DPPH and ABTS assays, though less potent than vitamin C. They also demonstrated significant antibacterial effects against multidrug-resistant

Gram-positive and Gram-negative bacteria. In a rat model, the extract protected against liver damage by enhancing antioxidant enzyme activity and reducing oxidative stress markers. These findings suggest *D. tripetala* as a potential treatment for microbial infections and oxidative stress-related conditions (Journal, 2023).

1.1.6 BIOACTIVITY

The increasing resistance of Plasmodium species to antimalarial drugs is a significant obstacle to malaria eradication. A study conducted by Ogbonnaya *et al.*, (2024). evaluated the antimalarial activity of *Dennettia tripetala* leaf extract and its N-hexane and water fractions in a rat model. Phytochemical screening of the N-hexane and water fractions was conducted using standard methods, and antimalarial efficacy was assessed through Peters' 4-day suppressive test, Rane's curative test, and a prophylactic model. The analysis revealed that both fractions contained varying levels of flavonoids, alkaloids, terpenoids, and saponins. Both fractions demonstrated significant antimalarial activity across all test models ($P < 0.05$), with the N-hexane fraction showing superior chemosuppressive and curative effects compared to the water fraction. The N-hexane fraction exhibited curative effects ranging from 62.3% to 72.4%, chemosuppressive effects from 51.2% to 88.5%, and chemoprophylactic activity from 32.1% to 61.2%. For comparison, *Combretum nigricans* butanol extract showed chemosuppressive effects of 40.3%, 54.1%, and 69.1%, therapeutic effects of 26.2%, 36.9%, and 34.5%, and chemoprophylaxis of 48.4%, 70.0%, and 87.4% at doses of 250–1500 mg/kg. These findings suggest that *Dennettia tripetala* solvent fractions possess significant antimalarial properties, potentially making them effective for various stages of malaria treatment.

1.1.7 METABOLISM

Dennetia tripetala, commonly known as pepper fruit, undergoes metabolism involving various bioactive compounds that contribute to its health benefits. The fruit is rich in essential nutrients such as carbohydrates, proteins, and fats, as well as secondary metabolites like alkaloids, flavonoids, tannins, and saponins, which are responsible for its medicinal properties (Okwu & Morah., 2004). The metabolism of these bioactive compounds begins with their digestion and absorption in the gastrointestinal tract. Alkaloids, for instance, are metabolized in the liver through enzymatic processes such as hydroxylation and oxidation, which enhance their bioavailability and pharmacological activity (Ezeja et al., 2011). Flavonoids, another significant component, are broken down by gut microbiota into smaller metabolites that can be absorbed and utilized by the body, contributing to antioxidant and anti-inflammatory effects (Oboh *et al.*, 2014). Moreover, *Dennetia tripetala* contains volatile oils and phenolic compounds that are metabolized to produce biologically active derivatives. These compounds exhibit antimicrobial and anti-hypertensive properties, which may influence intraocular and blood pressure (Iseghohi *et al.*, 2015). The metabolism of these compounds likely involves conjugation reactions such as glucuronidation and sulfation, facilitating their excretion from the body.

1.1.8 OVERVIEW OF ITS IMPORTANCE

Economic Importance; Pepper fruit is a significant crop for global trade, providing: employment opportunities which will supports millions of farmers and agricultural workers, improvement of economic growth which will contributes to local economies and national GDP and export revenue which can generates substantial foreign exchange earnings.

Digestive Health- Pepper fruit's fiber content promotes digestive regularity, preventing constipation and diverticulitis. The antioxidants and capsaicin also help alleviate symptoms of irritable bowel syndrome (IBS).

Cancer Prevention- A study on the anticancer effects of *Dennettia tripetala* extracts found that both aqueous and ethanol extracts reduced MCF-7 breast cancer cell viability in a dose-dependent manner. The aqueous extract had an IC₅₀ of 37.42 µg/ml, while the ethanol extract had 61.74 µg/ml, suggesting potential anticancer properties David *et al.*, (2024)

Neuroprotective Effects- Pepper fruit's antioxidants and capsaicin also provide neuroprotective benefits, shielding against neurodegenerative diseases like Alzheimer's and Parkinson's (Kim *et al.*, 2017). Capsaicin's ability to reduce inflammation and oxidative stress further supports brain health.

Culinary and Economic Significance- Pepper fruit is a staple ingredient in various cuisines worldwide, adding flavor, texture, and color to numerous dishes. As a major crop for global trade, pepper fruit provides a source of income for millions of farmers, contributing significantly to local economies (Journal, 2023).

Traditional Medicine- For centuries, pepper fruit has been utilized in traditional medicine for its therapeutic properties. It has been used to alleviate pain, digestive issues, and respiratory problems (Kim *et al.*, 2017; Lee *et al.*, 2012; Surh & Lee, 1996).

Ethnomedicinal Value: The findings of a research done by Moses *et al.*, (2024). supports the ethnomedicinal claims associated with *D. tripetala*, suggesting that the therapeutic properties attributed to its essential oil are likely due to the presence of the identified bioactive compounds. This reinforces the importance of traditional knowledge in guiding scientific research

Immune System Support- Pepper fruit's vitamin C content enhances immune function, boosting the production of white blood cells and activating natural killer cells (Lee *et al.*, 2012). This immune system support helps protect against infections and diseases.

Insecticidal effect; In 2017, *D. tripetala* powder was shown to be tolerated by rats when incorporated into their diet as a form of botanical pesticide (Nwosu *et al.*, 2017).

Fertility; In 2018, ethanolic extracts of *D. tripetala* fruits were shown to enhance the testosterone levels as well as the number and motility of sperm in rats (Obiandu and Green, 2018).

1.1.9 ANTIOXIDANT PROPERTIES

Pepper fruit's high antioxidant content helps protect cells from damage caused by free radicals, reducing the risk of chronic diseases such as cancer, cardiovascular disease, and neurodegenerative disorders (Lee *et al.*, 2012). Antioxidants like vitamin C and beta-carotene also enhance immune function, shielding against infections and illnesses.

The results of the research conducted by Umoh *et al.*, (2024). lend scientific support to the traditional applications of *Dennettia tripetala* in addressing ailments related to oxidative stress. The notable antioxidant properties identified in the study correspond with its historical uses in alleviating various health concerns, such as pain, inflammation, and respiratory issues.

Okolie *et al.*, (2014) conducted a study on the antioxidant properties of *Dennettia tripetala* root extract were evaluated, showing notable H₂O₂ and nitric oxide scavenging abilities, and a concentration dependent ferric ion-reducing power. The extract inhibited lipid peroxidation in frozen meat tissues, outperforming vitamin C in heart slices and matching vitamins C and E in testes and kidney slices. These findings highlight its potential for meat preservation during refrigeration.

Pepper fruit is a Nigerian medicinal plant used for various ailments and in traditional dishes.

Adebayo *et al.*, (2010) conducted a study comparing the antioxidant properties of aqueous

extracts from ripe (RPF) and unripe (UPF) fruits. RPF had higher total phenol content, while UPF exhibited greater antioxidant activities, including scavenging abilities and Fe chelation. Ripening increases phenol content but reduces overall antioxidant activity in pepper fruit.

1.1.10 PHYTOCHEMICAL PROPERTIES

Ihemeje *et al.*, (2013) carried out a phytochemical analysis on Pepper fruits and revealed the presence of anti-oxidants such as flavonoids and ascorbic acid in *Denettia tripetala*.

Research using methanol extract of Pepper fruit (*Dennettia tripetala*) leaves showed that *Dennettia tripetala* possesses strong antioxidant potentials in vitro (Odoh *et al.*, 2014).

Further experiment also revealed that the phenol content increases in ripening while the ascorbic and flavonoids contents did not change (Adedayo *et al.*, 2010). These antioxidants prevent and protect from damages caused by free radicals in the body

Also, phytochemical screening of the ethanolic extract revealed the presence of tannis, alkaloids, steriods, flavonoids, cardiac glycosides, saponins and terpenoids (Elekwa *et al.*, 2011).

Tannis-Tannins are group of polymeric phenolic substances capable of tanning leather or 13th precipitating gelatin from solution. It has been suggested that consumption of tannin containing beverages, especially green teas and red wines can cure or prevent a variety of illnesses including heart related diseases (Van-Burden and Robinson,1981).

Alkaloids- are a class of basic, naturally occurring organic compounds that contain at least one nitrogen atom.

Alkaloids have a wide range of pharmacological activities including antimalarial (e.g quinine), antiasthma (e.g.ephedrine), anticancer (e.g. homoharringtonine), cholinomimetic (e.g.

galantamine), vasodilatory (e.g. vincamine), antiarrhythmic (e.g. quinidine), analgesic (e.g. morphine), antibacterial (e.g. chelerythrine).

Flavonoids - Flavonoids are water soluble poly phenolic molecules with antioxidant activity which have many beneficial effects on the cardio vascular system (Evans,1989).

Epidemiological studies have illustrated that heart diseases are inversely related to flavonoid intake (Brown,1996). Flavonoids have also been reported to have vaso-dilatory and inhibitory effects on platelet aggregation thereby preventing coronary heart diseases (Okwu, 2001)

Cardiac glycosides- Cardiac glycosides have been variously used as diuretics and heart tonics due to their beneficial effects on the heart. Cardiac steroids are widely used in the modern treatment of congestive heart failure and for treatment of atrial fibrillation. They increase the force of contraction of the heart and are very useful for heart failure patients. They act by affecting the availability of intracellular Ca^{2+} for myocardial contraction or increasing the sensitivity of myocardial contractile proteins (Walker *et al.*, 2002).

Saponins- Saponins have been reported to have beneficial effects on blood cholesterol levels (Oyewole and Akingbala, 2011). They bind with bile salt and cholesterol in the intestinal tract. This binding causes a reduction of blood cholesterol by preventing its re- absorption.

Terpenoids-Terpenoids are synthesized from acetate units, and as such they share their origins with fatty acids. Terpenoids occur in nearly every natural food and have been associated with protection from and treatment of heart disease due to their antioxidant properties (Wagner and Elmadfa, 2003).

Capsaicin- Pepper fruit's antioxidants and capsaicin also provide neuroprotective benefits, shielding against neurodegenerative diseases like Alzheimer's and Parkinson's (Kim *et al.*, 2017). Capsaicin's ability to reduce inflammation and oxidative stress further supports brain health. These constituents/ phytochemicals provide a scientific basis for the use of DT in traditional medicine, saponins, tannins, and flavonoids, for instance, are also effective against diabetes. They also possess antimicrobial and anti-inflammatory properties (Sparg *et al.*, 2004)

1.1.11 ANTI-INFLAMMATORY EFFECT

Capsaicin's anti-inflammatory properties alleviate pain and reduce inflammation, making pepper fruit an effective natural remedy for conditions like arthritis, fibromyalgia, and psoriasis (Kim *et al.*, 2017). This anti-inflammatory action also helps mitigate symptoms of allergies and asthma.

A study evaluated the analgesic and anti-inflammatory effects of *Dennettia tripetala* essential oil (EO) in rodents. The essential oil showed significant pain-relief effects comparable to morphine and NSAIDs, with its action blocked by naloxone, suggesting both central and peripheral mechanisms. It also demonstrated strong anti-inflammatory activity similar to dexamethasone in a paw oedema model. These findings support the traditional use of *D. tripetala* in managing pain and fever. (Oyemitan *et al.*, 2008)

1.1.12 ANTI-MICROBIAL EFFECT

Studies at Delta State University, Abraka, have revealed that *Dennettia tripetala* (pepperfruit) possesses potent antimicrobial properties. Its essential oil and phenolic acid extract effectively inhibit the growth of harmful microorganisms, including *Staphylococcus aureus*, *Salmonella*, and *E. coli*, which commonly contaminate food. This suggests that pepperfruit could serve as a natural preservative for perishable foods, such as meat, particularly in areas with limited

refrigeration. Additionally, research has shown that the leaves of *Dennettia tripetala* successfully combat *Sclerotium rolfsii*, a fungus causing rot in cocoyam, both in laboratory and real-world settings. Multiple studies confirm the antimicrobial efficacy of *Dennettia tripetala*.

The essential oil of *Dennettia tripetala* exhibited notable antimicrobial activity against a range of microorganisms. The minimum inhibitory concentration (MIC) values revealed strong inhibitory effects, especially against *Klebsiella pneumoniae*, which had an MIC of 3.12%. This indicates that the oil may be effective in treating infections caused by this specific pathogen Moses *et al.*, (2024).

According to Ebanu *et al.*, (2016), the leaves were analyzed for their phytochemical content using both qualitative and quantitative methods with aqueous and ethanolic extracts.

Antimicrobial activity was evaluated using standard microbiological techniques. The study demonstrated that *Dennettia tripetala* and *Lasiandra africana* leaves contain abundant nutrients and phytochemicals, along with acceptable levels of anti-nutrients. Additionally, both plants exhibited significant antimicrobial activity against tested isolates.

Pepperfruit (*Dennettia tripetala*) extracts, including essential oils and phenolic acids, inhibited the growth of food-borne microorganisms such as bacteria and fungi. The essential oil showed greater antimicrobial activity than the phenolic acid. When applied to fresh, boiled, or roasted beef, the extracts significantly reduced or stabilized microbial populations, indicating their potential role in natural food preservation. (Ejechi.,2005)

1.1.13 CARDIOVASCULAR EFFECT

The capsaicin present in pepper fruit has been shown to lower cholesterol levels, reduce triglycerides, and prevent platelet aggregation, ultimately decreasing the risk of heart disease

(Liu *et al.*, 2013). Additionally, pepper fruit's potassium content helps regulate blood pressure, further contributing to cardiovascular health.

1.1.14 RESPIRATORY DISEASE EFFECT

Omigie *et al.*, (2017) investigated the respiratory effects of *Dennettia tripetala* (commonly known as pepper fruit) by measuring its impact on peak expiratory flow rate (PEFR). Their study involved healthy participants who consumed pepper fruit seeds, and their respiratory function was assessed using a calibrated Mini Wright's peak flow meter. The results showed a significant improvement in PEFR after consuming the seeds. This suggests that *Dennettia tripetala* may have a stimulatory effect on respiratory performance, potentially due to its phytochemical composition. The study highlighted the potential of *Dennettia tripetala* to enhance respiratory function, which might be linked to its ability to relax bronchial smooth muscle or influence central respiratory mechanisms.

1.1.15 ANTI-HYPERGLYCEMIC EFFECT

Analysis of pepper fruit extracts revealed the presence of various bioactive compounds, including glycosides, saponins, reducing sugars, fats and oils, alkaloids, carbohydrates, flavonoids, proteins, and tannins. These compounds are known for their potential in modulating glucose metabolism. The administration of *D. tripetala* extracts and fractions significantly reduced fasting blood glucose (FBG) levels in diabetic rats ($p < 0.05$). Acute treatment resulted in a notable decrease in blood glucose within 10 hours, while short-term treatment over 14 days further confirmed the extracts' potent hypoglycemic effects, demonstrating their efficacy in managing diabetes Abonyi *et al.*, (2020).

1.1.16 TOXICITY

A number of studies have been carried out to ascertain the toxicity of DT. Although DT has been reported to contain uvariopsin, an alkaloid which improves bile secretion and attenuates hepatic disorders, a study by Ofem *et al.*, (2014) showed that the ethanolic extract of DT fruits administered at a certain dose reduces bile production in normal healthy rats. The extract also caused an increase in sodium, potassium, and bicarbonate ions in bile and reduced the chloride and unconjugated bilirubin content of bile.

The effect of the ethanolic extract of DT on hematological parameters in normal healthy rats has also been investigated by Ikpi and Nku. Firstly, they carried out an acute toxicity test to determine the LD₅₀ of DT and a moderately high value of 251.19 g/kg·bw was gotten when the ethanolic extract of DT was administered intraperitoneally to normal healthy mice. Subsequently, they administered DT in normal saline orally to normal healthy rats and observed that, at low to moderate dose, DT may be hematotoxic to rats. Interestingly, the observed toxicity seemed to be relieved when the dose of DT administered was increased.

The toxic effects of the ethyl acetate root extract of DT have also been studied. An LD₅₀ value of 1120mg/kg was gotten from the intraperitoneal administration of the extract. Although, the extract exhibited mild toxicity on the liver, kidney, spleen, and blood cells, it was seemingly beneficial to the hearts of mice following prolonged exposure. The plant had significant phytochemical and antioxidant properties of medical interest and possessed toxic properties in rats when administered at a dose above 200 mg/Kg over a prolonged period of time. The administration of methanol leaves extract of *D. tripetala* at a dose over 100 mg/kg body weight for an extended period may induce toxicity to the liver and kidney, which could cause hepatic disease and renal dysfunction.

According to a study by Ugwoke *et al.*, (2014), the LD50 value for the ethanol extract of *Dennettia tripetala* seeds in rats was found to be approximately 500 mg/kg of body weight.

1.2 INTRAOCULAR PRESSURE

Intraocular pressure is defined by Merriam Webster Dictionary as the pressure within the eyeball that gives it a round firm shape and is caused by the aqueous humor and vitreous body. It is a measurement of the fluid pressure inside the eye.

IOP is maintained by the constant production and drainage of fluids. The eye can be thought of as a rigid sphere, where internal pressure is includes influenced by external forces and changes in volume. The aqueous humor, a fluid in the front part of the eye, plays a key role in regulating IOP through its dynamic movement. In contrast, the vitreous body, a gel-like substance in the back of the eye, has a relatively fixed volume and doesn't significantly impact IOP regulation.

Intraocular pressure is measured using a tonometer and intraocular pressure measurement of very important especially in evaluation of glaucoma.

1.2.1 INTRAOCULAR FLUIDS

These are fluids that makes up the eyes ball. They are the aqueous humor and vitreous humor.

These fluids can be divided into two portions:

Aqueous humor: Aqueous humor is a thin fluid present in the anterior chamber. It fills the space between lens and cornea. This space is divided into anterior and posterior chambers by iris. Both the chambers communicate with each other through pupil. The aqueous humor is found in front of the lens and vitreous humor, which lies between the posterior surface of the lens and the retina. Intraocular fluids (the aqueous humor and the vitreous humor), maintains sufficient pressure in

the eye ball to keep its shape. The aqueous humor occupies the anterior chamber- the space between the lens and cornea.

It is an optically clear freely flowing fluid, slightly alkaline and having properties similar to plasma in composition, but containing less protein and glucose and more lactose and ascorbic acid. It supplies nutrients to the avascular cornea and lens and also helps remove waste material from them.

Aqueous humor is continually being formed and reabsorbed. The balance between formation and reabsorption of aqueous humor regulates the total volume and pressure of the intraocular fluid (Guyton and Hall, 2006).

The vitreous humor is a transparent, colorless, gelatinous mass that fills the space in the eye between the lens and the retina (posterior chamber). It is surrounded by a layer of collagen called the vitreous membrane (or hyaloid membrane or vitreous cortex) separating it from the rest of the eye. It makes up four-fifths of the volume of the eyeball.

1.2.2 MAINTENANCE OF NORMAL INTRAOCULAR PRESSURE

Intraocular pressure is maintained through a precise balance between the production and drainage of aqueous humor. This equilibrium is essential for ocular health, and disruptions can lead to various eye pathologies, including glaucoma, uveitis, and retinal detachment. Sudden IOP spikes impose mechanical stress and ischemia on the retinal nerve fiber layer, while sudden drops can lead to the formation of gas microbubbles in the microvasculature, resulting in emboli and subsequent tissue damage. Chronically elevated intraocular pressure is particularly notorious for its role in primary open-angle glaucoma (POAG) and other vision-threatening conditions.

The regulation of intraocular pressure relies heavily on controlling aqueous humor outflow, which occurs primarily through the trabecular meshwork and involves the extracellular matrix in the juxtacanalicular tissue region near Schlemm's canal. Some theories propose that the extracellular matrix functions as a passive filter, adding physical resistance to aqueous humor outflow. Increases in extracellular matrix components like fibronectin and collagen may further restrict this outflow, potentially "clogging" the meshwork. More recent studies, however, suggest that alterations in the extracellular matrix may influence outflow by changing the trabecular meshwork's compliance or the contractile nature of trabecular cells.

An intricate homeostatic system governs intraocular pressure regulation, with the sympathetic nervous system modulating aqueous humor production directly through beta-2 and alpha-2 receptors, which increase and decrease secretion, respectively. Meanwhile, mechanical stress on trabecular meshwork cells from intraocular pressure changes triggers a signal cascade that elevates the activity of matrix metalloproteinases (MMPs), such as MMP14 and MMP2, promoting cell turnover in the TM. This turnover aids in maintaining AH outflow and overall IOP stability.

1.2.3 AQUEOUS PRODUCTION

Aqueous humor is a clear fluid produced by the ciliary epithelium located in the iris, ciliary body, and pars plana within the posterior chamber of the eye's anterior segment. Plasma filters through the capillary walls of the ciliary process, contributing to AH formation through diffusion (5%), ultrafiltration (15%), and active secretion (80%).

The primary secretion process uses an ATP-driven osmotic gradient to generate AH in the posterior chamber, independent of IOP. In contrast, AH production through ultrafiltration is influenced by plasma oncotic pressure, capillary blood pressure, and IOP.

The ciliary process consists of two layers of epithelial cells surrounding a capillary and interstitial tissue core. The innermost layer has nonpigmented ciliary epithelial cells, tightly linked by junctions, while the outer layer has pigmented ciliary epithelial cells joined by gap junctions. Both active secretion and ultrafiltration contribute to AH production. Plasma filtrate passes through capillary fenestrations into the interstitial space (ultrafiltration), with approximately 4% of plasma flow filtered by the capillaries.

The capillary wall serves as a key barrier against plasma proteins, but the tight junctions between nonpigmented ciliary epithelial cells are the main barrier. This structure, with high protein content in the tissue fluid, reduces the transcapillary oncotic pressure difference and increases oncotic pressure in the tissue fluid. Hydrostatic and oncotic pressure gradients across the ciliary epithelium move water into the processes from the posterior chamber, with secretion needed for fluid passage into the posterior chamber under normal conditions.

Only active transport across the ciliary epithelial layers allows fluid entry into the posterior chamber. AH production is about 2.5 $\mu\text{l}/\text{min}$, totaling approximately 3.5 ml daily, with production peaking around noon and dropping to its lowest during sleep.

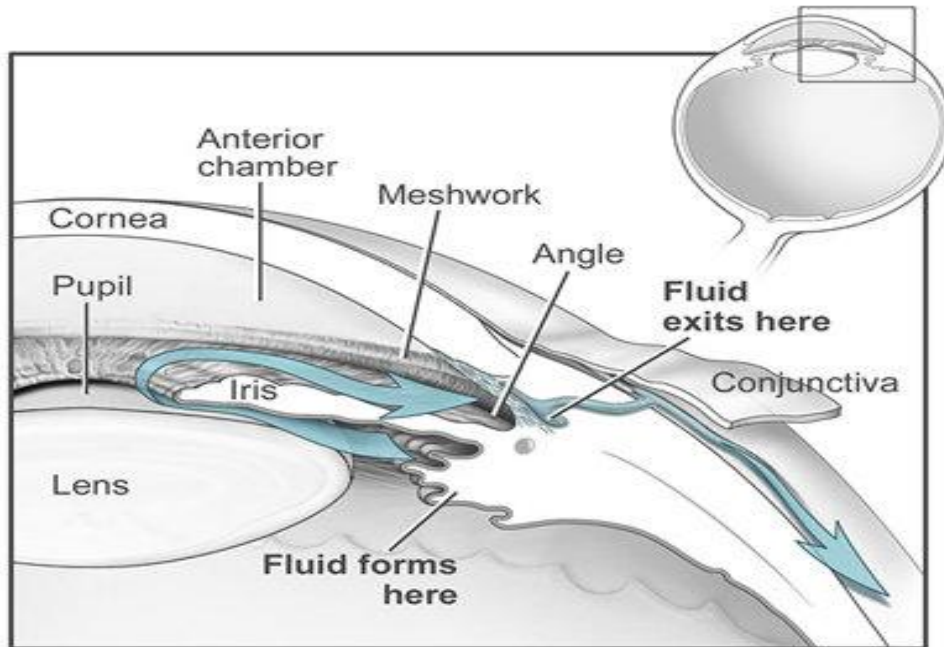


Figure 1.1: Diagram of the ciliary body showing ciliary processes. (Adapted from Guyton and Hall, 2006)

1.2.4 DRAINAGE OF AQUEOUS HUMOR

Aqueous humor flows from the posterior chamber through the pupil into the anterior chamber, where it exits the eye through three main pathways:

Trabecular Outflow (90%): The aqueous humor passes through the trabecular meshwork into the Schlemm canal, then drains into the episcleral veins. This pathway is pressure-sensitive, meaning that as intraocular pressure (IOP) increases, so does outflow.

Uveoscleral Drainage (10%): Here, the aqueous humor moves across the surface of the ciliary body into the suprachoroidal space, where it drains through venous circulation within the ciliary body, choroid, and sclera.

Iris Route: A small amount of aqueous humor also drains through the iris.

Trabecular Meshwork

The trabecular meshwork, located at the angle of the anterior chamber, acts as a filter for aqueous humor, with around 90% of it leaving the eye through this route. The inter-trabecular spaces within this meshwork are smaller than those of the uveal meshwork, creating more resistance to flow. The trabecular meshwork consists of three main parts:

Uveal Meshwork

The innermost layer, composed of cord-like strands covered in endothelial cells, which originate from the iris and ciliary body stroma. This layer has relatively large spaces that provide low resistance to aqueous flow.

Corneoscleral Meshwork

Located outside the uveal meshwork, this is the thickest part of the trabeculum, comprising layers of connective tissue strands with an endothelial-like cell covering.

Juxtacanalicular (Cribriform) Meshwork

The outermost part of the trabecular meshwork, connecting the corneoscleral meshwork to the Schlemm canal's inner wall. This section, made up of cells in a dense extracellular matrix with narrow spaces, provides the primary resistance to aqueous outflow under normal conditions.

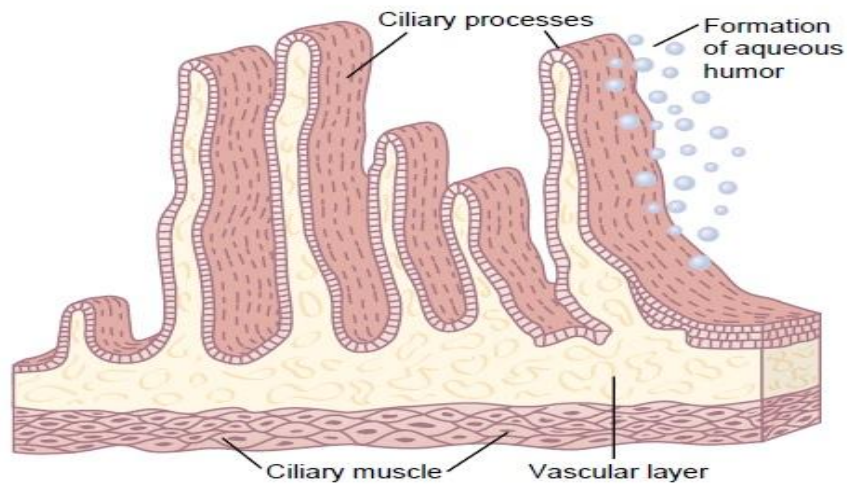


Figure 49–20

Anatomy of the ciliary processes. Aqueous humor is formed on surfaces.

Figure 1.2; showing the drainage system

Source: Researchgate.net

1.2.5 FACTORS AFFECTING INTRAOCULAR PRESSURE

Several factors can influence intraocular pressure (IOP), which is the fluid pressure within the eye. Key ones include;

Aqueous Humor Production and Outflow: The balance between the production and drainage of aqueous humor directly affects IOP. If the fluid builds up due to reduced drainage or increased production, it raises IOP.

Genetics: Studies have identified multiple genetic variants associated with increased IOP and glaucoma risk. These variants affect the functioning of the trabecular meshwork, the eye's drainage system, and the optic nerve. Genetic mutations can alter the production and drainage of aqueous humor leading to elevated IOP. Specific genetic factors are family history, genetic

utations, Ethnicity, genetic syndromes (example Axenfeld-Rieger syndrome and pigment dispersion syndrome) increase glaucoma risk. Genetic factors can: Increase IOP, Reduce IOP regulate and Influence response to treatment

Age: IOP generally increases with age as drainage channels in the eye become less efficient. The trabecular meshwork, responsible for fluid drainage, becomes less effective, causing fluid buildup and increased IOP. Additionally, the lens thickens with age, further obstructing fluid flow. The vitreous humor, the gel-like substance between the lens and retina, also undergoes changes that affect IOP.

Medical Conditions: Diabetes and hypertension are associated with higher IOP. Systemic diseases like thyroid dysfunction can also influence IOP.

Medications: Corticosteroids, often used to treat inflammation, can raise IOP when used over extended periods. Some medications for respiratory or bladder issues can also affect IOP.

Physical Activity and Body Position: Intense physical activities, head-down positions (e.g., yoga poses), or lying flat can temporarily increase IOP.

Time of Day: IOP fluctuates over the day, generally peaking in the morning and reducing by evening. Intraocular pressure varies throughout the night and day. The diurnal variation for normal eyes is between 3 and 6 mmHg and the variation may increase in glaucomatous eyes. During the night, intraocular pressure may not decrease despite the slower production of aqueous humor. Glaucoma patients' 24-hour IOP profiles may differ from those of healthy individuals.

Fitness and exercise: There is some inconclusive research that indicates that exercise could possibly affect IOP (some positively and some negatively). Moderate-intensity exercise, such as walking or jogging, temporarily lowers IOP for up to two hours. This decrease is attributed to:

Increased aqueous outflow, exercise stimulates the trabecular meshwork, improving fluid drainage and reduced blood pressure, which helps to lower systemic blood pressure, which decreases IOP.

Hydration and Diet: Caffeine intake can cause short-term increases in IOP. Excessive water intake over a short period can temporarily increase IOP. Dehydration can significantly increase IOP, while adequate hydration helps maintain healthy pressure. When the body is dehydrated intraocular pressure reduces while good hydration promotes IOP regulation. A well-balanced diet rich in essential nutrients can help manage IOP.

Environmental Factors: High altitudes and low temperatures can sometimes affect IOP, although these influences are generally minor but it has been found to be significant.

Hormonal Changes: Hormonal fluctuations (like during menstruation, pregnancy, or menopause) can influence IOP in some individuals.

1.2.6 MEASUREMENTS OF INTRAOCULAR PRESSURE

Goldmann Applanation Tonometer (GAT)

Introduced by Hans Goldmann in 1948, the Goldmann Applanation Tonometer remains the standard method for measuring intraocular pressure and is widely used in routine ophthalmic practice. This method involves applanation, which calculates the force necessary to flatten the cornea over a specified area. Based on the Imbert-Fick law, it approximates intraocular pressure by dividing the force applied by the flattened surface area. Higher IOP requires more force to applanate the cornea. Goldman applanation tonometry is typically used with a slit-lamp during eye exams. The procedure involves applying anesthetic drops and fluorescein dye, followed by using a cobalt blue-filtered light to observe the corneal tear film under the tonometer tip. The

clinician adjusts the instrument until two green semicircles align, indicating accurate flattening of the cornea. The IOP is then read from the device's calibrated dial.

While GAT is highly reliable, its accuracy can be affected by factors like central corneal thickness, corneal rigidity, astigmatism, and previous surgeries. Limitations include the need for skilled operation, use of topical anesthesia, and difficulties measuring irregular or scarred corneas. Additionally, it cannot be used in supine patients or those unable to cooperate.

Perkins and Draeger Applanation Tonometer

Perkins and Draeger handheld tonometers work similarly to GAT but are portable and suitable for settings without slit lamps, such as emergency rooms or operating theaters. These devices can measure IOP in both upright and supine positions. Although convenient, their portability can reduce stability, and they share limitations similar to GAT, including operator skill dependency and reduced precision on irregular corneas.

Non-contact Tonometer (NCT)

Developed in the 1970s, non-contact tonometer—commonly called "air-puff" tonometer—use a puff of air to applanate the cornea, with the returning air measured by sensors to determine IOP. They do not require topical anesthesia and are useful for screenings, especially in children or adults intolerant of contact methods. However, NCT is less accurate and more influenced by factors like CCT, making it unsuitable for glaucoma management.

Ocular-Response Analyzer (ORA) and Corvis ST Tonometer

The Ocular-Response Analyzer (ORA), introduced in 2005, is a non-contact device that measures corneal biomechanical properties, including corneal hysteresis, along with IOP. This

offers an advantage over GAT by accounting for variability in corneal structure. However, ORA tends to overestimate IOP at higher pressures, and its role in glaucoma management requires further study. The Corvis ST, launched in 2011, combines non-contact tonometry with a Scheimpflug camera to analyze corneal deformation during air indentation. While it is less influenced by corneal factors and provides precise readings, it often underestimates IOP compared to GAT.

Indentation Tonometry

Schiotz Tonometer

Developed in 1905, the Schiotz Tonometer uses a weighted plunger to indent the cornea, with IOP derived from a conversion chart. Though cost-effective and portable, it is prone to errors due to corneal rigidity, instrument variability, and positioning. It is rarely used today, except in certain pediatric or low-resource settings.

Tono-Pen

The Tono-Pen is a handheld device combining applanation and indentation principles to measure IOP. It averages multiple readings and can measure on irregular corneas or through contact lenses. While portable and versatile, its accuracy is affected by CCT, and it requires frequent calibration.

Pneumatonometer

The pneumatonometer uses a stream of air to indent the cornea and is equipped with a built-in transducer to convert force to IOP. It correlates well with GAT in normal IOP ranges but tends to overestimate pressure, limiting its clinical utility.

Rebound Tonometry

iCare Tonometer

The iCare tonometer is a portable device that measures IOP using a probe that bounces off the cornea, requiring no anesthesia. It is particularly useful in children, non-cooperative patients, and those allergic to fluorescein. While convenient and reliable for routine checks, elevated IOP readings should be confirmed with GAT.

Dynamic Contour Tonometry (DCT)

The DCT, introduced in 2003, calculates IOP using a contour-matched sensor that measures corneal pulsations. It provides readings independent of corneal thickness but is challenging to use in routine settings due to its learning curve and dependence on specialized equipment.

Continuous IOP Monitoring

Continuous IOP monitoring provides valuable insights into pressure fluctuations over 24 hours.

The Sensimed Triggerfish contact lens system offers real-time data collection but has limitations in accuracy and correlation with Goldman applanation tonometer. Implantable IOP sensors are another option but remain experimental and not yet widely available.

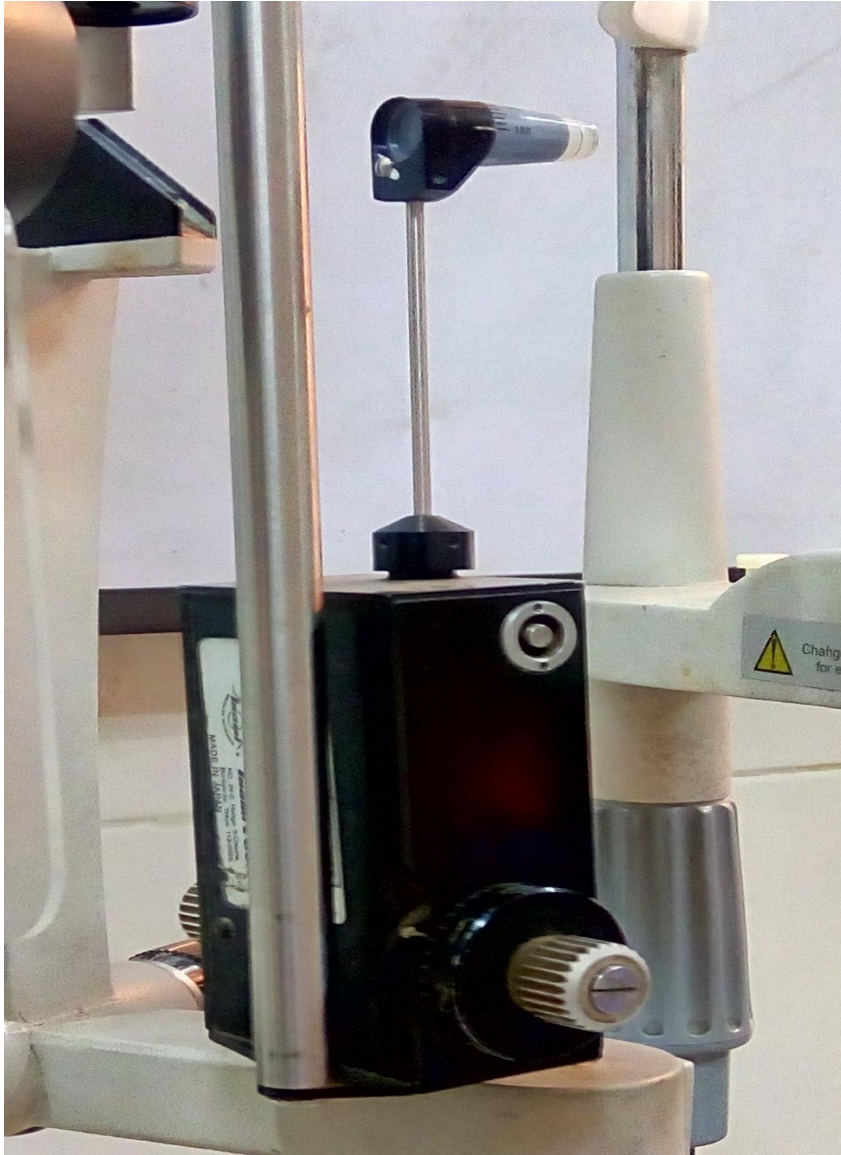


Figure 1.3; Goldmann Applanation Tonometer attached with Slit lamp biomicroscope

1.3 BLOOD PRESSURE

Blood pressure (BP) is the force exerted by circulating blood on the walls of blood vessels, the force makes a noise called Korotkoff sounds (Connie, 2006) as the heart pumps it throughout the body. It is a critical physiological parameter that reflects the efficiency of the cardiovascular system and is measured in millimeters of mercury (mmHg) using two values:

Systolic Blood Pressure: The higher value, recorded when the heart contracts (systole) and ejects blood into the arteries.

Diastolic Blood Pressure: The lower value, measured when the heart relaxes (diastole) and fills with blood. For example, a blood pressure reading of 120/80 mmHg means the systolic pressure is 120 mmHg, and the diastolic pressure is 80 mmHg.

1.3.1 PHYSIOLOGY OF BLOOD PRESSURE

During each heartbeat, blood pressure varies between a maximum systolic and a minimum diastolic pressure. The blood pressure in the circulation is principally due to the pumping action of the heart. However, blood pressure is also regulated by neural regulation from the brain, as well as osmotic regulation from the kidney. Differences in mean blood pressure drive the flow of blood around the circulation. The rate of mean blood flow depends on both blood pressure and the resistance to flow presented by the blood vessels. In the absence of hydrostatic effects (e.g. standing), mean blood pressure decreases as the circulating blood moves away from the heart through arteries and capillaries due to viscous losses of energy. Mean blood pressure drops over the whole circulation, although most of the fall occurs along the small arteries and arterioles. Pulsatility also diminishes in the smaller elements of the arterial circulation, although some transmitted pulsatility is observed in capillaries.

Gravity affects blood pressure via hydrostatic forces (e.g., during standing), and valves in veins, breathing, and pumping from contraction of skeletal muscles also influence blood pressure, particularly in veins. Blood pressure physiology relies on the complex interaction of five key factors: Cardiac output (the heart's pumping efficiency), peripheral resistance (blood vessel constriction or dilation), blood volume (total blood amount), vascular compliance (blood vessel

flexibility), regulatory mechanisms (nervous and hormonal controls). These factors constantly adjust to maintain optimal blood pressure, ensuring proper blood flow and oxygen delivery to organs and tissues. Imbalances can lead to hypertension (high blood pressure) or hypotension (low blood pressure), making understanding these processes vital for diagnosis and management.

1.3.2 MEASUREMENT OF BLOOD PRESSURE

The measurement of blood pressure using a mercury sphygmomanometer and stethoscope has been a longstanding practice in clinical settings, recognized for its accuracy and reliability. This method involves the use of a cuff that inflates to occlude blood flow, while a stethoscope is employed to detect the sounds of blood flow as pressure is released. The following sections detail the components and methodology involved in this traditional approach.

Components of the Sphygmomanometer

Cuff: A bag-shaped structure that wraps around the upper arm, designed to apply pressure to the artery (Iwata et al., 2019).

Pressure Measurement: The mercury column in the sphygmomanometer provides a direct measurement of pressure in millimeters of mercury (mm Hg), a standard unit in blood pressure assessment (McKay, 2008).

Stethoscope: Used to listen for Korotkoff sounds, which indicate systolic and diastolic pressures as the cuff deflates (McKay, 2008).

Measurement Methodology

Inflation and Deflation: The cuff is inflated until blood flow is completely occluded. As the cuff deflates, the first sound heard through the stethoscope indicates systolic pressure, while the last sound indicates diastolic pressure (Tetsuri et al., 2017).

Accuracy: This method is considered the "gold standard" due to its high level of measurement accuracy, although it requires proper technique and training (McKay, 2008).

While the mercury sphygmomanometer has been the traditional method for blood pressure measurement, there is a growing trend towards automated devices that may offer convenience and ease of use, albeit with varying degrees of accuracy compared to the classic method (Tetsuri et al., 2017).



Figure 1.4; Mercury sphygmomanometer and stethoscope

Source; Researchgate

1.3.3 RELATIONSHIP BETWEEN INTRAOCULAR PRESSURE AND BLOOD PRESSURE

Intraocular pressure (IOP) and blood pressure (BP) are two vital physiological parameters that are intricately linked. While IOP refers to the pressure exerted by the fluids in the eye, BP is the pressure exerted by blood on blood vessel walls. The positive correlation between IOP and BP is well-established. Studies have consistently shown that elevated BP can lead to increased IOP, while decreased BP can result in lower IOP (National Eye Institute, 2020). This relationship is attributed to the shared regulatory mechanisms that govern both IOP and BP. The autonomic nervous system, which regulates various bodily functions, including heart rate and blood vessel diameter, plays a crucial role in modulating both IOP and BP. Another key mechanism underlying the relationship between IOP and BP is vascular resistance. Changes in vascular

resistance can affect both BP and IOP. When vascular resistance increases, BP rises, leading to increased blood flow to the eye and elevated IOP. Conversely, decreased vascular resistance leads to lower BP and reduced IOP.

The dynamics of aqueous humor production and drainage also contribute to the relationship between IOP and BP. Aqueous humor, the clear fluid produced in the eye, helps maintain IOP. Changes in BP can influence aqueous humor dynamics, leading to fluctuations in IOP. The interplay between IOP and BP is central to understanding ocular health and disease. Ocular perfusion pressure, which reflects the balance between these two pressures, is a critical determinant of BF to ocular tissues. High IOP can reduce OPP and compromise BF, while low BP can have a similar effect, even in the absence of elevated IOP. This relationship underscores the importance of maintaining an optimal balance between BP and IOP to preserve ocular perfusion and prevent conditions like glaucoma. The autoregulatory capacity of ocular tissues to stabilize BF despite these fluctuations is essential, but when this mechanism fails, it may lead to optic nerve damage and the progression of glaucoma (Liang et al 2009).

1.3.4 HOW AGE AFFECTS IOP AND BP

Several population-based studies have examined the relationship between age, blood pressure (BP), and intraocular pressure (IOP). However, these studies have not consistently demonstrated a significant correlation among these variables. Age has been shown to influence both intraocular pressure (IOP) and blood pressure (BP) through various mechanisms. Research indicates that IOP tends to increase with advancing age, likely due to structural and functional changes in the eye, such as reduced aqueous humor outflow facility caused by trabecular meshwork degeneration. Similarly, BP tends to rise with age due to factors such as arterial stiffening and

increased vascular resistance, which are common age-related changes in the cardiovascular system (Queresha, 1995).

Furthermore, age-related increases in IOP and BP may be interconnected. Elevated BP can increase episcleral venous pressure, which could subsequently affect aqueous humor drainage and contribute to higher IOP. Queresha (1995) reported that in healthy individuals, both IOP and BP showed significant increases with age, suggesting that physiological aging alone, without underlying disease, may be sufficient to drive these changes. Additionally, there is evidence of a correlation between seasonal changes, IOP, and BP, with slightly higher values observed during winter months. It is hypothesized that variations in diurnal light exposure, atmospheric temperature, and pressure may influence these seasonal changes. Furthermore, factors such as changes in diet and body weight may also contribute to fluctuations in IOP and BP.

1.3.5 REGULATION OF INTRAOCULAR PRESSURE

The intraocular pressure (IOP) of the human eye remains relatively constant throughout life, even though aqueous humor is continuously produced and drained. However, the exact mechanism regulating IOP is not fully understood. It is believed that the outflow of aqueous humor from the anterior chamber into the canal of Schlemm plays a key role in maintaining this balance. The entrance to the canal is guarded by trabecular structures made up of lamellar plates stacked on top of one another. These plates are perforated with small openings, and their alignment affects fluid flow. When IOP increases above normal levels, the plates are thought to separate slightly, enlarging the perforations and allowing for rapid fluid outflow into the canal of Schlemm. This increased drainage reduces IOP back to normal. Conversely, when IOP is below normal, the plates compress against each other, restricting fluid loss until the pressure rises its normal range.

Additionally, nervous system regulation influences IOP by altering the resistance to fluid outflow and the rate of aqueous humor production. The ciliary epithelium's secretory activity, as well as the rate of blood flow to the eye, which affects aqueous humor secretion, are also controlled by the nervous system.

1.3.5 REGULATION OF BLOOD PRESSURE

The following mechanisms are responsible for arterial blood pressure

1. Baroreceptor Reflex (Klabunde, 2007):

The baroreceptor reflex is a rapid, short-term mechanism that regulates arterial blood pressure by adjusting the activity of the autonomic nervous system. Baroreceptors, located in the walls of the carotid sinuses and aortic arch, sense changes in blood pressure by detecting the stretch of arterial walls. When blood pressure rises, baroreceptors increase their firing rate, signaling the brainstem to reduce sympathetic nervous system activity and increase parasympathetic output. This leads to vasodilation, reduced heart rate, and decreased cardiac output, lowering blood pressure. Conversely, when blood pressure drops, baroreceptors reduce their firing rate, prompting increased sympathetic activity, vasoconstriction, and a rise in heart rate and cardiac output, thereby restoring blood pressure to normal levels.

2. Renin-Angiotensin System (RAS):

The renin-angiotensin system is a hormonal mechanism that regulates blood pressure and fluid balance over the long term. When blood pressure drops, the kidneys release the enzyme renin, which converts angiotensinogen (produced by the liver) into angiotensin I. Angiotensin I is then converted into angiotensin II by the angiotensin-converting enzyme (ACE) in the lungs.

Angiotensin II acts as a potent vasoconstrictor, increasing systemic vascular resistance and

raising blood pressure. It also stimulates the release of aldosterone from the adrenal glands and promotes sodium and water retention by the kidneys, further contributing to blood pressure regulation.

3. Aldosterone Release:

Aldosterone, a hormone produced by the adrenal cortex, plays a critical role in maintaining blood pressure by regulating sodium and water balance. Its release is stimulated by angiotensin II or elevated potassium levels. Aldosterone promotes sodium reabsorption and potassium excretion in the distal tubules and collecting ducts of the kidneys. By retaining sodium, water is also conserved, increasing blood volume and, consequently, arterial blood pressure. This mechanism works synergistically with the renin-angiotensin system to maintain long-term blood pressure stability.

1.4 STATEMENT OF PROBLEM

Glaucoma and hypertension are prevalent health issues that significantly contribute to global morbidity and mortality rates. Elevated intraocular pressure (IOP) is a primary risk factor for glaucoma, a leading cause of irreversible blindness worldwide. Similarly, hypertension, or high blood pressure, is a major risk factor for cardiovascular diseases, which are among the leading causes of death globally. *Dennettia tripetala* has been reported to possess hypotensive properties, yet the effect of graded doses of DT on IOP and blood pressure in humans remain underexplored. Therefore, there is a need to investigate whether extracts from *Dennettia tripetala* has a dose dependent effect on IOP and BP of humans.

1.5 AIMS AND OBJECTIVES

AIM

To investigate the effect of graded doses of the aqueous extract of *Dennettia tripetala* on intraocular pressure and blood pressure in normotensive subjects

OBJECTIVES

To determine if orally administered graded doses of aqueous extract of *Dennettia tripetala* fruit has a significant effect on intraocular pressure and blood pressure.

To determine if the effect of orally administered graded doses *Dennettia tripetala* on IOP and BP is dose dependent.

1.6 HYPOTHESIS

Null Hypothesis

Ho1: The graded doses extract of *Dennettia tripetala* has no effect on intraocular pressure and blood pressure of normotensive adults.

Alternate hypothesis

Ha1; The graded doses extract of *Dennettia tripetala* has an effect on intraocular pressure and blood pressure of normotensive subjects

1.7 SIGNIFICANCE OF STUDY

1) Results obtained from this study will add to existing literatures on the physiological effects of *Dennettia tripetala* and further enlighten eye care providers on possible effects of the plant on IOP and BP

2) A positive result from the study will provide a less expensive way to treat glaucoma, regulate intraocular pressure and blood pressure.

3) Highlighting the benefits of *Dennettia tripetala* can educate the public about safe and effective natural health remedies, as adjunct treatment for control of IOP and BP

1.8 DEFINITION OF TERMS

1. Normotensive; This refers to having a normal blood pressure. It is typically used to describe individuals whose blood pressure falls within the range considered healthy, usually around 120/80 mmHg according to standard medical guidelines.

2. Pepper fruit; *Dennettia tripetala* is a tropical plant belonging to the family Annonaceae, native to West Africa. It is commonly used for its culinary, medicinal, and cultural significance.

3. Pepper fruit extract; It is liquid gotten from the pepper fruit after an extraction process has been carried out.

4. Intraocular pressure; Intraocular pressure refers to the fluid pressure inside the eye, which is essential for maintaining the shape of the eye and ensuring its proper functioning. It is primarily determined by the balance between the production and drainage of aqueous humor, the clear fluid in the eye.

5. Blood pressure; This is the force exerted by circulating blood against the walls of the blood vessels, particularly the arteries. It is a vital sign and an important indicator of cardiovascular health. Blood pressure is measured in millimeters of mercury (mmHg)

6. Tonometry; This is a routine diagnostic procedure conducted in an optometry clinic to measure the intraocular pressure which is the pressure of the fluid inside the eye.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 BLOOD PRESSURE AND IOP

Due to the positive correlation between IOP and systemic blood pressure, it has been suggested that BP/IOP ratio is a better diagnostic criterion for glaucoma than IOP alone. An elevated IOP will cause a visual field loss only if the systemic blood pressure is high that the BP/IOP ratio is beyond a certain critical value

The study of Bulpitt *et al.*, (1986) showed that the higher the BP, the greater the IO, the greater the IOP was not related to sex, age, height or haemoglobin. They also formed the systemic pressure was more closely correlated with IOP than either the pulse pressure (systolic BP Diastolic BP) or mean BP. It has also been found that a 100mmHg rise in systolic BP resulted to a 2mmHg rise in IOP. This is not clinically significant but indicates a functional relationship between systolic BP and IOP.

2.2 EFFECT ON HEMATOLOGICAL PARAMETERS

Ikpi and Nku (2008) examined the effects of the ethanolic extract of *Dennettia tripetala* on the blood parameters of Wistar rats. Their study determined the median lethal dose (LD50) to be 251.19 g/kg·bw when administered intraperitoneally to mice. When given orally in normal saline to healthy rats, low to moderate doses were found to have hematotoxic effects. However, at higher doses, the toxicity appeared to decrease.

Salawu *et al.*, (2019) conducted a toxicity study on the aqueous menthol extract of *Dennettia tripetala* fruits in male albino rats. Twenty rats were divided into four groups: a control group receiving distilled water and three experimental groups receiving 100 mg/kg, 200 mg/kg, and 400 mg/kg of the extract over 14 days. The LD50 was established at 1265 mg/kg·bw, with doses of 1000 mg/kg·bw and above leading to toxicity and mortality. A dose-dependent reduction in body weight was observed in the experimental groups. Liver function was mostly unaffected, except for the 400 mg/kg group, which showed elevated bilirubin levels. Kidney function remained stable across groups, except for the highest dose, which resulted in increased creatinine, sodium, and potassium levels. Additionally, oxidative stress markers, including superoxide dismutase (SOD), glutathione-S-transferase (GST), glutathione peroxidase (GPx), and glutathione, were significantly reduced in the 200 mg/kg and 400 mg/kg groups, while the 100 mg/kg group showed no significant changes.

2.3 EFFECT ON INTRAOCULAR PRESSURE

Timothy and Okere (2008) conducted a preliminary study to examine the impact of *Dennettia tripetala* seed consumption on intraocular pressure (IOP). The study involved 40 healthy young volunteers with baseline IOPs ranging from 12–21 mmHg. Baseline IOP values were measured prior to ingestion of the seeds. Each subject was given 0.75 g of *Dennettia tripetala* seeds to ingest, and their IOP was measured at 30, 60, 90, and 120 minutes post-ingestion. The results

showed that 0.75 g of *Dennettia tripetala* seeds significantly reduced the mean IOP from 15.6 mmHg to 11.20 mmHg after 60 minutes. However, the IOP gradually returned toward baseline levels by 120 minutes post-ingestion.

Plant-derived treatments are gaining global attention for managing diseases, including glaucoma. Uzoamaka et al. (2023) investigated the effects of *Dennettia tripetala* aqueous seed extract (ASEDt) on intraocular pressure (IOP) and lipid profile in Wistar rats. The study, conducted at Abia State University, Nigeria, used 37 male albino rats, with 25 divided into five groups receiving different treatments, including cholesterol and varying doses of ASEDt. Results showed that 200mg/kg and 500mg/kg ASEDt significantly reduced IOP, with a greater effect at 500mg. Both doses also lowered total cholesterol (TC), triglycerides (TG), and LDL while increasing HDL. These findings suggest ASEDt may have potential benefits for ocular, cardiovascular, and public health management.

2.4 ANTI-GLAUCOMA EFFECT

A study by Chigozie *et al.*, (2023) investigated the effect of *Dennettia tripetala* seed extract on intraocular pressure (IOP) in 15 healthy male albino Wistar rats. The rats were divided into three groups (A, B, and C), each with five rats. Group A received a drop of ripe seed extract in one eye and Timolol in the other, while Group B received unripe seed extract in one eye and Timolol in the other. Group C served as the control, receiving only water. IOP was measured at 30-minute intervals for 120 minutes. Results showed that the ripe seed extract caused a significant peak reduction in IOP (31.2%) at 60 minutes, though the effect diminished toward baseline. The unripe extract led to a gradual and sustained decrease in IOP (17.9% at 120 minutes). Timolol showed the most consistent and highest IOP reduction, reaching 33.3% at 120 minutes. The

study suggests that the aqueous extract of ripe *D. tripetala* seeds may have potential anti-glaucoma effects.

According to Head and Kathleen (2001), flavonoids assist with collagen stabilization and synergize the effect of vitamin C. The effect of flavonoid in IOP reduction is thought to be as a result of the reduction in excessive permeability of blood aqueous membrane within the eye. The presence of lipoic acid (fatty acid) has been shown to increase glutathione in red blood cells and lacrimal fluid of glaucomatous patients thereby reducing the intraocular pressure.

2.5 EFFECT ON METABOLIC HEALTH

Yetunde *et al.*, (2020) investigated the effects of *Dennettia tripetala* supplementation on biochemical parameters in rats. Twenty-five rats were divided into five groups, with one serving as the control and the others receiving *Dennettia tripetala* fruits for 28 days. Blood analysis revealed a significant decrease ($p < 0.05$) in triglycerides and glucose, while total protein, catalase, and HDL levels increased significantly. No significant changes were observed in superoxide dismutase, albumin, cholesterol, or LDL levels. The study suggests that *Dennettia tripetala* has hypoglycemic, antioxidant, and hypolipidemic properties, potentially aiding in the prevention and management of conditions like coronary heart disease, diabetes, cancer, hypertension, and digestive disorders.

2.6 EFFECT ON HYPERTHYROIDISM

Ejere *et al.*, (2019) investigated the effects of *Dennettia tripetala* leaf extract on hyperthyroidism in *Rattus norvegicus*. Conducted at the University of Nigeria, Nsukka, the study spanned seven weeks and involved 72 male albino rats divided into six groups (A–F). Hyperthyroidism was induced in groups B–F using 600 $\mu\text{g}/\text{kg}$ Levothyroxine for 14 days. Group A (normal control)

and group B (hyperthyroid control) received only food and water, while group C was treated with Carbimazole. Groups D–F received the extract at doses of 100 mg/kg, 250 mg/kg, and 500 mg/kg. The study assessed cholesterol, triglycerides, lipoproteins, thyroid hormones, and thyroid histology. Phytochemical screening confirmed the presence of secondary metabolites, and toxicity tests showed no lethal effects even at 5000 mg/kg. By Day 7, the extract significantly influenced body weight, increasing cholesterol, LDL, triglycerides, and TSH while reducing HDL, T3, and T4. Histological analysis revealed no major thyroid changes. These findings suggest that *Dennettia tripetala* extract may help mitigate hyperthyroidism effects.

2.7 NUTRIENT CONTENT

Akpakpan *et al.*, (2019) analyzed the phytochemical and nutritional composition of unripe and ripe *Dennettia tripetala* fruits. The study, conducted at the University of Port Harcourt, assessed phytochemicals, proximate composition, minerals, and vitamins. Unripe DT fruits had significantly higher levels of terpenes, phytosterols, steroids, oxalates, saponins, alkaloids, and phytates, while ripe fruits contained more tannins, phenols, flavonoids, coumarins, and glycosides. Ripe fruits had higher ash and lipid content, whereas unripe fruits had more carbohydrates and crude fiber. Potassium was higher in ripe fruits, while zinc was higher in unripe fruits. Vitamin A, B1, B2, B3, B5, B7, B9, B12, and C were higher in ripe fruits, whereas unripe fruits had more vitamin B6 and K. The study concludes that both unripe and ripe DT fruits are rich in nutrients and phytochemicals, making them valuable dietary supplements.

The study carried out by Egharevba and Idah (2015), showed that the leaf has a similar phytochemical profile to the fruit except that the leaf lacks balsams (resin) and steroids. The seeds of *D. tripetala* showed the presence of Alkaloids, tannins, saponins, flavonoids, terpenoids,

steroids and cardiac glycosides. These bioactive compounds are the basis for therapeutic potentials of medicinal plants.

2.8 BIOCHEMICAL PROPERTIES

This study explores the therapeutic potential of *Dennettia tripetala* fruit, commonly used in African traditional medicine. The research examined its bioactive components, antimicrobial effects, and antioxidant properties using *in vitro* and *in vivo* models. Phytochemical screening revealed the presence of key compounds like flavonoids, tannins, and terpenoids. Antioxidant activity was assessed using DPPH and ABTS radical scavenging assays, showing notable free radical inhibition. Antibacterial tests demonstrated effectiveness against multidrug-resistant bacteria. Additionally, in a rat model, the extract provided liver protection by enhancing antioxidant enzyme activity and reducing oxidative stress. These findings suggest *Dennettia tripetala* as a potential natural remedy for microbial infections, oxidative stress, and liver damage.

Umoh *et al.*, (2024) investigated the chemical composition and antioxidant properties of the methanol extract from the stem bark of *Dennettia tripetala*. The stem bark was air-dried and extracted using 70% methanol. Quantitative phytochemical analysis revealed the presence of tannins, phenolics, alkaloids, flavonoids, saponins, and terpenoids, identified through *in vitro* methods and GC-MS. Antioxidant potential was assessed using FRAP, DPPH, and NO scavenging assays, along with total phenolic content evaluation. GC-MS detected bioactive compounds like phenol, eugenol, caryophyllene, and naphthalene. The extract demonstrated strong antioxidant activity, attributed to its high phenolic and flavonoid content. These findings support the traditional use of *D. tripetala* stem bark in managing oxidative stress-related conditions.

2.9 EFFECT ON BLOOD PRESSURE

Antioxidant Properties: The antioxidant activity of these compounds helps mitigate oxidative stress, which is linked to hypertension (Liu *et al.*, 2022)

Alkaloids: Known for their role in reducing oxidative stress and inflammation, alkaloids can also influence the renin-angiotensin-aldosterone system (RAAS), a key regulator of blood pressure (Sultana & Asif, 2017).

Flavonoids: These compounds are recognized for their vasodilatory effects, which can help lower blood pressure by relaxing blood vessels (Islam *et al.*, 2023).

Terpenoids and Saponins: These phytochemicals have been associated with vasodilatory effects, potentially aiding in the relaxation of blood vessels and lowering blood pressure (Muhammed *et al.*, 2021)

Edet *et al.*, (2002). identified phenanthrene alkaloids, specifically uvariopsine, stephenanthrine, and argentinine, along with the chromone dennettine, as bioactive compounds in *Dennettia tripetala*, which may contribute to its potential antihypertensive effects due to their pharmacological relevance

2.10 EFFECT ON LIVER AND KIDNEY FUNCTION

Akpakan *et al.*, (2017) investigated the effects of the ethanol extract of ripe *Dennettia tripetala* (Pepper Fruit) on liver and kidney function in male albino Wistar rats. The study involved 20 rats, each weighing between 160-210 g, divided into four groups of five animals. Group 4 served as the control, while Groups 1, 2, and 3 received oral doses of the ethanol extract at 262.20 mg/kg,

524.40 mg/kg, and 786.61 mg/kg daily for 30 days. The results indicated that the ethanol extract of *Dennettia tripetala* did not exhibit toxicity to the liver or kidneys.

A study by Omaye *et al.*, (2021) investigated the protective effects of *Dennettia tripetala* against liver and kidney damage caused by repeated exposure to carbon tetrachloride (CCl₄). Rats were given *Dennettia tripetala* extracts daily for 21 days, with CCl₄ administered from days 18 to 21.

This setup allowed researchers to assess the extract's protective properties over time.

Biochemical and histopathological analyses revealed that CCl₄ exposure led to increased liver enzyme activity, altered protein levels, lipid imbalances, and kidney dysfunction. Antioxidant enzyme activity declined, while oxidative stress markers rose. However, *D. tripetala* significantly reduced these adverse effects, preserving liver and kidney function. The study concluded that *D. tripetala* offers strong protection against chemical-induced organ damage, suggesting its potential as a therapeutic agent.

2.11 CONTRAINDICATION

In a study carried out by Imo *et al.*, (2023) the result showed that if the number of days of consumption of fruit extract of *Dennettia tripetala* is increased up to nine days, it may cause a significant increase in blood sugar level of the consumers. This means that individuals who have high blood pressure related challenge may be required not to consume fruit of *Dennettia tripetala* for a longer period. The effect of the seed extracts also caused an elevation of the blood sugar level of the test animals, but the increase is not statistically significant ($p > 0.05$).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 STUDY LOCATION

This study will be carried out in University of Benin Optometry Clinic, Benin City, Edo State

3.2 STUDY DESIGN

This is an experimental design which will consist of four groups of human subjects. Group A, B, C, and D. Group A, B and C will receive 50mg/kg, 75mg/kg and 100mg/kg body weight of *Dennettia tripetala* aqueous extract respectively while Group D will take 600ml of pure water. IOP and BP will be measured and recorded before and at 30 minutes interval for 180 minutes.

3.3 SAMPLING TECHNIQUE

Convenient Sampling method will be used in this study

3.4 STUDY POPULATION

The subjects to be used in this research are students of The University of Benin, Ugbowo Campus. The study will comprise 60 subjects of 40 females and 20 males. 15 subjects (group A), 15 subjects (group B), 15 subjects (group C) and 15 subjects as control all between the ages of 18-35 years who will meet the inclusion criteria. Healthy individuals with normal intraocular pressure ranging from 11-21mmHg and blood pressure ranging from 60-89 Diastolic BP and 100-130 Systolic blood pressure will be used for this study.

3.5 STUDY DURATION

The study will take place within a period of three months.

3.6 SAMPLE SIZE

Using Fischer's formula;

$$n = Z^2 P(1-P)/d^2$$

where;

n = sample size

Z = Statistical level of confidence of 95% (1.96)

P = 0.036 (3.6%)

d = Confidence interval (margin of error) 5% (d = 0.05)

$$n = 1.96^2 \times 0.036 (1-0.036)/0.05^2$$

$$n = 0.1333/0.0025$$

$$n = 53.32$$

Allowing for 10% Attribution factor

$$53.32 \times 0.1 = 5.332$$

$$\text{Total sample size} = 53.32 + 5.332 = 58.65$$

60 participants will be used for this study for credibility

3.7 INCLUSION CRITERIA

-Subject with intraocular pressure between 11-21 mmHg (normal), and normal systolic blood pressure of, (100-130mmHg) and normal diastolic blood pressure of 60- 89mmHg

-Healthy Male and female subjects within the age range of 18-35years who will give their consent to participate in the study.

3.8 EXCLUSION CRITERIA

-Subjects with intraocular pressure below 11mmHg and above 21mmHg and systolic blood pressure above 130mmHg and diastolic blood pressure below 89mmHg

-Subject with ocular pathologies and systemic disease

-Subjects below 18years and above 35years

-Subjects who will not give their consent to the study

-Subjects allergic to *Dennettia tripetala*

-Subjects currently using topical or systemic medication

3.9 RESEARCH MATERIALS

Fresh seeds of *Dennettia tripetala*

Marceration extraction apparatus

Glass Beakers

Measuring cylinder

Distilled water (Uniben pure water)

Blender

Washing bowls

Filter sieve

Weighing scale

Direct Ophthalmoscope

Perkins Applanation Tonometer

Anaesthetic 0.5 Lidocaine

Methylated spirit

Cotton wool

Fluorescein strip

Disposable plastic cups

Stethoscope

Mercury Sphygmomanometer

3.10 PROCEDURE

The following procedure was carried out after obtaining approval from the ethical committee of the Department of optometry University of Benin. Subjects that was used for this study will be selected from a screening exercise conducted in the University of Benin, Ugbowo Campus.

Thorough case history was taken on all subjects as well as ocular and general examination.

Ocular examination taken were Subjects who met the inclusion criteria was used in this study.

Informed consent was signed by each subject after a detailed explanation was given to them. The subjects were divided into four groups labeled A, B, C and D within the same age range.

Ocular and general examination conducted include

Case History

A thorough case history was carried out to ensure that there is no history of any ocular trauma, systemic or ocular disease, and current use of any systemic or topical ocular medication

Visual acuity testing;

Patient was properly positioned on the chair and the left eye was covered with an occluder to read with right eye, same was done for the right eye, then both eyes. This was done for record purposes and also for legal reasons.

External examination (Penlight test);

The patient was told to sit-up and look straight ahead, penlight was used on both eyes to examine the external adnexa for any abnormalities to know the set of people to rule out from partaking in the research.

Internal examination (Ophthalmoscopy)

This was carried out to examine the inside of the eyes, the subject was told to sit comfortably while fixating on the 6/60 letter of the VA chart, the ophthalmoscope was used to examine the right eye and the left eye to ensure and rule out any compromise to the retina and internal structure

Instruction to patient

Subjects was instructed not to eat before coming to the research clinic, and also to not wear any tight clothing for easy and accurate readings of IOP

Grouping of subjects

The selected 60 subjects were divided into 3 experimental group labeled A,B, C and one control group labeled D with each group having 15 subjects each. Group A, B, and C were to be orally administered 50mg/kg, 75mg/kg, 100mg/ kg body weight of *Dennettia tripetala* extract respectively on the day of the experiment while group D which is the control group was orally administered pure water only.

Pre administration of the extract

Subjects were asked to remove their shoes and the weights of the subjects were measured and recorded using a standardized weighing scale. The baseline IOP was measured and recorded using Perkins contact tonometer, likewise the baseline blood pressure was measured and recorded using the mercury sphygmomanometer and stethoscope.

Administration

After taking baseline measurement of IOP and BP The selected 60 subjects in group A, B, and C were orally administered 50mg/kg, 75mg/kg, 100mg/ kg body weight of *Dennettia tripetala* extract respectively on the day of the experiment. Group A was given 50mg/kg body weight, Group B was given 75mg/kg body weight and Group C was given 100mg/kg respectively on the day of the experiment. While group D which is the control group was orally administered pure water only. The doses of the aqueous extract were orally administered based on the body weight of each subject.

Intraocular pressure measurement;

Subjects was seated comfortably in a chair, the procedure was first explained to the patient before it commenced,

Thereafter, the intraocular pressure was measured at 30-minute interval, for 180 minutes. Each IOP measurement will be repeated three times and the average value will be recorded.

Blood pressure measurement;

Mercury sphygmomanometer was used, the blood pressure of the subject was first checked to ensure they meet the inclusion criteria. Baseline measurement was taken, subject was asked to sit

comfortably while resting the right hand on the arm rest, the cuffs were placed on the upper arm and the mercury column is at zero. The cuff is inflated with air using a bulb until the pressure exceeds the patient's systolic blood pressure, the air is slowly released from the cuff, allowing blood to flow again. The mercury column falls, indicating decreasing pressure. As the pressure drops, I listened with the stethoscope for the first sound of blood flowing through the artery, indicating the systolic blood pressure, the pressure will continue to drop, the sound of blood flowing through the artery changes, it becomes more muffled. The point at which the sound disappears indicates the diastolic blood pressure. The blood pressure reading is recorded as systolic pressure over diastolic pressure, measured in millimeters of mercury (mmHg). Each measurement will be repeated three times and the average value will be recorded.

Procedure for preparing *Dennettia tripetala* extract

Fresh *Dennettia tripetala* seeds will be bought from Uselu market in Benin City and would be brought to the department of Plant biology and biotechnology for identification. The seeds was grounded to powder after which it was weighed. Each dose in powdered form was measured into 600ml of pure water at room temperature using maceration extraction technique by the laboratory technician in the department of pharmacognosy. Standard solvent water volume of 500ml was used to produce a concentration of 50mg/kg, 75mg/kg and 100mg/kg of body weight. The weight of participants was measured in a scale and the aqueous extract was orally administered based on the body weight of each subject. Measuring cylinder was used to measure graded doses of the aqueous extract to be used for the experiment.

3.11 STATISTICAL ANALYSIS

Data obtained will be analyzed using Repeated Measures Analysis of Variance (ANOVA) and descriptive statistics as processed by the Statistical Package for Social Sciences (SPSS) Version 22. Results obtained will be expressed as mean \pm standard deviation (SD). A p value of less than 0.05 (<0.05) will be considered an indication of significance

3.12 LIMITATIONS OF STUDY

Ingestion of given doses of *Denettia tripetala* extract proved challenging as the subjects were unwilling to take the extract.

Subject became tired, uncomfortable and impatient as a result of multiple intraocular pressure and blood pressure measurements.

CHAPTER FOUR

4.0 RESULTS AND DATA ANALYSIS

4.1 Sociodemographic variable of the respondents

A total of 60 participants were recruited for this study and they were divided into 4 groups (Group A, B, C, D) comprising of 15 participants in each group. 10(66.7%) of the respondents in each group were females while 5(33.3%) were males. In group A, the mean age and weight were 22.13 ± 2.59 and 57.53 ± 8.11 respectively. In group B, the mean age and weight of the respondents were 22.33 ± 4.12 and 69.07 ± 9.78 respectively. In group C, the mean age and weight of the respondents were 22.33 ± 2.85 and 72.00 ± 17.13 respectively. In group D, the mean age and weight of the respondents were 22.73 ± 3.20 and 64.87 ± 6.85 . In summary, 40(66.7%) of the respondents were females while 20(33.3%) were males. The mean age and weight of the respondents were 22.38 ± 3.16 and 65.87 ± 12.21 respectively as shown in table 4.1.

Table 4.1: Sociodemographic variable of the respondents

Variable	Group A	Group B	Group C	Group D	Total
	N(%)	N(%)	N(%)	N(%)	N(%)
Gender					
Female	10(66.7%)	10(66.7%)	10(66.7%)	10(66.7%)	40(66.7%)
Male	5(33.3%)	5(33.3%)	5(33.3%)	5(33.3%)	20(33.3%)
Age(years)					
Mean± SD	22.13±2.59	22.33±4.12	22.33±2.85	22.73±3.20	22.38±3.16
Weight(kg)					
Mean± SD	57.53±8.11	69.07±9.78	72.00±17.13	64.87±6.85	65.87±12.21

GROUP A=Administered 50mg/kg weight of Dennetia tripetala extract, GROUP B= Administered 75mg/kg weight of Dennetia tripetala extract, GROUP C= Administered 100mg/kg weight of Dennetia tripetala extract, GROUP D= Administered pure water only.

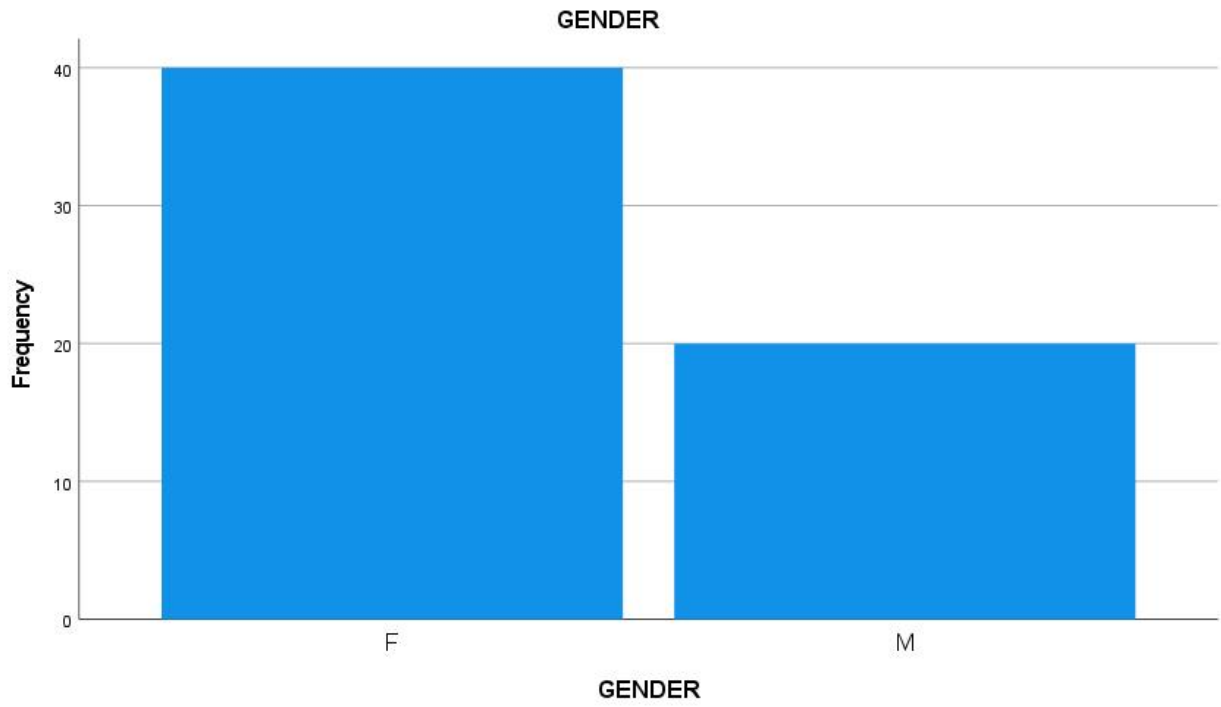


Fig 4.1 : Bar chart showing the gender distribution of the respondents

4.2 Descriptive statistics on Intraocular pressure and blood pressure of the respondents

The mean intraocular pressure at baseline, after 30mins, 60mins, 90mins, 120min and 180mins were 15.17 ± 2.64 , 14.35 ± 2.58 , 13.56 ± 2.65 , 13.33 ± 2.73 , 13.49 ± 2.62 and 14.71 ± 2.61 respectively.

The baseline SBP, baseline DBP, SBP and DBP after 30mins, SBP and DBP after 60mins, SBP and DBP after 90mins, SBP and DBP after 120mins, SBP and DBP after 180mins were 119.23 ± 5.92 , 76.82 ± 8.09 , 117.53 ± 6.00 , 75.65 ± 8.13 , 115.93 ± 5.89 , 73.18 ± 8.10 , 116.18 ± 6.11 , 72.52 ± 7.18 , 117.15 ± 6.28 and 73.37 ± 6.90 respectively as shown in table 4.2.

Table 4.2: Descriptive statistics on Intraocular pressure and blood pressure of the respondents

Variable	Group A	Group B	Group C	Group D	Total
	Mean± SD	Mean± SD	Mean± SD	Mean± SD	Mean± SD
1OP					
Baseline	15.53±2.49	15.44±2.65	14.82±2.60	14.90±3.02	15.17±2.64
After 30mins	14.65±2.23	14.06±2.65	14.03±2.94	14.66±2.63	14.35±2.58
After 60mins	13.67±2.15	13.14±2.44	12.95±3.25	14.50±2.65	13.56±2.65
After 90mins	12.73±2.02	13.07±2.25	12.73±3.37	14.79±2.80	13.33±2.73
After 120mins	12.51±2.20	13.98±2.10	12.81±2.96	14.57±2.73	13.49±2.62
After 180mins	14.46±2.41	15.53±2.36	14.18±3.09	14.66±2.58	14.71±2.61
Blood pressure					
Baseline SBP	119.07±7.29	119.47±6.03	119.93±1.67	118.47±7.38	119.23±5.92
Baseline DBP	74.93±8.20	76.67±10.69	77.67±4.63	78.00±8.19	76.82±8.09
SBP after 30mins	117.53±7.16	116.80±6.29	117.33±3.04	118.47±7.06	117.53±6.00
DBP after 30mins	73.60±9.09	74.27±11.15	77.27±2.69	77.47±7.19	75.65±8.13
SBP after 60mins	115.47±6.96	115.20±5.98	114.67±2.80	118.40±6.72	115.93±5.89
DBP after 60mins	70.27±8.00	71.13±10.66	74.07±3.67	77.27±7.29	73.18±8.10
SBP after 90mins	115.27±8.05	116.07±5.08	114.93±2.99	118.47±7.06	116.18±6.11
DBP after 90mins	70.53±8.05	71.47±8.21	72.13±3.29	75.93±7.49	72.52±7.18
SBP after 120mins	117.73±8.71	116.33±5.67	115.87±2.58	118.67±6.80	117.15±6.28
DBP after 120mins	72.13±8.05	72.33±6.91	72.93±4.04	76.07±7.79	73.37±6.90
SBP after 180mins	118.53±7.35	118.53±5.66	118.13±2.53	122.20±14.87	119.35±8.79
DBP after 180mins	75.27±7.26	75.33±7.89	75.13±5.88	76.73±8.24	75.37±7.24

4.3 Changes in intraocular pressure during the different time intervals

ANOVA with Repeated measures was conducted to examine the difference in intraocular pressure at the different time interval of measure which shows the effect of graded doses of *Dennettia tripetala* fruit on intraocular pressure. The findings revealed there was a significant effect of 50mg/kg of *Dennettia tripetala* fruit on intraocular pressure of the respondents ($F=13.54$, $P<0.001$). There was also a significant effect of 75mg/kg of *Dennettia tripetala* fruit on intraocular pressure of the respondents ($F=8.12$, $P<0.001$). There was a significant effect of 75mg/kg of *Dennettia tripetala* fruit on the intraocular pressure of the respondents ($F=8.46$, $p<0.001$). Finally, there was no significant effect of pure water on the intraocular pressure of the respondents ($F=0.448$, $P=0.694$) as shown in table 4.3.

Table 4.3: Changes in intraocular pressure during the different time intervals

	Mean Square	Df	F	p
Group A intraocular pressure	41.13	2.51	13.54	<0.001
Group B intraocular pressure	28.30	3.07	8.12	<0.001
Group C intraocular pressure	24.20	2.36	8.46	<0.001
Group D intraocular pressure	0.618	2.61	0.448	0.694

4.4 Changes in blood pressure during the different time intervals

ANOVA with Repeated measures was conducted to examine the difference in blood pressure at the different time interval of measure which shows the effect of graded doses of Dennettia

tripetala fruit on intraocular pressure. The findings revealed there was a significant effect on 50mg/kg of Dennettia tripetala fruit on SBP (F=7.31, P=0.008) and DBP (F=4.59, p=0.008). There was a significant effect of 75mg/kg of Dennettia tripetala fruit on SBP (F=13.91, P=<0.001) and DBP (F=4.51, P=0.007). Finally, there was a significant effect of 100mg/kg of Dennettia tripetala fruit on SBP (F=13.55, P=<0.001) and DBP (F=6.45, P=0.002). There was no significant effect of pure water on the SBP (F=1.044, p=0.327) and DBP (F=1.856, P=0.159) as shown in table 4.4

Table 4.4 changes in blood pressure during the different time intervals

	Mean Square	Df	F	P
Group A				
SBP	130.13	1.43	7.31	0.008
DBP	99.90	2.88	4.59	0.008
Group B				
SBP	71.30	2.74	13.91	<0.001
DBP	120.66	3.12	4.51	0.007
Group C				
SBP	132.63	2.35	13.55	<0.001
DBP	151.66	2.52	6.45	0.002
Group D				
SBP	165.87	1.04	1.044	0.327
DBP	18.48	2.70	1.856	0.159

Graph 1: Changes in Intraocular Pressure

Graph 1: Changes in Intraocular Pressure

This graph shows the effect of different doses of *Dennettia tripetala* on intraocular pressure over time. Groups A, B, and C show a reduction, while Group D remains stable.

Graph 2: Changes in Systolic Blood Pressure

This graph illustrates the effect of different doses of *Dennettia tripetala* on systolic blood pressure over time. Groups A, B, and C exhibit a reduction, whereas Group D remains relatively stable.

Graph 3: Changes in Diastolic Blood Pressure

This graph presents the changes in diastolic blood pressure over time. A noticeable decrease is observed in Groups A, B, and C, while Group D remains relatively unchanged.

CHAPTER FIVE

5.0 DISCUSSION OF FINDINGS

The aim of this study was to investigate the effect of graded doses of aqueous extract of *Dennettia tripetala* on intraocular pressure and blood pressure in normotensive subjects. The findings from this study showed that graded doses of aqueous extract of *Dennettia tripetala* reduced the intraocular pressure and blood pressure of normotensive though the reduction was not sustained at the differences doses and also throughout the different duration. At 30minutes, the consumption of 50mg/kg weight of Dennetia tripetala extract, results in the reduction of IOP by 5.67% (14.65mmHg) from a mean baseline of 15.53±2.49. This reduction was consistent at 60minutes by 11.98% (13.67mmHg), at 90minutes (12.73mmHg), at 120mins (12.51mmHg). The IOP returned to 14.46mmHg at 180mmHg. The consumption of 75mg/kg and 100mg/kg weight of Dennetia tripetala extract also resulted in the consistent reduction of IOP at 30minutes,

60minutes and 90minutes. The IOP at 120minutes and 180minutes were slightly higher than at 90minutes but lower than the baseline intraocular pressure.

The findings from this study also revealed there was a reduction in the systolic blood pressure by 1.29% (117.73mmHg) at 30minutes from a baseline of 119.07mmHg when 50mg/kg weight of *Dennettia tripetala* extract is consumed. The reduction was consistent at 60minutes by 3.02% (115.47mmHg) and 90minutes by 3.19% (115.27mmHg). The Blood pressure returned to 117.73mmHg and 118.53mmHg at 120minutes and 180minutes respectively. The consumption of 75mg/kg and 100mg/kg weight of *Dennettia tripetala* extract also resulted in the consistent reduction of systolic blood pressure at 30minutes, 60minutes, 90minutes. The blood pressure reading at 120minutes and 180minutes increased a bit but was still lower than the baseline blood pressure.

There was a significant effect of 50mg/kg, 75mg/kg and 100mg/kg of *Dennettia tripetala* fruit on intraocular pressure of the respondents (<0.001). This reduction in IOP recorded could be as a result of the presence of ascorbic acid, magnesium, flavonoid, melatonin, thiamin, vitamin B12, lipid acid in *Dennettia tripetala* (Timothy and Okere, 2008). It has been demonstrated that ascorbic acid supports the osmotic influx of water after blood osmolarity is artificially raised, which lowers IOP. 1.50% of the anterior chamber's contents are replenished every minute and that the aqueous portion of the chamber has a half-life of around 45 minutes, meaning that 2.80 ml is produced every day. Thus, ascorbic acid, a component of *D. tripetala* seed extract, decreased eye pressure via raising blood osmolarity when it was injected and absorbed into the eye (Ekenze *et al.*, 2023). Thus, ascorbic acid, a component of *D. tripetala* seed extract, decreased eye pressure via raising blood osmolarity when it was injected and absorbed into the eye. Because pigment cells typically circulate inside the aqueous and drain out via the trabecular

meshwork, the presence of ascorbic acid in the anterior chamber preserved the collagen fiber cells of the trabecular meshwork, preventing their shrinking, constriction, and obstruction. According to Timothy and Okere (2008), the rise in IOP after 60 and 120 minutes was most likely caused by insufficient ascorbic acid and magnesium in 0.75 g, which prevented IOP from continuing to decrease.

It is believed that flavonoids lower intraocular pressure by reducing the excessive permeability of the blood-aqueous barrier in the eye. By raising glutathione levels in glaucomatous patients' red blood cells and lacrimal fluid, lipoic acid (a fatty acid) most likely contributed to the decrease of intraocular pressure. Lastly, the presence of vitamin B, thiamine (vitamin B), and melatonin may have also helped to lower IOP. This is because glaucoma patients have been shown to have lower melatonin levels, and melatonin rhythms are reflected in normal diurnal rhythms of IOP fluctuation (Ekenze *et al.*, 2023).

There was also a significant effect of 50mg/kg, 75mg/kg and 100mg/kg of *Dennettia tripetala* fruit extract on blood pressure ($p < 0.05$) as it was seen that the blood pressure reduced at different time intervals. However, there was no significant effect of pure water on the intraocular pressure and blood pressure of the respondents ($p > 0.05$).

CHAPTER SIX

6.0 CONCLUSION

The ingestion of *Dennettia tripetala* resulted in the reduction of intraocular pressure and blood pressure for a duration of 2hours. There was a significant effect of graded doses of *Dennettia tripetala* fruit extract on intraocular pressure and blood pressure among the respondents.

6.1 RECOMMENDATION

Since glaucoma is one of the main causes of blindness in the world and hypertension poses as a major risk factor, there is a need for an affordable and widely accepted adjuvant treatment. For this reason,

1. Ingestion of *Dennettia tripetala* should be promoted as an adjuvant in glaucoma treatment
2. It should also be promoted as an adjuvant treatment in hypertensive patients.

3. More studies should be done on *D.tripetala* to gain better knowledge of its mechanism of action.
4. More subjects should be used in subsequent studies to be sure that its intraocular pressure reducing effect cuts across the entire population
5. More research should be done to provide *D.tripetala* tablets for individuals who can't drink the extract due to its pungent sensation.
6. Subsequent studies carried out on intraocular pressure using glaucoma patients.
7. Also subsequent studies should be carried to know if it affects other parameters like phoria, vergence and other ocular parameters.
8. The use of should be encouraged by health practitioners
9. Studies should be carried out to compare its effect with known antiglaucoma drugs.

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