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## Original Research Article

*Open Access*  
Online Journal

# Effect of Orally Administered Zingiber Officinale on the Intra Ocular Pressure of Experimental Rabbits

Received: 10-Mar-08

Revised: 02-Apr-08

Accepted: 16-Apr-08

## Abstract

**PURPOSE:** To determine the therapeutic effect of Ginger (*Zingiber officinale*) on increased intraocular pressure (IOP).

**METHODS:** Twenty male and female New Zealand rabbits divided into 5 groups (A, B, C, D and E) were used. Groups B and D were administered with topical atropine 1% for 2 weeks while groups A and C were not so treated and group E was used as control. After increased IOP was achieved in groups B and D, oral ginger (1.00 ml) obtained by hot (100 °C) extraction was administered to each rabbit in groups A and B while 1.0 ml of cold (37 °C) extracts of ginger was administered to groups C and D all twice daily.

**RESULTS:** There was significant decrease in mean IOP (within the range of  $3.0 \pm 1.0$  mmHg daily which finally stabilized at  $7.00 \pm 1.0$  mmHg) in all groups treated with both hot and cold extracts of ginger.

**CONCLUSION:** Ginger lowers IOP in rabbits' eyes and may be a useful agent in reducing IOP in humans as it is cheap, commonly available, relatively free from adverse effects and beneficial to all the major tissues of the body.

**Keywords:** Intraocular pressure, Ginger, Zingiber officinale, Topical application

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## Introduction

Normal intraocular pressure (IOP) has been defined as the average pressure which the normal eye can tolerate over a period of time without compromise to the integrity of the eye and ranges between 10 – 21mmHg with an average of 16 mmHg [1]. Therefore, IOP refers to the pressure within the globe of the eye, and thus the pressure exerted by the intra-ocular fluids of the eye [2]. Raised IOP has been implicated as one of the clinical triad of both primary and secondary glaucoma – others being the characteristic visual field loss and excavated optic disc [3]. Flammer [3] believed that it has been proven useful to apply the term glaucoma to all patients having an increased IOP (with or without glaucomatous damage), as well as to all patients suffering from glaucomatous damage (with or without a high IOP). Glaucoma is a blinding disease that causes visual loss by damaging the retinal nerve fibres extending through the optic nerve head along the visual pathway. Gala et al [4] listed causes of eye problems as being hereditary or acquired causes the major acquired ones being pathological and metabolic causes. Glaucoma can so be classified as Primary Open Angle Glaucoma having both hereditary and acquired implications.

About 12% of all blindness in the UK and USA are due to glaucoma [5]. Specifically, about 9.0% of Nigeria have been diagnosed with Primary Open Angle Glaucoma (POAG) [2]. POAG is just one of the several types of glaucoma. This is disturbing because farmers, retirees, and housewives are more disposed to POAG. The most significant diagnostic parameter is IOP variation. This is premised on the quest to unravel cheap, common and easy markers for the control or reduction of IOP. Investigations on the effect of vitamin C [6], exercise [7], moderate alcohol [8] have given indications that as there are several factors affecting IOP, there might also be numerous factors mitigating IOP increase.

Ginger (*Zingiber officinale*) belongs to the family called *Zingiberaceae*. It is a cane-like tuberous perennial plant native to Southern Asia but extensively cultivated throughout the tropical and sub-tropical regions of the world. Several studies on ginger have reported it being vital both as food supplement, condiment and medicinal herb. It is widely used in Asian, Indian and Arabic herbal traditions since ancient times. For example, in China it has been used to aid digestion, treat stomach upset, diarrhea and nausea for thousands of years. Other medicinal uses include common cold, flu like symptoms, headache, vomiting, painful periods, dyspepsia, flatulence, scurvy and impotence. The *Pen Tsao Chung* (3000 BC), China's first great herbal documentation, recommended ginger for colds, fever, tetanus and leprosy [9]. Velnet [10] also stated that distilled ginger water has in the past been regarded as one of the best ophthalmic remedies for cataract. Apart from its medicinal use, ginger is an important cooking spice even in modern times [10].

The dried rhizome of ginger consists of 1 – 4% volatile oils which are the pharmacological constituents of ginger. he oils are also sponsible for the unique smell and taste of ginger. The aromatic components are zingiberene and disabolene while the pungent components are the gingerols and shogoals which are credited with anti-nausea and anti-vomiting activities.

The aim of this work is to determine the effect of ginger on IOP.

## Materials and Methods

### Materials

Atropine 1.0%, novesine 1.4% and fluorescein strips were purchased from Alcon-Couvreur (Belgium), Merck (Sharp and Dohme – Chibret, MSD, USA) and Chauvin Pharmaceuticals (India), respectively

Ginger (*Zingiber officinale*) roots which was bought from local market in Benin City were

cut into pieces, dried and milled after which it was weighed. Some of the powdered root (200 g) was extracted with boiling water while another 200 g was extracted with distilled water at room temperature with soxhlet extractor (Quick Fit, UK) using standard procedures.

### Animals

New Zealand rabbits (20) were purchased from the same colony, examined by a veterinary doctor and then allowed to acclimatize to the laboratory condition for 2 weeks and fed on normal rabbit chow and water. They were then randomly assigned into five groups (A – E).

### Study design

Ethical approval was sought and granted by the Ethical Committee for Animal Studies of the Faculty of Pharmacy, University of Benin, Benin City prior to commencement of this study. The animals were grouped as follows:

*Group A: Fed with 1.0ml hot ginger extract daily for five days.*

*Group B: Received topical 1.0% atropine twice daily for 2 weeks to induce increased in IOP prior to oral administration of 1.0ml of hot ginger extract twice daily for 5 days.*

*Group C: Fed with 1.0 ml cold ginger extract daily for five days.*

*Group D: Received topical 1% atropine twice daily for 2 weeks to induce increase in IOP prior to oral administration of 1.0 ml of cold extract of ginger twice daily for 5 days.*

*Group E: Control.*

Oral administration of ginger extracts carried out using butterfly needles. Baseline IOP of each rabbit was taken to ensure no animal had abnormal IOP. Two drops of 0.4% novesine was applied topically to the two eyes of each animal and a fluorescein strip was inserted into the lower fornix of the

conjunctiva. A hand held Perkin Tonometer (HA-2 – Kowa Company Ltd, Japan) surface, which is the contacting portion of the prism, was sterilized and cleaned properly. Each rabbit was held to squat ventrally at the diagonal edge of a table (6 feet high) so as to maintain the gaze at normal panoramic position. The tonometer was held at the thumb wheel, and thus was turned while the tonometer surface was pressed lightly on the cornea. The examiner observes the doubling two green semi circles splitted on both sides. When these semi circles increased in size and became clear and distinct, forming almost a definite greenish circle, semi-contacting each other at their inside edges, the tonometer was removed and reading taken. The IOPs of both eyes of each animal were measured daily for the five days.

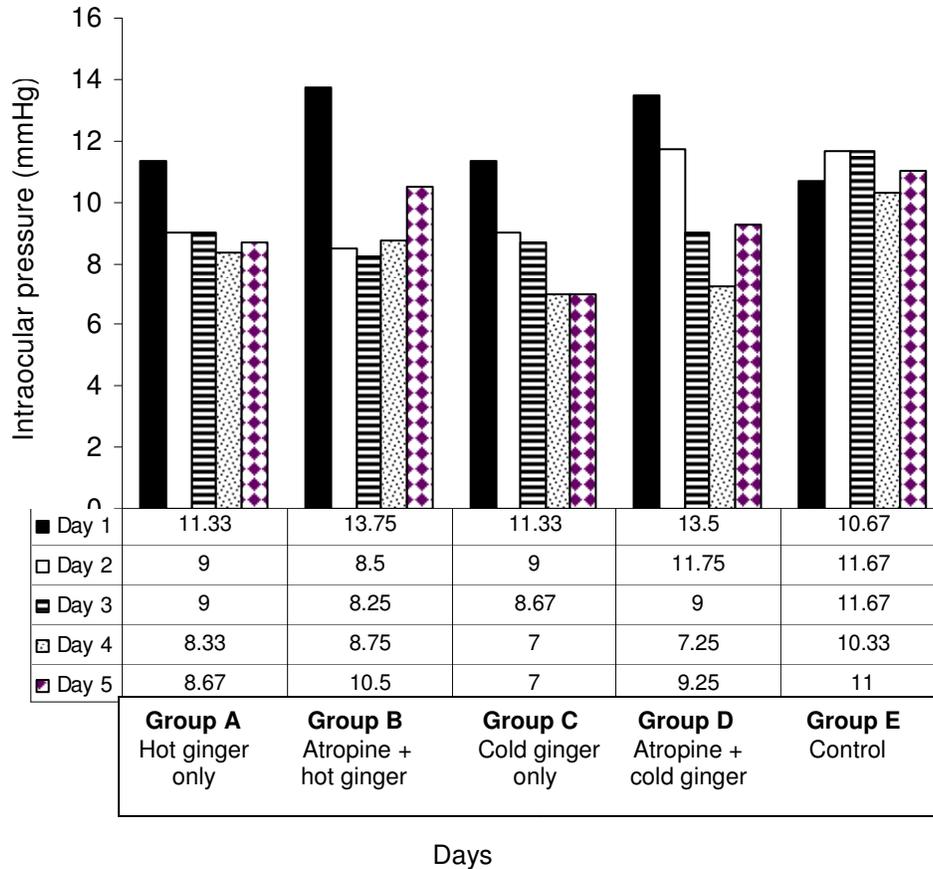
### Data analysis

The IOP data collected were analysed and expressed as mean. Statistical calculation was effected using one way analysis of variance (ANOVA). At 95% confidence interval, 2-tailed p values < 0.05 were considered significant.

### Results

Figure 1 showed the variation of IOP with time in days in the right eye. Atropine increased the mean IOP of groups B and D which were indicated in the results from the day of inception of treatment with both hot and cold ginger extracts. For group A, there was consistent decrease in IOP. In group B, the decrease was more pronounced for the second day and gradually went down only to increase on the 5<sup>th</sup> day. This decrease was more consistent in group C as it was in group A. There were similarities in the decrease in IOPs of Groups B and D, although the decrease in group B animals was much more pronounced and consistent.

Also the left eye showed the same trend of decrease (Figure 2) like that of the right eye especially for groups B and D in comparison with control (group E). This implied that the



**Figure 1:** Variation of intraocular pressure (IOP) with time in right eye (n=4)

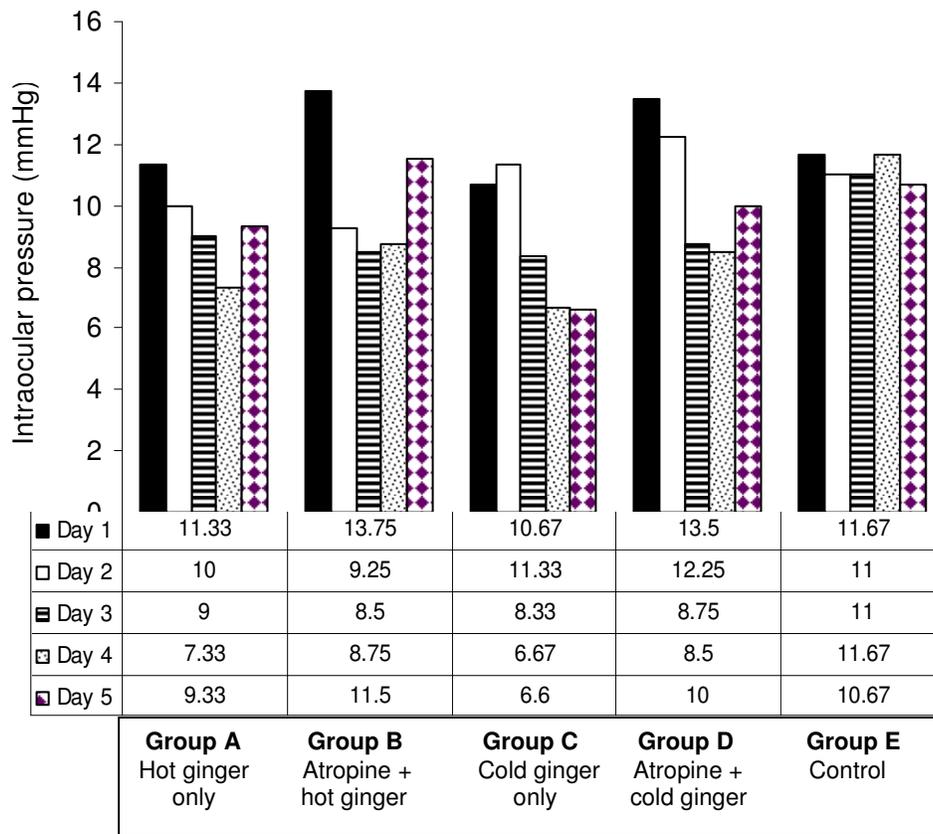
systemic effects of ginger extracts had binocular manifestation. There was no significant difference between the data for the two eyes.

### Discussion

Pharmacologically, mydriatic agents produce elevation of IOP because in mydriasis, the most peripheral of the anterior iris stroma is made to move forward towards the inner aspects of the uveoscleral meshwork, resulting in decreased trabecular outflow facility. This thus necessitated the use of Atropine. Corticosteroids also raise IOP using the same mechanism of action. However this was not used because of the

duration of time required to raise IOP with corticosteroids.

The results from figures 1 and 2 indicated that hot and cold extracts of ginger have the potential to lower IOP since the calculated f-value for right and left eyes are less than the critical f values for both eyes. Ginger root extracts have a wide array of pharmacological and physiological activities. The effects are specific to the different organs of the body. Griefenberg et al [11] indicated that several studies have suggested that it is more effective than placebo in reduction of symptoms associated with motion sickness. Also, Fischer et al [12] posited that at least two studies have indicated the potency of ginger in relieving



**Figure 2:** Variation of intraocular pressure (IOP) with time in left eye (n=4)

nausea and vomiting associated with pregnancy.

Studies by Arfeem et al [13] showed that ginger is a potent inhibitor of prostaglandins and leucotrienes synthesis which explains its effect as an anti-inflammatory agent. This is vital in reduction of IOP, because IOP is determined by the interaction between the rate of aqueous production and outflow resistance which has an inverse relationship with the rate of aqueous escape from the anterior chamber [6]. Guyer [14] explained that extracts of ginger have multiple pharmacological effects that includes antioxidants functions, inhibition of prostaglandins, leutotrienes and platelet aggregation coupled with cholesterol lowering activities.

Apart from prostaglandins inhibition, two other probable mechanisms are being elucidated on the effect of ginger on IOP. Asonye and Bawo [6] showed the singular antioxidant effect of vitamin C in lowering IOP. Ginger contains vitamin C and other varieties of antioxidants. The probable synergistic effects could reduce IOP. Also, the ability of ginger to lower increased IOP could be by its ability to thin out blood platelets thereby inhibiting platelet aggregation in the ciliary body thus enhancing out flow of aqueous humour.

Moreover, Zingibain the ginger proteolytic enzyme breaks down protein and displays anti-inflammatory properties. This is also a probable mechanism in enhancing IOP reduction. This could be implicated in the

increase in osmotic effect which subsequently creates an osmotic gradient<sup>[10]</sup>. Similarly, exercise could lower IOP by colloid osmotic effect or conceivably by increasing aqueous drainage through  $\beta$ -agonists- like action [7].

We are aware that several herbal medicinal products are being worked on for the reduction of IOP. For example, *Coleus forskolin* is a herb related to mint used in India. It is the only source of forskolin, a labdane diterpene compound which activates adenylate cyclase production, thus elevating cAMP whose abundance in the ciliary body reduces IOP when administered topically. Its mechanism of action is suggested to be by amplification of intracellular communication thus increasing aqueous flow rate [15]. Currently, some of the most efficacious drugs for reduction of IOP are for the very rich in our society as they are very exorbitant. This thus has necessitated our thorough research efforts attempting to find cheap, common, effective, efficacious products that would tremendously reduce IOP.

## Conclusion

Ginger lowers IOP in rabbits' eyes and may be a useful agent in reducing IOP in humans as it is cheap, commonly available, relatively free from adverse effects and beneficial to all the major tissues of the body. As IOP increase is the major predisposing factor for the manifestation of glaucoma (which currently is the second major cause of blindness in the world), ginger may serve a very useful source of medication for the prevention of blindness due to IOPs.

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