

# Effects of corn silk aqueous extract on intraocular pressure of ocular hypertensive human subjects

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## Abstract

Stigma/style of *Zea mays L* (Corn silk) has been documented to have hypotensive effect on blood pressure and to relieve oedema. However we are not aware of any literature on its hypotensive effect on intraocular pressure (IOP) of humans or animals. We studied the effects of water only, masked doses of corn silk aqueous extract (60 mg/kg, 130 mg/kg, 192.5 mg/kg and 260 mg/kg body weight) on the IOP and blood pressure (BP) of twenty normotensives and twenty ocular hypertensive subjects. Also we compared the effects of the varied doses of corn silk aqueous extract (CSAE) with masked doses (5 mg/kg and 10 mg/kg body weight) of acetazolamide on IOP of ocular hypertensive subjects only. The results showed that the last three doses of CSAE lowered

IOP and BP significantly ( $p < 0.001$ ) within eight hours of administration. The peak effect on IOP was observed after four hours while the peak effect on BP was observed after three hours of administration in the normotensives and ocular hypertensive subjects likewise the hypotensive effect was dose-dependent. The results also showed that 130 mg/kg body weight of CSAE produced the same hypotensive effect on IOP of ocular hypertensive subjects as 5 mg/kg body weight of acetazolamide. Therefore CSAE may have some IOP lowering effects that require further investigation in the management of ocular hypertension. (*S Afr Optom* 2013 72(3) 133-143)

**Key words:** Intraocular pressure, ocular hypertension, corn silk aqueous extract, acetazolamide

## Introduction

Corn silks are fine soft threads 10-20 cm long, commonly found on the corn. When fresh, they are like silk threads of a light green or yellow color<sup>1</sup>. Corn silks have been used in many parts of the world for the treatment of oedema, cystitis, kidney stones, nephritis and prostatitis<sup>2,3</sup>. Corn silk has both antioxidative and hypoglycemic activities<sup>4</sup>. It is also known to reduce blood pressure in animals<sup>5</sup>, however studies on the

effect of corn silks extract on intraocular pressure in animals and humans are lacking. Intraocular pressure is the measure of how tense the globe is. Normal IOP has been defined as the average pressure, which the normal eye can tolerate over a period of time without compromise to the integrity of the eye, or without glaucomatous damage<sup>6</sup>. The range of normal human intraocular pressure<sup>7</sup> is 11-21 mmHg. The term 'ocular hypertension' is used when the intraocular pressure is found to be greater than 21 mmHg on two

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consecutive occasions, in the absence of detectable glaucomatous damage<sup>7,8</sup>.

Previous researchers have reported that changes in blood pressure result in changes in intraocular pressure without drug intervention in humans and animals studies<sup>9-11</sup> and Leske *et al*<sup>12</sup>, (1996) concluded that raised systemic pressure preceded raised IOP in a given patient<sup>12</sup>. Since CSAE has hypotensive effects on systemic blood pressure<sup>5</sup>, there is a need to provide baseline data on the changes in IOP when CSAE is administered. Likewise, the need to create awareness among eye care practitioners on the efficacy of CSAE in reducing IOP suggested we compare its effect with a known IOP-reducing drug like acetazolamide. Acetazolamide (Diamox) is a potent carbonic anhydrase inhibitor, effective in the control of fluid secretion in ocular hypertension and glaucoma by decreasing the formation of aqueous humor in the human eye, resulting in lowered intraocular pressure<sup>13</sup>. It is a white crystalline, odorless tablet, weakly acidic, very slightly soluble in water and slightly soluble in alcohol<sup>14</sup>. Common side effects of using this drug include numbness and tingling in the fingers and toes, taste alterations (parageusia), blurred vision<sup>15</sup>, metabolic acidosis<sup>16</sup>, increased risk of developing calcium oxalate and calcium phosphate kidney stones<sup>17</sup> as well as frequent urination<sup>18</sup>.

The prevailing incidence of ocular hypertension and glaucoma and its subsequent diagnosis in the Nigerian society is growing at an alarming rate especially among young people<sup>19</sup>. Ocular hypertension is a precursor to glaucoma which is a sight-threatening ocular disease. Glaucoma is managed with topical medications such as prostaglandins and beta-blockers most often without oral medication. In Nigeria with severe raised intraocular pressure, oral medication such as carbonic anhydrase inhibitor (acetazolamide) is commonly used in conjunction with topical anti-glaucoma drugs to lower IOP. Due to the undesirable side effects of acetazolamide, often an alternative treatment may be preferred.

## Materials and Methods

### Subjects

Forty subjects, nineteen (19) males and twenty one (21) females were randomly selected from the

University community in a screening exercise carried out in the University of Benin Optometry Clinic in Benin City, Edo State Nigeria. Informed consent was obtained from each subject after detailed explanations of the procedures. Approval for the study was granted by the Ethics and Research Committee of the University of Benin Teaching Hospital, and was performed in accordance with the guidelines of the Declaration of Helsinki. The subjects were divided into two groups of twenty each. Group A comprised of twenty ocular normotensives, aged between 22 and 32 (mean age of  $25.17 \pm 2.72$ ) years. Group B comprised of twenty ocular hypertensives, aged between 22 and 35 (mean age of  $26.36 \pm 2.84$ ) years. They were instructed to abstain from all medication a week before and during the period of the experiments. The subjects were instructed to wear shirts without tight collars, ties and long sleeves for easy and accurate measurements of BP and IOP. Likewise they were instructed to abstain from liquid food, water, juice and beverages in the morning before presenting for the studies since these may affect readings. All the subjects emptied their bladders and each subject was weighed and body weight recorded on each experimental day before they drank water, CSAE, or acetazolamide. Experiments commenced at 9am every morning. During the screening exercise, the case history of each subject was taken. External and internal examinations of the anterior and posterior segments of the eyes of each subject were carried out to rule out abnormalities. Though the central corneal thickness was not assessed due to non availability of ultrasound pachymeter, but direct ophthalmoscopy was carried out using a Keeler ophthalmoscope; to rule out pathological cupping, asymmetry of 0.2 or more between the two eyes in any individual subject, cup: disc ratio greater than 20%, loss of neuroretinal rim, and retinal nerve fibre layer atrophy. Intraocular pressure was measured with the Kowa HA-2-hand-held applanation tonometer. Blood pressure was measured with U-MEC mercurial sphygmomanometer and Sprague stethoscope (Model No 112).

### Inclusion criteria

The ocular hypertensive subjects were those newly diagnosed from the screening exercise and had not started any treatment. They had IOP greater than 21

mmHg in three consecutive measurements; at 9 am, 3 pm and 6 pm. These three readings were taken during the screening exercise in order to observe the diurnal variations in their IOP before selection. Similar measurements of IOP were taken in the selection of the normotensive subjects and those who had IOP less than 21 mmHg were selected for the study. The selected subjects in the two groups had their visual fields assessed using Octopus 900 Haag-streit model to rule out visual field defects, had their ocular fundus assessed to ensure no loss of neural disc tissue from the assessment of the thickness, symmetry and color of the neuro retinal rim. Although the relationship between their IOP and CCT was not analyzed; there was no remarkable ocular or medical history in all the subjects selected for this study. All the subjects were non-alcoholics and non-smokers.

#### *Exclusion criteria*

Subjects who were on topical and/or systemic medications and those with ocular or systemic disease were excluded from the study.

#### *Description of procedure*

Subjects who met the selection criteria were recruited for the study. It was a masked study in which different doses of CSAE were prepared and masked with different labels by the laboratory technicians in the Pharmacognosy department of the University of Benin, so that the four observers who measured and recorded the IOP and BP of the subjects had no prior knowledge of the dose administered to each subject. Each dose of 60 mg/kg, 130 mg/kg, 192.5 mg/kg and 260 mg/kg body wt. of CSAE were masked and labeled "W, X, Y, and Z" respectively. In experiment 1, each labeled dose was administered, orally to the same subject in the ocular hypertensive group and the normotensive group; at two weeks intervals. In experiment 2, each dose of 5 mg/kg or 10 mg/kg body weight of acetazolamide dissolved in 600 ml of water were masked and labeled "S and T". Each labeled dose was administered orally at two weeks interval on the same subjects. During the experiment, IOP and BP were measured at 0 hour (baseline), and at every hour, after oral administration of water, CSAE or acetazolamide, until IOP and BP returned to baseline values.

### **Experiment 1**

Day 1 of the experiment, 600 ml of distilled water masked and labeled "V" was administered orally to each subject in groups A and B to serve as control. IOP and BP were measured at 0 hour (before administration) and every hour for eight hours after administration to observe for placebo effect.

Day 2, each subject in Groups A and B had 600 ml of a dose of CSAE masked and labeled "W" administered orally. Measurements of IOP and BP were repeated as in day 1.

Day 16 of the experiment, 600 ml of distilled water masked and labeled "V" was repeatedly administered orally to each subject in groups A and B. IOP and BP were measured and recorded as in day 1.

Day 17, each subject in Groups A and B had 600 ml of another masked dose of CSAE labeled "Y" administered orally. Measurements of IOP and BP were repeated as in day 1.

Day 31 of the experiment, 600 ml of distilled water masked and labeled "V" was repeatedly administered orally to each subject in groups A and B. IOP and BP were measured and recorded as in day 1.

Day 32, each subject in Groups A and B had 600 ml of another dose of CSAE masked and labeled "X" administered orally. Measurements were repeated as in day 1.

Day 46 of the experiment, 600 ml of distilled water masked and labeled "V" was administered orally to each subject in groups A and B. IOP and BP were measured and recorded as in day 1.

Likewise on day 47, each subject in Groups A and B had 600 ml of another dose of CSAE masked and labeled "Z" administered orally. Measurements were repeated as in day 1. The subjects were allowed to rest for two weeks thereafter only group B subjects were invited again for experiment 2.

### **Experiment 2**

Day 61 of the experiment, 600 ml of distilled water masked and labeled "V" was administered orally to each subject in group B only; to serve as control. IOP and BP were measured and recorded as in day 1.

Day 62: Each subject in Group B had a masked dose of acetazolamide dissolved in 600 ml of distilled

water; labeled “S” administered orally. Measurements of IOP and BP were repeated as experiment 1 above.

Day 76 of the experiment, 600 ml of distilled water masked and labeled “V” was administered orally to each subject in group B. Measurements of IOP and BP were repeated as experiment 1 above.

Day 77: Each subject in Group B had another masked dose of acetazolamide dissolved in 600 ml of distilled water; labeled “T” administered orally. Measurements of IOP and BP were repeated as experiment 1 above.

#### *Intraocular pressure measurement*

The cornea of the right eye was superficially anesthetized with one drop of 0.5% tetracaine. The end of a sterile, fluorescein strip was moistened with one drop of distilled water and applied to the subject's temporal bulbar conjunctiva. Each subject's reading was measured using the Kowa HA-2-hand-held applanation tonometer while the subject sat comfortably and relaxed on the examination chair with the head resting against the head-rest. The contact prism of the tonometer was aligned exactly with the apex of the cornea of the right eye and the pressure-recording dial was slowly rotated by the observer until the inner side of the top ring was aligned with the inner side of the bottom ring. The pressure reading was recorded at this point. The same procedure was repeated for the left eye.

#### *Preparation of cornsilk aqueous extract*

The methodology of Velaquez *et al*<sup>2</sup> and Jiyang *et al*<sup>4</sup> were adopted in the preparation of CSAE. Corn silks from a cultivated corn farm were harvested fresh from their corn combs when the combs were still seedless because at this stage the silks are non-pollinated. When the corn combs yield their seeds they can no longer be used because their silks are already pollinated. Their moisture content was removed by air-drying at room temperature ( $36.0 \pm 10^\circ\text{C}$ ) for 72 hours in the Department of Pharmacognosy of the University of Benin. Extracts were prepared in the Department of Pharmacognosy of the University of Benin by laboratory technicians by adding 480 grams of the corn silks to 7.0 L of boiling water. Immediately after boiling the heat was turned off and after 20 minutes solutions were filtered and allowed to cool; thereafter different doses were obtained by

dilution principle. 600 ml was the standard volume administered orally based on body weight of each subject in the normotensive (NT) and ocular hypertensive (OHT) groups. 600 ml contained 41.14 g of the CSAE and 520 mg/kg body wt. of the CSAE for the individual whose body weight is 80 kg. 300 ml of the CSAE added to 300 ml of distilled water contained 20.57 g of CSAE and 260 mg/kg body wt. of CSAE. 225 ml of CSAE added to 375 ml of distilled water contained 15.4 g of CSAE and 192.5 mg/kg body wt. of CSAE. 150 ml of CSAE added to 450 ml of distilled water contained 10.28 g of CSAE and 130 mg/kg body wt. of CSAE. 75 ml of CSAE added to 525 ml of distilled water contained 5.14 g of CSAE and 60 mg/kg body wt. of CSAE. For the various body weight of the subjects, their doses were determined by calculating the grams of CSAE for their body weight and calculating the volume of CSAE that should be added to water for each body weight.

#### *Statistical analysis*

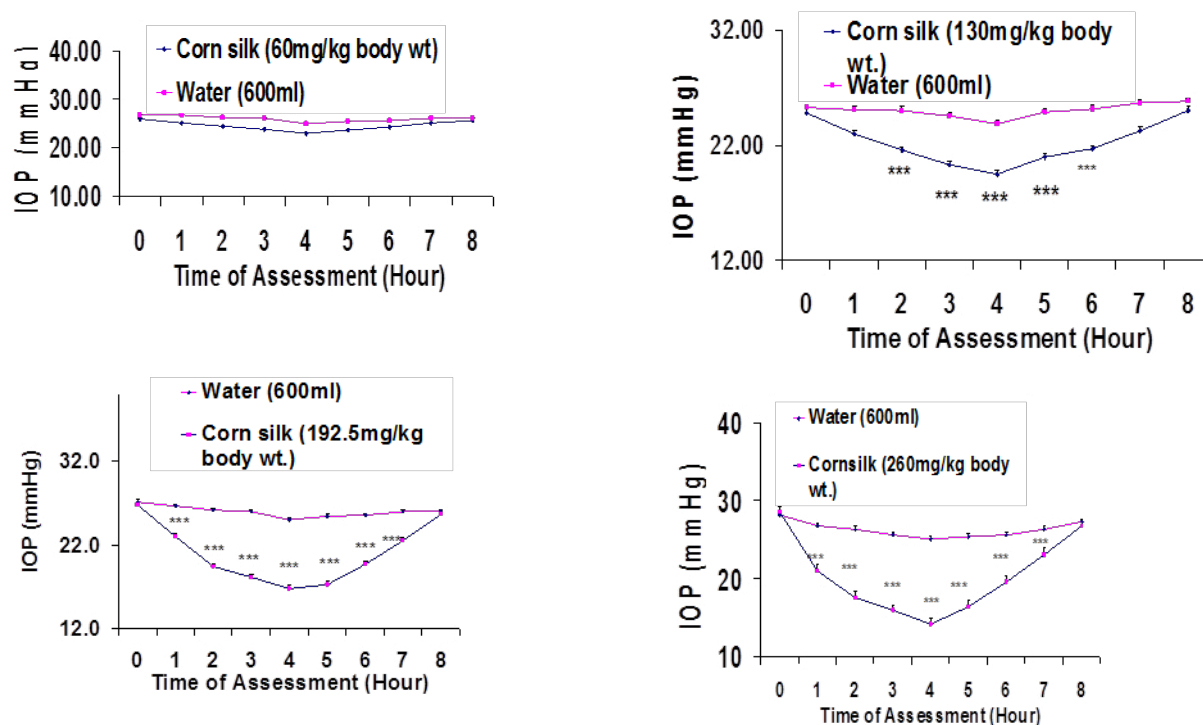
All the data in this study were analyzed with SPSS version 15. A multivariate Analysis of Variance (ANOVA) and *Post-hoc* Least Significant Difference (LSD) were used to determine if CSAE had significant effect on IOP and at what hour is the difference significant. Paired *t*-tests were employed to compare data between cornsilk aqueous extract and acetazolamide. Significance was declared when probabilities values were  $p < 0.05$ .

#### **Results**

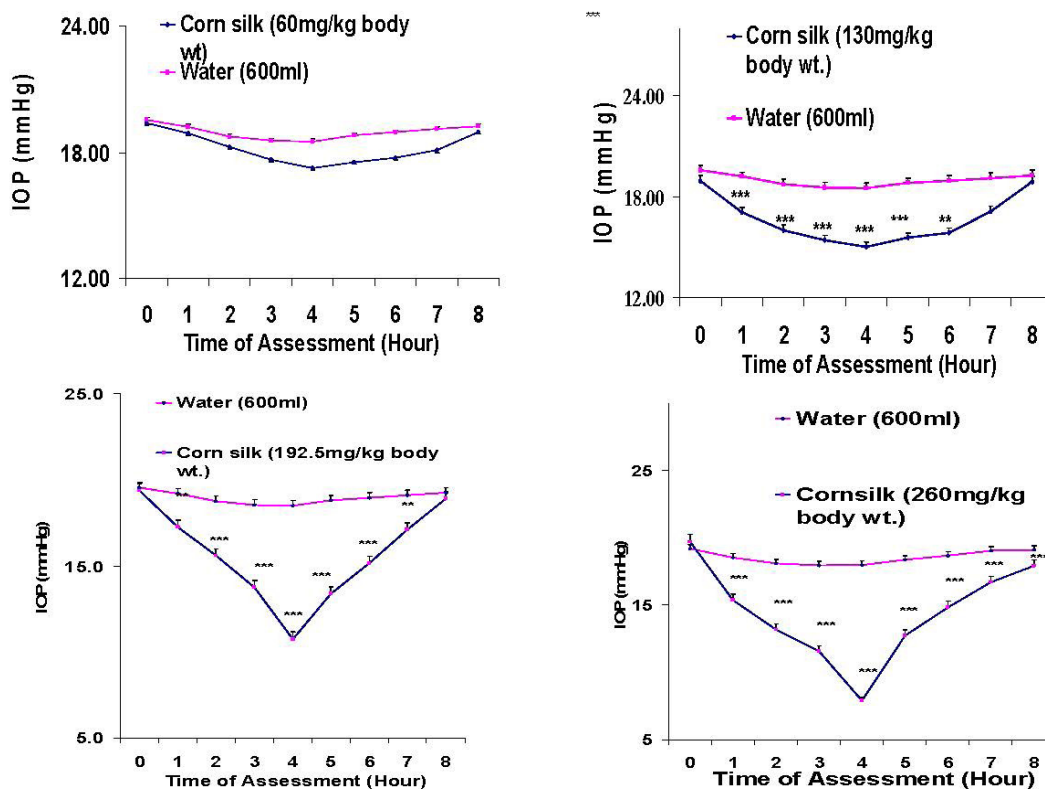
There were no significant differences in mean IOP responses of the right compared to the left eyes. Therefore, to avoid duplication, results of right eye only are presented. The varied doses of (60 mg/kg, 130 mg/kg, 192.5 mg/kg, and 260 mg/kg) body weight of CSAE labeled “W, X, Y and Z” were unmasked and their effects on IOP were compared to that of distilled water in Figure 1 for ocular hypertensives and in Figure 2 for normotensive subjects. There was a similar fall in mean IOP of the two groups and the peak of fall was after four hours of administration of CSAE, thereafter IOP rose and returned to baseline values after eight hours. The response of IOP to 60 mg/kg body wt. of CSAE compared to distilled water in the two groups was not significant, but the responses



of IOP to 130 mg/kg, 192.5 mg/kg and 260 mg/kg body wt. of CSAE compared to distilled water in the two groups were statistically significant ( $p < 0.001$ ).



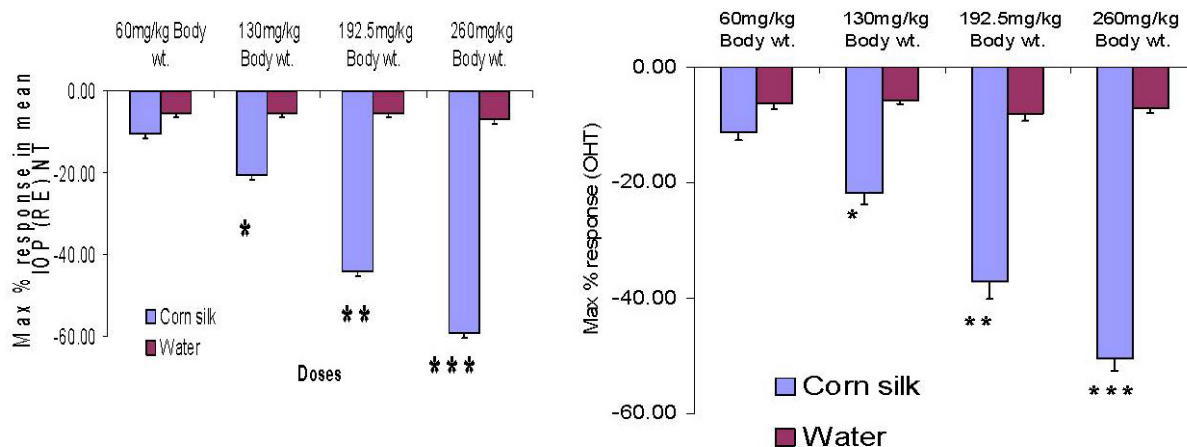
**Figure 1:** The mean difference in IOP was significant ( $p < 0.001$ ) after administering 130 mg/kg, 192.5 mg/kg and 260 mg/kg body wt. of CSAE, across different time of assessment in right eye of ocular hypertensives. Maximum fall in mean IOP was after four hours.



**Figure 2:** The mean difference in IOP was significant ( $p < 0.001$ ) after administering 130 mg/kg, 192.5 mg/kg and 260 mg/kg body wt. of CSAE, across different time of assessment in right eye of normotensives. Maximum fall in mean IOP was after four hours. (\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ )

Figure 3 shows the maximum percentage change in mean IOP of the right eye in ocular hypertensive and normotensive groups which occurred after four hours of administering CSAE compared to water (control). The maximum percentage changes in the mean IOP when 60 mg/kg, 130 mg/kg, 192.5 mg/kg, and 260 mg/kg of CSAE were administered from their control (water) in the right eye of ocular hypertensives are

( $-5.04 \pm 0.29\%$ ,  $-16.01 \pm 1.45\%$ ,  $-29.07 \pm 1.83\%$  and  $-43.34 \pm 1.33\%$ ) respectively. These values were similar to those obtained in normotensives which were: ( $-5.20 \pm 0.04\%$ ,  $-15.12 \pm 0.21\%$ ,  $-38.70 \pm 0.31\%$  and  $-52.48 \pm 0.07\%$ ) respectively. Figure 3 also showed that the response of IOP to CSAE is dose-dependent in the two groups.



**Figure 3:** The response of IOP to CSAE was dose dependent. The higher the dose of CSAE administered, the greater the fall in the percentage mean IOP in normotensives (NT) and ocular hypertensives (OHT) right eye.

**Table 1:** MABP across the different time of assessment after administering CSAE compared to water (control) in ocular hypertensive subjects (OHT).

Assessment Time (hour)	MABP (mmHg) OHT (60 mg/Kg Body wt.) (Mean $\pm$ S.E.M)	MABP (mmHg) OHT (130 mg/Kg Body wt.) (Mean $\pm$ S.E.M)	MABP (mmHg) OHT (192.5 mg/Kg Body wt.) (Mean $\pm$ S.E.M)	MABP (mmHg) OHT (260 mg/Kg Body wt.) (Mean $\pm$ S.E.M)
0 hr	87.78 $\pm$ 1.39	82.41 $\pm$ 1.19	86.57 $\pm$ 1.14	89.14 $\pm$ 1.08
1 hr	80.63 $\pm$ 1.51	79.57 $\pm$ 1.40	79.73 $\pm$ 1.49	80.26 $\pm$ 1.46
2 hrs	79.03 $\pm$ 1.53	77.03 $\pm$ 1.46	77.32 $\pm$ 1.47	74.73 $\pm$ 1.59
3 hrs	77.61 $\pm$ 1.66	73.53 $\pm$ 1.54	73.08 $\pm$ 1.57	68.88 $\pm$ 1.62
4 hrs	78.28 $\pm$ 1.58	75.96 $\pm$ 1.57	75.39 $\pm$ 1.54	73.70 $\pm$ 1.56
5 hrs	78.88 $\pm$ 1.59	76.80 $\pm$ 1.48	76.94 $\pm$ 1.51	76.71 $\pm$ 1.51
6 hrs	80.98 $\pm$ 1.60	78.84 $\pm$ 1.51	79.55 $\pm$ 1.67	79.74 $\pm$ 1.53
7 hrs	82.38 $\pm$ 1.50	81.06 $\pm$ 1.41	81.71 $\pm$ 1.60	82.35 $\pm$ 1.49
8 hrs	83.04 $\pm$ 1.56	82.81 $\pm$ 1.36	84.11 $\pm$ 1.62	84.98 $\pm$ 1.45

The mean arterial blood pressure (MABP) was calculated from the measured systolic and diastolic blood pressure of the ocular hypertensive and normotensive subjects. The MABP is the diastolic pressure plus one-third of pulse pressure. Pulse pressure is the difference between the systolic pressure and the diastolic pressure. Tables 1 and 2 showed changes in the MABP which occurred after three hours of administering varied doses of CSAE to the two groups. The maximum fall occurred after three hours of administering each dose of CSAE. The

last three doses of CSAE except 60 mg/kg body wt. gave a statistically significant difference ( $p < 0.001$ ) in the MABP of the ocular hypertensives and their normotensive control subjects.

Table 3 shows the maximum percentage changes in the MABP which occurred after three hours of administering CSAE in the two groups. The response of MABP to CSAE is also dose dependent. The higher the dose of CSAE administered the greater the fall in the MABP in ocular hypertensives (OHT) and normotensives (NT) groups.

**Table 2:** MABP across the different time of assessment after administering CSAE compared to water (control) in normotensive subjects (NT).

Assessment Time (hour)	MABP (mmHg) NT (60 mg/Kg Body wt.) (Mean $\pm$ S.E.M)	MABP (mmHg) NT (130 mg/Kg Body wt.) (Mean $\pm$ S.E.M)	MABP (mmHg) NT (192.5 mg/Kg Body wt.) (Mean $\pm$ S.E.M)	MABP (mmHg) NT (260 mg/Kg Body wt.) (Mean $\pm$ S.E.M)
0 hr	84.82 $\pm$ 1.43	85.88 $\pm$ 1.16	85.92 $\pm$ 1.24	88.70 $\pm$ 1.15
1 hr	78.82 $\pm$ 1.34	80.68 $\pm$ 1.39	79.41 $\pm$ 1.46	80.62 $\pm$ 1.54
2 hrs	77.11 $\pm$ 1.47	78.03 $\pm$ 1.44	76.62 $\pm$ 1.49	75.28 $\pm$ 1.56
3 hrs	76.14 $\pm$ 1.37	76.71 $\pm$ 1.49	72.56 $\pm$ 1.57	69.79 $\pm$ 1.51
4 hrs	77.52 $\pm$ 1.36	78.54 $\pm$ 1.42	75.03 $\pm$ 1.53	73.41 $\pm$ 1.58
5 hrs	78.01 $\pm$ 1.38	79.48 $\pm$ 1.53	76.42 $\pm$ 1.50	76.26 $\pm$ 1.47
6 hrs	78.82 $\pm$ 1.34	80.78 $\pm$ 1.47	78.53 $\pm$ 1.54	78.28 $\pm$ 1.48
7 hrs	79.74 $\pm$ 1.31	81.83 $\pm$ 1.52	80.95 $\pm$ 1.47	80.96 $\pm$ 1.44
8 hrs	82.15 $\pm$ 1.16	83.90 $\pm$ 1.52	84.64 $\pm$ 1.46	83.89 $\pm$ 1.40

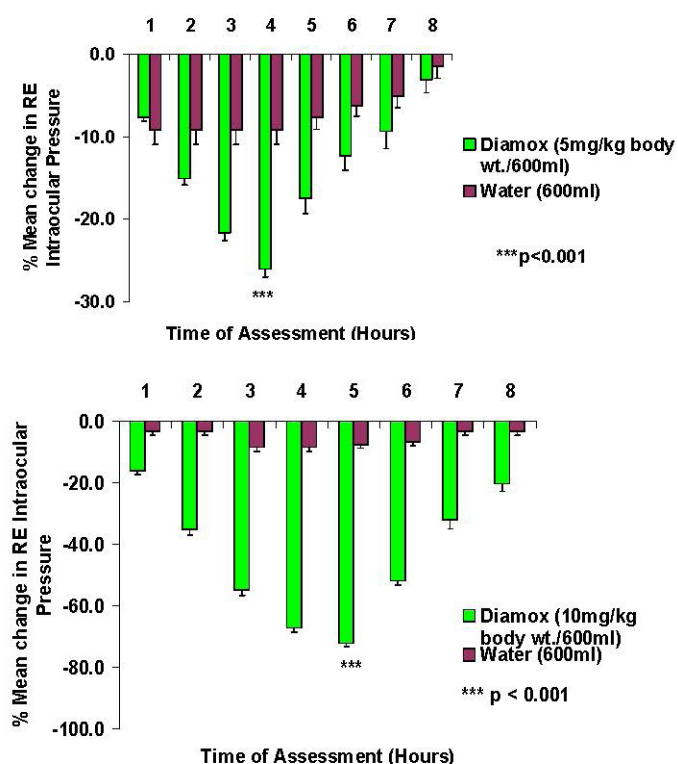
**Table 3:** Maximum percentage changes in MABP with varied doses of CSAE compared to water (control) in ocular hypertensives and normotensive subjects.

Varied doses of CSAE	Maximum % change in MABP at the peak of fall (3hrs) in ocular hypertensives	Maximum % change in MABP at the peak of fall (3hrs) in normotensives
60 mg/kg	-1.95 $\pm$ 0.06 %	-2.67 $\pm$ 0.04 %
130 mg/kg	-8.32 $\pm$ 0.35 % *	-8.79 $\pm$ 0.51 % *
192.5 mg/kg	-13.55 $\pm$ 0.58 % **	-14.16 $\pm$ 0.16 % **
260 mg/kg	-18.36 $\pm$ 0.50 % ***	-19.29 $\pm$ 0.15 % ***

Note: \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$

The response of IOP to 5 mg/kg and 10 mg/kg body weight of acetazolamide (Diamox) in the right eye across different time of assessment in ocular hypertensives is shown in Figure 4 and is statistically significant ( $p < 0.001$ ) for the two doses. Maximum percentage fall in mean IOP when 5 mg/kg body wt. of acetazolamide was compared to water was  $-16.9 \pm 0.84\%$ . While the maximum percentage fall in mean IOP when 10 mg/kg body wt. of acetazolamide was compared to water in ocular hypertensive subjects was  $-64.7 \pm 1.33\%$ .

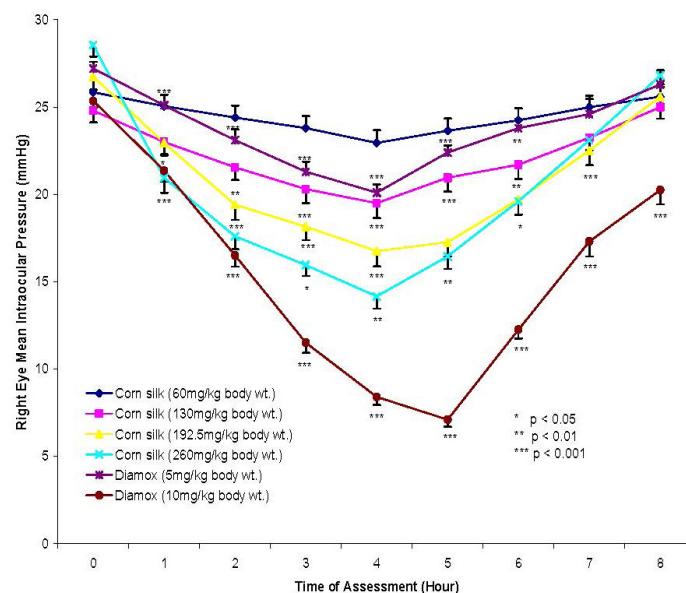
Comparisons were made between the responses of mean IOP to CSAE and acetazolamide across the different time of assessment. Figure 5 showed the IOP response to varied doses of CSAE and acetazolamide (Diamox).



**Figure 4:** The peak of fall in percentage mean IOP for 5 mg/kg of acetazolamide was after four hours but the peak of fall for 10 mg/kg of acetazolamide was after five hours of administration.

Comparison was made between the maximum percentage change in mean IOP, after administering 130 mg/kg body wt. of CSAE and 5 mg/kg body

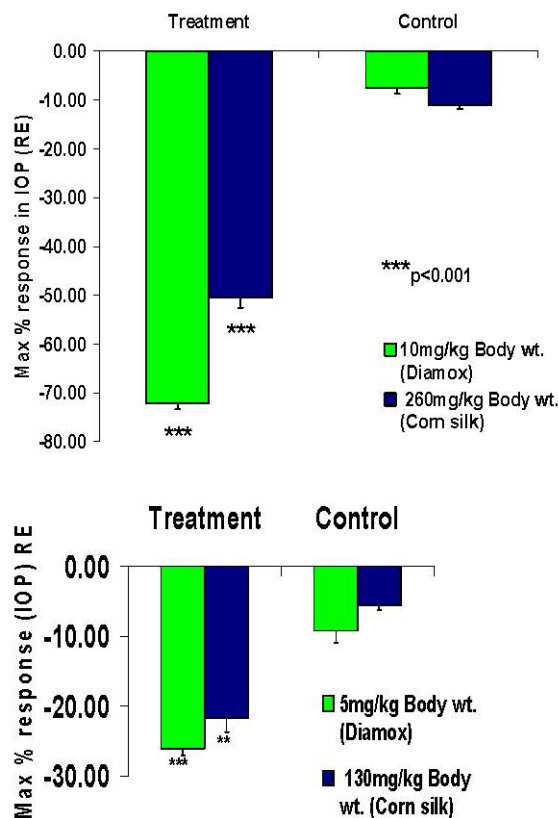
wt. of acetazolamide to ocular hypertensive subjects and there was practically no difference in maximum percentage fall in IOP of the right eye. Maximum percentage fall in mean IOP for CSAE compared to water was  $-16.01 \pm 1.45\%$  while for acetazolamide compared to water was  $-16.9 \pm 0.84\%$  as shown in Figure 6. After administering 260 mg/kg body wt. of CSAE and 10 mg/kg body wt. of acetazolamide to ocular hypertensive subjects; maximum percentage fall in mean IOP for CSAE was  $-43.34 \pm 1.32\%$  while for acetazolamide was  $-64.7 \pm 1.33\%$  in the right eye. These were statistically significant percentage falls ( $p < 0.001$ ) in mean IOP. The difference in the maximum percentage change in mean IOP with 10 mg/kg of acetazolamide compared to 260 mg/kg of CSAE was statistically significant ( $p < 0.05$ ).



**Figure 5:** Mean IOP response to varied doses of CSAE compared to acetazolamide (Diamox) in ocular hypertensives. The IOP response to 10 mg/kg body wt. of acetazolamide was most significant.

The maximum hypotensive effect of acetazolamide on MABP occurred after three hours. Compared with CSAE using *t*-test, 5 mg/kg body wt. of acetazolamide produced the same effect on MABP as 192.5 mg/kg body wt. of CSAE and 10 mg/kg body wt. of acetazolamide reduced MABP significantly ( $p < 0.003$ ) more than 260 mg/kg body wt. of CSAE in the ocular hypertensives.





**Figure 6:** Maximum percentage fall in mean IOP after administering (5 mg/kg and 10 mg/kg) acetazolamide and (130 mg/kg and 260 mg/kg) CSAE compared to water (control) in the right eye of ocular hypertensive subjects.

**Table 4:** Maximum % response of MABP after administering acetazolamide and CSAE to OHT

Varied doses of CSAE and ACETAZOLAMIDE	Maximum % response of MABP after 3hrs of administering CSAE and DIAMOX (Mean± SEM )
60 mg/kg body weight of CSAE	1.95± 0.06%
130 mg/kg body weight of CSAE	8.32± 0.35% *
192.5 mg/kg body weight of CSAE	13.55± 0.58% **
260 mg/kg body weight of CSAE	18.36± 0.50%***
5 mg/kg body weight of ACETAZOLAMIDE	12.62± 0.22% **
10 mg/kg body weight of ACETAZOLAMIDE	21.34± 0.50% ***

\* $p<0.05$ ,

\*\* $p<0.01$ ,

\*\*\* $p<0.001$

## Discussion

The results of this study showed that CSAE lowered intraocular pressure significantly in ocular hypertensives and in their normotensive subjects. The peak of fall in mean IOP was after four hours of administering CSAE. This was preceded by the peak of fall in MABP which occurred after three hours of administration. The hypotensive effects of CSAE on IOP and MABP depended largely on dosage administration. The result of this study on the hypotensive effect of CSAE on MABP agrees with the study of Mirza<sup>5</sup>, (2004). In 2004 she studied the effect of various doses of ethanolic extract of *Zea mays* Linn on blood pressure in rats. Her study showed that, an increase in the dose of *Zea mays* ethanolic extract caused an increase in percentage fall in MABP.

There are reported studies to show that changes in systemic blood pressure results in direct changes in IOP in humans and animals studies. Previously published studies<sup>9-12</sup> has confirmed an association of blood pressure with IOP. Vaajanen *et al*<sup>10</sup> (2008) evaluated the relationship between BP and IOP using hypertensive rats and the results suggested a positive relation between BP and IOP. Castejon *et al*<sup>11</sup> (2010) studied the effect of acute increase in blood pressure on intraocular pressure in humans and found a linear relationship between BP and IOP variations. They concluded that isometric exercise in humans shows that IOP rises significantly and rapidly with kinetics close to those of BP, and the two values are linearly related. Leske *et al*<sup>12</sup> (1996) carried out a case-control study which evaluated systemic hypertension as one of the risk factors for open-angle glaucoma and high intraocular pressure (IOP), their results confirmed an association of blood pressure with IOP. They concluded that raised systemic blood pressure preceded raised IOP in a given patient. In this study it was observed that the fall in MABP preceded the fall in mean IOP.

Comparison of hypotensive effect of CSAE and acetazolamide on IOP revealed that 5 mg/kg body wt. of acetazolamide produced practically the same hypotensive effect on IOP as 130 mg/kg body wt. of CSAE. Likewise 5 mg/kg body wt. of acetazolamide produced same hypotensive effect on MABP as 192.5 mg/kg body wt. of CSAE. It was observed in this study that a few of the subjects reported various side effects such as “tingling” sensation in the extremities,

nausea, vomiting and diarrhea with administration of 10 mg/kg body wt. of acetazolamide. These side effects were not reported by these subjects with administration of even the highest dose of CSAE used in this human study. Researchers<sup>2, 19, 20</sup> have reported that the principal constituents of corn silk are harmless therefore it can be concluded that corn silk tea is as safe as other widely used green tea. Previous studies of toxicity assay of corn silk extract by Velazquez *et al*<sup>2</sup> (2005) reported that no toxic effects or deaths were observed with doses as high as 1.0, 2.0 and 4.0 g/kg body wt. of corn silk extract administered during 72 hours observation in 50 male and female mice. Likewise the toxicological studies of ethanolic extract of *Zea mays* Linn on 24 albino rats by Mirza<sup>21</sup> (2004) showed no toxic effects or gross histological changes in vital organs of the rats when autopsy was done after six weeks of oral administration of 2.5, 5.0, and 7.5 g/kg body wt. of *Zea mays* ethanolic extract.

The hypotensive effect of 10 mg/kg body weight of acetazolamide on MABP was significantly higher than 260mg/kg body wt. of CSAE; therefore acetazolamide may not be a drug of choice for patients whose systemic blood pressure will not require a significant fall in the course of therapy for ocular hypertension.

## Conclusion

The study has shown that CSAE lowered IOP significantly in hypertensive human eyes and in their normotensive controls. This reduction is dose-dependent and may be as a consequence of a fall in blood pressure which preceded the fall in IOP or may be as a result of some unknown phytochemical constituents present in the CSAE. The study also showed that 130 mg/kg body wt. of CSAE has the same IOP lowering effect as 5 mg/kg body wt. of acetazolamide and 130 mg/kg body wt. of CSAE has a far less lowering effect on MABP than 5 mg/kg body wt. of acetazolamide. Since 5 mg/kg body wt. of acetazolamide is the recommended dose<sup>13</sup> for management of ocular conditions such as glaucoma and ocular hypertension when the need arises, then 130 mg/kg body wt. of CSAE may serve as an alternative therapy to 5 mg/kg body wt. of acetazolamide since it has the same IOP lowering effect and a less hypotensive effect on MABP. Corn silk is relatively cheap, affordable and innocuous therefore it may be

an alternative traditional treatment to acetazolamide. This may be of great benefit in African society considering the prevalence of glaucoma and the cost of conventional treatment.

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## References

1. Fazilatun N, Zhari I, Nornisah M. Antimicrobial activities of extracts and flavonoid glycosides of Corn Silk (*Zeamays* L). *Intl J Biotech Wellness Indus* 2012 **1** 115-121.
2. Velazquez DVO, Xavier HS, Batista JEM, Castro-Chavas C. *Zea mays* L. Extracts modify glomerular function and potassium urinary excretion in conscious rats. *Phytomedicine* 2005 **12** 363-369.
3. Grases F, March JG, Ramis M, Costa-Bauza A. The influence of *Zea mays* on urinary risk factors for kidney stones in rats. *Phytotherapy Res* 1993 **7** 146-149.
4. Jianyou G, Tongjun L, Linna H, Yongmei L. The effects of corn silk on glycaemic metabolism. *J Nutrition Metabolism* 2009 **6** 47-52.
5. Mirza M. Hypotensive activity of ethanolic extracts of *Zea mays* Linn (corn silk) in rats. . In: *Diuretic activity of certain plants used in traditional system of Medicine*. A PhD Thesis deposited in Pakistan Research Repository, Higher Education Commission Pakistan. 2004 pp 107-114.
6. Ira SS. Aqueous humour dynamics. *Am J Optom Physiol Opt* 1977 **53** 202-205.
7. Kanski J J. Glaucoma. *Clinical Ophthalmology: A Systemic Approach*, 5<sup>th</sup> ed., Butterworth-Heinemann, Elsevier Science Limited, 2003 pp 193-198.
8. Sembulingam K, Sembulingam P. Intraocular pressure and Glaucoma. *Essentials of Medical Physiology*, 5<sup>th</sup> ed., Jaypee Brothers Medical Publishers, 2010 pp 930-934.
9. Klein BE, Klein R, Knudtson MD. Intraocular pressure and systemic blood pressure: longitudinal perspective: the Beaver Dam Eye Study. *British J Ophthalmol* 2005 **89** 284-287.
10. Vaajanen A., Mervaala E, Oksala O, and Vapaatalo H. Is there a relationship between blood pressure and intraocular pressure? An experimental study in hypertensive rats. *Curr Eye Res* 2008 **33** 325-332.
11. Castejon H, Chiquet C, Savy O, Baguet JP, Khayi H, Tamisier R, Bourdon L, Romanet JP. Effect of acute increase in blood pressure on intraocular pressure in pigs and humans. *Invest Ophthalmol Vis Sci* 2010 **51** 1599-1605.
12. Leske MC, Warheit-Roberts L, Wu SY. Open-angle glaucoma and ocular hypertension: the Long Island Glaucoma Case-control Study. *Ophthalmic Epidemiol* 1996 **3** 85-96.
13. Becker B. Decrease in intraocular pressure in man by a carbonic anhydrase inhibitor, Diamox: a preliminary report. *Am J Ophthalmol* 1954 **37** 13-15.

14. Friedenwald JS. Current studies on acetazoleamide (Diamox) and aqueous humor flow. *Am J Ophthalmol* 1955 **40** 139-147.
15. Epstein DL, Grant WM. Carbonic anhydrase inhibitor side effects. *Arch Ophthalmol* 1977 **95** 1378-1382.
16. Heller I, Halevy J, Cohen S, Theodor E. Significant metabolic acidosis induced by acetazolamide: not a rare complication. *Arch Intern Med* 1985 **145** 1815-1817.
17. Howlett SA. Renal failure associated with acetazolamide therapy for glaucoma. *South Med J* 1975 **68** 504-506.
18. Higenbottam T, Ogg CS, Saxton HM. Acute renal failure from the use of acetazolamide (Diamox). *Postgrad Med J* 1978 **54** 127-128.
19. Iwuagwu OF, Megwas UA, Irem-Azode A. A study on the gender difference in the prevalence of glaucoma. *J Afr Council Optom* 2007 **1** 104-110.
20. Loomis TA. *Essentials of Toxicology*, 3<sup>rd</sup> ed. Philadelphia Lea and Febiger 1978 pp.18- 203.
21. Mirza M. Toxicological studies of ethanolic extracts of *Zea mays* Linn (corn silk) in rats. In: *Diuretic activity of certain plants used in traditional system of medicine*. A PhD Thesis deposited in 2007 at the Pakistan Research Repository, Higher Education Commission Pakistan. 2004 pp 58-62.7.