The Effect of Anabasis articulata Stems Extract on Lowering Intraocular Pressure in the Glaucoma Rat Model(Conference Paper)# Waleed K. Abdulsahib*

9th scientific conference conference sponsored by College of Pharmacy, University of Baghdad 25-26 August 2021 *Department of Pharmacology and Toxicology, College of Pharmacy, Al-Farahidi University, Baghdad, Iraq. Abstract

High intraocular pressure (IOP) is a recognized risk factor for glaucoma and optic nerve injury, and it is one of the primary causes of vision loss globally. Anabasis articulata (AA) is a desert plant found in Iraq. The extract of AA is used for the treatment of diabetes, fever, eczema, and kidney infections. The study aims to evaluate the antioxidant effect of methanol extract of AA on intraocular pressure in the glaucoma rat model. Fortytwo rats were allocated into seven groups, each with six animals; group 1 (normal), group 2 (control), in which animals were induced to have elevated IOP by betamethasone suspension injection, groups 3,4 and 5 for evaluating the effect of 50,100 and 150 mg/kg/day of the tested extract, respectively, and the remaining two groups (group 6 and 7) for evaluating oral acetazolamide and topical timolol 0.5% respectively. Betamethasone was used for the induction. Measure the IOP every 2 days for 2 weeks. The daily dose of AA extract (50 mg/kg/day) for 6 days significantly reduces intraocular pressure (p < 0.05), from (34.23 ± 0.58) to (32.83 ± 1.38) mmHg when compared with the control group. In group 4, IOP decreased significantly from (35.5 ± 1.37) to (31.35 ± 0.40) mmHg (p < 0.05) after 1 week of treatment. In group 5, the significant (p < 0.001) IOP reduction from (35.66±0.39) to (31.88 ± 0.74) mmHg started on day 6 and continued until the end of the experiment, reaching (24.53 ± 0.53) mmHg (p < 0.001). The antioxidant and anti-angiogenic properties of AA make it a promising adjuvant treatment for glaucoma.

Keywords: Anabasis articulata, glaucoma, antioxidant, extract, betamethasone, intraocular pressure. تأثير مستخلص سيقان ال Anabasis Articulata في خفض ضغط العين لداء الزرق المستحدث في

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ارتفاع ضغط العين هو عامل خطير يؤدي للإصابة بداء الزَرَق وكذلك إصابة العصب البصري ، ويعتبر ارتفاع ضغط العين أحد الأسباب الرئيسية لفقدان البصر على مستوى العالم .

العجرم (Anabasis articulata) هو نبات صحر اوي موجود في العراق ويستخدم لعلاج مرض السكري والحمى والأكزيما وكذلك التهابات الكلى. الهدف من الدراسة هو تقييم التأثير المضاد للأكسدة لمستخلص الميثانول لنبتة العجرم على ضغط العين المستحدث في الجرذان. تم تقسيم اثنين وأربعين جرذا إلى سبع مجموعات ، كل مجموعة تحوي ستة حيوانات: المجموعة ١ (طبيعة) ، المجموعة ٢ (مجموعة التحكم) ، حيث تم استحداث ضغط العين المرتفع في هذه المجموعة عن طريق حقنَّ معلَّق البيتاميثازون ، المجموعة الثالثة والرابعة والخامسة استخدمت لتقييم تأثير ، ٥ و ١٠٠ و ١٥٠ ملغم / كغم / يوميا من المستخلص على التوالي ، والمجمو عتان المتبقيتان (المجموعة ٦ و ٧) لتقييم تأثير الأسيتاز ولاميد الفموي والتيمولول الموضعي ٥,٠٪ على التوالي. تم قياس ضغط العين كل يومين ولمدة أسبوعين. أظهرت نتائج الجرعة اليومية من المستخلص (50 مجم / كغم / يوم) ولمدَّة ٦ أيام انها تقال بشَّكل ملحوظ من ضغط العين (p< 0.05) ، حيث انخفض الضغط من (٣٤,٢٣ ± ٥،٨٣) إلى (٣٢,٨٣ ± ٨ /١,١) مم زئبَّق بالمقارنة مع المجموعة الضابطة. وكذلك انخفض الصَّغط في المُّجموعة الرابعة بشكل ملحوظ من (٥,٥٥ ± ٣٧,١) إلى (٣١,٣٥ ± ٤٠,٠) مَم زَنبق (p < 0.05) p) بعد أسبوع من العلاج. وفي المجموعة ٥ ، بدأ الانخفاض المعنوي (p < 0.001) للضُغط من (٠,٣٩ ± ٣٥,٦٩) إلى (٣١,٨٨ ± ٢٤,٥٣) مم زئبق في اليوم السادس واستمر حتى نهاية التجربة ، ليصل إلى (٢٤,٥٣ لَـ ٣،٥,٠) ممّ زئبق(p< 0.001) . استنتج من الدراسة ان الخصائص المضادة للأكسدة والمضادة لتولد الأوعية لنبتة العجرم تجعله علاجًا مساعدًا واعدًا لداء الزرق.

الكلمات المفتاحية: العجرم ، مضاد الاكسدة،ضغط العين، البيتاميثازون ، داء الزرق.

Introduction

High intraocular pressure (IOP) is a recognized risk factor for glaucoma and optic nerve injury, ⁽¹⁾, and it is one of the most common causes of blindness in the world (2). Glaucoma affected approximately 64.3 million people worldwide in 2013, putting them at risk of blindness. This number is expected to rise to 76.0 million in 2020 and 111.8 million in 2040⁽³⁾. The buildup of aqueous humor (AH) in the anterior chamber, which is mostly caused by the eye's failure to discharge aqueous fluid effectively, results in a high IOP⁽⁴⁾. Blood flowing through the ciliary body's arteries is the main cause of aqueous humor. In the posterior chamber, the ciliary body between the iris and lens

secretes aqueous humor, the fluid of this region

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moves from the posterior to the anterior chamber between the cornea and the iris before being emptied from the eye at the iridocorneal junction⁽⁵⁾.

Increased IOP is thought to be a chief risk factor for the gradual loss of retinal ganglion cells (RGCs).

According to previous research, the longer the IOP rise, the more severe the optic nerve consequences ⁽⁶⁾. Medication, surgery, and laser therapy are all common glaucoma treatments. Ocular hypotensive medications either reduce or improve trabecular meshwork, Schlemm's canal, and uveoscleral outflow⁽⁷⁾. On the other hand, most clinical medications can produce adverse effects, and natural plant extracts may provide an alternate medication source⁽⁸⁾.

Herbal medicines have grown in importance as a subject of study for health care around the world ⁽⁹⁾. Anabasis articulata (AA), also known as Ajrem, Eshnan, or Berry Bearing Glasswort, is a desert plant found in Iraq, Algeria, Syria, and Egypt. In folk medicine, AA is used to treat diabetes, fever, eczema, and kidney infections⁽¹⁰⁾. Many studies after the phytochemical screening on AA discovered the availability of coumarins, anthraquinones, unsaturated sterols or triterpenoids, alkaloids, saponin, phenolics, flavonoids, iridoids, and tannins as active components that may have many pharmacological effects (11). Additionally, recent studies have shown that the main ingredients identified by Gas chromatography-mass spectrometry (GC-MS) of methanol extracts are tannins, saponins, flavonoids, phenolics, and alkaloid compounds (12). AA has recently become the focus of research due to the diversity of its composition and effectiveness. However, the scientific literature on the beneficial effects of AA on glaucoma patients is limited. Thus, the goal of this study is to evaluate the effect of AA on intraocular pressure in a glaucoma rat model.

Materials and Methods

Preparation of plant extract

Anabasis articulata (Forssk.) Moq. (Amaranthaceae) stems were obtained from a Baghdad-based herbal apothecary and authenticated by Assistant Professor Dr. Ibrahim Salih Abbas plants. (Ph.D. Medicinal pharmacognosy Department, College of Pharmacy, A1-Mustansiriyah University, Iraq). The plant's specimen (99334) was deposited in the Herbarium of Al Farahidi University- Faculty of Pharmacy. The maceration process (cold process) was carried out by soaking plant stems (powdered) in a container stopped with 70% v/v ethanol and allowing for 72 hours of frequent turmoil at room temperature in the bath, after which the crude material was extracted using a vacuum-concentrated rotary evaporator and kept in a dry bottle and firmly screened. **Experimental** animals

Forty- two Sprague Dawley rats of both sexes, aged about 8 months were used in the experiment. Animals maintain a 12-hour light/dark cycle and are kept at 25 ± 3 C°. Rats were free to access clean water ad libitum and rodent diet. The institutional animal care and use committee of Al-Farahidi University, Pharmacy College approved the research protocol, and the conduction of the work was performed according to the association of research in vision and ophthalmology (ARVO). Group 1: animals were injected 0.2 ml distilled water Subconjunctivally (SO) and this group is considered a normal group. Group 2: animals were induced to have elevated IOP by 0.2 ml betamethasone suspension SO injection. Groups 3,4, and 5: these groups were used to evaluate the effect of 50,100, and 150 mg/kg/day of the herb, respectively. The remaining two groups (groups 6 and 7) were used to evaluate oral acetazolamide (at a dose of 78 mg/kg/day) and topical timolol 0.5 percent (twice daily), respectively, and these groups were considered positive. Asteroid suspension of 0.03 ml betamethasone containing a mixture of (betamethasone dipropionate 2 mg and betamethasone sodium phosphate 5mg) / ml was used for induction of elevated IOP. (Diprofos*, MSD)⁽¹³⁾. Syringe gauge 30 was used (Pic, UK) for subconjunctival steroids. After injection, one drop of antibiotic Ofloxacin (Pioneer, Iraq) was used to prevent future infections of the eye (14). In all animal groups, the right eye was used to induce chronic glaucoma models by weekly SO betamethasone for 4 weeks⁽¹⁵⁾, and the left eye was used to evaluate whether oral test extracts had any adverse effects on the eyes. After 7 days of induction, rats with an IOP increase of more than 32 mmHg were included in the test group. AccuPen Handheld Tonometer (Accutome, USA) is used to measure intraocular pressure every 2 days. All readings were taken in the morning (10 am) to exclude diurnal changes in IOP. Three doses of methanol extract of AA stems (50, 100, and 150 mg/dose/day) were orally administered by gastric tube gavage for 14 days to study the effect of the extract in controlling elevated IOP.

Bodyweight was measured every week to study the adverse effect of steroids and the potential beneficial effect of AA. A blood sample was withdrawn before and after treatment with AA to measure the serum level of Lactate dehydrogenase (LDH), malondialdehyde (MDA), glutathione peroxidase (GP), catalase (CAT), and superoxide dismutase (SOD).In previous studies, the safety of the extract was studied, and the LD 50 was even calculated. The doses used have no toxic effects. *Statistical analysis*

All data are represented in this study as mean± standard deviation(SD) (6 animals for each group). Bodyweight changes, serum level of the biochemical parameters, and IOP were investigated using one-way analysis of variance (ANOVA) using version 23 of IBM SPSS and then multiple comparison tests of type T- Tukey. Statistical significance is defined as a P-value < 0.05.

Results

Bodyweight effect in a steroid-induced model of glaucoma

As displayed in a table (1) and figure 1, a significant decrease in mean body weight (p < 0.05) was detected in the second group (control group), but not in the first group 1 (normal group). After 7 days of oral intake of 100 mg of the tested extract, a

significant increase (p < 0.05) in average body weight was observed in group 4 compared to group 2, as shown in table (1). Group 5 shows a significant (p < 0.05) increase in body weight after 14 days of treatment compared to the control group. The weight of animals in the fourth group after 2 weeks increased significantly (p < 0.05) when compared to the third group. Although the administration of 150 mg (group 5) resulted in a greater increase in body weight, there was no significant difference when compared to group 4 (p < 0.05). Acetazolamide did not affect body weight when compared to the control group (p=0.88).

Table 1. Effect of *Anabasis articulata* extracts on the body weight in the betamethasone-induced chronic glaucoma model.

Groups	Bodyweight (gram)					
	Before induction	After 7 days of induction	After 14 days of induction			
Normal	216.33±2.25	227.83± 5.03	252.83± 4.62			
Control	212.83± 1.94	196.66± 2.80 *	207.33± 1.75 *			
AA treatment 50 mg	213.66± 3.38	199.83±4.79	208.16± 2.13			
AA treatment 100 mg	217.83 ± 5.41	210.50± 6.74 **	218.83± 6.64 **			
AA treatment 150 mg	219.83 ± 3.71	206.00± 7.21	215.00± 4.47 **			
Acetazolamide	217.16 ± 4.53	202.66±4.08	208.83± 3.76			

results are denoted as mean \pm standard deviation (n=6). * p < 0.05 means there is a significant difference compared with the normal group, ** p < 0.05 means there is a significant difference compared with the control group. AA: *Anabasis articulate*

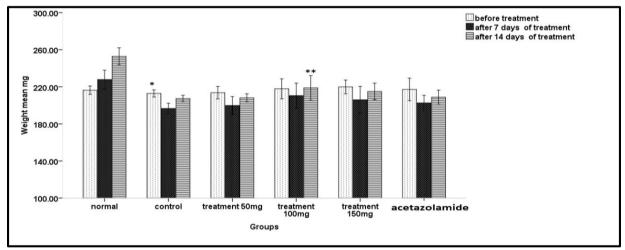


Figure 1. The effect of induction agent (betamethasone suspension), *Anabasis articulata* (50, 100, and 150 mg/ kg/ day) and (50 mg/kg/day) for Acetazolamide on body weight (n= 6). * p less than 0.05 denote a significant difference when compared to the normal group, **p less than 0.05 denote a significant difference compared to the control group. Data represented as mean \pm SD. Error bar represents the standard deviation of the mean.

Effect of Anabasis articulata on IOP

Subconjunctival injection of steroids in the second group of rats increased the intraocular pressure from (18.75 ± 0.44) to (34.58 ± 0.97) mmHg. Compared with the normal group, these changes are significant (p < 0.05), as shown in figure 2. One week later, the increase in intraocular pressure in the control group was still significant (p< 0.001) (34.76\pm0.9 mmHg). In addition, the intraocular pressure at the end of the study was still high $(35.01\pm0.69 \text{ mmHg})$ (p<0.001) compared to the

normal group (18.66±0.45). Figure 2 shows the daily dose of AA extract (50 mg/kg/day) for 6 days significantly reduces intraocular pressure (p < 0.05), from (34.23± 0.58) to (32.83± 1.38) mmHg when compared with the control group. The maximum drop in intraocular pressure (28.51±0.52 mmHg) (p<0.05) was reached on day 14. In group 4, IOP decreased significantly from (35.5±1.37) to (31.35±0.40) mmHg (p < 0.05) after 1 week of treatment. On day 14, there was the greatest pressure reduction (24.76±0.69), which was significant

compared with the control group (p < 0.001), as shown in figure 3. On days 6 and 12, group 4 produces a significant IOP reduction when compared to group 3 (p < 0.05). In group 5, the significant (p< 0.001) IOP reduction from (35.66±0.39) to (31.88±0.74) mmHg started on day 6 and continued until the end of the experiment, reaching (24.53±0.53) mmHg (p< 0.001), as shown in figure4. No superiority of 150 mg over 100 mg. Positive control groups: group 6 (acetazolamide) and group 7 (timolol) significantly reduced intraocular pressure (p < 0.001) from (35.31±0.77) to (30.58 ± 0.49) ; from (36.03 ± 0.49) to (28.11 ± 0.64) mmHg respectively.as presented in figure 5 and 6. Figure 7 shows that all doses of AA reduce the IOP significantly after 2 weeks of treatment. Finally, acetazolamide and timolol were more effective in reducing IOP during the study period (p < 0.05) compared to all doses of the extract.

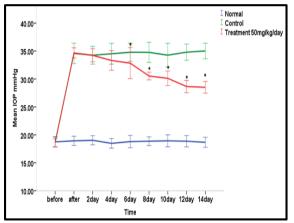


Figure 2. Effect of *Anabasis articulata* stems extract (50 mg/kg/day) on mean IOP in a chronic glaucoma model in rats. *p < 0.05 means there is a significant difference compared with the control group.

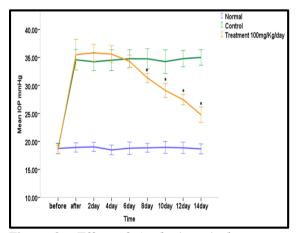


Figure 3. Effect of *Anabasis articulata* stems extract (100 mg/kg/day) on mean IOP in a chronic glaucoma model in rats. p < 0.05 means there is a significant difference compared with the control group.

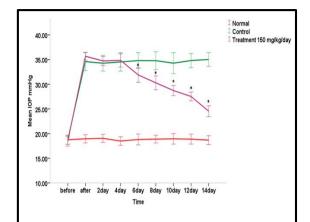


Figure 4. Effect of *Anabasis articulata* stems extract (150 mg/kg/day) on mean IOP in a chronic glaucoma model in rats. p < 0.05 means there is a significant difference compared with the control group.

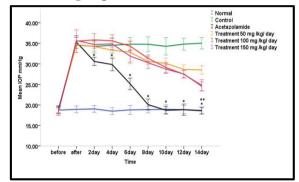


Figure 5. Comparison between different doses of *Anabasis articulata* stems extract and topical timolol (0.5%) on mean IOP in a chronic glaucoma model in rats. *p < 0.05 means there is a significant difference compared with the control group, **p < 0.05 means there is a significant difference compared with groups 3,4, and 5.

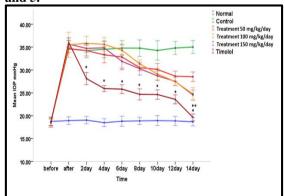


Figure 6. The comparison effect between different doses of *Anabasis articulata* stems extract and topical timolol (0.5%) on mean IOP in a chronic glaucoma model in rats. *p < 0.05 means there is a significant difference compared with the control group **p < 0.05 means there is a significant difference start difference sta

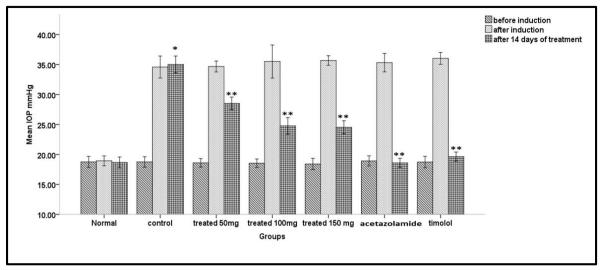


Figure 7. The comparison effect between different doses of *Anabasis articulata* stems extract, acetazolamide, and topical timolol (0.5%) on mean intraocular pressure after 2 weeks of treatment in a chronic model of glaucoma in rats. *p < 0.05 means there is a significant difference compared with the normal group, **p < 0.05 means there is a significant difference compared with the control group.

Effects of Anabasis articulata extract on serum levels of some oxidative stress parameters.

Table (2) shows the effect of 3 doses of the extract on the serum levels of five biological parameters in steroid-induced glaucoma after 2 weeks of treatment. In group 2 (control) the serum levels of LDH & MDA increased significantly (p<0.05), whereas those of GP, CAT, and SOD decreased significantly (p<0.05) when compared to the normal group. After 2 weeks of oral administration of extract in all treatment groups (3,4

and 5), led to a trend of significantly decreased in the serum levels of LDH and MDA and a significant increase in the serum level of GP, CAT, and SOD (p<0.05) compared to control group. Compared with the third group, the second group showed the preferred effect in reducing the levels of LDH and MDA and increasing the levels of GP, CAT, and SOD (p<0.05). In addition, the antioxidant activity of the fourth group was more significant than that of the fifth group (p<0.05), resulting in the effect of the fourth group being better than that of the fifth group.

Table 2. The effect of Anabasis articulata extract on serum levels of biological parameters in a chronic model
of glaucoma in rats after 2 weeks of treatment.

Groups	LDH	SOD (U/mg)	MDA (mmol/	CAT	GP
	(U/L)		mg)	(U/ mg)	(U/ mg)
Normal	1769.94 ± 12.70	116.35 ± 1.77	1.17 ± 0.130	65.73 ± 0.41	1.15 ± 0.022
Control	$2319.42 \pm 6.94^*$	$71.14 \pm 0.84^{*}$	$1.43 \pm 0.031^*$	$25.47 \pm 0.15^{*}$	$0.56 \pm 0.017^{*}$
Treatment 50 mg	1320.26± 12.53 ^a	86.32± 0.53 ^a	1.23± 0.037 ^a	30.77± 0.28 ^a	0.64± 0.036 ^a
Treatment 100 mg	1486.91±7.15 ac	101.48± 1.32 ac	1.33 ± 0.037	35.49± 0.33 ac	0.95 ± 0.017 ac
Treatment 150 mg	1416.41±3.66 ad	95.99± 1.38 ad	1.14 ± 0.034 ad	31.44± 0.22 ^{ad}	0.83 ± 0.020 ad

Results are denoted as mean \pm standard deviation (n=6). * p < 0.05 denote a significant difference when compared to the normal group, ^a p < 0.05 denote a significant difference when compared with the control group, ^c p<0.05 denote a significant difference when compared with the 50 mg treatment group. ^d p<0.05 denote a significant difference when compared with the 100 mg treatment group. LDH: lactic dehydrogenase; SOD: superoxide dismutase; MDA: malondialdehyde; CAT, catalase; GP, glutathione peroxidase.

Discussion

Glaucoma is the world's second-largest reason of blindness, in which the optic nerve and RGCs gradually degenerate ⁽¹⁶⁾. High IOP is still the most well-recognized risk factor for glaucomatous optic nerve injury, even though other variables may play a role in glaucoma. ⁽¹⁷⁾. The effect of AA extract on IOP in a rat model of steroid-induced glaucoma was investigated in this work. Steroid-induced glaucoma resulted in a noteworthy elevation in IOP and a drop in mean rat weight, according to the findings. Steroid-induced IOP elevation is said to be dose-dependent and associated with known systemic adverse consequences such as weight loss⁽¹³⁾. Although weight gain is a common side effect of glucocorticoids in humans⁽¹⁸⁾, irritation of the stomach is moreover prevalent, which could lead to appetite and weight loss in rats⁽¹⁸⁾. However, after 14 days of AA administration, bodyweight loss slightly recovered when compared to the control group. IOP increased above 32 mmHg in the steroid groups,

indicating that the glaucoma model was efficiently produced. The experiment results displayed that all doses of AA reduce IOP noticeably after 2 weeks, with 100 mg/kg/day being the most effective. The control group had considerably higher LDH and MDA levels and marked lowering effects on SOD, GP, and CAT levels, indicating that the glaucoma rats were under a lot of oxidative stress. After fourteen days of treatment, 50 mg of AA administered daily caused an apparent decrease in LDH and MDA levels and a momentous rise in SOD, GP, and CAT levels in the experimental groups. Groups 4 and 5 demonstrated a similar trend, but with greater antioxidant effects than group 3. The experimental results show that AA extract increased the glaucoma rats' intrinsic antioxidant capabilities.

In addition to laser treatment and surgical procedures, the most frequent treatment method for glaucoma is lowering IOP with medical therapy. To reduce IOP, medical therapy employs two mechanisms: boosting outflow drainage and inhibiting aqueous humor formation. ⁽¹⁹⁾. According to reports, antioxidant pretreatment markedly reduces the influence of oxidative stress on the trabecular meshwork (TM) (20). It has been reported that AA has a high clearance rate of free radicals of 2',2'-diphenyl-1-picrahydrazyl (DPPH)^(21,22). The high content of tannins, saponins, flavonoids, phenolics, and alkaloid compounds in AA is attributed to its antioxidant activity (21). There is growing evidence that reactive oxygen species be a factor in the pathogenesis of primary open-angle glaucoma.⁽²³⁾. The association between antioxidant component content, in vivo / in vitro antioxidant abilities, and IOP-reducing effect suggests that oxidative stress is important in the progress of IOP elevation and glaucoma-related lesions $^{(20)}$. TNF- α is a pro-inflammatory cytokine with antiinflammatory and neuroprotective properties. Furthermore, this cytokine has two different receptors: TNF-R1 and TNF-R2, and its activity varies depending on which of these two receptors is activated. Stimulation of the first receptor results in the recruitment of immune cells, which causes inflammation, as well as the activation of enzymes that cause oxidative stress (18). The second, on the other hand, support tissue homeostasis and promotes tissue regeneration, and so plays an active role in neuroprotection ⁽²⁰⁾. This result requires stimulation of the NFkB pathway by TNF-R2(24), which translocates into the nucleus of cortical neurons and likely protects against excitotoxicity. TNF-, on the other hand, has been proven in vitro to trigger RGC cell death by activating caspase-3 and -8 or by oxidative stress produced by mitochondrial malfunction. ⁽²⁵⁾. The increment in ROS production can also result in the death of the neuronal cell. The ROS that activates the NFkB pathway in glial cells induces inflammation, which then stimulates NADPH oxidase, which produces more ROS, creating a vicious cycle. As a result of the herbs' antioxidant activity, this vicious cycle will be broken. Based on our findings, the antioxidant effect of AA could be linked to reduce IOP and decrease RGCs death. Oxidative stress is caused by an elevation in ROS that exceeds the tissue's antioxidant capacity, which contributes to the aging process by generating and accelerating cellular senescence. The defective mitochondrial function in glaucoma patients' TM cells makes these cells abnormally vulnerable to Ca⁺⁺ stress, resulting in IOP control failure.

In glaucoma patients, several inflammatory molecules are upregulated. Vascular endothelial growth factor (VEGF), interleukins, and TNF are a few examples ⁽²³⁾. The optic axon is affected by VEGF activators such as hypoxia and NO, though the mechanism is unknown⁽²⁶⁾. Elevated VEGF levels in the anterior segment may be the primary cause of the remodeling process in TM tissues (16). Most of these mediators can induce extracellular matrix remodeling and change functions of cytoskeletal in the TM during glaucoma⁽²⁷⁾. Specifically, IL6, which increases in response to oxidative stress, IL8 can modify the permeability of Schlemm's canal endothelial cells and has also been connected to the induction of senescence and the modification of barrier functions of the TM endothelium in pig eyes (28). Previous research has shown that AA has an important anti-angiogenesis effect by inhibiting VEGF, and this action will increase the extract's efficacy in lowering IOP and preventing the progression of glaucoma disease^{(22,29).} Furthermore, male and female rats given AA for acute and chronic toxicity in previous studies revealed no observable adverse effects at doses greater than 5000 mg/kg, indicating that AA is safe for use as a therapeutic supplement $^{(12)}$.

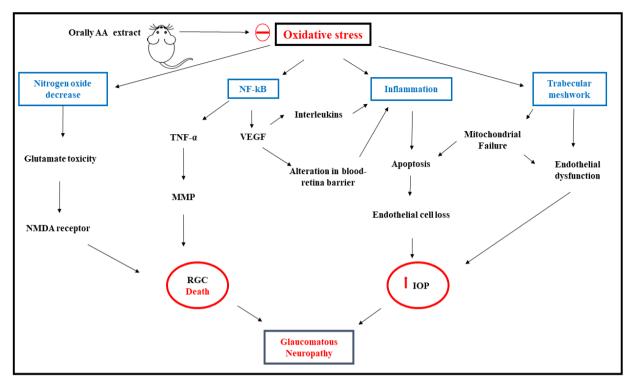


Figure 8. Supposed mechanism of action of oral administration of *Anabasis articulata* for treatment of glaucoma. Oxidative stress can cause alteration in the conventional outflow pathway, leading to IOP elevation and induce apoptosis that leads to RGC death (30). TNF- α : tumor necrosis factor- α ; NF-kB: nuclear factor-kappa; MMP: mitochondrial membrane potential; IOP: intraocular pressure; VEGF: vascular endothelial growth factor.

Conclusion

The antioxidant and anti-angiogenic properties of AA make it a promising adjuvant treatment for glaucoma patients. More studies with larger sample sizes are needed to evaluate the longer-lasting effects of AA treatment.

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Conflict of interests

There are no conflicts of interest declared by the author.

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References

- Schuster AK, Erb C, Hoffmann EM, Dietlein T, Pfeiffer N. The Diagnosis and Treatment of Glaucoma. Dtsch Arztebl Int. 2020 Mar;117(13):225–34.
- He S, Stankowska DL, Ellis DZ, Krishnamoorthy RR, Yorio T. Targets of Neuroprotection in Glaucoma. J Ocul Pharmacol Ther Off J Assoc Ocul Pharmacol Ther. 2018;34(1–2):85–106.

- **3.** Tham Y-C, Li X, Wong TY, Quigley HA, Aung T, Cheng C-Y. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121(11):2081–90.
- 4. Hussein MQ, Kadim HM, Abdulsahib WK. Effect of Telmisartan on Intra-Ocular Pressure in induced Open Angle Glaucoma in Rabbits. Int J Sci Res ISSN. 2017;6(10):1565–661.
- 5. Abdulsahib WK, Al-Zubaidy A, Sahib HB, Kathem SH. Tolerable ocular hypotensive effect of topically applied sildenafil in ocular in normotensive and betamethasone-induced hypertensive rabbits. Int J Pharm Sci Rev Res. 2015;35(1):96–102.
- 6. Krishnan A, Kocab AJ, Zacks DN, Marshak-Rothstein A, Gregory-Ksander M. A small peptide antagonist of the Fas receptor inhibits neuroinflammation and prevents axon degeneration and retinal ganglion cell death in an inducible mouse model of glaucoma. J Neuroinflammation. 2019 Sep;16(1):184.
- 7. Mead B, Tomarev S. Evaluating retinal ganglion cell loss and dysfunction. Exp Eye Res. 2016 Oct;151:96–106.
- **8.** Abdulsahib WK, Abood SJ. Effect of digoxin ophthalmic solutions on the intraocular pressure in rabbits. Drug Invent Today. 2020;14(1):5–9.

- **9.** Abdulsahib WK. Future Therapeutic Strategies in the Glaucoma Management. J Adv Med Pharm Sci. 2020;22(7):40–9.
- **10.** Abdulsahib WK, Abd AH, Qasim BJ, Sahib HB. Antiangiogenesis and antioxidant effect of anabasis articulata stems extracts. Int J Pharm Sci Rev Res. 2016;41(2):88–94.
- **11.** Hussein ZA, Rajab NA. Formulation and Characterization of Bromocriptine Mesylate as Liquid Self-Nano Emulsifying Drug Delivery System. Iraqi J Pharm Sci). 2018;27(2):93–101.
- **12.** Mahmood FM, Abdulsahib WK. Acute Toxicity of Methanolic Extract of Anabasis articulata Stems [Internet]. Vol. 6, International Journal of Science and Research (IJSR). 2015. Available from: www.ijsr.net
- **13.** Abdulsahib WK and AJS. The effect of Calcium channel blocker in the Betamethasone-induced Glaucoma model in rabbits. J Adv Pharm Educ Res. 2021;11(1):135–40.
- Abdulsahib WK. The Effect of Levamlodipine in Glucose-Induced Acute Model of Glaucoma in Rabbits. Open Access Maced J Med Sci. 2021;9(A):505–9.
- Melena J, Santafé J, Segarra J. Betamethasoneinduced ocular hypertension in rabbits. Methods Find Exp Clin Pharmacol. 1997 Oct;19(8):553–8.
- **16.** Fry LE, Fahy E, Chrysostomou V, Hui F, Tang J, van Wijngaarden P, et al. The coma in glaucoma: Retinal ganglion cell dysfunction and recovery. Prog Retin Eye Res. 2018 Jul;65:77–92.
- **17.** Abdulsahib WK, Fadhil OQ, Tizkam HH. Effect of topically applied nimodipine on the intraocular pressure on ocular normotensive and betamethasone-induced hypertensive eyes in rabbits. Int J Res Pharm Sci. 2019 Oct 1;10(4):2727–32.
- 18. Horng C-T, Yang Y-L, Chen C-C, Huang Y-S, Chen C, Chen F-A. Intraocular pressurelowering effect of Cordyceps cicadae mycelia extract in a glaucoma rat model. Int J Med Sci. 2021;18(4):1007.
- **19.** Ahn HR, Yang JW, Kim JY, Lee CY, Kim T-J, Jung SH. The intraocular pressure-lowering effect of persimmon leaves (Diospyros kaki) in a mouse model of glaucoma. Int J Mol Sci. 2019;20(21):5268.
- **20.** Saccà SC, Corazza P, Gandolfi S, Ferrari D, Sukkar S, Iorio EL, et al. Substances of interest

that support glaucoma therapy. Nutrients. 2019;11(2):239.

- **21.** Benhammou N, Ghambaza N, Benabdelkader S, Atik-Bekkara F, Panovska FK. Phytochemicals and antioxidant properties of extracts from the root and stems of Anabasis articulata. Int Food Res J. 2013;20(5):2057.
- 22. Abdulsahib WK, Abd AH, Qasim J. Antiangiogenic Activity of Iraqi Anabasis articulata Stems In vivo Study. Int J Sci Res ISSN [Internet]. 2013;5(9). Available from: www.ijsr.net
- **23.** Kimura A, Namekata K, Guo X, Noro T, Harada C, Harada T. Targeting oxidative stress for treatment of glaucoma and optic neuritis. Oxid Med Cell Longev. 2017;2017.
- 24. Al-Radeef MY, Abood SJ, Abdulsahib WK, Hamad SO. Comparing the effect of dexamethasone, normal saline, and metoclopramide on prevention of postoperative nausea, vomiting and pain in patient undergoing cholecystectomy laparoscopic or open appendectomy: a randomized clinical trial. Open Access Maced J Med Sci. 2020;8(B):139-44.
- **25.** Wei X, Cho K-S, Thee EF, Jager MJ, Chen DF. Neuroinflammation and microglia in glaucoma: time for a paradigm shift. J Neurosci Res. 2019 Jan;97(1):70–6.
- **26.** Abdulsahib WK, Fadhil OQ, Abood SJ. Antimicrobial susceptibility pattern isolated from different clinical samples in Baghdad hospitals. J Adv Pharm Educ Res Jan-Mar. 2020;10(1).
- Sun H, Zhu Q, Guo P, Zhang Y, Tighe S, Zhu Y. Trabecular meshwork cells are a valuable resource for cellular therapy of glaucoma. J Cell Mol Med. 2019 Mar;23(3):1678–86.
- **28.** Chen J, Liu X, Zhong Y. Interleukin-17A: The Key Cytokine in Neurodegenerative Diseases. Front Aging Neurosci. 2020;12:566922.
- **29.** Abudalsahib W, Abd A, Jumaa B. Antiangiogenic Activity of Iraqi Anabasis articulata Stems In vivo Study. Int J Sci Res. 2016;5(9).
- 30. Pinazo-Duran MD, Shoaie-Nia K, Zanon-Moreno V, Sanz-Gonzalez SM, Del Castillo JB, Garcia-Medina JJ. Strategies to Reduce Oxidative Stress in Glaucoma Patients. Curr Neuropharmacol. 2018;16(7):903–18.



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