

The Use of Certain Cannabis Derivatives (Canasol) in Glaucoma

Written by Manley West

Manley West, O.M., Ph.D., is a professor of pharmacology at the University of the West Indies in Kingston, Jamaica. Introduction Glaucoma may be defined as a group of ocular conditions characterized by raised intraocular pressure. Approximately 300 persons per 100,000 suffer from glaucoma. The prevalence increases with age and involves about 1 percent of the population over 40. Almost 80,000 Americans are blind from glaucoma, which makes the disease the leading cause of preventable blindness in the United States. More than 2 million Americans have glaucoma of one form or another. Primary open angle glaucoma is the most common form; it causes insidious, asymptomatic, bilateral visual loss. About 15 percent of Caucasians with glaucoma have closed angle glaucoma, and this percentage may even be higher in Asians. Glaucoma is more prevalent, begins earlier in life, and progresses faster among blacks than among other races. Jamaica, in particular, with a population of about 3 million has about 3 percent of this number suffering from glaucoma.

Normal intraocular pressure is from 10 to 20 mm Hg. Elevated intraocular pressure is usually associated with damage to the optic disk and visual field loss. In spite of a fundamental interest and research in this area, the precise mechanism by which ocular hypertension damages the optic disk is not clearly understood.

Aqueous humor is the fluid that circulates within the eyes to provide nourishment to the tissues. It is produced by the ciliary processes in the posterior chamber of the eyes and passes from the posterior chamber through the pupil to the anterior chamber of the eyes and exits through the outflow system at the peripheral angle of the anterior chamber. Two factors are really important in the dynamics of aqueous humor: (1) irregularities in the inflow mechanism or aqueous humor production, and (2) abnormalities in drainage or outflow of the aqueous humor. The inflow should balance outflow to maintain a steady state of intraocular pressure. Reducing aqueous production and hence inflow should be an accepted method of reducing intraocular pressure in all forms of glaucoma. The treatment involves a medical or surgical approach. The surgical approach should be used only after all medical attempts have failed.

At present we do not know how either endogenous or exogenous stimulators or inhibitors may alter aqueous humor formation and intraocular pressure. However, the adenylate cyclase complex in the ciliary process acts to reduce flow in a manner that is not known. It is known that the cholera toxin induces a watery diarrhea by stimulating an intestinal epithelia adenylate cyclase with the result of sodium and water being drawn into the lumen of the intestines (Gregory et al. 1981). This same toxin increases endolymph production in the inner ear. Stimulation of adenylate cyclase activity will accelerate production of cyclic AMP in epithelial cells and cause movement of fluid from the basal to the apical portion of the cells and hence into the lumen. It is known that cyclic AMP will increase the permeability of luminal membranes. It is also known that adrenaline enhances the intraocular accumulation of cyclic AMP by activating adenylate cyclase. The same line of reasoning holds for the ciliary epithelium, but the movement of fluid is reversed due to the invagination of the optical vesicles during the development of the eye. Therefore, it should not be difficult to accept that the receptor complex in the secretory tissues of eye, the ciliary processes, may be the area where research should be directed to find an acceptable medication for glaucoma.

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Treatment

The management of glaucoma is best left to the ophthalmologist, but the size and importance of the problem calls for the cooperation of other health professionals. The medical treatment is divided into two major areas: (1) reduction of aqueous humor production and (2) facilitation of aqueous humor outflow. Canasol is a fairly new drug that reduces inflow and has significant advantages when compared to the synthetic drugs.

Current antiglaucoma medications are not always effective and have significant side effects. Pilocarpine and other miotic drugs (which constrict the pupil, thereby increasing the fluid outflow) may cause blurred vision during the day due to ciliary body spasm and impaired vision at night caused by miosis. Furthermore, the miotics may contribute to the development of cataracts and may predispose the patient to uveitis and retinal detachment. The carbonic anhydrase inhibitors, such as Diamox, can produce electrolyte imbalance, fatigue, decreased appetite and weight loss, and kidney stones. Epinephrine eyedrops may cause eye pain or headache because they dilate the pupils (to inhibit the inflow of fluid). Because they can be absorbed into the circulation, they may also cause heart palpitations and nervousness. The most popular glaucoma medication is Timoptic (generic name, timolol maleate), a beta-blocker, which is believed to decrease eye fluid production. Initial adverse reactions noted were mild ocular irritation and a slight reduction in the resting heart rate. Later reports identified problems associated with nerves, digestion, vision, skin, and respiration (Miller 1980; the Harvard Medical School Health Letter 1979).

Canasol

For many years it was observed in Israel and the United States that the Cannabis plant has ocular hypotensive effects, and vast sums of money were invested in these countries in research to develop therapeutically useful compounds. These ocular hypotensive compounds represent a new class of chemicals that are more potent in reducing intraocular pressure than most of the other accepted drugs used clinically and with none of their side effects.

Canasol is a sterile ophthalmic preparation developed from Cannabis sativa specifically for the management of glaucoma. It is the result of ten years of basic scientific and clinical research done at the University of the West Indies in the pharmacology and ophthalmology departments and in private ophthalmic clinics (West and Lockhart 1978,1980). (See Table 1 and Figure 1.)

Whereas international researchers concentrated their efforts on some cannabinoids that are psychoactive, at the University of the West Indies our research efforts were directed at other compounds of this plant since we were looking at long-term therapy. Now that the effectiveness of Canasol in glaucoma has been established in the Caribbean region and, according to private communication, in Australia, New Zealand, Colombia, and England, research is being directed at its mode and mechanism of action (Gutierrez and Gutierrez 1995). There is evidence that we may be looking at adrenergic receptor control of aqueous humor dynamics. Here Canasol could make a significant contribution to ophthalmology.

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Pupil Size (mmm)	Before Use		2 Weeks		4 Weeks		8 Weeks	
	R	L	R	L	R	L	R	L
6	30	30	22	22	16	16	16	16
6	26	34	22	26	20	24	18	18
6	22	26	18	18	20	20	16	16
5	32	32	26	26	20	20	18	18
6	38	28	22	22	16	16	18	18
6	26	26	20	20	14	14	16	16
6	34	34	26	26	20	20	18	18
Mean	28.29	30	28.28	22.86	18.00	18.57	17.14	17.14
S.E.	1.53	1.31	1.11	1.12	0.97	1.29	0.40	0.40
6	30	30	16	16	18	18		
4	30	32	24	24	18	18		
5	26	26	16	16	18	18		
6	28	28	24	24	20	20		
4	30	40	26	28	22	22		
5	32	34	24	24	18	18		
6	28	26	22	20	16	16		
4	30	30	24	24	16	16		
5	42	34	28	28	32	32		
6	40	32	38	30	38	30		
6	28	28	20	20	22	24		
4	30	30	22	24	18	18		
5	40	40	30	30	26	26		
6	44	46	38	38	24	24		
5	26	26	20	20	20	20		
5	32	32	22	18	22	18		
Mean	32.25	32.13	24.63	24.00	21.75	21.13		
S.E.	1.46	1.42	1.70	1.61	1.49	1.21		

Table 1. Canasol 0.1 Percent in Glaucoma

Reduction in intraocular pressure in patients with glaucoma after treatment with Canasol 0.1 percent w/v eyedrops over eight weeks. The lower portion of the table shows the changes over four weeks.

R = right eye L = left eye

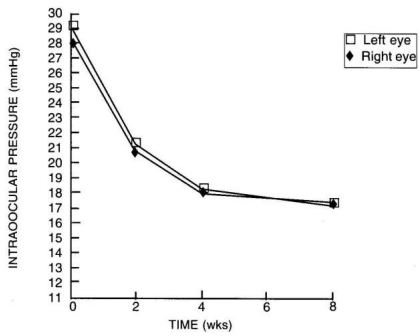


Figure 1

Effect of Canasol 0.1 percent solution on intraocular pressure in patients with glaucoma. The graph shows the reduction in intraocular pressure over time for both eyes.

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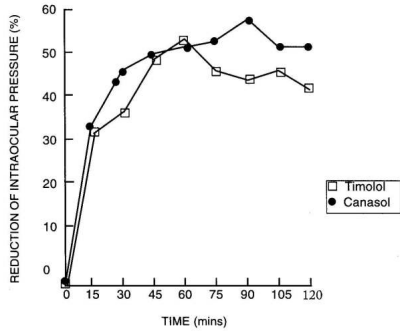


Figure 3.

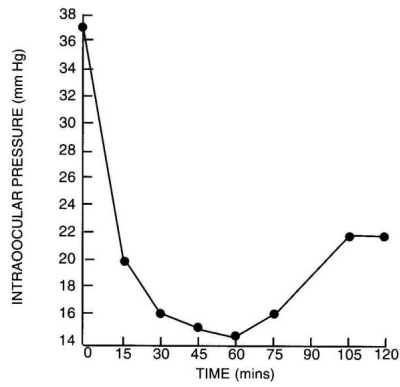


Figure 4.