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Original Article

# Efficacy and safety of 1% forskolin eye drops in open angle glaucoma – An open label study

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## Abstract

*Purpose:* Current treatment for glaucoma includes beta-blockers and prostaglandin analogues which have their own disadvantages. Thus a need exists for new ocular hypotensive agents that are more efficacious and have fewer side effects. Therefore, forskolin eye drops 1%, through herbal product; a clinical trial was carried out for the safety and efficacy in the treatment of open angle glaucoma.
*Methods:* Ninety adult male/female patients of 18–60 years of age, of either sex, suffering from open angle glaucoma with an intraocular pressure (IOP) of more than 24 mm Hg were enrolled in the study. Patients were advised to instill 2 drops thrice a day (8:00 h, 14:00 h and 20:00 h) and tonometric readings were recorded on baseline visit and on Visit 2, i.e. end of 1st week, Visit 3–2nd week, Visit 4–3rd week, and Visit 5–4th week. The reduction in IOP across each time point from untreated baseline visit and reduction in IOP across various study visits were measured.
*Results:* The mean (95% CI) difference in reduction in IOP was 4.5 mm Hg ($P < 0.05$) in the right eye and was 5.4 mm Hg ($p < 0.05$) in the left eye from baseline visit (Visit 1) to final visit (Visit 5).
*Conclusions:* Forskolin 1% eye drops can be a safe alternative to beta blockers in glaucoma patients having concomitant asthma.

**Keywords**: Intraocular pressure, Xalatan, Timolol, Open angle glaucoma, Hypotensive


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## Introduction

Glaucoma is a leading cause of blindness and vision loss.[1] It is the most frequent cause of irreversible blindness worldwide and the second most frequent cause of irreversible blindness worldwide after cataract[2] and therefore improved methods of screening and therapy for glaucoma are urgently needed.[3] Persistent high intraocular pressure which characterizes this condition, can lead to worsening of the disease.[4] Currently, there are many drugs available for lowering IOP acting through various mechanisms; however, for adequate control of the IOP along with the minimal side effects, new drugs are the need of the hour.

*Coleus forskohlii* is an aromatic herb growing all over India from the Himalayas to Southern India. From the roots of this plant is extracted forskolin and it has been studied over the last three decades as a very interesting biological tool.

Current treatment for glaucoma includes beta-blockers and prostaglandin analogues. Beta blockers show systemic side effects that affect the heart and lungs while the

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increased iris pigmentation with prostaglandin analogues is a disadvantage.[5] A need exists for new ocular hypotensive agents that are more efficacious and have fewer side effects than those used currently. Results from previous pilot exploratory studies indicate that forskolin eye drops may improve the overall symptoms of glaucoma. The current study on forskolin 1% eye drops, confirms the efficacy of the product over a large sample size, and could be an alternative in asthmatic patients having glaucoma, who are contradicted to use conventional beta blockers.

## Materials and methods

The clinical study was approved by the Drug Controller General of India (DCGI), New Delhi and the trial was conducted in accordance with the Good Clinical Practice guidelines and by adhering to all the tenets of the Declaration of Helsinki. Forskolin 1% eye drops study material was supplied by the manufacturer Sami Labs Limited, India, This trial involved 90 adult patients screened and enrolled at three clinical centers across India. With respective Institutional Ethics Committee approvals, patients diagnosed with open angle glaucoma with an IOP of more than 24 mm/Hg, who had not received miotic therapy for 24 h and systemic therapy for at least 4 days, were enrolled. The nature and purpose of the trial were explained in detail to all participants and their informed consent was obtained, in writing.

Subjects who met all the Inclusion Criteria but none of the exclusion criteria were selected for the current study: Inclusion Criteria – (a) Adult male or female subjects having primary open angle glaucoma, (b) Glaucoma with IOP of more than 24 mm Hg, (c) No miotic or other therapy 24 h before, (d) Off systemic therapy for glaucoma for at least four days, (e) Informed consent given. Exclusion Criteria – (a) Subjects with conditions such as secondary or closed angle glaucoma, bronchial asthma, chronic obstructive pulmonary disease, uncompensated cardiac failure, pregnancy, sinus bradycardia or 2nd or 3rd degree atrio-ventricular block were excluded from the trial, (b) Subjects, who have taken any anti-inflammatory ophthalmic dose in the past 3 months, were barred. (c) Subjects having concurrent drug intake e.g. $\beta$ blockers and diamox were also excluded. (d) Pregnancy was also exclusion for this trial. A washout period of 4 weeks has been maintained from the day of screening as per international recommendations.[6]

The enrolled patients were assessed for demographic, complete clinical and physical examination including severity of eye symptoms. Concomitant treatment was also noted (see Table 1). Patients underwent an IOP recording by a validated Goldmann applanation tonometry using a mean of 2 readings at 0 h before study medication was instilled in the affected eye/eyes. Readings were recorded for the right and left eye and both the eyes were analyzed as separate entries. After administering 2 drops of forskolin 1% in the affected eye, tonometric readings were subsequently taken at 0.5, 1, 2, 3, 4, 5 and 6 h. For these IOP measurements, the subjects were to relax 15 min before, and two readings were taken in supine position. These readings were recorded in duplicate, and a mean of two readings was considered for statistical analysis.

The study duration was for 4 weeks. There were 4 follow up visits besides baseline visit (Week 2–Week 5).

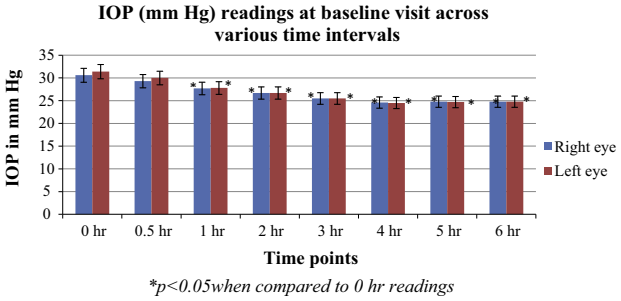


**Figure 1.** Figures indicate mean decrease in IOP (mm Hg) at baseline visit across various time intervals i.e. 0 h, 0.5 h, 1 h, 2 h, 3 h, 4 h, 5 h and 6 h – postinstillation of forskolin eye drops (1%) [Right & Left Eye]. After administration of first dose (two drops) of forskolin 1% eye drops, decrease in IOP was observed at the first reading (30 min. after administration), reached statistical significance from 1 h onward and IOP continued to drop till 4 h and then remained at plateau for next 2 h.

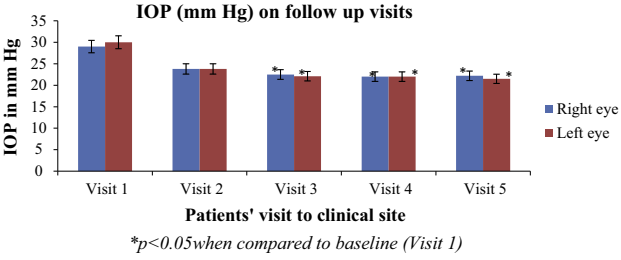


**Figure 2.** Figure presents effect of treatment on IOP at every follow up visit. It represents the mean decrease in IOP at the first time interval of every follow up visit i.e. Visits 2–5. There was a considerable decrease in the IOP at the first follow-up visit, and reached a statistical significance from second follow up visit (Visit 3) which was maintained till the last study visit.

Throughout the study duration, patients were to instill 2 drops of study medication, 3 times a day (8:00 h, 14:00 h and 20:00 h). Patients were advised not to instill the medication on the morning of the follow up visits, during which, the signs, symptoms and adverse effects were recorded on the Case Record Form. On the day of visit to the clinical site, after administering 2 drops of forskolin 1% in the affected eye, tonometric readings were subsequently taken at 0.5, 1, 2, 3, 4, 5 and 6 h. A qualified personnel who was independent of the study was designated by the Principal Investigator for IOP measurements to avoid potential bias. Tonometric readings were recorded in duplicates and a mean of two readings was considered at the respective time intervals. The same process was followed during all the subsequent visits. Physical and clinical examination, assessment of adverse events and concomitant medications were recorded on all the follow up visits as well. Adverse events were evaluated by asking patients a general query about their state of health since their respective previous or earlier study visits.

## Results

Across three clinical centers, ninety subjects (53 males and 37 females) participated in this trial and their mean age was 51.6 ± 11.9 years, and weight 66.0 ± 13.7 kg. Other patient demographic characteristics are depicted in Table 2, as mean