# CHAPTER II

## REVIEW OF RELATED LITERATURE

**Latanoprost**, a topical prostaglandin, has become an important addition to the glaucoma regimens because of its ability to reduce the intraocular pressure with an improved therapeutic index, as compared to older medications. [7]

### Mechanism of Action

Latanoprost is a new prostaglandin analogue developed to reduce the intraocular pressure in glaucoma. It has an interesting mode of action, in that it increases the uveoscleral outflow of aqueous humor in primates. In this outflow pathway, the aqueous humor percolates through the ciliary muscle, suprachoroidal space, and the sclera instead of exiting the eye through the trabecular meshwork and Schlemm canal. In humans, latanoprost has also been shown to increase the uveoscleral outflow. [8]

**Efficacy**

There have been many reports on the efficacy of latanoprost. The result from three big study groups, the UK [9,10], the Scandinavian[11] and the USA[12] Latanoprost Study Group, comparing latanoprost 0.005% administered once daily to timolol 0.5% administered twice daily, have shown that the mean IOP reduction from baseline in latanoprost treated group ranged from 5.5 – 8.6 mmHg (equivalent to 25-35 % reduction), greater than the control group (4.9-8.3 mmHg (-25%)). In a study conducted in Italy[13], in patients whose IOP was inadequately controlled with timolol, adding latanoprost to timolol treatment reduced diurnal IOP by 6.1 $\pm$ 0.3 mmHg (-28%), adding pilocarpine to timolol treatment reduced diurnal IOP by 4.2 $\pm$ 0.3 mmHg (-19%), and switching from timolol to latanoprost monotherapy reduced diurnal IOP by 5.5 $\pm$ 0.3 mmHg (-25%). In another clinical trial in Scandinavia, in patients whose IOP could not be controlled with timolol alone, a two–dose regimen of 0.005% latanoprost in combination with 0.5% timolol resulted in marked and sustained reduction of IOP by about 30–33% throughout the treatment period.

There are also reports that latanoprost has higher efficacy than other new drugs such as unoprostone and dorzolamide. [14,15] In summary, latanoprost is the most efficacious one in lowering IOP. [16]

**Adverse Effects**

Latanoprost undergoes little metabolism in the eye, and once it has entered the blood circulation, it is rapidly metabolized and excreted. Its half-life in blood circulation is very short, about 17 minutes. Hence, it can be regarded as oculoselective, and systemic side effects should not occur. [8]

However, there are some reports about ocular side effects of latanoprost. Mild to moderate conjunctival hyperemia, increased iris pigmentation and superficial punctate keratitis were observed in many clinical trials. [9-11,17,18,19] The clinical implications and long–term risk of the iris color change are not yet known. Johnstone M.A. reported 43 patients who developed hypertrichosis and increased pigmentation of eyelashes and adjacent hair in the region of the ipsilateral eyelids of patients treated with unilateral topical latanoprost. [20] Other side effects reported are increased eyelid pigmentation and iris cyst, associated with use of latanoprost.[21,22] Cystoid macular edema and iritis are also reported.[23] Currently, there has been no study in Thailand that has the following criteria:

1. Comparison between latanoprost and combination of pilocarpine with timolol in open-angle glaucoma or ocular hypertension patients who had inadequate control of IOP with timolol treatment.

2. Randomized controlled trial.

3. A large sample size, enough to establish statistical and clinical significance.

Therefore, we conducted this study to compare the effectiveness, the side effects and the cost-effectiveness of this new drug to the old one.