

I. Mikheyteva<sup>1</sup>, G. Grigorieva<sup>2</sup>, N. Pasechnikova<sup>1</sup>, S. Kolomiichuk<sup>1</sup>, T. Siroshatanenko<sup>1</sup>, N. Konakhovich<sup>2</sup>

<sup>1</sup> The Filatov Institute of Eye Diseases and Tissue Therapy of the NAMS of Ukraine; Odesa, Ukraine

<sup>2</sup> Institute of Pharmacology and Toxicology of NAMS of Ukraine; Kyiv, Ukraine

## INTRODUCTION

Latanoprost (L) is the most commonly used prostaglandin analog for glaucoma treatment. All hypotensive topical medications have a relatively short effect due to low penetration of topical across the corneal epithelium, which causes the need for their daily application for a long time. Because there is a growing need for prolonging the treatment effect and thus improving L treatment efficacy and patient compliance, it is important to study various sustained drug delivery systems for L agents.

Liposomal phospholipid preparations of L are promising for combining prolonged pharmacotherapeutic IOP regulation with various ways of drug delivery to the eye. Consequently, it is important to study the potential of novel liposomal preparations of L for optimization of pharmacotherapeutic effect and compliance in patients with elevated IOP.

## AIM

To establish the dynamics of intraocular pressure (IOP) with time and the duration of the hypotensive effect of the original liposomal form of latanoprost applied by instillations into the conjunctiva sac and subconjunctival injection for the experimental glaucoma (EG) in rabbits.

## METHOD

Ophthalmic experiments were carried out on chinchilla rabbits (1 year old, weighing 2.5 - 3 kg). The rabbits were divided into four groups: Group I - EG was simulated and treated with instillations of liposomal form of L (n = 7); Group II - EG was modeled and treated with subconjunctival administration of liposomal form of L (n = 7); Group III - EG was modeled without treatment (n = 7); Group IV - intact control. EG was induced by two injections of 0.1 ml of 0.3% carbomer in isotonic solution into the anterior chamber of the eyes at 10 days interval. Subconjunctival administration of the liposomal form of L was applied by a 0.1 ml single injection immediately after the formation of the EG. Treatment of animals with instillations of liposomal form of L was carried out daily in the evening, one drop in both eyes. Follow-up duration was 10 weeks. IOP monitoring was carried out at key stages of the experiment for each group of animals.

## RESULTS

At baseline, in randomized animals, the IOP was within the normal range (11.8-12.4 mmHg), with no significant difference.

After EG modeling was performed, in each group, there was a persistent increase in IOP to 18.8 to 19.4 mmHg, which was 51-65% higher than at baseline (p < 0.001).

In Gr1, before the application of topical liposomal L, the IOP was 64.6% higher than at baseline (p < 0.001). In the presence of application of topical L, the IOP was significantly decreased at each IOP measurement time point, but was still statistically significantly higher than at baseline (Fig. 1). The reduction in elevated IOP began at week 1, and increased at week 3. It is noteworthy that at each IOP measurement time point, the IOP in Gr1 (animals with EG treated with topical liposomal L) was 30.5% lower than in animals of Gr3 (untreated animals with EG) (p < 0.001), indicating a significant hypotensive effect of daily topical liposomal L treatment.

In animals of Gr 2, a single subconjunctival injection of liposomal L resulted in apparently normalized IOP at each IOP measurement time point, with no significant difference from baseline (Fig. 2). In addition, the IOP in animals with EG treated with a single subconjunctival injection of liposomal L was 36.7% lower than in untreated animals with EG (p < 0.001).

## CONCLUSIONS

Our animal study demonstrated that a ten-week daily local treatment with a new liposomal latanoprost formulation for EG had an apparent hypotensive effect, with a 30.5% reduction in IOP compared to baseline (p < 0.001).

A single subconjunctival injection of the liposomal L formulation resulted in a 36.7% reduction in IOP compared to baseline (p < 0.001), with the effect being as long as 10 weeks. Finally, subconjunctival injection of the examined liposomal latanoprost formulation is promising in the treatment of patients with elevated IOP, with a potential improvement in pharmacologic efficacy and patient compliance in the treatment of patients with ocular hypertension or glaucoma. The results obtained in the experiment on the EG model indicate a significant hypotensive effect of long-term instillations and a single subconjunctival injection of the original liposomal composition of L with an emphasis on the effect of a single subconjunctival injection of the medicine, which is clearly prolonged up to 10 weeks.

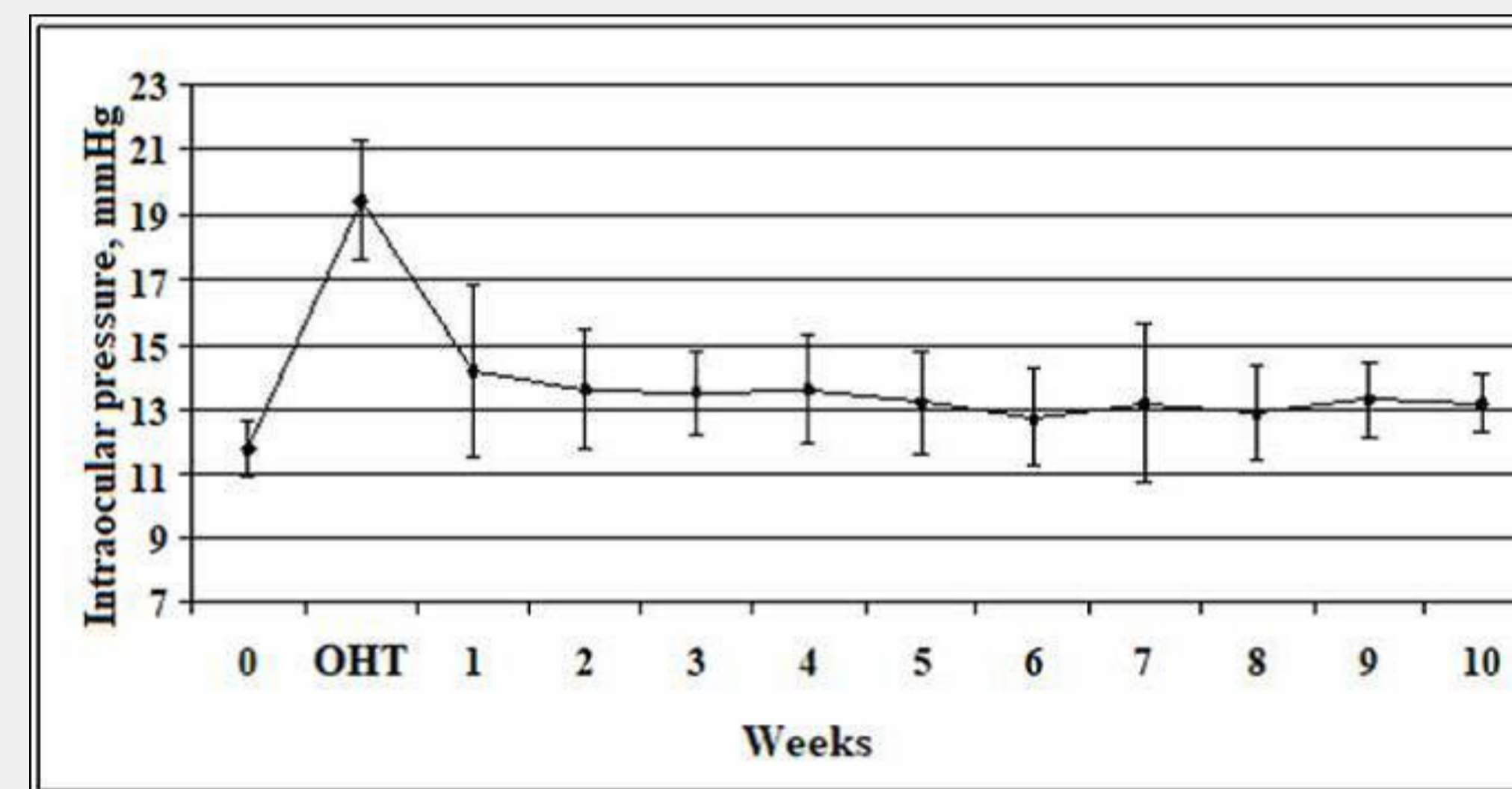


Fig. 1. Changes in intraocular pressure (IOP assessed in mmHg, mean ± standard deviation) with time in rabbits with experimental glaucoma treated with daily topical liposomal latanoprost

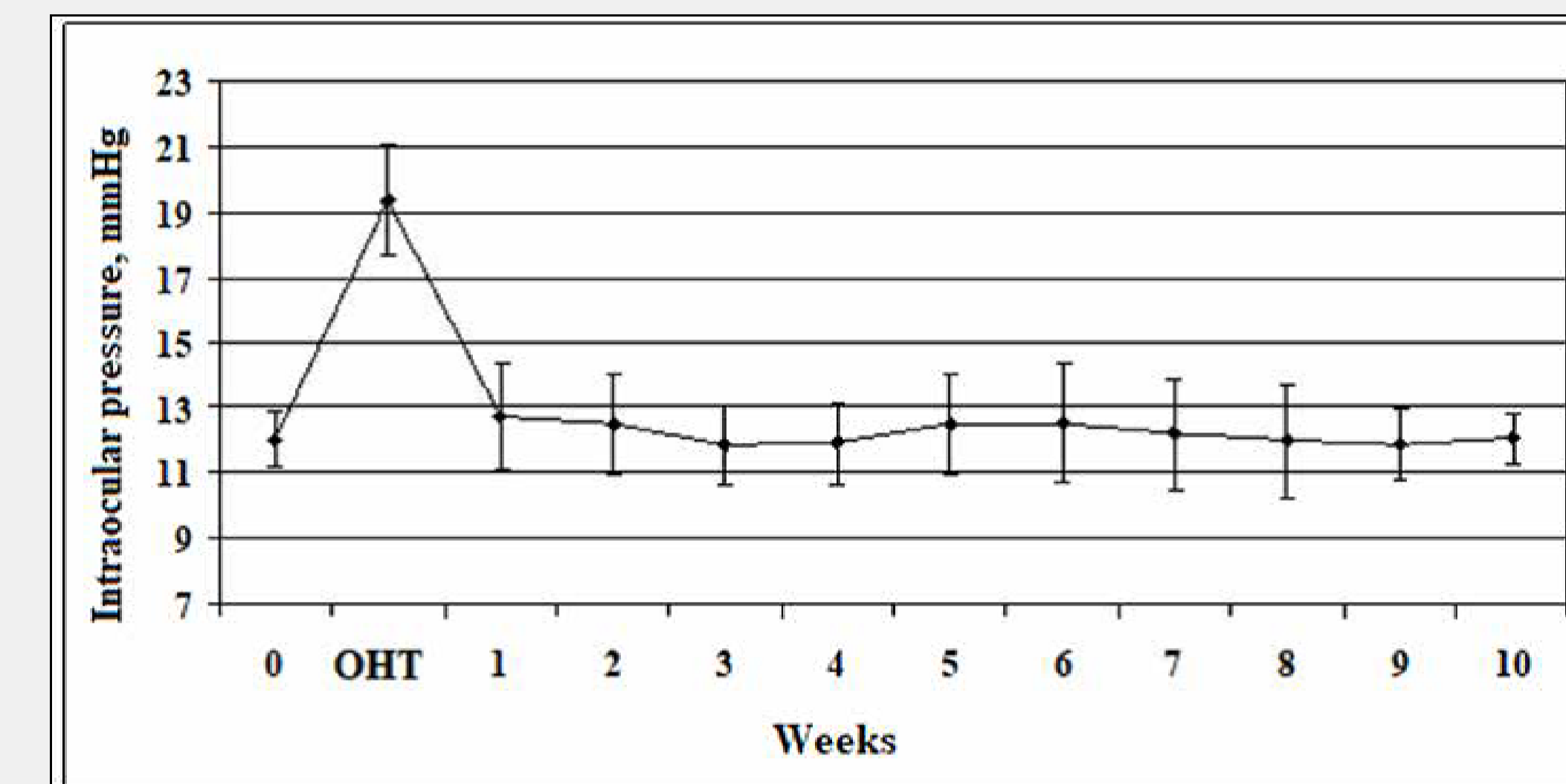


Fig. 2. Changes in intraocular pressure (IOP assessed in mmHg, mean ± standard deviation) with time in rabbits with experimental glaucoma treated with a single subconjunctival injection of liposomal latanoprost

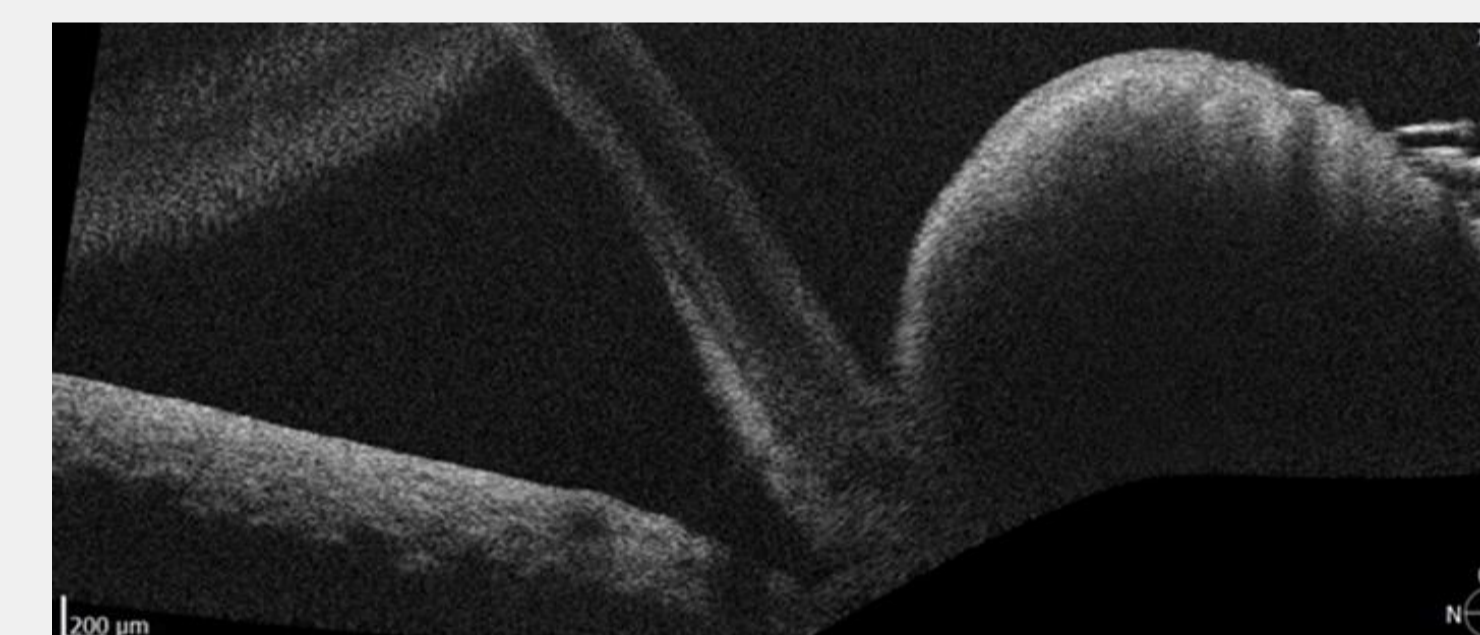


Fig. 3. OCT of the anterior part of the rabbit eye immediately after subconjunctival injection of liposomal latanoprost

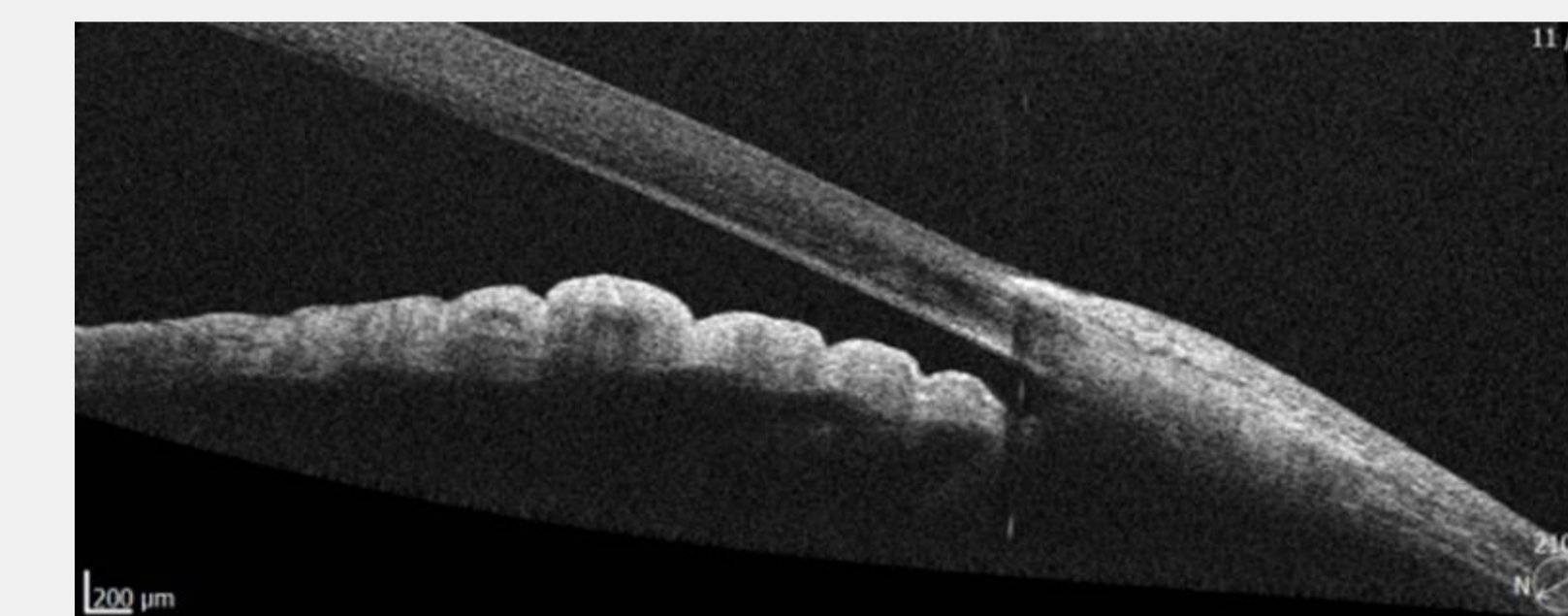


Fig.4 Long-term results of OCT of the anterior part of the eye of a rabbit with experimental glaucoma 90 days after subconjunctival injection of liposomal latanoprost

## REFERENCES

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## CONTACT INFORMATION

Irina Mikheyteva, head of biochemistry department, Filatov Institute of Eye Diseases and Tissue Therapy of the NAMS of Ukraine, e-mail: [filatovbiochem@ukr.net](mailto:filatovbiochem@ukr.net)

Address: Frantsuzskii Bulvar, 49/51

65061, Odessa, Ukraine