brane-bound enzymes, and the membrane's lipid bilayer.

Indeed, increased value of the information being transferred is achievable owing to the presence of various receptor subtypes [9]. RP such as neurohypophyseal hormones, enkephalins, and substance P have been shown to be capable of acting on the cell by binding to receptors for other bioregulators [10,15]. Some RP can influence the activity of membrane-bound proteins in a direct fashion [4]. Furthermore, recent experimental evidence indicates that many peptides are able to interact directly with the plasma membrane lipid matrix of the effector cell [1,3,5-8,12,14].

The role of the peptide-lipid interactions mentioned above may be visualized as follows. By being adsorbed on the lipid bilayer, RP molecules can acquire the particular conformation required for their binding to the receptors, and this property probably enables the cell to receive information from various conformers of one peptide that are present in solution. Then, RP molecules residing in the lipid environment can influence various membrane-bound proteins and also can modify physicochemical characteristics of the plasma membrane lipid matrix itself. As a result, the quantity and, consequently, the value of the information carried by the RP and received by the cell can be considerably increased.

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Effect of Low-Dose Emoxypine and Pyridoxine Hydrochloride on Human Cataract and Glaucoma

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Synthetic antioxidants have been extensively used in ophthalmological practice as preparations protecting the retina from damage developing in the activation of free-radical oxidation reactions. The concept underlying their use implies that disturbances in the oxidative processes and antioxidation protection mechanisms affect the membrane structures of the

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TABLE 1. Changes in Visual Acuity in Patients with Cataract as a Function of Time of Administration of 0.02% PH Solution ($M \pm m$)

Experimental conditions	Time of PH administration, days			
	0	10	20	30
without correction	0.24±0.03	0.38±0.04*	0.55±0.01*	0.42±0.07*
with correction	0.51±0.05	0.58±0.04*	0.74±0.04*	0.75±0.05*
	n=63	n=51	n=29	n=16

Note: here and in Tables 2–5 *: improvement in comparison with baseline, $p<0.05$.

eyes [5, 8]. Antioxidation protection in the eye structures is provided for by native lipophilic antioxidants such as tocopherols, melanoproteins of the pigment epithelium, and enzymatic systems (superoxide dismutase, glutathione peroxidase).

In 1986 a new antioxidative preparation, emoxypine, was introduced into ophthalmological practice. Developed at the Department of the Kinetics of Chemical and Biological Processes, Institute of Chemical Physics of the Russian Academy of Sciences [11], it is used in a concentration of 1% for the treatment of hemophthalmia. Its native analog, pyridoxine hydrochloride (PH), is used in a concentration of 0.4% in Furanvit eye drops (Italy) for the treatment of keratitis and inflammatory eye diseases.

Since the activation of lipid peroxidation in the aqueous humor and lens tissues is implicated in the pathogenesis of cataract [1-3, 7], substances acting as antioxidants are being increasingly used for the treatment and prophylaxis of cataract development [9]. The activation of lipid peroxidation is also observed in the development of glaucoma [4], suggesting the efficacy of the use of antioxidant for the treatment of this condition as well.

In the present study the effect of emoxypine and PH on human cataract and glaucoma was investigated.

MATERIALS AND METHODS

The effect of aqueous solutions of PH in concentrations of 0.2 and 0.02% (10^{-2} and 10^{-3} M) and emoxypine in a concentration of 0.015% (10^{-3} M) was studied in the treatment of outpatients with early stage cataract and glaucoma. Apart from the effect of low doses of the preparations, the response of eyes of different colors to the treatment was evaluated. The preparations were instilled in a volume of two drops twice a day during 20 to 30 days. Special methods of investigation were used on 33 patients with cataract (63 eyes) and on 17 patients with glaucoma (33 eyes) of different genesis. The pupillary response to the instillation of the preparation was evaluated on the normal eyes of 10 volunteers. The ophthalmological studies included evaluation of visual acuity, perimetry, tonometry, electronic tonography, biomicroscopy, ophthalmoscopy, pupillometry, and ophthalmosphygmography. The studies were conducted before and after the instillation of the solutions during the first hour, every ten days of the first month, and then the patients were followed up as mentioned below. The apparatus used included a Granitsa all-purpose projection perigraph, an OTG-01 electronic tonograph, and a slit lamp.

The statistical analysis of the experimental data based on the comparison of the indexes recorded in the course of treatment for each patient was performed with the use of Student's t test.

RESULTS

The effect of PH on human cataract was tested every 10 days after the beginning of treatment. Visual acuity and visual field were tested. A subjective effect of vision improvement was recorded as early as 3 to 5 days after the beginning of treatment (muscae volitantes and black spots disappeared, and eye fatigue during close work was reduced).

Table 1 shows the data on the changes in visual acuity with and without correction in patients 10, 20, and 30 days after the instillation of 0.02% PH.

TABLE 2. Visual Field in Patients with Cataract as a Function of Time of Administration of 0.02% PH Solution ($M \pm m$)

Eye color	Enlargement of visual field, days			
	0	10	20	30
light	431±11	48±10*	26±7*	50±9*
	n=15	n=7	n=7	n=6
dark	454±10	23±5*	21±11	21±36
	n=12	n=8	n=4	n=3
p**	0.1	0.05		

Note: **: significance level in analysis of difference between light and dark eyes.

TABLE 3. Changes in Visual Acuity and Visual Field after Daily Instillations of 0.2% PH Solution (2 Drops Twice a Day) ($M \pm m$)

Experimental conditions	Time of PH administration, days			
	0	10	20	30
Visus with correction	0.68±0.10 n=20	0.75±0.10 n=12	0.82±0.10 n=9	0.50±0.05 n=5
ΔVisus		0.21±0.05*	0.26±0.04*	−0.15±0.03*
Visual field	476.7±7.9	499±20		508±11
Enlargement of visual field		27.0±13.0		28.3±8.1*

With this strength of PH solution 86% of the patients with cataract showed improvement of visual functions; there was no improvement in the rest of the patients, and no cases of impairment of vision were observed. It should be noted that the fact of improvement itself was not related to the color of the patients' eyes. The degree of improvement was slightly higher in the patients with light-colored eyes, although it was not significantly different from that in the patients with dark eyes. The treatment with 0.02% PH also resulted in a marked enlargement of the visual field in patients with early stage cataract. It is worth noting that the response of dark and light eyes to the action of the preparation was reliably different, the light eyes being more sensitive (Table 2).

For an evaluation of the long-term effect of the preparation the visual functions were tested in 15 patients during one month after the end of the 30-day course of treatment. The improvement obtained during the treatment persisted throughout this period.

A small group of patients (11) (mean age 63±5 years) was given a 0.2% solution of PH for the treatment of cataract. Table 3 shows the data on the changes of the visual field after the instillation of 0.2% solution over 30 days.

It can be seen from Table 3 that an improvement in visual acuity for the use of 0.2% PH is observed only for 20 days. A longer course of treatment can result in a slight impairment of visual acuity with a simultaneous enlargement of the visual field. A study of the effect of 0.2% PH on the hydrodynamic indexes of human cataract revealed that the intraocular pressure (P_0), the rate of intraocular fluid secretion (F), the rate of intraocular fluid drainage (C), and Becker's coefficient ($K_B = P_0/C$) were virtually unchanged 60 min after instillation and 10 and 20 days after administration (Table 4). The changes in the hydrodynamic indexes of the eyes of cataract patients were significant only 25 min after the instillation of the preparation.

Table 4 shows that at any schedule of administration the intraocular pressure tended to drop, which suggests the efficacy of the concentration used for the treatment of patients with glaucoma.

Glaucoma patients were given PH in a dose of 0.02% while receiving conventional treatment with 1% pilocarpine.

Table 5 presents the hemodynamic indexes of the eyes of glaucoma patients undergoing combined treatment with pyridoxine hydrochloride and pilocarpine.

The data in the table show that the use of 0.02% PH solution potentiates the pilocarpine effect in glaucoma, while the intraocular pressure and Becker's coefficient are reduced.

Pilocarpine belongs to a group of preparations which are known to have a stimulating effect on the m-cholinoreactive structures of the parasympathetic nerves innervating the iris constrictor muscle, causing the pupil to constrict and thus reducing the intraocular pressure. Pyridoxine hydrochloride presumably potentiates the cholinomimetic effect of pilocarpine. The study of the direct effect of 0.02% PH solution on the pupillary response in a group of subjects (21), including both healthy persons and patients with cataract and glaucoma, revealed a significant reduction in the pupillary diameter 10 min after instillation: $\Delta d = 0.23 \pm 0.04$ mm ($p < 0.001$). No marked differences between the normal and affected eyes were noted.

The effect of 0.015% emoxypine solution on the pupillary response and tonographic characteristics of

TABLE 4. Changes in Intraocular Pressure (P_0), Rate of Intraocular Fluid Secretion (F), Rate of the Intraocular Fluid Drainage (C), and Becker's Coefficient (C_B) 25 min after Instillation and 10 and 20 Days after Administration of 0.02% PH Solution to Patients with Cataract ($M \pm m$)

Time	P_0	C	F	C_B
25 min n=30	−1.09±0.46*	+0.027±0.007*	+0.014±0.050	−36±11*
10 days n=17	−0.65±0.43	+0.013±0.007	−0.42±0.22	+10±10
20 days n=10	−1.12±0.59	+0.048±0.008	+0.135±0.310	−7.0±17.0

TABLE 5. Changes in Intraocular Pressure (P_0), Rate of Intraocular Fluid Secretion (F), Rate of Intraocular Fluid Drainage (C), and Becker's Coefficient (C_B) 25 min after Instillation and 10 and 20 Days after Administration of 0.02% PH Solution for the Treatment of Patients with Glaucoma Continuously Using 1% Pilocarpine Drops for a Number of Years ($M \pm m$)

Time	P_0	C	F	C_B
25 min $n=12$	-2.97 ± 0.92*	$+0.021 \pm 0.022$	-0.43 ± 0.21	-20 ± 30
10 days $n=17$	-4.94 ± 1.29*	$+0.024 \pm 0.014$	nonreliable	-169 ± 63*
20 days $n=9$	$+3.71 \pm 1.82$	$+0.04 \pm 0.02$	$+1.38 \pm 0.74$	-136 ± 59*
30 days $n=8$	-6.39 ± 1.96*	$+0.03 \pm 0.02$	-0.55 ± 0.18*	-131 ± 59*

19 patients with early stage cataract (38 eyes) was studied by the double-blind method. The patients of the first group (10) were given physiological saline, whereas the patients of the second group (9) were given emoxypine solution. The pupillary diameter was measured before and 20-30 min (the first measurement) and 40-60 min (the second measurement) after the instillation. Tonography was performed before and during the first hour after the instillation. Physiological saline did not change the diameter of the pupil or the tonographic indexes, whereas 0.015% emoxypine solution tended to reduce the pupillary diameter on the average by 0.14 mm ($p<0.001$) 20 to 30 min after the instillation and by 0.33 mm ($p<0.001$) 40 to 60 min after the instillation, the intraocular pressure being reduced by 1.68 ± 0.61 ($p<0.05$). Thus, the data obtained suggest that low doses of PH and emoxypine are effective in the treatment of patients with glaucoma and early stage cataract. The effect of the preparations may be associated with the influence of the doses used on the membranes of the cellular structures. Antioxidants are known to change not only the rate of lipid peroxidation but also the lipid composition and the structural characteristics of the lipid matrix, which in turn is responsible for alterations in the activity of the membrane proteins and receptors [5, 10]. From the evidence about the changes in the pupillary diameter the conclusion can be drawn that low doses of emoxypine and PH act upon the cholinoreceptive structures of the sphincter. The effect may be either direct or mediated via the cell membrane by changing the sensitivity of the cholinoreceptors to exogenous and endogenous transmitters.

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