LITERATURE CITED

1. M. I. Agadzhanov, D. M. Gevorkyan, et al., in: Problems in Neurochemistry [in Russian], Leningrad (1977), p. 130.
2. Yu. A. Vladimirov and A. I. Archakov, Peroxidation of Lipids in Biological Membranes [in Russian], Moscow (1972).
3. R. N. Glebov and G. N. Kryzhanovskii, Usp. Fiziol. Nauk, No. 3, 523 (1981).
4. V. E. Kagan, O. A. Azizova, and Yu. V. Arkhipenko, Biofizika, 22, 625 (1977).
5. G. N. Kryzhanovskii, Zh. Nevropatol. Psikhiat., 76, 1730 (1974).
6. G. N. Kryzhanovskii, E. V. Nikushkin, V. E. Braslavskii, and R. N. Glebov, Byull. Éksp. Biol. Med., 89, 14 (1980).
7. Yu. N. Lyaskovskaya, N. N. Krylova, V. P. Volovinskaya, et al., in: The Use of Chemical Preservatives, Antioxidants, Stabilizers, and Ion-Exchange Resins in the Meat Industry [in Russian], Moscow (1967), p. 52.
8. F. Z. Meerson, V. E. Kagan, L. L. Prilipko, et al., Byull. Éksp. Biol. Med., 87, 404 (1979).
9. S. M. Nikolaev, "The effect of sodium selenite, α-tocopherol, and a combination of both on the course of experimental myocardial infarction," Author's Abstract of Candidate's Dissertation, Moscow (1976).
10. A. Y. Sun, Biochim. Biophys. Acta, 266, 350 (1972).

ACTION OF ODIFALINE AND DIFRIL ON THE CATECHOLAMINE CONTENT IN ADRENERGIC NERVE FIBERS IN VARIOUS RAT ORGANS

L. A. Strinskaya, G. R. Leont'eva, O. M. Avakyan, and V. A. Govyrin

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KEY WORDS: adrenergic innervation; heart; vessels; drugs.

Odifaline – 3-phenyl-3-O-hydroxyphenyl-N-(phenylisopropyl)propylamine – is an original coronary dilator, structurally similar to difril,* which has been used in the treatment of angina pectoris and myocardial infarction [11]. The properties of difril, according to data in the literature, are due to its mobilizing action on catecholamine reserves in adrenergic nerves [4, 6] and to its ability to inhibit transmembrane transport of Ca^{++} ions [8]. The action of odifaline and difril has been studied mainly in tissue homogenates by the use of biochemical methods [1, 9], and to a lesser degree, radiographically; only isolated studies have been undertaken by histochemical methods [8, 12, 13]. However, despite their great value, these investigations do not reflect the dynamics of action of the drugs.

It was accordingly decided to study the dynamics of action of difril and odifaline on the catecholamine content in peripheral adrenergic nerves of various organs with different types of sympathetic innervation.

EXPERIMENTAL METHOD

Experiments were carried out on 200 male Wistar albino rats weighing 150-200 g. A suspension of odifaline or difril, made up in a 0.5% solution of carboxymethylcellulose, was injected intraperitoneally in a dose of 50 mg/kg. The animals were killed 1, 6, 12, 18, 24, and 30 h after a single injection of the drug; 6 to 10 animals were investigated at each time. Rats receiving an intraperitoneal injection of a 0.5% solution of car-

*Prenylamine.

Laboratory of Adrenergic Mechanisms, A. L. Mndzhoyan Institute of Fine Organic Chemistry, Erevan. Laboratory of Development of the Adaptive and Trophic Function of the Nervous System, I. M. Sechenov Institute of Evolutionary Physiology and Biochemistry, Academy of Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.)

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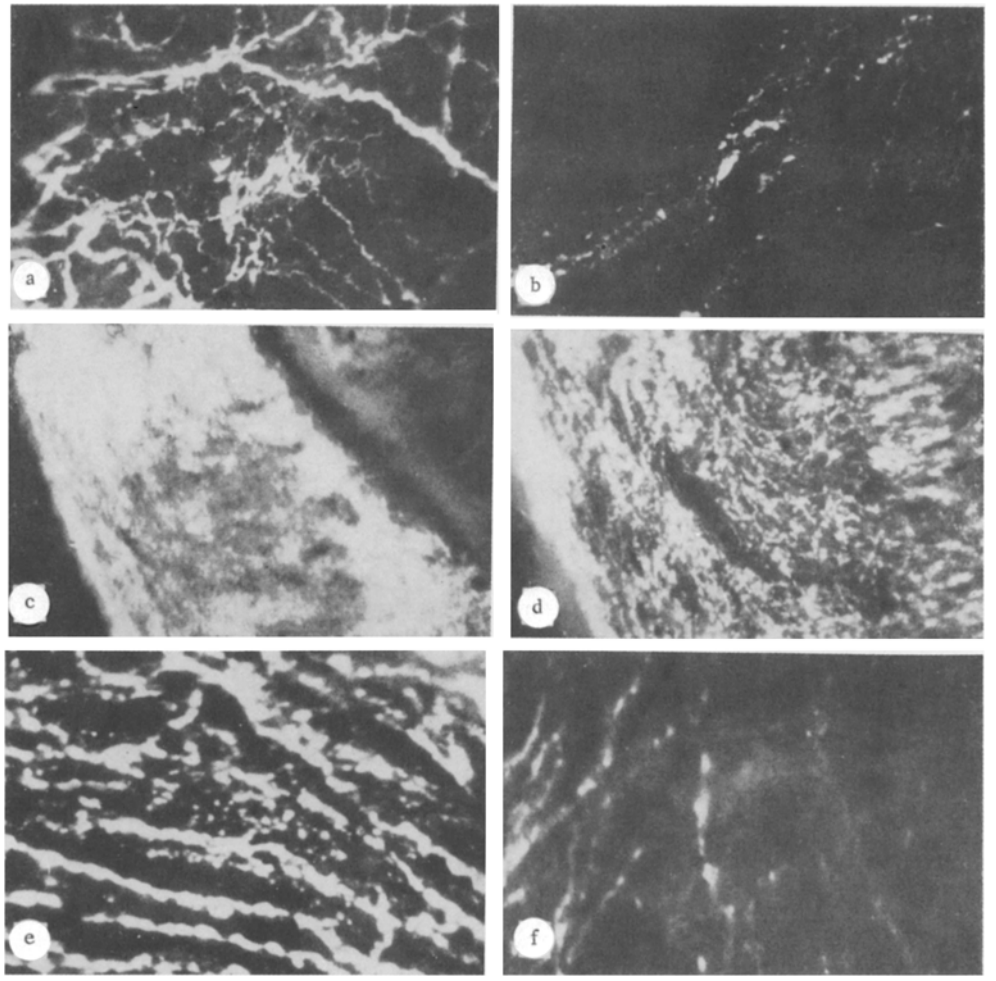

Fig. 1. Adrenergic nerve plexus detected by Axelsson's histochemical method in rat organs: opening of chorda tendinea of atrioventricular valve (total preparation) under normal conditions (a) and 6 h after injection of odifaline (b); vas deferens (40-μ sections) under normal conditions (c) and 1 h after injection of difril (d); mesenteric vein (total preparation) under normal conditions (e) and 1 h after injection of odifaline (f).

boxymethylcellulose only, in a dose of 0.5 ml/100 g body weight, which gives a mild mobilizing effect, most marked in veins, were used as the control. The iris, mesenteric artery and vein, atrioventricular heart valve, myocardium of the right auricle, and the vas deferens were investigated by a histochemical method [5]. Frozen sections 40 μ thick were cut from the last two organs, and total preparations were obtained from the rest. The intensity of fluorescence of adrenergic nerves was measured by the FMÉL-1 photometric attachment (× 90 objective), with a small probe covering an area of 1.1 mm^2, and expressed in conventional units.

EXPERIMENTAL RESULTS

The investigation showed a decrease in catecholamine reserves in adrenergic structures under the influence of difril and odifaline. The decrease first began to appear in the preterminal part of adrenergic fibers, whereas the terminal portions, varicose expansions, and bodies of chromaffin cells (in the heart valves) were more resistant to the action of the drugs. The decrease in catecholamine reserves, starting during the first hours after administration of the drugs, did not affect the adrenergic fibers uniformly, but only in some parts (Fig. 1); after a longer period, however, the decrease in fluorescence, amounting sometimes to total disappearance, was observed over the whole of the adrenergic plexus.

The results showed that adrenergic nerves of different organs react differently to administration of these two drugs. For instance, vascular nerves of the iris, in which complete disppearance of fluorescence occurred later than in nerves to the radial muscle, were the most resistant to the mobilizing action of difril and odifaline.

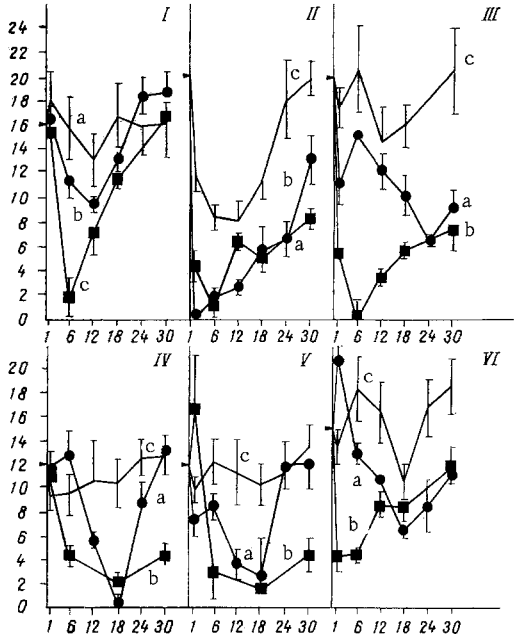

Fig. 2. Changes in intensity of fluorescence in adrenergic nerve fibers of different organs of rats under the influence of difril (a), odifaline (b), and in the control (c). Abscissa, time (in h) after injection of drug; ordinate, intensity of fluorescence (in conventional units, μA) (mean initial catecholamine level indicated by arrows). I) Artery, II) vein, III) atrioventricular heart valve, IV) myocardium, V) vas deferens, VI) iris.

In the atrioventricular heart valve the bodies of the chromaffin cells were not completely denuded of catecholamines in general (Fig. 1a, b), and their original catecholamine level was restored, just as in the vascular nerves of the iris, sooner than in nerves in the cusps of the valve. As will be clear from Fig. 2, the myocardium of the right atrium and the vas deferens, organs receiving a direct sympathetic innervation [3], reacted similarly to administration of difril and odifaline. The original level of catecholamine fluorescence was the same in both organs, the mobilizing effect of the drugs increased gradually to reach a maximum after 18 h, after which complete or almost complete restoration of the catecholamine reserves took place within a relatively short period (6 h).

In the iris and the cusps of the heart valves, organs with mixed adrenergic innervation, a considerable difference was found both in the original catecholamine content and in the action of difril and odifaline: the action of difril developed after 18-24 h, whereas odifaline gave rise to maximal mobilization of the reserves during the first 6 h after its injection.

Blood vessels occupied a special place with respect to their reaction to odifaline and difril. The initial intensity of fluorescence in the adrenergic nerves of the mesenteric artery was rather lower than in the parallel veins. The vein was the most sensitive organ to the effect of the drugs. Difril and odifaline acted sooner on the vein, more strongly, and for longer than on the parallel artery (Fig. 2). In most abdominal veins in mammals the noradrenalin content per unit of smooth-muscle component is greater than in arteries [3], and the reactivity of the smooth muscles of the capacitive vessels in response to sympathetic effects is higher than that of resistive vessels [10].

Difril and odifaline, during the first few hours after injection, did not reduce, but increased the intensity of fluorescence in the vas deferens and iris – organs with the richest adrenergic innervation. This effect was observed in the iris 1 h after injection of difril, and in the vas deferens 1 h after injection of odifaline. This may depend to some extent on increased liberation of monoamines into the blood from the adrenals under the influence of difril [8] and, in consequence of this, an increase in the uptake of catecholamines by the numerous adrenergic nerves of these organs.

These experiments thus revealed differences in the response of adrenergic nerves of different organs to the action of difril and odifaline. Denudation of the catecholamine depots in the adrenergic fibers and organs with direct, indirect, and mixed innervation, and also in blood vessels, followed a different course. These results suggest that adrenergic nerves in organs and tissues are heterogeneous. Furthermore, since the most intensive and prolonged denudation of the endogenous catecholamine reserves was observed in the adrenergic nerves of the veins, by contrast with arteries, it can be concluded that a definite role in the changes arising in the circulatory system under the influence of difril and odifaline and in the therapeutic coronary dilator and hypotensive effect of these drugs, is played by their effect on veins.

LITERATURE CITED

1. O. M. Avakyan and A. A. Kaltrikyan, Biol. Zh. Armenii, No. 2, 142 (1979).
2. V. A. Govyrin and G. R. Leont'eva, Zh. Évol. Biokhim, Fiziol., 7, 145 (1971).
3. V. A. Govyrin and A. D. Bukinich, Arkh. Anat., No. 12, 30 (1974).
4. P. O. Manolov, Farmatsiya (Sofia), 21, 2 (1971).
5. S. Axelsson, A. Bjorklund, B. Falck, et al., Acta Physiol. Scand., 87, 57 (1973).
6. H. Grobecker and T. Malmfors, Arch. Exp. Pathol. Pharmakol., 266, 51 (1970).
7. E. Höflich, Med. Welt (Stuttgart), 28, 1747 (1977).
8. W. Kloot, K. Hiroshi, and K. Kuniko, Gen. Pharmacol., 6, 63 (1975).
9. B. R. Mackenna, Acta Physiol. Scand., 63, 413 (1965).
10. S. Mellander, Acta Physiol. Scand., 50, Suppl. 176 (1960).
11. P. A. Nasmyth, Physiol. Pharmacol., 4, 129 (1967).
12. K. C. Nielson and C. Owman, Circulat. Res., 21, 45 (1967).
13. F. Wohlrab, Arch. Exp. Pathol. Pharmakol., 243, 382 (1962).

EFFECT OF ETHIMIZOLE ON PERMEABILITY OF THE BLOOD–CELL BARRIER IN CARBON TETRACHLORIDE-POISONING-INDUCED HEPATITIS

V. E. Neiko

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KEY WORDS: hepatitis; blood–cell barrier; protective action of ethimizole.

Acute and chronic hepatitis are among the more important forms of liver disease in medical practice [2, 8, 9]. In experimental hepatitis changes arising in the parenchyma and blood vessels of the liver closely resemble those observed in man in the active phase of chronic hepatitis [4].

Stabilization of lysosomal membranes is disturbed in the hepatocytes and Kupffer cells of rats with experimental hepatitis, and this is associated with changes in the activity of lysosomal enzymes [5].

The object of the present investigation was to study the effect of ethimizole* on permeability of the blood–cell barrier of the internal organs in experimental hepatitis due to CCl_4 poisoning.

EXPERIMENTAL METHOD

Ethimizole was injected intramuscularly into the experimental animals twice a day as a 0.3% solution in a dose of 0.3 mg/kg body weight for 7 days [1, 3, 6].

*1-Ethylimidazole-4,5-dicarboxylic acid-bis-methylamide.

Department of Pathological Physiology, Ivano-Frankovsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.)

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