dles of collagen fibers hyalinized in places. In areas of the gland adjacent to the pseudocyst sclerosis and lipomatosis progressed.

In the group of animals treated with tageflar the boundary zone was greatly reduced in size. In it, just as in the control, tubulo-epithelial reconstruction of the acini took place. However, unlike in the control the tubulo-epithelial complexes were less numerous and were formed by flattened, dystrophic EP, which were subsequently replaced by connective tissue.

Administration of tageflar in a dose of 0.1 mg/kg thus had a marked effect on the morphogenesis of experimental pancreatitis. The most important and characteristic features of the pathomorphosis of pancreatitis in this case are: 1) accelerated formation of complete necrosis of irreversibly damaged EP and reduction in size of the perifocal zone of necrobiosis with reconstruction of acini into tubulo-epithelial complexes; 2) considerable preservation of the microcirculation in the zone of necrosis of the parenchyma with intensification of PML-infiltration of necrotic tissues of the gland, acceleration of their elimination and organization of foci of injury; 3) inhibition of sclerosis and lipomatosis formation in the pancreas; 4) lowering of the blood levels of pancreatic enzymes in the hemorrhage stage of experimental pancreatitis.

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EFFECT OF ZIXORIN ON DIURESIS AND RENAL TRANSPORT OF XENOBIOTICS

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KEY WORDS: zixorin; diuresis; tubular secretion of kidneys

Zixorin (Gedeon Richter, Hungary), a new inducer of the mono-oxygenase system, has been widely used in a number of conditions when stimulation of glucuronide formation and excretion of foreign substances has been required. In the character of this action it resembles phenobarbital [6]. It was shown previously that an inducer of microsomal enzymes, studied at the Institute of Cytology and Genetics, Siberian branch, Academy of Sciences of the USSR, potentiates tubular secretion in the kidneys [1].

It was decided to study zixorin in this respect. This was important also because zixorin has an immunomodulating action, and in particular, it stimulates antibody formation and phagocytosis [4]. Meanwhile it has been shown that immunostimulators accelerate tubular transport of foreign substances [2]. Besides tubular secretion, it was also decided to study the effect of zixorin on other processes in the kidneys, namely diuresis and sodium and potassium excretion, which may be of practical importance.

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TABLE 1. Effect of Zixorin (given for 4 days in a dose of 100 mg/kg internally) on Maximal Diodone Transport in Rats (M ± m; n = 14)

Parameter	Control	Experiment
Diuresis, ml/min	0,091±0,018	0,093±0,009
Filtration, ml/min	0,90±0,094	0,98±0,060*
Secretion of diodone, mg/min	0,27±0,021	0,39±0,036**

Legend. *p < 0.05, **p < 0.02 compared with control.

TABLE 2. Effect of Zixorin (100 mg/kg, internally) on 24-Hourly Diuresis and on Water Diuresis in Rats (M ± m)

Parameter	24-hourly diuresis, ml		Water diuresis, ml/3 h	
	control	expt.	control	expt.
Diuresis	9,1±0,98	8,8±1,36	6,4±0,37	6,9±0,30
Excretion, μM, of sodium	26,9±2,17	32,4±5,53	29,2±3,67	25,2±3,84
potassium	624±32	603±63	108±7,8	110±17
creatinine	31±2,1	34±2,2		

EXPERIMENTAL METHOD

Experiments were carried out on 62 noninbred rats weighing 160-200 g. The effect on diuresis was studied in chronic experiments on animals, kept in individual metabolism cages, constantly receiving food with free access to water. The 24-hourly diuresis and excretion of sodium, potassium, and creatinine were determined. The last of these was used as an indicator of glomerular filtration. In experiments to study diuresis the drug was given 1 h before water loading (5% of body weight) and urine was collected after 3 h. Tubular secretion was studied in chronic experiments by the method in [3] and in acute experiments, by determining maximal diodone transport. Zixorin was given internally in a dose of 100 mg/kg body weight. To study the effect of zixorin on tubular secretion, the drug was given daily for 4 days. The level of diodone secretion was determined in the initial period (twice or three times), after the first and fourth doses, and also 3 and 7 days after the end of the course.

EXPERIMENTAL RESULTS

Zixorin stimulated tubular secretion and this effect lasted for the first few days after the end of the course (Fig. 1). To verify this result, acute experiments were carried out to determine maximal diodone transport. In this case, the possibility that changes in glomerular filtration could have an effect was completely ruled out, and secretion was expressed in absolute quantities of transported substrate. As will be clear from Table 1, zixorin did not change glomerular filtration but it increased the maximal secretion of diodone significantly (by 44%).

After administration of zixorin the 24-hourly diuresis and excretion of sodium, potassium, and creatinine remained virtually unchanged (Table 2). No changes in diuresis likewise were observed after water loading. This confirms that zixorin has no effect on renal transport of water and electrolytes.

The stimulating effect of zixorin on tubular secretion in the kidneys may indicate a definite connection between the mono-oxygenase and the secretory and transport systems of the kidneys, more especially because they both are involved in protection of the body against xenobiotics. The character of this connection is not yet clear. In a study of interaction between the mono-oxygenase and immune systems, reciprocal relationships were found [5]. In

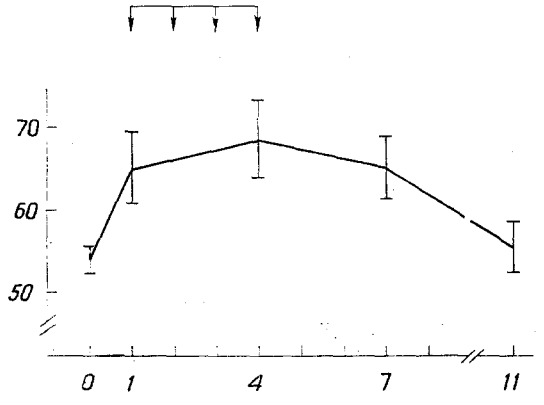

Fig. 1. Effect of zixorin on tubular secretion in rats. Abscissa, time of observation (in days); ordinate, excretion of diodone (in %/h). 0) Average initial data. Arrows indicate administration of zixorin (100 mg/kg, internally).

the case which we studied, the mono-oxygenase system of cytochromes and tubular secretion in the kidneys reacted in the same direction to the inducer.

The results thus indicate that inducers of microsomal enzymes may stimulate tubular transport of xenobiotics in the kidney without affecting diuresis or sodium and potassium excretion.

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