

HEPATOPROTECTIVE EFFECT ON SPIROCYCLIC OXINDOLIC DERIVATE IN THE CONDITIONS OF ACUTE LIVER'S ISCHEMIA

Zhurenko D.S., Lukienko O.V., Tsubanova N.A.

The National University of Pharmacy, Kharkiv, Ukraine

zidikor@gmail.com

Hypoxic hepatitis, also known as ischaemic hepatitis or shock liver, is an acute liver injury caused by hepatic hypoxia. Cardiac failure, respiratory failure and septic shock are the main underlying conditions. In each of these conditions, several haemodynamic mechanisms lead to hepatic hypoxia. A shock state is observed in only 50% of cases. Current trends in modern medicine and pharmacy is to create, study and implementation in medical practice drugs with multiple organ action, namely anti-hypoxic, hepatoprotective and ability to restore energy metabolism in the damaged liver cells in the treatment and prevention of ischemic and reperfusion injury of the liver tissue and its microvasculature. Promising compound in this aspect can be considered a new substance - 4,3'-spiro[(2-amino-3-nitrile-4,5-dihydropyrano[3,2-c]chromen-5-one)-5-methyl-2'-oxindole], connection 77, by the structure of the nucleus of the molecule (4H-pyrano [3,2-c] chromen) is a structural analogue of melatonin. Influence was studied the spirocyclic oxindolic derivate in a dose 5 mg/kg and preparations of comparison vita-melatonin (5 mg/kg) and thiotriazolin (48 mg/kg) on lethality on animals, activity of cytolysis, free-radical oxidization and functional activity of the liver in the conditions of acute experimental ischemia is studied. At ischemia of the liver without pharmacological protection of animals groups control pathology there was a high mortality rate (64,3%), which was significantly indicating the severity of the condition and figure significantly higher than in the group of control rats (0%, $p < 0,001$). Therapeutic and prophylactic administration of the compound 77 and comparator drugs significantly reduced the percentage of mortality in all three experimental groups, but it should be noted that the protective effect of compound 77 was the most pronounced and has reduced the mortality rate to 0%, what is significantly exceeded this figure vita-melatonin (40 %, $p < 0,001$) and hepatoprotector thiotriazoline (25%, $p < 0,01$). Compound 77 showed marked membrane protective effect of significantly reducing the cytolytic activity of enzymes in the blood serum. The expressed antioxidant, anticytolytic action spirocyclic oxindolic derivate in dose 5 mg/kg is established. It is found that the total hepatoprotective effect of new substance exceeds activity of preparations of comparison of vita-melatonin and thiotriazolin. It is proved that the a new substance to had significant hepatoprotective activity due to multicomponent mechanism of action, namely, antihypoxic, antioxidant, cytoprotective properties.