

EVALUATING CYCVALON ACTIVITY UNDER CONDITIONS OF CHRONIC ENDOTOXICOSIS MODELS IN RATS

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Using the results of instrumental and numerical investigations of structure – activity relationships at derivatives and structural analogs of cinnamic acid, we predicted and then experimentally proved the action of the new bile-expelling drug cycvalon (a cyclohexanone derivative) in rats under the chronic model endotoxiosis. The drug effectively prevented cytotoxic damage of liver and kidney tissues and the vascular and fibroplastic mechanisms. At the same time, cycvalon is of low effectiveness with respect to the development of lung tissue damage, chronic pneumonia, and pneumofibrosis.

Chronic endotoxiosis (CET) is developed in many pathological states involving the supply of endotoxins – bacterial wall components – into the systemic blood flow. Since free-radical oxidation is among the main processes in CET pathogenesis, it is expedient to treat this disease using antioxidants and drugs possessing hypolipidemic and cytoprotective properties. The present state of CET therapy can by no means be considered satisfactory, which makes necessary the search for new drugs effective in the treatment of this disease [1].

One promising drug for the treatment of CET is cycvalon, a structural analog of cinnamic acid, which is known to exhibit antioxidant, bile-expelling, hypolipidemic, and hepatoprotector properties [2]. This study was devoted to evaluating the efficacy of cycvalon action on the experimental models of CET in rats.

METHODS OF INVESTIGATION

The drug efficacy was evaluated using an experimental model of CET developed at the Chair of Pathological Anatomy of the Volgograd State Medical University [3]. The experiments were performed on 32 laboratory white mongrel rats weighing 180–220 g divided into test and control groups, each containing 4–5 animals. The model CET (control groups) was induced by administering tetrachloromethane (CCl_4) in a dose of 5 ml/kg with a cheese – oil mixture before meals five times a week, followed by the intraperitoneal injection of a solution of bacterial lipopoly-

saccharides from *Sal. typhimurium* (Sigma, USA) in a dose of 0.2 ml/kg on the sixth day. Upon this treatment the lethality of animals in the untreated control group approached 10% within 30 days and reached 40–50% by 60 days. The reference (intact) group consisted of animals under standard vivarium conditions. Animals in the test groups received, in addition to CCl_4 , cycvalon in a dose of 5 ml/kg with a cheese – oil mixture.

After the observation period, the tissues of liver, lung and kidney taken from animals of all groups were characterized by morphological techniques using hematoxylin staining [4]. The morphometric examination was performed using the conventional principles of systemic quantitative analysis [5]. The samples of tissues were examined and characterized using a computer-controlled setup Vi Morpho 4.0 (Russia) including a binocular microscope, high-resolution video camera, a personal computer, color printer, and the corresponding software package.

The liver was histomorphometrically studied with determination of the volume fraction (VF m^3) of connective tissues (including interlobular partitions) and hepatocytes; the average volume ($\text{AV, } \mu\text{m}^3$) of hepatocyte nuclei and Kupffer's cells. Analogous investigation was performed for the lung cells, which were characterized by the VF of connective tissues and alveolocytes and the AV of alveolar nuclei and alveolar macrophages. The histomorphometric investigation of kidneys included evaluation of the VF of glomerular capillaries and connective tissues and the AV of nuclei (determined separately for the proximal and distal nephron tubules). In order to characterize the CET

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