AN APPRAISAL OF SINGLE ORGANS AND TISSUES LOADING AFTER XENOBIOTIC INVASION IN ORGANISM BY MEANS OF EXTRACTIONS POTENCIES CALCULATED USING FIRST PASS EFFECT (MODEL METHOTREXATE) IN RATS

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In the study of effect of New Chemical Entity (NCE) entering in organism it is advantageous to know the concentration of its loading the single organs and tissues. The greater stress is, the higher probability of undesirable effect and higher influence of pathologically changed organ function on effect kinetics and dosing can originate. The indicator of the stress degree can be the extraction potency (EP) of organ and tissues calculated using AUCs of plasma levels after administration of NCE in part of blood circuit before and after supplying the studied organ or area (2). Subtracting relation between these AUCs from one it is possible obtain the EP of studied organ (3). Using the application of NCE intravenously, retrogradly in carotis dextra, intraperitoneally, perorally, intraduodenally and in vein portal in groups of rat males narcotised by 60 mg/kg i.p., it is possible to calculate AUC of levels estimated from 5 samples of blood uptaken in 5 intervals up to 120 min and than the EP of lung, liver, mesenteric apparatus, gastro enteric tract, intestinal wall and also the rest of organism. This is demonstrated in case of methotrexate (1) where the stress corresponding to extraction activity index is for lung 0,158,liver – 0.118, Git – 0.959, intestine – 0.989, for submucose and mesentery 0.2, for the rest of organism without peritoneum – 0.51. It is possible to conclude, that the risk for lung and liver is very equal, the highest for gastrointestinal tract and the site of maximal absorption after p.o. administration is the gastric wall.

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