



## Elimination kinetics of the novel prodrug cinazepam possessing psychotropic activity in mice

Sergei I. Schukin<sup>1</sup>, Vladymyr G. Zinkovsky<sup>2</sup>, Olga V. Zhuk<sup>2</sup>

<sup>1</sup>Department of Biology, Odessa National University, Dvoryanskaya 2, Odessa 65000, Ukraine

<sup>2</sup>University of Opole, Department of Biotechnology and Molecular Biology, Kominka 4, PL 45-035 Opole, Poland

**Correspondence:** Olga Zhuk, e-mail: olga\_zhuk@uni.opole.pl

---

### Abstract:

The kinetics of excretion of the novel tranquilizer cinazepam (3-hydroxy-7-bromo-5-(*ortho*-chlorophenyl)-1,2-dihydro-3H-1,4-benzodiazepin-2-one hemisuccinate (I)) in mice after a single administration and different schemes of multiple administration were determined. Mass balance was studied daily in excretions of mice (feces and urine) for 5–10 days. We observed that monoexponential renal excretion of <sup>14</sup>C-cinazepam and its metabolites predominated with all dosage regimens. Cinazepam and its metabolites were almost fully (> 90%) eliminated in urine and feces over the period of study (5–10 days), which means that no significant accumulation of the drug in the body occurred. The kinetic parameters of drug excretion were not significantly different after a single injection compared with those following multiple doses of <sup>14</sup>C-cinazepam administration. This finding suggests the absence of induction (repression) of enzymatic systems after multiple administration and lack of influence on the kinetic scheme of cinazepam elimination from mice.

In our work, we also presented a modification of the Mansgeldorf's method for analysis of kinetic parameters during multiple administration of the tranquilizer. We demonstrated that our modified approach could be equally and efficiently applied for interpreting experimental data during a single dose administration and after chronic administration of xenobiotics. The use of this method made it possible to evaluate the relative efficiency of elimination processes and to find current values for excretion constants during sampling intervals.

### Key words:

cinazepam, elimination, single and multiple administration, mice, modifications of Mansgeldorf's method

---