

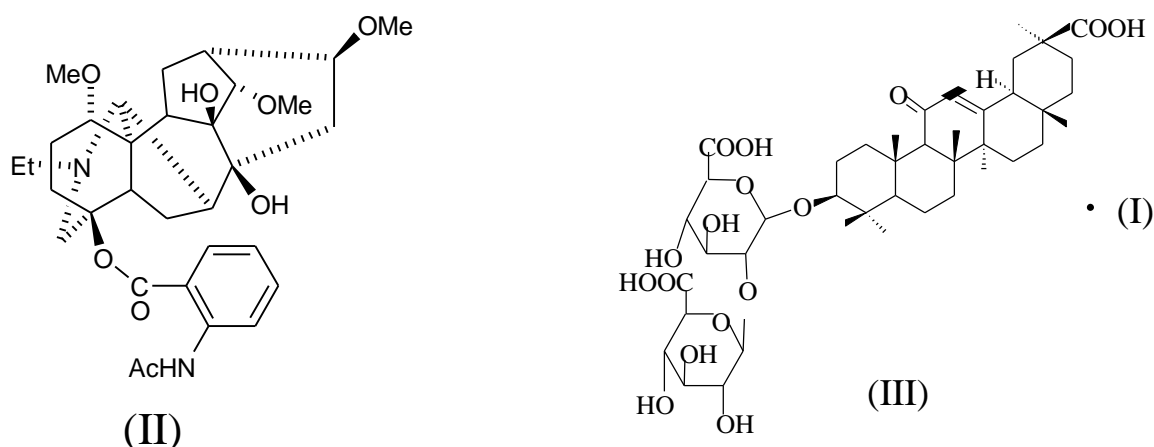
## Lappaconitin and its Derivatives - Psychotropic Agents

Lyudmila N. Popova, Margarita P. Dolgikh, Nikolai A. Deys, Tatiana G. Tolstikova,

Natalya A. Pankrushina, Elvira E. Shults

*Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 9 prosp.Akad.Lavrent'eva, 630090 Novosibirsk, Russia . Fax: +7(383 2) 344752. E-mail: benzol@nioch.nsc.ru*

Alkaloids of different *Aconitum* species are employed as analgesic and antirheumatics in traditional Chinese folk medicine. On the basis of lappaconitin (I) an antiarytmic drug allapinine was established. Unfortunately, the clinical trials had limited success, mainly due to its extremely high toxicity. The objective of the present study was to examine the psychotropic activity of the major *Aconitum* alkaloid lappaconitine, its N-oxide (II) (produced by oxidation of (I) with m-Cl-PBA) and the salts of (I) with  $\alpha$ -glycyrrhizic acid (1:2) (compound III).



Male albino mice were used to test toxicity and psychotropic activity on (  $20 \pm 2$  g). The  $LD_{50}$  values were estimated by the standard method of Karber. The toxicity of compounds (II) and (III) was 60-100 times more lower than those of lappaconitin.

Lappaconitin (I) and its derivatives (II) possess stimulative activity on the dopamine receptors, salts (III) - on the serotonin receptors.

Compounds (I) and (II) blocked activity of reserpine, exert antagonism to the corasole, nicotine, acetylcholine; decreased the narcotic action of chloralhydrate. Lappaconitin (I) and its N-oxide (II) exert a depressive action in the "Head twitch" test. Compounds (I) and (II) induced psychomotor stimulation of the apomorphine and L-DOPA - stimulation dopamine system.

Salts (III) exert strongly stimulative action on CNS. The compound possess nicotinic acetylcholinomimetic and analeptic activity ( induced convulsant action nicotine, acetylcholine and corasole).

Compound (III) blocked action of reserpine, potentiated of the chloralhydrate sleeping times, strongly stimulative effect of 5-oxytriphthophane - stimulation serotonin system.