careful examination of endogenous 3',5' GMP changes during the smooth muscle responses. This work was supported by US PHS Grants HE14534 and HE14179. We thank Dr. J. F. Kuo for his interest and helpful discussion about this work.

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Similarity between the effects of dimethyl and monomethyl tricyclic drugs on reserpine effects in the frog and 5-hydroxytryptamine uptake by human blood platelets

We have previously observed that the tertiary (dimethyl) tricyclic antidepressants, imipramine and amitriptyline, are much stronger than their secondary (monomethyl) derivatives, desipramine and nortriptyline, in enhancing the effects of reserpine in the frog (Oxenkrug & Lapin, 1971). Our data were confirmed by Frank (1971). The effects of reserpine (loss of the righting reflex and appearance of twitches of the extremities) are presumably related to activation of the central 5-hydroxytryptamine (5-HT) processes (Lapin, Oxenkrug & others, 1970). The tertiary compounds are also reported to be more potent than secondary ones in blocking the uptake of 5-HT into central neurons (Carlsson, 1970) and into blood platelets (Todrick & Tait, 1969). The latter were a useful model for the neuronal uptake of 5-HT (see Pletscher, 1968).

Recently we compared the influence of aminopropyl derivatives (imipramine and desipramine) with that of the corresponding β-aminopropionyl derivatives (IPK-17 and IPK-18) of dibenzazepine on the effects of resperine in the frog and on the uptake of 5-HT by human blood platelets. Dimethyl (IPK-17) and monomethyl (IPK-18) β-aminopropionyl dibenzazepine (synthesized in Leningrad Technological Institute) have the imipramine-like pharmacological spectrum (Lapin, 1966; Lapin & Schelkunov, 1968).

Male frogs (*Rana temporaria*) were used as described earlier (Oxenkrug & Lapin, 1971). The uptake of 5-HT by human blood platelets was studied under conditions similar to those described by Ahtee & Saarnivaara (1971) with the exception that we precipitated proteins with 0·1N $HClO_4$. The statistical significance of the results was determined by Student's *t*-test.

Table 1. *Influence of compounds on the effects of reserpine in the frog.*

	Minimal effective doses (mg kg^{-1}) for: Inhibition of righting reflexes after pretreatment with phenelzine (25 mg kg^{-1}) + reserpine (10 mg kg^{-1})	Appearance of twitches after pretreatment with phenelzine (25 mg kg^{-1}) + reserpine (10 mg kg^{-1})
Imipramine	2·5	2·5
Desipramine	20·0	20·0
IPK–17	10·0	10·0
IPK–18	5·0	5·0

Table 2. *Influence of compounds on the uptake of 5-HT by human platelets.*

	Inhibition of 5-HT uptake %			
	3×10^{-5}M	$P<$**	3×10^{-6}M	$P<$**
Imipramine	83·80 ± 2·01 (3)*	0·002	51·35 ± 3·41 (6)	0·001
Desipramine	76·60 ± 7·84 (3)	0·01	28·70 ± 4·86 (6)	0·002
IPK-17	64·00 ± 5·76 (3)	0·01	18·66 ± 3·46 (6)	n.s.
IPK-18	74·60 ± 8·75 (3)	0·002	56·86 ± 7·45 (6)	0·001

* Number of experiments in parentheses.
** In comparison with control (without 5-HT). At 3×10^{-6}M P (imipramine–desipramine) $<0·02$; P (IPK-17–IPK-18) $<0·01$.

Tables 1 and 2 show that drugs IPK-17 and IPK-18, like imipramine and desipramine, enhanced the effects of resperine in the frog and inhibited the uptake of 5-HT by human blood platelets. Amongst the β-aminopropionyl agents *vs* aminopropyl agents, the monomethyl derivative was stronger than the dimethyl derivative in both tests. The same "inverse" order of potency was described for the bicyclic compounds Lu 3-010 [1-(3-methylaminopropyl)-1-phenyl-3,3-dimethylphthalane] and its corresponding tertiary amine (Lu 3-009) (Ahtee & Saarnivaara, 1971). Hence desmonomethylation does not always result in enhancing the 5HT-positive properties.

The correlation in the action of the studied agents in both tests suggests that potentiation of the effects of reserpine in the frog by tricyclic antidepressants is related to inhibition of the reuptake of 5-HT from the synaptic cleft into presynaptic nerve endings. This leads to an increase of the amount of free 5-HT acting on the specific receptors.

Both tests may be useful for investigation of the 5-HT effects that play an important role in the mechanism of thymoanaleptic action of psychotropic drugs (see Carlsson, Corrodi & others, 1969; Lapin & Oxenkrug, 1969).

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A new chemotherapeutic property of metronidazole: effect against oxyurids in mice

Metronidazole, 1-(2′-hydroxyethyl)-2-methyl-5-nitroimidazole, was first found to be effective against genito-urinary trichomoniasis (Cosar & Julou, 1959). Later, it was shown to be useful in the treatment of giardiasis (Mandoul, Dargelos & Millan, 1961), acute ulcerative gingivitis (Shinn, 1962) and amoebiasis (Powell, Macleod & others, 1966). It was also claimed to be effective in controlling acute clinical manifestations in cases of dracunculosis (Pardanani & Kothari, 1970). Metronidazole is therefore an established antiprotozoal agent with broad-spectrum activity. We have found it effective against oxyurids, the common intestinal helminth of rodents.

Experiments were carried out in laboratory bred SRC strain albino mice of either sex. Previously uninfected mice, 18–20 g, grouped according to sex, were kept in association with other mice infected with oxyurids of both the species, *Aspiculuris tetraptera* and *Syphacia obvelata*. After 20 days a random sample showed the infections to be established uniformly. The newly infected mice were distributed in cages, 5 in each, according to sex and weight. Metronidazole, at different doses, was suspended in 0·2% tragacanth and 0·2 ml of the suspension was administered by gavage. Either a single dose or three once daily doses were given. For every treated group a similarly infected group was kept as control. On the 5th day after the start of treatment, both the treated and control group mice were killed and individual, intestines and caecae were examined microscopically for the presence of oxyurids. At single doses of metronidazole of 225 mg kg^{-1} and above and after three daily doses of 75 mg kg^{-1} and above, there was 100% clearance of oxyurids while the controls all remained infected.

These results prove that the rodent oxyurids are susceptible to metronidazole. This compound is well tolerated and does not produce serious toxic effects. In view of the findings, it may prove active against pinworms, *Enterobius vermicularis*, in man.

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