The effect of neuroleptic derivatives of butyrophenone on the uptake of 5-HT by human blood platelets

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The uptake of 5-HT by blood platelets is a useful model for the neuronal uptake of 5-HT (Paasonen, 1965) and it is generally accepted that impramine-like drugs are the most potent inhibitors of this uptake (Tuomisto, 1974). Neuroleptic derivatives of phenothiazine inhibit the uptake of 5-HT by human (Todrick & Tait, 1969) and rabbit (Ahtee & Paasonen, 1968) blood platelets. However, the influence of derivatives of butyrophenone on the uptake of 5-HT by blood platelets has not been studied. I have therefore examined the influence of five derivatives of butyrophenone on the uptake of 5-HT by human blood platelets.

The rate of uptake was evaluated by the rise of 5-HT content in platelets during 5 min incubation of 1 ml of platelet rich plasma with 1 μg 5-HT at 37° (Oxenkrug, 1975). 5-HT content in platelets was determined spectrofluorimetrically (Oxenkrug, 1973). IC50 values were calculated by Dr V. N. Amatuni according to the program published by Finney (1972).

In each experiment a blood pool from 2–3 healthy donors was used. All drugs were dissolved in saline and added (in 0·1 ml) to platelet-rich plasma 5 min before the 5-HT.

The derivatives of butyrophenone inhibited the uptake of 5-HT, though not as strongly as imipramine (see Table 1).

The inhibiting effect of the derivatives on 5-HT uptake by blood platelets suggest that they could inhibit 5-HT reuptake in neurons. This supposition corresponds with the observation of Kannengiesser, Hunt & Raynaud (1973) that haloperidol inhibited the uptake of ^{14}C-5-HT by synaptosomes from rat brain. The inhibition of 5-HT reuptake from the synaptic cleft to the presynaptic nerve ending enhances the quantity of 5-HT molecules that influence the postsynaptic receptors (Modigh, 1973). Thus, the inhibition of 5-HT uptake by haloperidol and its derivatives supports their 5-HT-positive effect.

Table 1. *The effect of compounds on the uptake of 5-HT by human blood platelets.*

	Inhibition of 5-HT uptake in % (means ± s.e. from 6 exp.)*			IC50 (means ± s.e.)
	10^{-6} M	10^{-5} M	3×10^{-5} M	
Imipramine	71·85 ± 4·53	91·66 ± 2·12		$4{\cdot}52\times10^{-7}$ $\pm0{\cdot}93\times10^{-7}$**
Trifluperidol	34·00 ± 5·75	64·67 ± 3·39	75·00 ± 1·75	$3{\cdot}46\times10^{-6}$ $\pm0{\cdot}86\pm10^{-6}$***
Spiramid	22·17 ± 6·16	48·67 ± 3·96	70·84 ± 2·94	$8{\cdot}47\times10^{-6}$ $\pm0{\cdot}17\times10^{-6}$***
Fluanisone	31·34 ± 3·96	44·17 ± 5·45	62·34 ± 2·21	$1{\cdot}10\times10^{-5}$ $\pm0{\cdot}53\times10^{-5}$***
Haloperidol	16·84 ± 4·25	45·54 ± 4·56	67·00 ± 4·65	$1{\cdot}13\times10^{-5}$ $\pm0{\cdot}21\times10^{-5}$***
Droperidol	23·67 ± 4·97	40·00 ± 4·23	56·60 ± 1·22	$1{\cdot}90\times10^{-6}$ $\pm0{\cdot}60\times10^{-6}$***

* All results are statistically significant ($P<0{\cdot}02$, Student's t-test) in comparison with control (saline instead of drugs).
** Statistically significant ($P<0{\cdot}01$) in comparison with each drug.
*** Statistically significant ($P<0{\cdot}01$) in comparison with imipramine, trifluoperidol and spiramid.

At present the antimanic action of haloperidol is associated primarily with its ability to block dopaminergic receptors (Janssen, 1967). According to the 'permissive' hypothesis of Prange (1974) the 5-HT-positive effect is a component of antimanic action. The data obtained allow the suggestion that the 5-HT-positive effect of haloperidol and its derivatives may play a definite role in the drug's antimanic activity.

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