

# Letters to the Editor

## ANTICHOLINESTERASE ACTIVITY OF BUFOTENINE

Sir,

Bufotenine (5-hydroxy-N, N-dimethyltryptamine) has been shown to be the hallucinogenic principle of several plants used in mystico-religious tribal rites (3). Chemically it is a close structural analogue of physostigmine. The present communication reports the anticholinesterase activity of bufotenine. Both *in vitro* and *in vivo* methods have been used and the results have been compared with those obtained with physostigmine.

*In vitro* studies were done by the biological assay technique of Hemsworth and West (4). Blood was collected from dogs using heparinised syringe, and centrifuged for 10 min so as to separate the R.B.C. and plasma. The plasma was drained off and measured. The R.B.Cs. were washed with 0.9% saline and then haemolysed in a volume of distilled water corresponding to the volume of plasma. One ml of plasma or 1 ml of haemolysed R. B. Cs. were taken in a series of test tubes. They were divided into three sets. In the first set only acetylcholine bromide (10  $\mu\text{g}$  in 2 ml) was added, in the second and third set graded doses of physostigmine and bufotenine, respectively, were added and then acetylcholine bromide was added in the same dose as in the first set. All the test tubes belonging to the different sets were incubated at 37° for 30 min. In the absence of an inhibitor acetylcholine was completely destroyed by the cholinesterase (CHE) present in the plasma (psuedo) and R.B.Cs., (true). In the presence of an inhibitor (physostigmine or bufotenine), the residual acetylcholine was biologically assayed on frog rectus abdominis muscle preparation by the method of Richter and Crossland (6). The sample was bracketted between two doses of known acetylcholine differing by a factor of two. The amount of acetylcholine present in the sample was calculated by plotting log dose-response curve of the standard acetylcholine and reading of the response of that of the unknown sample. The amounts of plasma, R.B.C., physostigmine and bufotenine used, had no effect of their own on this tissue. The concentrations of physostigmine and bufotenine required to completely antagonise plasma (psuedo) were 2.0  $\mu\text{g}/\text{ml}$  and 45  $\mu\text{g}/\text{ml}$  respectively and those required for R.B.C. (true) cholinesterase were 2.0 and 45.5  $\mu\text{g}/\text{ml}$ , respectively, (means of ten experiments). The  $\text{ED}_{50}$ , of physostigmine against both types of cholinesterases were 0.8  $\mu\text{g}/\text{ml}$  respectively and those of bufotenine were 27.5  $\mu\text{g}/\text{ml}$  respectively. Thus the activity of both the drugs was equal against either type of cholinesterase.

*In vivo* studies were done using the chromodacryorrhea test (2) in albino rats. Acetylcholine (2mg/kg, sc) was injected in albino rats (100-150 g) and those secreting red tears within 10 min were selected for further studies. The animals were divided into groups of ten each. One group served as control and received only saline while in the other groups different doses of physostigmine or bufotenine were injected intraperitoneally. Thirty min later a small dose

of acetylcholine (0.2 mg/kg sc) was injected into all the groups. The rats were examined for the presence of red tears at 2 min intervals upto 14 min, by touching a piece of filter paper on the conjunctiva. Physostigmine produced a positive response in all the animals at a dose of 0.1 mg/kg while bufotenine showed similar activity at a dose of 2.5 mg/kg. None of the saline treated control animals showed the presence of red tears.

The results show that bufotenine has both *in vitro* and *in vivo* anticholinesterase activity, similar to that of physostigmine but 20-30 times weaker.

Bufotenine has recently been shown to be a potent histamine releaser (1). Earlier reports (5) suggest that its major pharmacological actions are due to its nicotinic activity. The present study implicates it in yet another physiological transmitter activity. Serotonin, of which bufotenine is the N-dimethylated derivative, has been reported to produce cholinesterase inhibition, both *in vitro* and *in vivo* (5). It is also of interest to note that LSD and psilocybin have been shown to possess anticholinesterase activity (6) and like bufotenine, are potent hallucinogenic agents.

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