THE OXYTOCIC ACTIVITY OF DL-5-HYDROXYTRYPTOPHAN

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Incubation of the isolated rat uterus with α-methyldopa or bromolysergic acid diethylamide produces a complete inhibition of oxytocic activity of 5-hydroxytryptophan.

STUDYING the formation of 5-hydroxytryptamine (5-HT) in X-irradiated aqueous solution of 5-hydroxytryptophan (5-HTP) we observed that 5-HTP possesses a slight oxytocic activity, the sensitivity threshold being 5×10^{-5}. It seemed to us of interest to find out if this activity can be attributed to 5-HTP itself or to its decarboxylation product 5-HT. For that reason the influence of α-methyl-β-(3,4-dihydroxyphenyl)alanine (α-methyldopa) which is an inhibitor of 5-hydroxy-L-tryptophan decarboxylase, and bromolysergic acid diethylamide (bromLSD) which is an antagonist of 5-HT, was investigated on the oxytocic activity of 5-HTP.

METHODS

The isolated oestrous rat uterus suspended in de Jalon solution (Gaddum, Peart and Vogt, 1949) was used to test the oxytocic activity. The

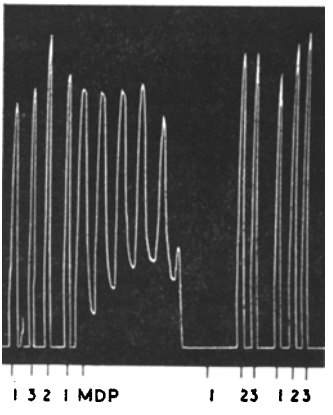

FIG. 1. Isolated oestrous rat uterus, 1, 0·1 mg./ml. 5-hydroxytryptophan. 2, 0·003 μg./ml. 5-hydroxytryptamine. 3, 0·15 μg./ml. acetylcholine. MDP, 1·5 mg./ml. of α-methyldopa. 10 min.

temperature of the organ bath was 28–29°. The following substances were used, DL-5-hydroxytryptophan monohydrate (Roche, England); 5-hydroxytryptamine creatinine sulphate monohydrate (Fluka, Switzerland); α-methyl-β-(3,4-dihydroxyphenyl)alanine (M.D.); bromolysergic acid diethylamide (Sandoz, Switzerland); acetylcholine hydrochloride (Roche, Switzerland).

RESULTS

As shown in Fig. 1 the oxytocic activity of 5-HTP was completely inhibited by α-methyldopa, while this activity of 5-HT and acetylcholine remained unaltered. In few experiments, besides the complete inhibition of 5-HTP, a partial and transient inhibition of 5-HT was observed (Fig. 2). 5-HT and 5-HTP were both completely antagonised by bromLSD (Fig. 3).

Discussion

It is well known that α-methyldopa is an inhibitor of 5-hydroxytryptophan-L-decarboxylase (Westermann, Balzer and Knell, 1958). Since 5-HTP is inhibited by this agent in our experimental work, it is very likely that its oxytocic activity can be ascribed to 5-HT formed by decarboxylation in the uterus tissue. The experiments with bromLSD, an antagonist

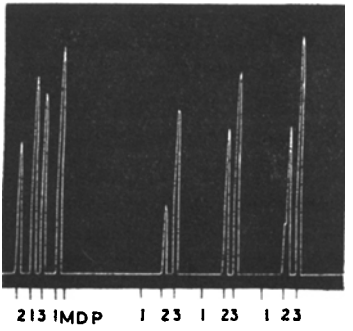

FIG. 2. Isolated oestrous rat uterus. 1, 0·3 mg./ml. 5-hydroxytryptophan. 2, 0·004 μg./ml. 5-hydroxytryptamine. 3, 0·1 μg./ml. acetylcholine. MDP, 2·5 mg./ml. α-methyldopa. 10 min.

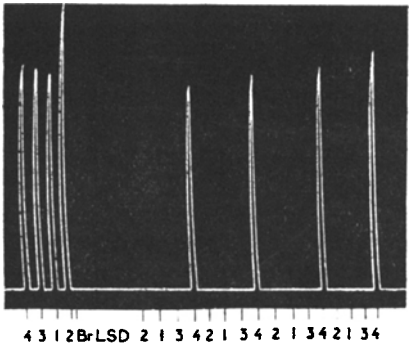

FIG. 3. Isolated oestrous rat uterus. 1, 0·05 mg./ml. 5-hydroxytryptophan. 2, 0·1 mg./ml. 5-hydroxytryptophan. 3, 0·004 μg./ml. 5-hydroxytryptamine. 4, 0·1 μg./ml. acetylcholine. BrLSD, 0·1 μg./ml. bromLSD. 5 min.

of 5-HT (Cerletti and Konsett, 1956), also support this presumption. Reported observations might suggest the presence of 5-HTP decarboxylase in the tissue of uterus. This possibility should be taken into account while using the uterus as test organ for studies on the biosynthesis of 5-HT.

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