PHARMACOLOGY

INFLUENCE OF APOMORPHINE ON THE INACTIVATION OF ADRENALIN IN THE CAT ORGANISM

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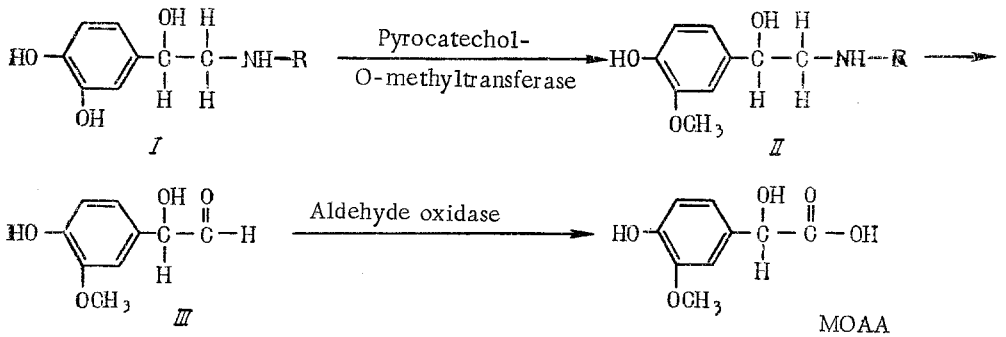
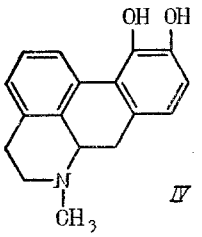
In recent years, data have appeared indicating that the main pathway of inactivation of noradrenalin and adrenalin (I) in the organism consists of methylation of the hydroxyl groups situated in the meta-position to the side chain, catalyzed by pyrocatechol-O-methyltransferase [1-4]. The O-methylated derivatives of pyrocatecholamines (II) formed in this case undergo oxidative deamination under the influence of monoamine oxidase, with conversion to 3-methoxy-4-hydroxyamygdalic aldehyde (III), which then, under the influence of aldehyde oxidase, is converted to 3-methoxy-4-hydroxyamygdalic acid (MOAA).



Since the structure of apomorphine (IV) contains a pyrocatechol group, there was some basis for believing that apomorphine may serve as a substrate for pyrocatechol-O-methyltransferase, and thus, may exert an inhibiting effect upon the process of O-methylation of pyrocatecholamines.



The purpose of this work was to investigate the influence of apomorphine upon the MOAA content in the urine of cats during adrenalin loading.

*Deceased.

MOAA Content in the Urine of Control Cats and Cats that Received Apomorphine

Control		Experiment	
animal no.	MOAA content	animal no.	MOAA content
1	52	7	27
2	28	8	15
3	27	9	15
4	32	10	17
5	60	11	10
6	60	12	10

EXPERIMENTAL PROCEDURE

The experiments were conducted on 12 cats, placed under ethaminal narcosis (80 mg/kg intraperitoneally). The urinary bladders of the animals were entirely evacuated before the experiment by puncture. Six cats received apomorphine hydrochloride through the jugular vein in a dose of 10 mg/kg in the form of a 1% solution; the remaining cats (controls) received the corresponding amount of isotonic sodium chloride solution intravenously. After 20 min, all the animals received intramuscular injections of adrenaline hydrochloride in a dose of 0.5 mg/kg, in the form of a 0.02% solution, and after 3 h, all the urine was collected from them for investigation for MOAA content.

MOAA was determined according to the method of Pisano, et al. [5]. MOAA was extracted from acidified and sodium chloride-saturated urine with ethyl acetate, from which it was transferred to a sodium carbonate solution. Then the MOAA was oxidized to vanillin, by adding periodate. The excess periodate was reduced with metabisulfite in the presence of acetate–phosphate buffer. After this, vanillin was extracted with toluene and transferred to sodium carbonate solution, in which the vanillin concentration was determined spectrophotometrically.

EXPERIMENTAL RESULTS

The data obtained are presented in the table in arbitrary extinction units, multiplied by 10^3. In the statistical treatment of the results, it was found that the MOAA content in the urine of the control cats is 41.4 (20.5-62.3) arbitrary units, while in the cats that received apomorphine it is 13.4 (9.4-17.4) arbitrary units (the confidence limits of the averages at $P = 0.05$ are presented in parentheses). The difference in the MOAA content in the urine among the control animals and among the animals that received apomorphine is statistically significant ($0.002 < P < 0.01$). The MOAA content in the urine does not depend on the amount of diuresis, which is not significantly changed under the influence of apomorphine.

Thus, the data that we obtained indicated that apomorphine statistically reliably inhibits O-methylation of adrenalin in the cat organism. This phenomenon is evidently explained by the fact that apomorphine itself serves as a substrate for pyrocatechol-O-methyltransferase.

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