phase, however, to a less extent, as do exogenously administered PGE_1 and PGE_2 (1–50 ng/ml). (ii) The ganglionic relay in the peripheral part of the hypogastric nerve was extremely sensitive to the inhibitory substance (cf. Fig. 2), and the same was found for exogeneous PG (0·1–0·4 ng/ml). (iii) Incubation of the vas deferens with an inhibitor of PG synthesis (5,8,11,14-eicosatetraynoic acid, ETA, 1–20 μg/ml) (Downing, Ahern & Bachta, 1970)| led to a partial or total abolishment of the endogeneous inhibition. (iv) Release of prostaglandin-like material, mainly resembling PGE_2, from the vas deferens on nerve stimulation, was established by silicic acid thin-layer chromatography (Gréen & Samuelsson, 1964).

It can be concluded from the present results that the mechanical response of the isolated vas deferens to nerve stimulation is under a dual influence from excitatory and inhibitory agents. Several experimental data support the hypothesis that the endogenous inhibition could be due to release of prostaglandins that are acting by restricting the amount of noradrenaline liberated from adrenergic nerves by stimulation (cf. Hedqvist, 1970; Wennmalm, 1971). With regard to the effectiveness of the autoinhibition described even at very low frequencies of stimulation (2–5 Hz), it is tempting to suggest that this process might play a modulating role in the nerve-induced mechanical activity of this organ in *in vivo* conditions, as recently suggested by Wennmalm (1971) for the rabbit heart. Furthermore, the results provide the first indications of an inhibitory action of PG on ganglionic neuro-transmission.

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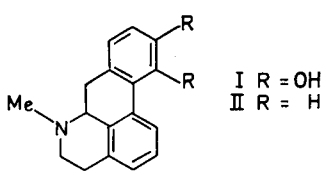
On the dopamine-like action of apomorphine

Apomorphine (I) elicits a gnawing compulsion in rats which is due to stimulation of inhibitory dopaminergic neurons in the corpus striatum (Ernst, 1967, 1969; Ernst & Smelik, 1966; Ungerstedt, Butcher, & others, 1969). It apparently reduces the impulse flow of these neurons by a negative feedback mechanism arising from dopamine receptor stimulation, although an indirect mechanism involving the release of dopamine from central stores has also been implicated (Fekete, Kurti & Pribusz, 1970). However, pretreatment with iproniazid does not potentiate apomorphine-induced gnawing (Ernst, 1967), and apomorphine both retards the utilization of brain dopamine (Andén, Rubenson, & others, 1967) and inhibits its biosynthesis (Goldstein, Freedman, & Backstrom, 1970). It is therefore likely that apomorphine acts directly



I R = OH
II R = H

on central dopamine receptors in producing gnawing effects, and it also appears to produce peripheral vasodilation by an action upon peripheral dopamine receptors (Yeh, McNay & Goldberg, 1969). From molecular orbital calculations, it has been concluded that the important part of the apomorphine molecule in its interaction with dopamine receptors is not the dihydroxytetrahydroaminonaphthalene moiety but the tetrahydroisoquinoline moiety (Kier & Truitt, 1970). We dispute this conclusion, and our results, and those of others, show it to be erroneous.

Gnawing was measured in male Porton rats (200–250 g) in metal cages with wire grid bottoms (Ernst, 1967). Apomorphine hydrochloride (5 mg/kg, i.p.) consistently produced a syndrome of stereotyped licking accompanied by periods of gnawing, in both normal and iproniazid-pretreated rats. Aporphine (II), tetrahydroisoquinoline, *N*-methyltetrahydroisoquinoline, or phenethylamine, administered (i.p.) as their hydrochlorides, produced no gnawing or licking movements at doses up to 20 mg/kg. The five compounds were also compared with dopamine for depressor effects on the blood pressure of urethanized rabbits (Burn & Rand, 1958). Apomorphine was twice as potent as dopamine (minimum effective dose, 0·05 mg/kg, i.v.) while aporphine had less than one-fifth the potency of dopamine; the other compounds produced pressor effects except for *N*-methyltetrahydroisoquinoline which was inactive.

If Kier and Truitt are correct, then one would have expected that aporphine and the two isoquinoline derivatives would have had apomorphine-like effects on dopamine receptors, while phenethylamine might also attain a folded conformation corresponding to that proposed for the dopamine pharmacophore. The structural requirements for dopamine-like renal vasodilatation are very specific (Goldberg, Sonneville & McNay, 1968), and phenethylamine and the two isoquinolines (Hanna & Shutt, 1953) do not have vasodilator properties in contrast to apomorphine. Our results support these findings and suggest that similar structural specificity exists in the central nervous system. Apomorphine is reported to be inactive on dopaminergic neurons in *Helix aspersa* (Woodruff & Walker, 1969) but the invertebrate nervous system may well differ from that in the mammal. Our thesis is therefore that if apomorphine, in producing dopamine-like effects, acts on dopamine receptors then it does so in a way which intimately involves the dihydroxytetrahydroaminonaphthalene moiety.

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