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THE ACTION OF SOME AMINES RELATED TO ADRENALINE: METHOXY-PHENYLISO-PROPYLAMINES

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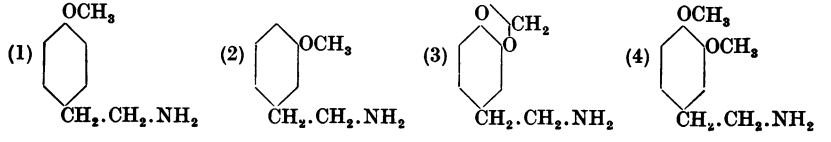
In previous papers [Epstein, Gunn & Virden, 1932; Elphick & Gunn, 1934] an account has been given of the actions of certain compounds, related to adrenaline in so far as they possess the phenylethylamine skeleton, in which a (—H) has been replaced by (—OCH_3) either on the benzene ring or on the ethylamine side-chain or on both. Determinations were made especially of (*a*) the toxicity, (*b*) the action on the central nervous system and (*c*) the presence or absence of peripheral sympathomimetic action, of the compounds investigated.

In the present paper a similar account is given of the actions of certain methoxy derivatives of phenylisopropylamine (benzedrine). As the investigation is primarily concerned with those derivatives rather than with benzedrine itself, which is only used here for comparison, no attempt has been made to discuss the already considerable literature on the latter substance.

To indicate the object of this paper, a brief summary is necessary of the results arrived at in the two papers mentioned, and, to facilitate comparison, the compounds used in the present paper are numbered consecutively with those in the previous papers.

Epstein *et al.* [1932] investigated

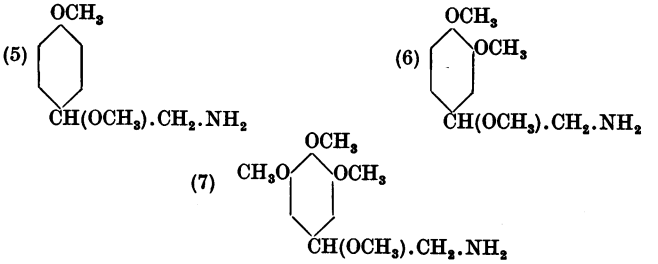
(1) *p*-Methoxy-phenylethylamine.
(2) *m*-Methoxy-phenylethylamine.
(3) 3 : 4-Methylenedioxy-phenylethylamine.
(4) 3 : 4-Dimethoxy-phenylethylamine.



The minimum lethal dose per kg. by intraperitoneal injection for mice was found to be approximately (1) 0·15 g., (2) 0·23 g., (3) 0·30 g. and (4) 0·42 g. The first three compounds all stimulate the central nervous system but with some differences in the site of action; the fourth compound produces only depression. The first three compounds produce a peripheral sympathomimetic action in cats but not in rodents, while the fourth has no sympathomimetic action in any of these animals. All four compounds have a direct stimulant action on smooth muscle. In the decerebrate cat compounds (1) and (2) have about 1/300, compound (3) about 1/400, of the pressor activity of adrenaline.

Elphick & Gunn [1934] investigated the following compounds, with a view to determining the effect of introduction of a methoxyl group in the β position of the ethylamine side-chain.

(5) *p*-Methoxyphenyl-methoxyethylamine.
(6) 3 : 4-Dimethoxyphenyl-methoxyethylamine.
(7) 3 : 4 : 5-Trimethoxyphenyl-methoxyethylamine.

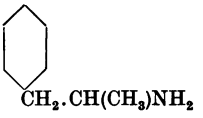


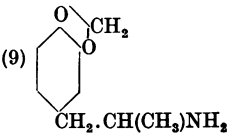
This addition of a methoxyl group to the side-chain diminishes physiological activity as compared with that of the corresponding compounds lacking this methoxyl group. Thus compound (5) differs from compound (1) as follows: it possesses about two-fifths of the toxicity for mice and of the pressor action in decerebrate cats; it has lost the sympathomimetic action which the latter compound exhibits in cats and it has a weaker stimulant action on the central nervous system.

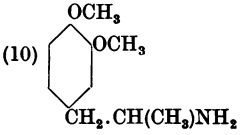
The present paper deals with the following compounds:

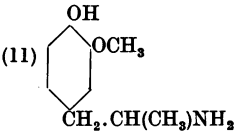
(8) β-Phenyl-isopropylamine ("benzedrine").
(9) 3 : 4-Methylenedioxyphenyl-isopropylamine.
(10) 3 : 4-Dimethoxyphenyl-isopropylamine.
(11) 3-Methoxy : 4-hydroxyphenyl-isopropylamine.

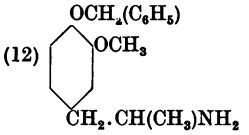
(12) 3-Methoxy : 4-phenylmethoxyphenyl-isopropylamine.
(13) 3-Phenylmethoxy : 4-methoxyphenyl-isopropylamine.

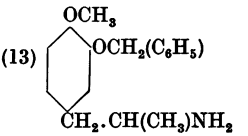
(8) 

(9) 

(10) 

(11) 

(12) 

(13) 

Toxicity

The minimum lethal dose was determined in mice by intraperitoneal injection. As the available quantity of most of the drugs was not sufficient to permit the determination of lethality in groups of animals, the approximate minimal lethal dose was estimated by administration of graded doses, not less than ten animals being used for each assay. The following table gives the minimal lethal dose in grams of drug per kilogram of animal:

Compound	(8)—0·12	Compound	(11)—0·70
,,	(9)—0·12	,,	(12)—0·12
,,	(10)—0·25	,,	(13)—0·20

Some points in regard to the relative toxicities of the first four of these compounds are of interest when compared with the findings in the previous two papers. Epstein *et al.* [1932] found that, in compounds of this series with an ethylamine side-chain, the 3 : 4-dimethoxy compound was less toxic than the 3 : 4-methylenedioxy compound, which in turn was less toxic than either the *p*- or *m*-methoxy compound. Elphick & Gunn [1934] found that in compounds with a methoxy-ethylamine side-chain the 3 : 4-dimethoxy compound was less toxic than the *p*-methoxy compound. In the present group with an isopropylamine side-chain the dimethoxy compound (10) is again less toxic than the 3 : 4-methylenedioxy compound (9). Though all the possible compounds necessary for a complete comparison have not been available, it can be said from these experiments that, with three different types of side-chain, the 3 : 4-

dimethoxyphenyl compounds are less toxic than the 3 : 4-methylenedioxy compounds, which latter are less toxic than the *p*- or *m*-methoxy compounds.

With regard to compound (11), 3-methoxy: 4-hydroxyphenylisopropylamine, no compound with this nucleus has been previously investigated. Alles [1933] found that the introduction of a phenolic hydroxyl group in the *p*-position lowered the toxicity of both phenylethylamine and of phenylisopropylamine. Epstein *et al.* [1932] found that *p*-hydroxyphenylethylamine is less toxic than *m*-methoxyphenylethylamine. The result of adding both groups to the nucleus could, therefore, hardly be predicted. Actually the result is greatly to diminish the toxicity of phenylisopropylamine. In other words this compound also suggests that the presence of a phenolic hydroxyl group in the *p*-position diminishes toxicity.

Lastly, by comparison of the toxicities of compounds (3) and (4) with compounds (9) and (10), it appears that the isopropylamine side-chain renders a compound more toxic than the corresponding compound with an ethylamine side-chain. Alles [1933] came to the same conclusion with a different set of compounds.

In all our experiments toxicity has been determined mainly by intraperitoneal injection in mice. Reservation must be made that identical relations may not hold good for other animals.

Symptoms produced

In the investigation of compounds related to adrenaline, attention has usually been focused upon the pressor and the sympathomimetic actions, relatively little being known about the action of most compounds on the central nervous system.

Epstein *et al.* showed that methylation of a single —OH group in the para position changed *p*-hydroxy-phenylethylamine from a depressant into a convulsant. They also found that *m*-methoxy- and methylenedioxy-phenylethylamine had a stimulant action on the central nervous system, whereas the dimethoxy compound was almost purely depressant. Since the discovery of the central stimulant properties of benzedrine and of its use in various conditions of nervous depression, more interest has been aroused in the action of such compounds on the central nervous system. We have investigated the nervous symptoms produced by the present series of compounds in mice, by simple observation and also by cinematograph records. It is impossible by "clinical" notes to record all

the symptoms, and a cinematograph record of the symptoms of intoxication of an animal not only gives a more complete record and one which can be scrutinized repeatedly but also enables a comparison to be made with symptoms produced by other compounds in other experiments done at other times. Even with cinematographic aid, only a crude diagnosis of the site of action on the central nervous system can be made. Several of the compounds under consideration produce a type of stimulation of the central nervous system closely resembling that produced by benzedrine, but the symptoms produced by different compounds are not identical, indicating minor differences in the site or intensity of action. Similar differences would almost certainly be exhibited also in man, with consequent differences in their therapeutic values.

A description of the symptoms produced by each compound would require lengthy protocols, and it will suffice for the present purpose to enumerate the chief symptoms produced in mice by benzedrine itself and then briefly to compare with those the symptoms produced by the other derivatives.

Benzedrine (compound 8) produces in the first instance the following effects: increased motor activity with jerky progression and frequent spontaneous leaps, sometimes accompanied by squealing, tremors, champing of the jaws and panting respiration; convulsions definitely of the cortical type with no marked effect on the spinal reflexes. If the dose is sufficiently large, paralytic symptoms supervene, respiration becomes slower and death appears to be due to respiratory paralysis.

Compound (9) produces very similar effects, the convulsive movements being rather more violent. As the discovery of a compound belonging to the benzedrine group which would have a more powerful stimulating effect on the central nervous system than benzedrine itself would be not only of pharmacological interest, but probably of therapeutic value, further experiments were done to compare compounds (8) and (9). The symptoms produced in rabbits were very similar in the case of both compounds. Both produced a great increase in motor activity and a very marked acceleration of respiration. A dose of 0·02 g./kg. of compound (9) in one rabbit increased the respiration rate from 60 to 240 per min. A symptom produced by both compounds is one which we have not observed with other stimulants of the central nervous system. As a warning signal, or in some cases possibly as a sexual manifestation, rabbits raise their hindquarters and bring the hind legs down with a thud on the ground. During the period of stimulation with compound (9), this symptom occurs repeatedly, and it was found also to occur with benze-

drine. It may be a useful localizing symptom. In blood-pressure experiments on spinal cats it was found that compound (9), if in sufficient doses, almost invariably produces reflex movements, whereas these were not observed with benzedrine. Also in experiments on the intact cat, deeply anaesthetized with ether, compound (9) evoked movements, but compound (8) did not.

From the experiments mentioned on mice, rabbits and cats we came to the conclusion that methylene-dioxyphenyl-isopropylamine is a more powerful stimulant to the central nervous system than phenyl-isopropylamine.

Compound (10) produced slight tremors and ataxia, with no marked stimulant effect. The superior stimulant effect of compound (9) over compound (10) affords a parallel to the phenylethylamine compounds, in which case also the methylenedioxy compound (3) has a much more powerful stimulant action than the dimethoxy compound (4).

Compound (11) was of interest as it possesses a phenolic —OH in the *p*-position and a phenolic methoxyl in the *m*-position. Alles [1933] found that the hydroxyphenyl derivatives had less marked effect in awakening animals from anaesthesia than the corresponding phenyl derivatives. Epstein *et al.* [1932] found, from the mere symptoms of poisoning, that in the case of the phenylethylamines a phenolic —OH suppressed stimulation while a phenolic —OCH_3 preserved or increased it. In a compound with both groups (11) the influence of the hydroxy group seems to preponderate; for it was found to have only a very slight stimulant action, producing slight tremors but no gross convulsive movements.

Compounds (12) and (13) produce a clonic convulsive effect, being definitely more stimulant than compound (10). The stimulant effect is less enduring than with compound (9).

A study of these compounds, so far as they have been available, shows agreement and permits the following conclusions in regard to the stimulation of the central nervous system:

(1) With an isopropylamine side-chain, the compounds may be arranged, in diminishing intensity of stimulation, in the following order of modification of the phenyl nucleus:

$$CH_2\begin{matrix}O\\O\end{matrix} > H- > \begin{matrix}CH_3O-\\CH_3O-\end{matrix} > \begin{matrix}HO\\CH_3O-\end{matrix}$$

The degree of stimulation of the nervous system was estimated, from the cinematograph and observational records, mainly by the intensity, frequency and duration of the convulsive movements.

(2) So far as compounds of this series have been available for comparison, the isopropylamine side-chain renders a compound more stimulating to the central nervous system than the ethylamine side-chain. Thus phenylisopropylamine is more stimulant than phenylethylamine and the methylenedioxy- and dimethoxy-isopropylamines are more stimulant than the corresponding ethylamine compounds. The same difference has been found to be true of some other compounds at present under investigation with different phenolic nuclei.

Isolated mammalian heart

In the case of compounds (1), (2) and (3), it was found that they produced typical sympathomimetic effects (augmentation and acceleration) on the perfused heart of the cat but no such effect on the heart of

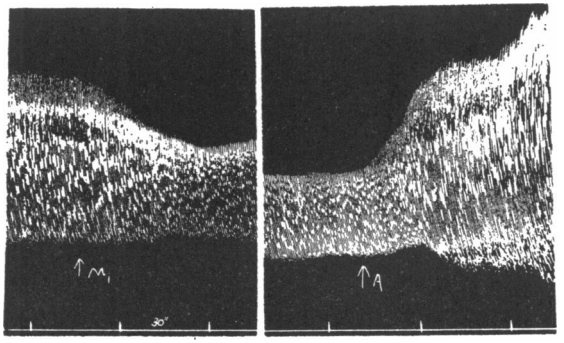


Fig. 1. Isolated perfused rabbit's heart: showing ($\uparrow M_1$) depressant action of methylenedioxy-phenylisopropylamine (1 in 25,000) contrasted with ($\uparrow A$) sympathomimetic effect of adrenaline (1 in 5,000,000).

the rabbit. It was, in fact, these experiments that first suggested, what was afterwards confirmed for other tissues, that sympathomimetic responses to these compounds might differ in the cat and in rodents. The reaction of the hearts of cats and rabbits to the new series of compounds was, therefore, of interest.

In the case of compounds (8)–(13) it was found also that none of them produced any characteristic sympathomimetic effect on the perfused heart of the rabbit. Fig. 1, for example, shows a purely depressant action of compound (9), 1 in 25,000, contrasted with the typical effect later produced in the same heart, by adrenaline 1 in 5,000,000. On the cat's heart, however, typical augmentation and acceleration was obtained, especially with compounds (8), (9) and (11). Fig. 2 shows the absence of

effect with 1 in 50,000 of compound (11) on the rabbit's heart (upper tracing) and the typical sympathomimetic effect of the same strength of

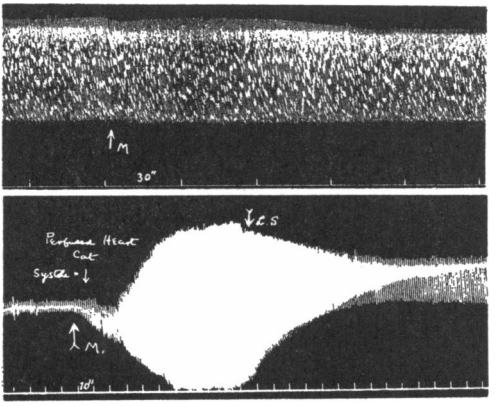


Fig. 2. Isolated perfused mammalian hearts: showing (upper tracing) absence of effect of 3-methoxy : 4-hydroxy-phenylisopropylamine (1 in 50,000) in the rabbit's heart, contrasted with the sympathomimetic effect (lower tracing) of the same solution in the cat's heart.

solution on the cat's heart (lower tracing). Fig. 3 shows almost equal effects produced on the cat's heart, by injection into the side tube of the perfusion apparatus, of 0·1 μg. adrenaline (*a*) and 5 μg. of compound (11). The effect of benzedrine itself was qualitatively similar.

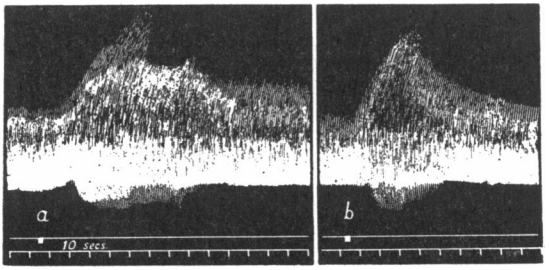


Fig. 3. Isolated perfused cat's heart: showing similarity of effect produced by (*a*) 5 μg. of 3-methoxy : 4-hydroxy-phenylisopropylamine and (*b*) 0·1 μg. adrenaline.

Compounds (10), (12) and (13) produced only depression of the heart, even in the cat. Fig. 4 shows the depression produced by 0·5 mg. of compound (12) (*b*) and compound (13) (*c*), as contrasted with 0·1 μg. adrenaline (*a*).

So far as the evidence from the perfused heart is concerned, therefore, a sympathomimetic effect is obtained in the cat with compounds (8), (9)

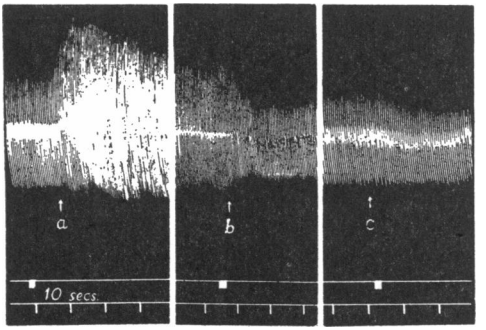


Fig. 4. Isolated perfused cat's heart: showing (*a*) sympathomimetic action of 0·1 μg. adrenaline, (*b*) depressant action of 5 mg. of compound (12), and (*c*) of compound (13).

and (11) but not with compounds (10), (12) and (13), and no clear sympathomimetic effect is obtained in the rabbit with any of these compounds.

Blood pressure

Blood pressure experiments were done on spinal cats, on cats anaesthetized with ether, and on rabbits anaesthetized either with urethane or ether. While qualitative effects on blood pressure were readily decided, quantitative effects involving comparison of two compounds were difficult to measure accurately.

Nearly all workers with compounds of this type have noted that a previous injection of one compound may modify the effect of subsequent injections either of the same, or of related, compounds. This being the case, one might hope to make quantitative comparisons by utilizing only the first injection in each animal, the experimental conditions being the same in each case; but, even so, it was found that there were fairly wide differences even with the same dose in different individuals of the same species. In these respects, most of these compounds differ from adrenaline with which the usual experience is that one can obtain almost identical rises of blood pressure with repeated identical doses in the same animal, even if these injections are closely spaced.

The following experiment may be cited as an example of a quite

common result. In a spinal cat, the following doses were given at 15 min. intervals with the resulting rises in blood pressure:

Dose and drug	Rise of blood pressure
10 μg. adrenaline	120 mm.
1 mg. compound 11	100 „
1 mg. „	82 „
2 mg. „	106 „
5 mg. „	96 „
1 mg. „	46 „
10 μg. adrenaline	120 „

With successive doses of compound (11), the rise of pressure produced was not proportional to the dose, 1 mg. producing first a rise of 100 mm., then of 82 mm., and, after a total dose of 9 mg., only 46 mm. On the other hand a dose of 10 μg. adrenaline produced the same effect after 10 mg. of compound (11) as it had done in the beginning. Often there was some reduction in the pressor effect of adrenaline following previous doses of these compounds, but it seemed always to retain its effect on repetition better than did any of the other compounds.

The following statements are based upon a large number of experiments but must be taken with the reservations mentioned above.

(*a*) *Cats*

Compounds (8), (9) and (11) all produced marked pressor effects lasting longer, for an equivalent rise of pressure, than the effects of

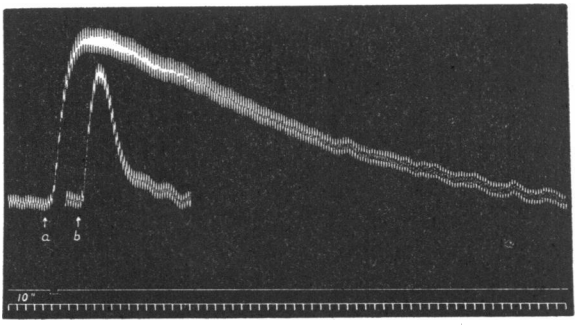


Fig. 5. Spinal cat, blood pressure: showing (*a*) prolonged effect of 5 mg. of 3 methoxy : 4-hydroxy-phenylisopropylamine, as compared with (*b*) 10 μg. of adrenaline.

adrenaline. Of these, compound (11) was most powerful, 2 mg. producing a rise equal in height to that produced by 10 μg. adrenaline; in other words it has about 1/200 of the pressor activity of adrenaline. The pressor effect of it is, however, much more lasting. Fig. 5 shows the effect of 5 mg. of compound (11) (*a* in figure) compared with that of

10 μg. adrenaline (*b* in figure). The first injection produced a rise of blood pressure of 125 mm., the second injection 95 mm. After adrenaline,

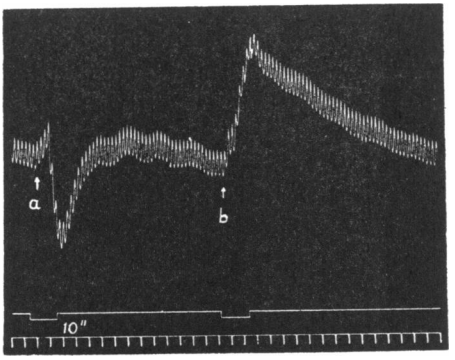


Fig. 6. Spinal cat, blood pressure after ergotoxine: showing "reversal" by adrenaline (10 μg.) at (*a*) but not by 3-methoxy : 4-hydroxy-phenylisopropylamine (2 mg.) at (*b*).

the blood pressure reached its normal level in 2 min., but, with compound (11), blood pressure did not reach the normal level until after 10 min. The prolonged duration of the pressor effect of this compound, coupled with

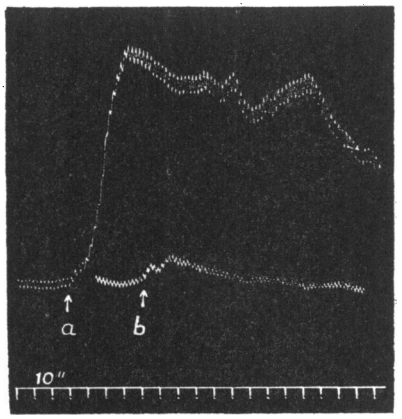


Fig. 7. Spinal cat, blood pressure: showing (*a*) pronounced rise of pressure by 1 mg. of methylenedioxy-phenylisopropylamine and (*b*) slight rise of pressure by 1 mg. dimethoxy-phenylisopropylamine.

its low toxicity and absence of stimulant action on the central nervous system, suggest that it might be of therapeutic value for raising blood pressure, especially in cases where central stimulation is to be avoided.

The pressor effect of compound (11) is not "reversed" by doses of ergotoxine which reverse the effect of adrenaline. Fig. 6 shows the effect of 10 μg. adrenaline after ergotoxine. This dose which, previous to the injection of ergotoxine, had produced a rise of 95 mm. now produced a fall of 40 mm., but 2 mg. of compound (11) still produced a rise of 60 mm., only slightly less than was produced by the same dose previous to ergotoxine. Detrick, Millikan, Modern & Thienes [1937] found that ergotamine sometimes increased and sometimes diminished the pressor effect of benzedrine but did not reverse it.

With the phenylethylamine group of compounds it was found by Epstein, *et al.* that the pressor effect of the methylenedioxy compound (3) was much greater than that of the dimethoxy compound (4). The same is true of the phenylisopropylamine group. Fig. 7 shows the effects of 1 mg. each of compounds (9) and (10). The former produced a very pronounced rise of pressure (*a*) while the pressor effect of the latter (*b*) was negligible.

(*b*) *Rabbits*

In rabbits, anaesthetized with ether or urethane, the rise of pressure produced by all compounds (8)–(11) was less than that produced by corresponding doses in the spinal cat. This was true even if the vagi were

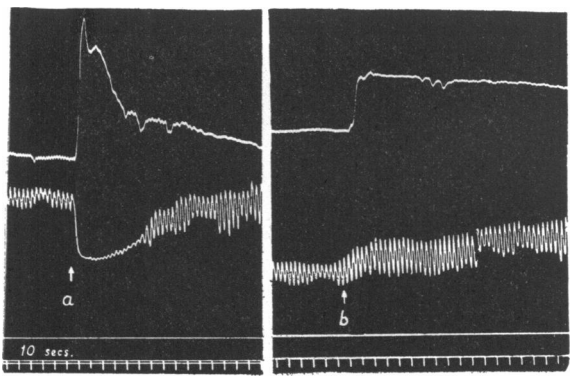


Fig. 8. Rabbit, urethane anaesthesia, record of blood pressure (upper tracing) and intestinal movements (lower tracing): showing (*a*) transient rise of pressure and inhibition of intestinal tone and movements by adrenaline (20 μg.) and (*b*) more prolonged rise of pressure and stimulation of intestinal tone and movements by 25 mg. of compound (11).

cut, and is also characteristic of adrenaline itself. With repeated equal doses the pressor effects were more quickly diminished, or even replaced by a fall, in the rabbit than in the cat.

Fig. 8 shows the effect of 20 μg. adrenaline, which produced a rise of 72 mm. (*a*), and of 25 mg. compound (11), which produced a rise of 32 mm. The effect of the latter was, however, much more lasting.

With regard to compounds (12) and (13), the former had a slight pressor action in small doses (1–3 mg.), but the latter none. With larger doses (5–10 mg.) both substances produced a fall of pressure.

Uterus

As the response of the uterus to sympathetic stimulation varies in different species of animal, this organ supplies a convenient test for sympathomimetic action.

On the isolated non-pregnant cat's uterus all compounds (8)–(11) produced marked stimulation. Fig. 9 shows the effect of benzedrine 1 in

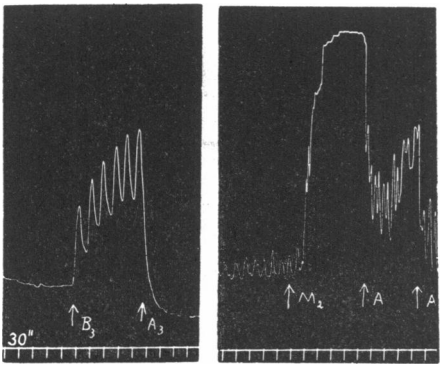


Fig. 9. Isolated uterus of non-pregnant cat: showing at B_3 stimulation of muscle by benzedrine (1 in 100,000) and at A_3 relaxation of muscle by adrenaline (1 in 50,000,000); at M_2 stimulation by compound (9) (1 in 100,000), with subsequent relaxation, at *A*, by adrenaline (1 in 25,000,000).

100,000 (B_3), which produced a rise of tone with induction of increased rhythmic movements. Adrenaline, 1 in 50,000,000, promptly relaxed the uterus (A_3). In the same tracing at M_2, compound (9), 1 in 100,000, was added to the bath and produced a vigorous sustained contraction of the uterus. The addition of adrenaline, 1 in 25,000,000, relaxed the uterus, but two applications failed to abolish the rhythmic movements. Similar effects were obtained with compounds (10) and (11). It is evident from these experiments that, so far as the cat's uterus is concerned, these compounds do not have a sympathomimetic action. The corresponding compounds of the phenylethylamine group usually inhibited the contractions of the non-pregnant cat's uterus in low concentrations, though

stronger solutions caused contraction even in a uterus which was inhibited in the usual manner by adrenaline.

The rabbit's uterus was also always stimulated by compounds (8)–(11).

Compounds (12) and (13), on the other hand, if in strong concentrations always relaxed the uteri both of cats and rabbits. The effect was slower in onset than that of adrenaline and suggested a simple muscular depression rather than a sympathomimetic inhibition.

Intestine

The exsected intestine of the *rabbit* was usually stimulated by compounds (8)–(11). Fig. 10 shows this effect produced by benzedrine (B_1) and compound 11 (M), the concentration being 1 in 10,000 in both cases.

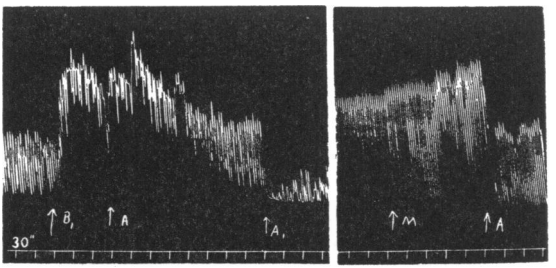


Fig. 10. Isolated intestine of rabbit: showing stimulation of intestinal movements by benzedrine (1 in 10,000) at B, and by compound (11) (1 in 10,000) at M, with relaxation by adrenaline (1 in 10,000,000), in both cases, at A.

Adrenaline, 1 in 10,000,000 (A), caused inhibition of the intestine after both compounds. Fig. 8 shows stimulation of the intestine *in situ* with compound (11) (b in tracing) as contrasted with the inhibition produced by adrenaline (a in tracing).

Usually these compounds in low concentrations stimulated also the isolated intestine of the *cat*. In the intestine *in situ*, however, they all produced relaxation. From these experiments on the isolated uterus and intestine of the cat, it would seem that the phenylisopropylamine compounds have more direct stimulant action and less sympathomimetic action than the corresponding phenylethylamine compounds.

Compounds (12) and (13) relax the isolated intestine of both cat and rabbit. This is in accord with the effects of these compounds on other tissues. For example, in rabbits and cats, they both have mainly a depressor effect on blood pressure, weaken the contraction of the perfused heart and relax the uterus as well as the intestine. All the effects are,

therefore, compatible with a general depressant action on involuntary muscle. The addition of the phenyl group in these compounds has, therefore, not only removed all trace of a sympathomimetic action but has changed the stimulant action on involuntary muscle, which is so characteristic of the other compounds, into a depressant one.

Conclusions

The actions of some derivatives of phenylisopropylamine (benzedrine) have been investigated and compared with those of corresponding compounds of phenylethylamine, the pharmacology of which has previously been described.

Subject to reservations mentioned in the text, the following main conclusions can be drawn from a study of this series of compounds:

1. With the same phenyl nucleus, the isopropylamine side-chain renders a compound more toxic, more stimulant to the central nervous system and less completely "sympathomimetic" than the corresponding compound with an ethylamine side-chain.

2. Whether the side-chain be ethylamine or isopropylamine, a methylenedioxy compound is more toxic, more stimulant to the central nervous system and more completely "sympathomimetic" than a dimethoxy compound.

3. The presence of a HO— group in the para position renders a compound less toxic, less stimulant to the central nervous system, but more completely sympathomimetic than when there is H— or CH_3O— in this position.

4. Many compounds of the type under consideration retain the power of producing the characteristic peripheral sympathomimetic actions of adrenaline in cats when they cease to produce these effects in rodents. In rabbits the augmentor-accelerator effects on the perfused heart are absent or inconspicuous, whereas in cats they are pronounced; and in rodents the action on smooth muscle is one of general stimulation, independent of the effects of sympathetic stimulation, whereas in cats the various motor and inhibitor effects that adrenaline produces on the smooth muscle of different organs are more faithfully reproduced.

5. In the case of dimethoxy-phenylisopropylamine, if an additional phenyl nucleus is introduced into the methoxy group in either the 3 : or 4 : position, this change renders the compound more stimulant to the central nervous system, but the stimulant action on smooth muscle is replaced by a depressant one.

6. Two of the compounds have properties which may prove of therapeutic value. 3-Methoxy : 4-hydroxy-phenylisopropylamine has a pressor action much more lasting than that produced by adrenaline. It has a low toxicity and may be found useful for raising blood pressure in cases where a stimulant action on brain is undesirable. 3 : 4-Methylenedioxy-phenylisopropylamine is a more powerful stimulant of the central nervous system than phenylisopropylamine (benzedrine) in mice, rabbits and cats, and may prove superior to the latter in this respect also in man.

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