38 Mechanism of Cardiovascular Actions of Heptanolamines. J. GARRETT and W. OSSWALD (Portugal).

On the basis of experimental results chiefly obtained on the papillary muscle preparation, heptaminol (6-amino-2-methyl-2-heptanol hydrochloride; 2831 RP) and methylheptaminol (6-methylamino-2-methyl-2-heptanol hydrochloride; 3738 RP; Aranthol) were proposed for clinical use as myocardial stimulants with cardiotonic actions similar to those of cardiac glycosides. However, as these aliphatic amines show definite sympathomimetic effects, it is necessary to elucidate the mechanism of their actions on the heart, in order to determine if digitalis-like properties are involved in these effects.

Tests used in the present study included blood pressure and nictitating membrane of the cat, guinea pig and rabbit isolated atria, isolated rabbit car, ECG of the cat and the dog, ballistocardiogram of the dog, isolated seminal vesicles of the guinea pig, and rabbit intestine. The effects of heptaminol and methylheptaminol on these tests were compared with those of suitable drugs (catecholamines, tyramine, k-strophantin), the influence of atropine, cocaine and reserpine being also investigated.

The results of the present experiments show that both heptanolamines have a long-lasting cardiostimulant action, which is abolished by cocaine and absent in reserpine-treated animals. The pharmacological activity of these drugs may be entirely attributed to an indirect sympathomimetic action of the tyramine type, possibly due to the liberation of endogenous catecholamines. None of the experimental findings is consistent with the alleged digitalis-like action of these compounds.

39a Substances Hypotensives dans des Extraits Trichloracetiques de Coeurs de Lapins. J. JACOB et L. MAITRE (France).

Des extraits trichloracétiques de coeurs de lapins ont été purifiés et fractionnés avec les méthodes, légèrement modifiées, de Von Euler *et al.*[1] (adsorption sur alumine) et de Crawford *et al.*[2] et Vogt[3] (chromatographie sur papier, milieu phénol-HCl).

Ils contiennent une (ou des) substances(s) thermostable(s), abondante(s) surtout dans les éluats de la bande voisine de la ligne de départ mais migrant de façon diffuse, et qui provoque(nt) de l'hypotension chez le rat non démédullé et de la bradycardie sur l'oreillette isolée de rat. Il ne s'agit ni de dérivés de la choline, ni d'histamine, ni de 5-hydroxytryptamine, ni d'une amine catéchique hypotensive. L'effet tensionnel ressemble, sans lui être identique, à celui de l'adénosine; il est réduit par l'hexamethonium.

En outre, dans 9 cas sur 11, les éluats des bandes correspondant au RF de l'isopropylnoradrénaline ont eu des effets hypotenseurs et (ou) inotropes positifs (en opposition aux éluats des bandes correspondant à l'adrénaline qui étaient hypertenseurs et moins actifs sur l'oreillette isolée).

Les activités ont varié, correspondant à 0·5–11 mg d'isopropylnoradrénaline par gramme de coeur (soit 0·05 à 1·2 pour cent des amines catéchiques totales). Toutefois ces valeurs sont incertaines: l'isopropylnoradrénaline est très labile à ces concentrations, et les équivalents déduits des pouvoirs hypotenseurs étaient nettement supérieurs à ceux trouvés dans les essais sur l'oreillette; ceci plaide contre l'identification du principe actif à l'isopropylnoradrénaline ou tout au moins contre l'obtention de cette dernière sans contaminants.

1. VON EULER and ORWEN (1955), *Acta Physiol. Scand.*, **33,** Suppl. 118, 1.
2. CRAWFORD and OUTSCHOORN (1951), *Brit. J. Pharmacol.*, **6,** 8.
3. VOGT (1952), *Brit. J. Pharmacol.*, **7,** 325.

39b Hypotensive Substances in Trichloracetic Acid Extracts of the Rabbit Heart. J. JACOB and L. MAITRE (France).

Trichloracetic acid extracts of rabbit heart were purified and fractionated by slightly modified methods described by von Euler *et al.*[1] (adsorption on aluminium), by Crawford *et al.*[2] and by Vogt[3] (paper chromatography with phenol-HCl).

They contain one or more substances which are thermostable and abundant, particularly in the eluate of the band next to the origin, but migrate diffusely and provoke hypotension in the non-medullated rat and bradycardia in the isolated rat-auricle. The substance (or substances) in question is not a derivative of choline or histamine nor of 5-hydroxytryptamine nor of a catecholic hypotensive amine. The effect on blood pressure resembles that of adenosine without being identical with it; it is reduced by hexamethonium.

In addition, in 9 of 11 cases, the eluates of bands which correspond to the RF value of isopropylnoradrenaline had hypotensive effects and (or) positive inotropic effects (in contrast with eluates of the bands which correspond to adrenaline which were hypertensive and less active on the isolated auricle).

The activities varied; they corresponded to 0·5–11 mg of isopropylnoradrenaline per gram of heart (or 0·05 to 1·2 per cent of the total catecholamines). However, these values are uncertain: isopropyl-noradrenaline is very labile in these concentrations, and the equivalents which were arrived at from hypotensive potency were definitely higher than those found in tests on the auricle. This indicates that the active principle is not identical with isopropyl-noradrenaline or at least that it has not been obtained uncontaminated.