Der Zusammenhang von MAO-Hemmung und Abschwächung der NA-Wirkung ist nicht klar. Neuere Befunde, wonach die Ansprechbarkeit der Arterienwand von der Konzentration des endogenen NA in der Gefässwand abhängt, bieten eine Erklärungsmöglichkeit. Reserpin, welches den Gehalt von endogenem NA in den Arterien vermindert, erhöht deren Empfindlichkeit auf exogenes NA[11]. Möglicherweise bewirkt IIH Zunahme von endogenem NA in der Gefässwand, wobei im Gegensatz zu Reserpin eine Verminderung der NA-Empfindlichkeit der Aorta zustande kommt.

Im Myokard steigt der Gehalt von endogenem NA nach IIH-Behandlung an[12]. Ferner bewirkt injiziertes NA stärkeren Anstieg dieses Amins im Myokard nach Vorbehandlung mit IIH als ohne Vorbehandlung[13]. Es bleibt noch abzuklären, ob IIH den NA-Stoffwechsel in der Aortenwand in gleicher Weise beeinflusst wie im Herzen.

Verminderte Ansprechbarkeit des Gefäßsystems auf NA könnte das Zustandekommen von orthostatischer Hypotonie beim Menschen während IIH-Behandlung möglicherweise erklären.

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Abteilung für experimentelle Medizin der F. Hoffmann-La Roche & Co. AG., Basel, 6. Mai 1959.

Summary

Twenty hours after pretreatment of rabbits with the monoamine oxidase inhibitor N_2-isopropyl-isonicotinic acid hydrazide (IIH) the norepinephrine induced contraction of the isolated aorta was significantly reduced; the 5-hydroxytryptamine sensitivity could not be changed significantly. Isonicotinic acid hydrazide (INH), a weak monoamine oxidase inhibitor, had no significant effect on the norepinephrine and 5-hydroxytryptamine sensitivity of the aorta.

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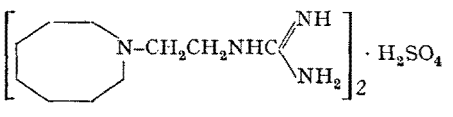
[2-(Octahydro-1-azocinyl)-ethyl]-guanidine sulfate (CIBA 5864-SU), a New Synthetic Antihypertensive Agent

SU-5864, which is [2-(octahydro-1-azocinyl)-ethyl]-guanidine sulfate has been studied to ascertain its antihypertensive properties in animals:



$7^1/_2$ to 15 mg/kg intravenously of SU-5864 markedly lowered the arterial pressure of unanesthetized renal and neurogenic hypertensive dogs while its effects on the arterial pressure of the unanesthetized normotensive dog were slight. In the anesthetized normotensive dog SU-5864 inhibited carotid occlusion reflex pressor responses and antagonized the severe pressor responses elicited by high doses of amphetamine.

Marked delayed relaxation of the nictitating membranes of dogs and cats was produced by 10 to 15 mg/kg SU-5864 intravenously. As demonstrated in the cat this relaxation was associated with a blockade of transmission somewhere in the cervical sympathetic trunk-smooth muscle complex, such that the nictitating membranes could not be retracted by preganglionic faradization. Except for a very transient period SU-5864 did not interfere with transmission across the superior cervical ganglion nor with the conduction along pre- or post-ganglionic nerve fibers. However, at the same time that the nictitating membranes could not be retracted by nerve stimulation, they were demonstrated to be hypersensitive to injected norepinephrine. From these data we infer that SU-5864 must produce an inhibition of the release and/or distribution of transmitter substances from sympathetic nerve terminals.

The effects described above last for periods ranging from 5 to 20 days following a single intravenous administration of SU-5864.

A convenient method of preparation utilized octahydroazocine[1] as starting material. Treatment with chloroacetonitrile gave the octahydro-1-azocineacetonitrile, b.p. 114–118°C/14 mm; $n_D^{24} = 1{\cdot}4720$; calculated for $C_9H_{16}N_2$: C 71·11; H 10·61; N 18·43; Found: C 71·17; H 10·62; N 18·36. Lithium aluminium hydride reduction of the nitrile yielded octahydro-1-azocineethylamine, b.p. 108–111°C/14 mm; $n_D^{22} = 1{\cdot}4830$; calculated for $C_9H_{20}H_2$: C 69·29; H 12·92; N 17·96; Found: C 69·26; H 12·94; N 17·89. Reaction of the amine with S-methylisothiourea sulfate resulted in the formation of the above described SU-5864 which was recrystallized from aqueous ethanol and melted with decomposition at 276–281°C; calculated for $(C_{10}H_{22}N_4)_2 \cdot H_2SO_4$: C 48·55; H 9·37; N 22·65; S 6·48; Found: C 48·49; H 9·51; N 22·49; S 6·33.

R. A. Maxwell, R. P. Mull, and A. J. Plummer

Research Department, CIBA Pharmaceutical Products Inc., Summit (New Jersey), May 4, 1959.

Résumé

On décrit la chimie et la pharmacologie d'un nouvel agent antihypertenseur.

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On the Relation between the Secretion of the Perivascular Mast Cells and the Serum Level of Mucoproteins

The mast cells are well known as producers of histamine, 5-hydroxytryptamine, heparin, and hyaluronic acid[1]. We have already demonstrated their secretory changes under experimental conditions[2–4] resulting in a heparinemia[5–8]

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