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Pharmacological Profile of Novel Dithiodibenzamides

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The aim of this study was to synthesize three different dithiodibenzamides and to compare their effects on isolated heart and smooth muscle preparations [1]. The three compounds only differed in the substitution on the phenylendiamine moiety. Compound **1** is an o-phenylendiamine derivative, compound **2** is the m-phenylendiamine derivative and compound **3** is the p-phenylendiamine derivative. All three compounds have the same substitution pattern. Compound **1** caused a highly potent negative inotropic effect on papillary muscles with an IC_{50} of 0.39 µmol/l (n=4). The spasmolytic effect on terminal ilea was 10 times weaker with an IC_{50} of 3.85 µmol/l (n=4), while the effect on vascular smooth muscle was even less (aorta: IC_{50}>100, n=5; ateria pulmonalis: IC_{50}= 34.5 µmol/l, n=7). Substance **2** resulted in an IC_{50} value of 1.68 µmol/l (n=4) for the negative inotropy. The spasmolytic effect of **2** was similar to compound **1** with an IC_{50} of 3.1 µmol/l (n=5). Vasodilating effects were again less pronounced (ateria pulmonalis: IC_{50}= 32.2 µmol/l, n=5; aorta: IC_{50}>14, n=5). Derivative **3** had no effect on papillary muscles up to a concentration 100 µmol/l and showed a weak vasodilating activity.

The spasmolytic effect of this derivative was potent with an IC_{50} of 5.9 µmol/l (n=5).

Our investigations show that the paraphenylendiamine derivative lacks in cardiovascular effects, while the spasmolytic effect is predominant. On the other hand a substitution in the ortho and meta position of the phenylendiamine results in a strong negative inotropic effect.

The synthesis of the compounds and the investigation of their pharmacological profiles are presented.

[1] Reiter M. [Evaluation of inotropically active drugs on isolated papillary muscle]. Arzneimittelforschung. 1967; 17: 1249–1253. PMid:5632870