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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 IC50 of 0.39 µmol/l (n=4). The spasmolytic effect on terminal ilea was 10 times weaker with an IC50 of 3.85 µmol/l (n=4), while the effect on vascular smooth muscle was even less (aorta: IC50>100, n=5; ateria pulmonalis: IC50= 34.5 µmol/l, n=7). Substance 2 resulted in an IC50 value of 1.68 µmol/l (n=4) for the negative inotropy. The spasmolytic effect of 2 was similar to compound 1 with an IC50 of 3.1 µmol/l (n=5). Vasodilating effects were again less pronounced (ateria pulmonalis: IC50= 32.2 µmol/l, n=5; aorta: IC50>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 IC50 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.


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