

Vasodilating, spasmolytic, inotropic and chronotropic activities of curcuminoids from *Curcuma longa* in isolated organ preparations of guinea pigs

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Abstract

Turmeric is a yellowish orange spice, widely used in Asian cuisine and obtained from the rhizome of *Curcuma longa*. It is a mixture of three curcuminoids namely, curcumin, demethoxycurcumin and bisdemethoxycurcumin. Turmeric has been used as a medicinal substance since ancient times for respiratory and gastrointestinal problems. The aim of the present study was to investigate which curcuminoid contributes to the observed pharmacological activities, all three curcuminoids, the major curcumin metabolite tetrahydrocurcumin, and the non-enzymatic curcumin hydrolysis products ferulic acid, feruloyl methane and vanillin were analyzed for spasmolytic, inotropic and chronotropic activity. Furthermore, their uptake in respective tissue samples was also investigated and correlated with activity. Spasmolytic activity was determined in guinea pig ileum, aorta and pulmonary artery. Inotropic and chronotropic activity was determined on guinea pig papillary muscles and right atrium respectively, while tissue uptake was quantified by using high-performance liquid chromatography (HPLC). All the curcuminoids exhibited significant spasmolytic activity with highest EC₅₀ values for bisdemethoxycurcumin ($5.8 \pm 0.6 \mu\text{M}$) followed by curcumin ($12.9 \pm 0.7 \mu\text{M}$), demethoxycurcumin ($16.8 \pm 3 \mu\text{M}$) and tetrahydrocurcumin ($22.9 \pm 1.5 \mu\text{M}$). While only demethoxycurcumin was able to significantly relax the pulmonary artery with EC₅₀ value of $15.78 \pm 0.85 \mu\text{M}$. All three curcuminoids showed mild negative chronotropic effects in the isolated right atrium; tetrahydrocurcumin demonstrated no activity. Curcumin and bisdemethoxycurcumin also showed mild positive inotropic effect whereas demethoxycurcumin and tetrahydrocurcumin exhibited weak negative inotropic one. Interestingly, ferulic acid, feruloyl methane and vanillin demonstrated no pharmacological activity at all in the various isolated organs. All three curcuminoids and tetrahydrocurcumin showed high uptake into the various tissues where concentrations correlated with pharmacological activity. The results indicate pronounced differences in the in vitro pharmacological activities of curcumin, demethoxycurcumin, bisdemethoxycurcumin and tetrahydrocurcumin which have to be considered in humans after per-oral intake of turmeric powder.