

A Bufadienolide-Enriched Fraction of *Bryophyllum pinnatum* Inhibits Human Myometrial Contractility *In Vitro*

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Introduction: *Bryophyllum pinnatum* has been used in the treatment of premature labour, first in anthroposophic hospitals and, recently, in conventional settings often as an add-on medication [1, 2]. However, the compounds contributing to the tocolytic effect are still unknown.

Aims: To investigate the effects of a flavonoids-enriched fraction (FEF), the corresponding flavonoid aglycon mixture (A-Mix), a bufadienolide-enriched fraction (BEF) [3], and *B. pinnatum* juice (BPJ) on human myometrial contractility *in vitro*.

Methods: Myometrial biopsies were collected during elective Caesarean section. Strips of tissue were mounted in an organ bath system (myograph), and spontaneous contractions were recorded. Aliquots of a stock solution of FEF, A-Mix, BEF, *B. pinnatum* juice (BPJ) or a vehicle control (Krebs solution or DMSO), were repeatedly added (4 times) in 20-min intervals. The strength (i.e. AUC and amplitude) and the frequency of contractions were recorded for each 20-min period. After a washout period, vitality of strips was observed for additional 30 min. Cell viability assays were performed with the human myometrial hTERT cell line.

Results: Compared to initial values, the repeated addition of FEF, A-Mix, BEF or BPJ led to significantly lower contraction strength (AUC and amplitude) in a concentration-dependent manner (in all cases, $p < 0.05$). BEF was the most active (e.g. 1 $\mu\text{g}/\text{mL}$ BEF lowered AUC to $40.1 \pm 11.8\%$ of initial, whereas 150 $\mu\text{g}/\text{mL}$ FEF, 6.2 $\mu\text{g}/\text{mL}$ A-Mix, and 1% BPJ (i.e. 10 $\mu\text{g}/\text{mL}$) were required to obtain comparable inhibition). All test substances, except A-Mix, led to a progressive increase of contraction frequency. A-Mix, BEF and BPJ did not decrease viability of hTERT cells at concentrations up to 40 $\mu\text{g}/\text{ml}$, 15 $\mu\text{g}/\text{ml}$ and, FEF only at the highest test concentration of 1000 $\mu\text{g}/\text{ml}$.

Conclusion: The data confirm previous observations showing that *in vitro* myometrial contractility can be inhibited by *B. pinnatum* leaf press juice and fractions without affecting viability. The fraction enriched in bufadienolides appears mainly responsible for the observed relaxant effect.

Keywords: *B. pinnatum*, bufadienolides, flavonoids, myometrium, *in vitro*

References:

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