

### A163 Preliminary characterization of the effect of *Artemisia afra* on guinea pig airway muscle

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The objective of this study was to assess the bronchodilator potential of *Artemisia afra* (AA), a plant frequently advocated for the treatment of asthma in South African traditional medicine. Aqueous extracts of the aerial parts of the locally collected plant were prepared and its effect on histamine (His)-, methacholine (Mch)- and LTD4 – induced contraction of guinea pig airway smooth muscle determined using the zigzag cut tracheal muscle preparation. The effects of AA on the guinea pig tracheal muscle were quite complex. AA had no direct effect on tracheal muscle, but in muscle exposed to Mch and then washed, 1 & 2 % AA solutions produced major contractile responses, which was fully inhibited by ipratropium ( $1.67 \times 10^{-3}$  M) and mepyramine ( $4.13 \times 10^{-10}$  M), while 10 to 30% AA produced relaxation (53% relaxation with 20% AA). Such sensitisation was not evident after exposure to His and LTD4. AA (0.1 to 30 %) also inhibited the contractions induced by Mch ( $6.67 \times 10^{-8}$  M), His ( $6.67 \times 10^{-6}$  M) and LTD4 ( $2.13 \times 10^{-9}$  M) in a dose dependent manner with a relative order of potency (based on AA concentration producing 50% of relaxation of agonist-induced contraction) of 10: 11.1: 8.9 for Mch: His: LTD4, respectively. In the presence of 2% AA the log dose response curve (LDRC) for Mch was displaced upwards at lower concentrations ( $< 10^{-6}$  M), while EC<sub>50</sub> ( $3.37 \times 10^{-7}$  M vs  $1.82 \times 10^{-7}$  M) remained unchanged, but in presence of 20% AA a pronounced non-parallel shift to the right occurred (EC<sub>50</sub>:  $2.2 \times 10^{-6}$  M vs  $1.82 \times 10^{-7}$  M; and Hill Slopes: 1.029 vs 0.6022, respectively). In presence of 2% AA there was no change in LDRC for His, but 20% AA caused pronounced shift to the right (EC<sub>50</sub>:  $2.92 \times 10^{-5}$  M vs  $4.21 \times 10^{-6}$  M and Hill slopes 0.9918 vs 2.553). Finally, propranolol ( $6.67 \times 10^{-5}$  M) inhibited the dose dependent relaxation produced by 1 to 30 % AA of Mch –induced contraction (by as much as 65.83% for 30% AA), but the relaxant effect could not be fully reversed by beta blockade. AA thus is able to reverse the actions that several mediators implicated in asthma pathology have on tracheal smooth muscle and has significant potential as a bronchodilator. The mechanisms for AA's relaxant activity is however complex and most likely attributable to the presence of more than one active principle.

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### A164 Cardiovascular properties of *Cedrelopsis grevei*

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*Cedrelopsis grevei* Baill. (Meliaceae) is an endemic species from Madagascar, traditionally used to relieve muscle fatigue when the bark is soaked in hot water. Previous phytochemical investigations have shown its bark to contain chromones (1), coumarins (2) together with limonoids (3). Recently, we exposed a bio-guided isolation leading to the structural elucidation of four known and a new coumarins, which participate to the vasorelaxation of extract (4).

We submit now the cardiovascular properties of the hydroalcoholic extract from *C. grevei* bark. This crude extract was able to decrease blood pressure and to induce relaxation on rat thoracic aorta, at the level of both smooth muscle and endothelium. Daily oral administration of normotensive rats with the crude extract (80 mg/kg) for four weeks produced a decrease in blood pressure and modified vascular reactivity with an improved endothelium-dependent vasodilatation, using acetylcholine to control the functionality of endothelium.

These cardiovascular properties encouraged us to continue the pharmacological study about *C. grevei*.

**References:** 1. Dean, FM. et al. (1971) *Phytochemistry* 10: 3221. 2. Eshiett, IT. et al. (1968) *J. Chem. Soc.* 481. 3. Mulholland, DA. et al. (1999) *Tetrahedron* 55: 11547. 4. Rabenau, I. et al. (2001) *Int. PSE Symposium*, Lausanne.