**Capsaicin and neurokinin A-induced bronchoconstriction in the anaesthetised guinea-pig: evidence for a direct action of menthol on isolated bronchial smooth muscle**

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**Abstract**

1. For many years menthol has been used in the treatment of respiratory disorders although, a bronchodilator effect of menthol has yet to be described. Using the bronchoconstrictors capsaicin (acting via stimulating the release of neuropeptides from sensory afferents) and neurokinin A (NKA) we have raised airways resistance in the guinea-pig (GP) and studied the effect of menthol on both capsaicin and NKA-induced bronchoconstriction *in vivo*. *In vitro* the effect of menthol on acetylcholine (ACh) and KCl precontracted GP bronchi was also studied.
2. GP (*n*=13) were anaesthetized (urethane 1.5 g kg−1, i.p.) and a bolus injection of capsaicin (7.5 μg ml−1, i.v.) or infusion of NKA (1 μg min−1, i.v.) was given either in the presence of air (0.81 min−1) or air impregnated with menthol vapour (7.5 μg l−1) freely breathed from a tracheal cannula via a T-piece. Airways resistance (*R*aw) and ventilation were measured throughout. Bronchi of mean internal diameter (1029+73.6 μm; *n*=24) were removed from GP (*n*=16) and mounted in the Cambustion myograph. Bronchial rings were maximally precontracted with 80 mM KC1 or 2 mM ACh. Relaxation due to a cumulative dose of menthol (1–3000 μM) was measured.
3. Menthol produced a significant (*P*<0.05) 51.3% reversal of the capsaicin-induced increase in *R*aw, and also inhibited the significant (*P*<0.05) reduction in minute ventilation (Ve) associated with the capsaicin-induced increased in *R*aw. Menthol also caused a significant (*P*<0.05) 41% reversal of the NKA-induced increase in *R*aw. The NKA-induced decrease in Ve was again significantly (*P*<0.05) reversed with menthol inhalation. Menthol caused a significant (*P*<0.001) dose-dependent relaxation of KCl and ACh precontracted bronchi.
4. We have shown that menthol attenuates both capsaicin and NKA-induced bronchoconstriction *in vivo* and relaxes KCl and ACh preconstricted bronchi *in vitro*. Menthol inhibition of NKA and capsaicin-induced bronchoconstriction could be, in part, explained by a direct action of menthol on bronchial smooth muscle.

**Keywords:** Menthol, capsaicin, neurokinin A, airways resistance, bronchodilatation