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## Respiratory Physiology and Neurobiology

Volume 156, Issue 1, 15 April 2007, Pages 69-78

## Influence of epithelium on beta-adrenoceptor desensitization of guinea pig tracheal smooth muscle

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## Abstract

The effect of tissue incubation with a  $\beta_2$ -agonist of denuded and intact epithelium trachea on the responsiveness to isoprenaline and  $\beta$ -receptor blocked by propranolol (CR-1) was examined in this study. We examined the effect of epithelium removal on the  $\beta$ -adrenoceptor desensitization resulting from incubation of guinea pig trachea in the  $\beta$ -adrenergic agonist isoprenaline (10  $\mu$ M). Desensitization was measured as the change in  $EC_{50}$ , the concentration of  $\beta$ -agonist that produced 50% relaxation of tracheal rings contracted with methacholine. As a second measure of desensitization, we measured the shift in  $EC_{50}$  resulting from incubation of tracheal rings with the  $\beta$ -adrenoceptor antagonist propranolol (20 nM), expressed as CR-1 ([post-propranolol  $EC_{50}$ /baseline  $EC_{50}$ ] - 1). Initially, we measured desensitization immediately after incubation in isoprenaline; subsequently, we repeated the protocol and allowed a 30 min rest between the end of incubation and the measurement. The sensitivity of denuded epithelium trachea to isoprenaline and (CR-1) was significantly higher than that of intact epithelium only in non-incubated preparations ( $p < 0.05$  to  $p < 0.001$ ). Incubation to isoprenaline caused a significant reduction in the tracheal response to isoprenaline in both the denuded groups ( $p < 0.005$  for both cases) and intact epithelium groups ( $p < 0.05$  for both cases). Incubation to isoprenaline also caused a significant reduction in (CR-1) value in both the denuded groups ( $p < 0.005$  for group 2 and  $p < 0.001$  for group 4) and intact epithelium only in group 1 ( $p < 0.05$ ). However, the changes in  $EC_{50}$  due to tissue incubation with isoprenaline were significantly greater in denuded than intact epithelium trachea ( $p < 0.05$  for all cases) and for CR-1 value only in groups 1 and 2 ( $p < 0.05$ ). These results indicate decrease in both tracheal response to  $\beta$ -agonist (tolerance) and CR-1 (due to incubation of tissues with isoprenaline), which were greater in denuded epithelium groups. © 2006 Elsevier B.V. All rights reserved.

## Reaxys Database Information

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## Author keywords

Adrenergic receptors; Asthma; Desensitization; Epithelium; Tolerance; Tracheal responsiveness

## Indexed Keywords

EMTREE drug terms: beta adrenergic receptor; beta adrenergic receptor blocking agent; beta adrenergic receptor stimulating agent; isoprenaline; methacholine; propranolol

EMTREE medical terms: animal tissue; article; asthma; concentration (parameters); desensitization; drug tolerance; guinea pig; muscle contraction; muscle relaxation; nonhuman; priority journal; trachea mucosa; trachea muscle

MeSH: Adrenergic beta-Agonists; Adrenergic beta-Antagonists; Animals; Dose-Response Relationship, Drug; Drug Interactions; Epithelium; Guinea Pigs; Isoproterenol; Muscle, Smooth; Propranolol; Random Allocation; Receptors, Adrenergic, beta; Statistics, Nonparametric; Trachea Medline is the source for the MeSH terms of this document.

Chemicals and CAS Registry Numbers: isoprenaline, 299-95-6, 51-30-9, 6700-39-6, 7683-59-2; methacholine, 55-92-5; propranolol, 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; Adrenergic beta-Agonists; Adrenergic beta-Antagonists; Isoproterenol, 7683-59-2; Propranolol, 525-66-6; Receptors, Adrenergic, beta

Manufacturers: Drug manufacturer: Sigma, United Kingdom.

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