

Stimulation of both β_2 - and β_3 -adrenoceptors produces relaxation of myogenic contractions of mouse isolated urinary bladder

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Objectives

The involvement of β -adrenoceptors (β -ARs) in urinary bladder relaxation during urine storage has been described, but the distribution of the subtypes varies among species.

It is well established that bladder relaxation is primarily mediated by both β_2 - and β_3 -ARs in rat⁽¹⁾ and pig⁽²⁾ and by β_3 -AR in dog⁽¹⁾, primates⁽³⁾ and human^(4,5). While a role for both β_2 - and β_3 -ARs in the mouse bladder has recently been demonstrated⁽⁶⁾, the relative roles of the two subtypes are unclear.

The objective of the present study was to determine the relative roles of β_2 - and β_3 -ARs in mouse urinary bladder relaxation by directly comparing the activity of selective agonists and antagonists under the same experimental conditions. The role of the urothelium in these responses was also evaluated.

Methods

Urinary bladders were obtained from adult female C57/Bl6 mice (aged 11-13 weeks) sacrificed by cervical dislocation.

Bladders were bisected (the urothelium removed in some experiments) and bladder halves mounted in 5 mL organ baths under 0.5 g of initial tension in the presence of prazosin (1 μ M) in order to block α_1 -ARs.

CGP-20712 (β_1 -AR antagonist at 300 nM), ICI118,551 (β_2 -AR antagonist at 30 nM), L748,337 (β_3 -AR antagonist at 1, 3 or 10 μ M) or their vehicle (0.001% DMSO in distilled water) were added into the organ bath followed 20 min later by stimulation with KCl (30 mM).

Once contractions to KCl stabilized, cumulative concentration-response curves to β -AR agonists (fenoterol, a β_2 -AR selective agonist; CL316,243, a β_3 -AR selective agonist; isoproterenol, a non-selective β -AR agonist) were constructed.

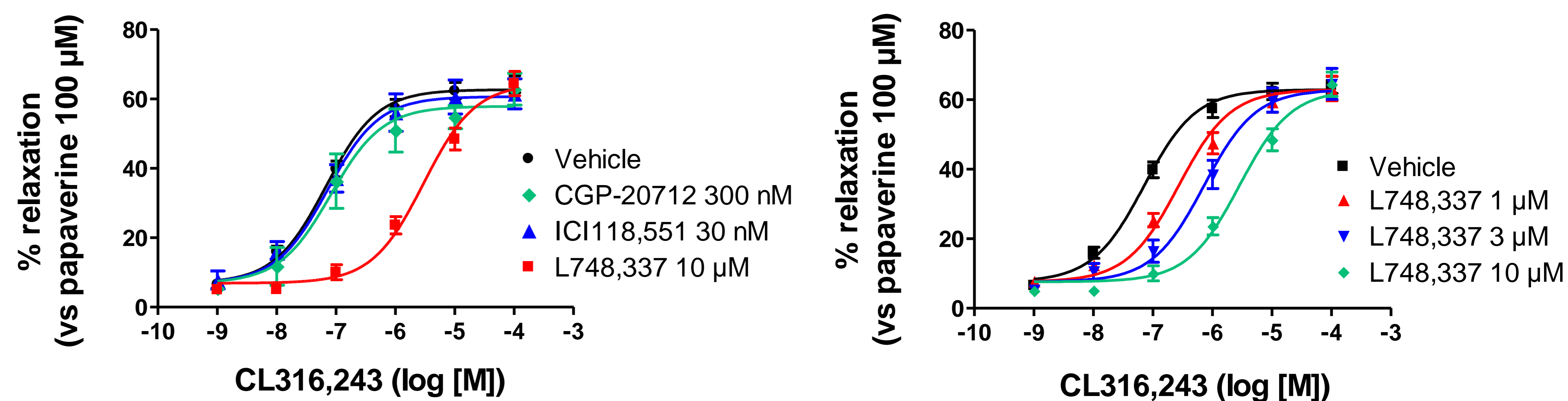
Results are expressed as a percentage of the maximal relaxation produced by papaverine (100 μ M).

Conclusions

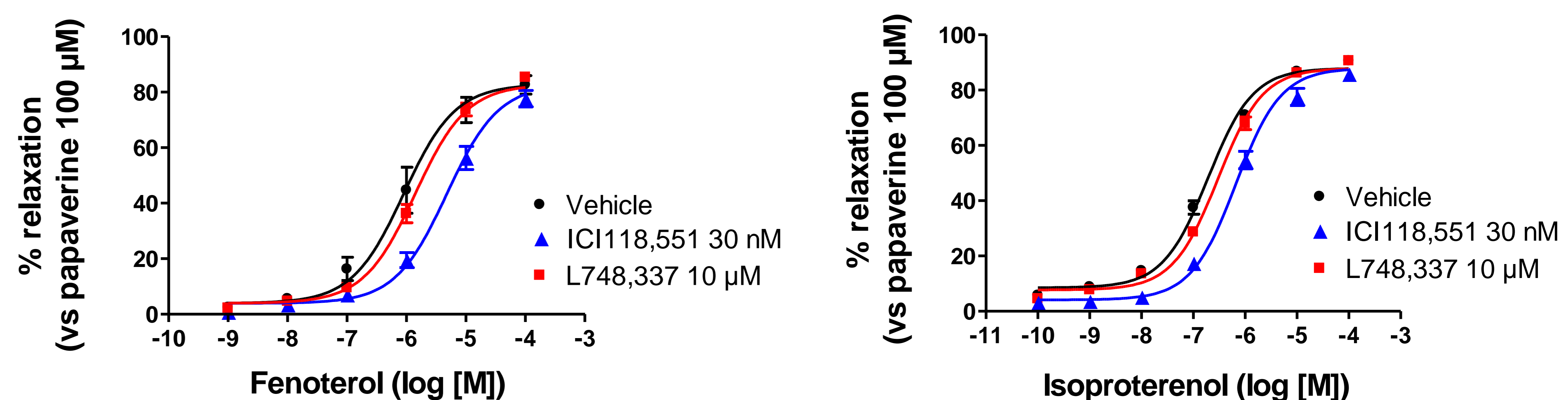
The β_3 -AR selective agonist CL316,243 and the β_2 -AR selective agonist fenoterol are both able to inhibit myogenic contractions of mouse urinary bladder strips, confirming the functional presence of both β_2 - and β_3 -AR subtypes. In addition, while CL316,243 and fenoterol act through β_3 - and β_2 -ARs, respectively, isoproterenol appears to produce relaxation primarily through β_2 -ARs. However, the stimulation of β_2 -ARs produces a greater degree of inhibition than stimulation of β_3 -ARs, indicating a greater role for β_2 -ARs in the relaxation of mouse urinary bladder. Finally, removal of the urothelium does not appear to significantly affect the response of mouse urinary bladder strips to β -AR stimulation.

Results

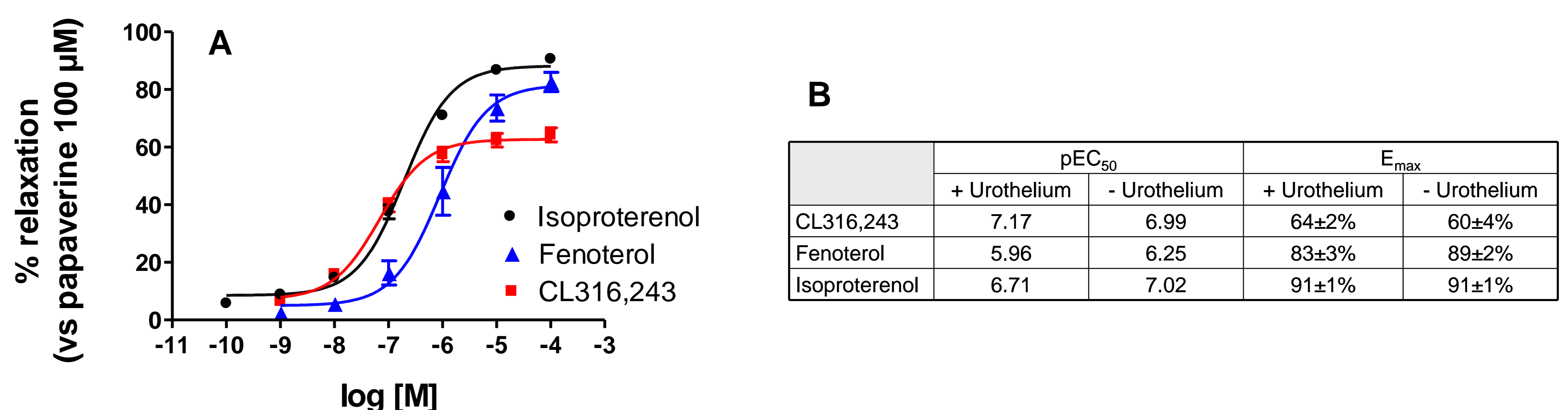
Effects of β -AR antagonists on CL316,243-mediated relaxation of urothelium intact mouse urinary bladder strips pre-contracted with 30 mM KCl



Effects of β -AR antagonists on fenoterol and isoproterenol-mediated relaxation of urothelium intact mouse urinary bladder strips pre-contracted with 30 mM KCl



Comparison of relaxant effects of β -AR agonists in the presence of urothelium (A) and the effect of urothelium removal (B)



No significant change was observed in pEC₅₀ and E_{max} values for β -AR agonists after removal of the urothelium.

References

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