

Bond University
Research Repository



The urothelium and lamina propria as an alternative target for clinical antimuscarinics

Veer, Vineesha; Chess-Williams, Russ; Moro, Christian

Licence:
Free to read

[Link to output in Bond University research repository.](#)

Recommended citation(APA):
Veer, V., Chess-Williams, R., & Moro, C. (2022). *The urothelium and lamina propria as an alternative target for clinical antimuscarinics*. 181. Abstract from 2022 Australian Physiological Society/Australian Society for Biophysics Scientific Meeting, Hobart, Tasmania, Australia.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

For more information, or if you believe that this document breaches copyright, please contact the Bond University research repository coordinator.



Scientific Meeting

Australian
Physiological
Society

Australian
Society for
Biophysics

HOBART · TASMANIA · NOVEMBER 2022

CONFERENCE PROCEEDINGS (V52)



20 -23 NOVEMBER 2022

HOSTED BY

UNIVERSITY of
TASMANIA 





The urothelium and lamina propria as an alternative target for clinical antimuscarinics

Vineesha Veer¹, Russ Chess-Williams¹, Christian Moro¹.

¹ Faculty of Health Sciences and Medicine, Bond University, Robina, Australia

Introduction: Overactive bladder is the most common type of bladder dysfunction and involves spontaneous contractions of the urinary bladder during the filling phase. The first-line pharmaceutical therapies for managing this disorder are antimuscarinics (Moro et al., 2011), which have a primary action of blocking the action of acetylcholine in the urothelium and lamina propria (Nardulli et al., 2012). However, more than 70% of patients who are administered these drugs cease their treatment regimen due to lower than expected treatment benefits or adverse side effects (Vouri et al., 2019). The reason for this is unclear, although this does suggest a varied effectiveness or selectivity of antimuscarinics on urinary bladder tissue. **Aim:** This study aims to find the differences in the abilities to inhibit contractions of the U&LP for commonly prescribed clinical antimuscarinics. **Methods:** Strips of porcine U&LP were mounted in carbogen-gassed Krebs-bicarbonate solution at 37°C. The tissues were paired with carbachol concentration-response curves performed in the absence or presence of clinically used antimuscarinics. The concentration for each antagonist was chosen at which the inhibited contractions reached a significant, but sub-maximal, extent. pEC₅₀ values for each curve were analysed and estimated affinities calculated. Ethical approval was not required for this study as tissues were sourced from the local abattoir after slaughter for the routine commercial provision of food. **Results:** The clinical antimuscarinics producing right parallel shifts from the control in the U&LP (concentration; n value; estimated affinity or pK_D; paired Student's two-tailed t-test) included oxybutynin (1µM; 18; 7.08; p<0.001), solifenacin (1µM; 11; 6.88; p<0.001), darifenacin (100nM; 10; 6.48; p<0.001), tolterodine (1µM; 10; 8.00; p<0.001), trospium (100nM; 10; 7.63; p<0.001) and fesoterodine (100nM; 11; 7.40; p<0.001). Propiverine (concentration; n value; paired Student's two-tailed t-test) did not produce a shift (1µM; 11; p=0.50). **Conclusion:** The data highlights a variance in the effectiveness of each clinically used antimuscarinic to antagonise the response to muscarinic receptor activation of the U&LP.

Moro C, Uchiyama J and Chess-Williams R (2011) 'Urothelial/Lamina Propria Spontaneous Activity and the Role of M3 Muscarinic Receptors in Mediating Rate Responses to Stretch and Carbachol', *Urology*, **78(6)**:1442.e9–1442.e15, doi:10.1016/j.urology.2011.08.039.

Nardulli R, Losavio E, Ranieri M, Fiore P, Megna G, Bellomo RG, Cristella G and Megna M (2012) 'Combined Antimuscarinics for Treatment of Neurogenic Overactive Bladder', *Int J Immunopathol Pharmacol*., **25(1_suppl)**:35–41, doi:10.1177/03946320120250S106.

Vouri SM, Schootman M, Strobe SA, Xian H and Olsen MA (2019) 'Antimuscarinic use and discontinuation in an older adult population', *Arch Gerontol Geriatr*, **80**:1–11, doi:10.1016/j.archger.2018.09.005.