

***In vitro* antimicrobial activity of cell-free supernatants from asymptomatic bacteriuria (ABU) isolates against multi-drug resistant uropathogenic *Escherichia coli* (UPEC)**

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Abstract

Background: Multi-drug resistant uropathogenic *Escherichia coli* (UPEC) cause > 80% of community acquired urinary tract infections (UTIs), and > 40% of nosocomial UTIs. Preliminary evidence suggests a beneficial role for UPEC's commensal counterparts, asymptomatic bacteriuria (ABU), in establishing bacterial interference against UPEC. The aim of this study was to analyse the antimicrobial activity of cell free supernatant's (CFS) from ABU isolates against UPEC.

Methods: *In vitro* antagonistic effects of nine uncharacterised ABU isolates were compared against the inhibitory affect induced by the prototype ABU isolate, *E. coli* 83972. Turbidimetric growth assays were performed using the CFS of the ABU isolates against eight clinically relevant UPEC to characterise the antimicrobial activity. Subsequent analysis was completed on BAGEL4 to identify potential bacteriocin encoding genes.

Results: CFSs from all nine ABU isolates exhibited superior inhibition against UPEC growth when compared to *E. coli* 83972. Initial *in vitro* safety assessments revealed that the ABU isolates are weak biofilm formers and generally susceptible to first-line antibiotics, indicating

low virulence. The ABU isolate PUTS58 proved to be the most effective, displaying the greatest antimicrobial activity against the indicator isolates. Additionally, cross-immunity assays revealed that UPEC 5 displayed strong activity against six of its fellow UPEC isolates, similar to PUTS58 in efficacy, thereby warranting further investigation.

Conclusion: ABU isolates represent promising candidates as urinary microbiome-based therapeutics, thus, the mechanism of competitive interference needs to be explored. Moreover, should PUTS58 exhibit strong efficacy in urogenital-like environments, it could be a suitable agent for therapeutic bladder colonisation.