

Title: Promising FDA-approved drugs with efflux pump inhibitory activities against clinical isolates of *Staphylococcus aureus*

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Staphylococcus aureus is an opportunistic pathogen that causes wide range of nosocomial and community-acquired infections, which have spread worldwide leading to an urgent need for developing effective anti-staphylococcal agents. Efflux is an important resistance mechanism that bacteria used to fight the antimicrobial action. This study aimed to investigate the efflux mechanism in *S. aureus* and assess diclofenac, domperidone, glyceryl trinitrate and metformin as potential efflux pump inhibitors that can be used in combination with antibiotics for treating topical infections caused by *S. aureus*. Efflux was detected qualitatively by the ethidium bromide Cart-Wheel method followed by investigating the presence of efflux genes by polymerase chain reaction. Twenty-six isolates were selected for further investigation of efflux by Cart-Wheel method in absence and presence of tested compounds followed by quantitative efflux assay. Furthermore, antibiotics minimum inhibitory concentrations in absence and presence of tested compounds were determined. The effects of tested drugs on expression levels of efflux genes *norA*, *fexA* and *tetK* were determined by quantitative real time-polymerase chain reaction. Efflux was found in 65.3% of isolates, the prevalence of *norA*, *tetK*, *fexA* and *msrA* genes were 91.7%, 77.8%, 27.8% and 6.9%. Efflux assay revealed that tested drugs had potential efflux inhibitory activities, reduced the antibiotic's MICs and significantly decreased the relative expression of efflux genes. In conclusion, Diclofenac sodium, domperidone and glyceryl trinitrate showed higher efflux inhibitory activities than verapamil and metformin. This study showed that diclofenac sodium, glyceryl trinitrate and domperidone have efflux pump inhibitory activities against *S. aureus*.

Biography

Safaa has completed Bachelor of Pharmaceutical Sciences from Zagazig University, Egypt, 2009; Master of Pharmaceutical Sciences (Microbiology & Immunology), Zagazig University, 2016 and Doctor of Philosophy, Pharmaceutical Sciences (Microbiology & Immunology), Zagazig University, 2022. Her current job: Lecturer in Microbiology department at Faculty of Pharmacy, Zagazig University and a member of Pharmacists Syndicate.