OBJECTIVES

Resistance of microorganisms to many classes of antibiotics and other drugs is a major problem throughout the world. This antimicrobial resistance can be mediated by various mechanisms such as enzymatic inactivation of the drug, alteration of the target and decreased intracellular concentration of the antimicrobial. Among the given mechanisms, the last mechanism is mediated by either decreased influx or increased efflux or a combination of both. Recently, efflux has become increasingly recognized as a major component of resistance. Some efflux pumps selectively extrude specific antibiotics such as macrolides, lincosamides and/or streptogramins and tetracyclines, whereas others, referred to as multiple drug resistance pumps, expel a variety of structurally diverse anti-infectives with different modes of action. This phenomenon, whereby a single transporter is able to recognize and transport multiple antimicrobials with no common structural homology, was first described in the late 1980s in higher eukaryotes where P-glycoprotein was found to play a role in resistance to anti-cancer chemotherapeutic agents. Later, it became apparent that efflux systems were also present in microorganisms. Efflux pump inhibitors offer considerable promise as therapeutic agents, as they should restore the activity of standard antibiotics. Hence the main objectives of current study are:

1. Identification of novel drug targets, which are common in the selected species of *Staphylococcus*, *Streptococcus*, *Klebsiella* and *Shigella*, and identification of putative drugs for selected novel drug targets.

2. Identification of common multidrug resistant (MDR) proteins in selected species of *Staphylococcus*, *Streptococcus*, *Klebsiella* and *Shigella*, and identification of potent drug-like molecules for selected MDR proteins.

3. Proteome mining of selected pathogens to identify novel bacteriocins; study of binding affinity of experimentally confirmed bacteriocins and cyclotides with identified novel drug targets and MDR proteins.

4. Biological confirmation of identified drug-like molecules against selected pathogens through antimicrobial study.