3 RATIONALE, AIM AND OBJECTIVES
3.1 Rationale
The clinical strains of *P. aeruginosa* and *A. baumannii* resistant to most of the antibiotics, such as penicillins, cephalosporins, aminoglycosides, fluoroquinolones have been observed. To worsen it further, there has also been an emergence of strains resistant to the last resort antibiotics, the carbapenems (Mehta et al. 2007; Pawar et al. 2008; Rosenthal et al. 2010). Thus, there has been an increasing threat of pan drug resistance among these bacteria, necessitating the development of new therapeutic strategies to control their infections.

Drugs targeting bacterial growth pose the risk of resistance development due to the selective pressure exerted, and hence, anti-virulence approach has been followed as a promising therapeutic target, which can be effective in controlling infections by reducing bacteria’s pathogenicity and it also does not exert any life-death pressure (Clatworthy et al. 2007).

Since the last decade, quorum sensing (QS) – a bacterial communication system via signaling molecules, is being studied critically. This process is significant for many pathogens for the expression of virulence factors (Ch. 2 Section 2.3). Hence, controlling quorum sensing will further control virulence of the pathogen. The signaling pathway of QS is also known to regulate virulence and biofilm maturation in the pathogens, *P. aeruginosa* and *A. baumannii*; hence, inhibiting QS in these organisms can facilitate reduction of their pathogenicity. Thus, it was hypothesized that targeting QS of the above pathogens, may prove to be fruitful in the development of new anti-infective drugs.

Literature search on QS inhibition revealed many studies focussed on controlling virulence in *P. aeruginosa*, by inhibition of its AHL-QS systems, and further testing their *in vivo* efficacy. Some of them were able to facilitate bacterial clearance, improving the survival chances of infected animals. As per the available literature, the antibiotic, azithromycin, has been reported to be effective in preventing ventilator associated *Pseudomonas* pneumonia in pilot clinical trials (van Delden et al. 2012). Only recently, few studies have focussed on the inhibition of QS to control *A. baumannii* biofilms. So,
there has been an increasing demand for more compounds possessing anti-QS potential, for an effective therapy against the pathogens under study.

Since many decades, herbal drugs are known to be effective and safe in terms of toxicity, when used appropriately and due to their treasure of diverse, complex bioactive molecules, their tremendous medicinal values are being realized throughout the world. For the present study, five Indian medicinal plants were selected, based on the criteria which included factors such as availability, not known to possess bactericidal activity against Gram negative bacteria, not studied previously for QS inhibition, and being least toxic to humans.

The present study was thus designed to screen five plants, *Rubia cordifolia* Linn. (Common name – Manjistha), *Tinospora cordifolia* (Willd.) Miers. (Guduchi), *Picrorhiza kurroa* Royle Ex Benth. (Katuka), *Bauhinia variegata* Linn. (Kanchanara) and *Cassia fistula* Linn. (Aragvadha) for anti-quorum sensing activity w.r.t. *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, further test their ability to inhibit QS regulated virulence and biofilms and identify the bioactive molecule/s present in the plant extract.
3.2 Aim

To evaluate the activity of some Indian medicinal plants used in traditional medicine against quorum sensing mechanism which is responsible for biofilm formation and virulence in opportunistic, nosocomial pathogens such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*

3.3 Objectives

- To screen plant extracts for the presence of activity against QS of *P. aeruginosa* and *A. baumannii*.
- To evaluate the anti-QS plant extracts for inhibition of QS controlled biofilm formation and virulence in wild type and clinical strains of *P. aeruginosa* and *A. baumannii*.
- To detect the phytochemicals present in the plant extract/s showing significant anti-quorum sensing activity.
- To fractionate selected plant extracts and identify the phytochemicals responsible for anti-QS activity.