1 INTRODUCTION
Antimicrobial resistance is a ticking time-bomb not only for the UK, but also for the world. We need to work with everyone to ensure the apocalyptic scenario of widespread antimicrobial resistance does not become a reality. This threat is arguably as important as climate change.

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The prevalence of the superbugs with the ability to surmount the inhibitory effects of most antibiotics is well known to the medical community. These organisms are often associated with mortality and morbidity, and due to the high resistance levels, the treatment of their infections causes extended hospital stays as well as increased expenses. Since more than a decade ago, it was common to detect multidrug resistant (MDR) strains in many pathogenic species such as *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Enterobacter* sp., *Streptococcus pneumonia*, *Mycobacterium tuberculosis*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, etc. However, the rapid development and dissemination of resistance traits among a wide range of bacterial species is now challenging the medical sector with the appearance of extensively drug resistant (XDR) and totally drug resistant (TDR) strains, or collectively the superbugs. Their tolerance to most of the available antimicrobials has left very limited therapeutic options to treat their infections. Hence, the phenomenon of drug resistance in bacteria is intimating the development of new and effective infection control strategies, and as rightly said by Daves, it is needed to consider antimicrobial resistance as a serious issue, and work together to win the battle against these bugs (Davies & Davies 2010; McCarthy 2013).

1.1 Evolution of antibiotic resistance

The history of antibiotics began with the discovery of penicillin in 1928 by Sir Alexander Fleming. However, the first effective antibiotics available for human use were the sulphonamides, in 1937. Further, up to 1950s, the industry witnessed the development of various generations of antibiotics with the ability to act on a broader range of organisms and by employing different mechanisms of action. These mechanisms include inhibition of DNA synthesis, inhibition of protein synthesis, increasing membrane permeability of
the bacterial cells, etc. Later on, in the period of 1960 to 2000, the rate at which new antibiotics were discovered declined substantially, while the emergence of resistant strains approached the human race at a rapid pace. However, it should be noted that the history of antimicrobial resistance dates back to the time of antibiotic discovery or even before. In the late 1930s, along with the introduction of sulphonamides, the evidence of bacterial resistance to the drug was also reported. The presence of bacterial penicillinase was also identified in 1940, even before the drug was marketed on a commercial basis. The production of antibiotics by many bacteria and fungi is a natural phenomenon, and many bacteria have naturally evolved mechanisms to protect themselves from the harmful effects of these antimicrobials (Davies & Davies 2010).

The slow course of natural evolution accelerated due to the human interference in terms of the enormous use of antibiotics for various purposes. This includes the antibiotic consumption for common infections such as cold, cough, etc. which is generally caused by viruses, and antibiotics are ineffective against them; commercial applications in hand care and household cleaning products, sterility procedures, etc. They are also used as growth factor in animal feed, wherein sub-therapeutic dose is administered to the animals, for therapeutic or prophylactic purpose in aquaculture, etc. To add on this, the antibiotics are disposed off inappropriately to the soil environment, which is host to a variety of useful and harmful bacteria. All of this exposes the antibiotics to bacteria at a lower than its effective concentration, causing chemical induced mutations which get accumulated and eventually lead to antibiotic resistance. Further, the selective pressure on bacterial growth exerted by the antibiotics promotes survival of the fittest, i.e. the resistant bacterial strains, while the susceptible strains get killed. Hence, the population of resistant strains goes on increasing while the sensitive ones get depleted. Additionally, the capability of bacteria to exchange resistance encoding genes among different species leads to the build-up of multiple resistance traits in the organisms, and the consequent evolution of MDR, XDR and TDR strains (Davies & Davies 2010).
1.2 **Origins of antimicrobial resistance**

The genes encoding antibiotic resistance have been found to reside in the bacterial chromosome as well as plasmids. The genes may be inherently present or acquired through mutations and horizontal gene transfer (HGT) between the same or related bacterial species (Roberts 2012).

1.2.1 **Mutations**

Spontaneous mutations occur during normal DNA replication, as a simple error that alters the base composition of a gene; mutations may occur by exposure to ultra-violet (UV) light, chemicals; and by insertion or deletion of mobile DNA elements such as transposons and integrons. Mutations arising from DNA replication errors or UV exposure may be silent, or may cause a different amino acid substitution of the protein expressed. Such alterations in the target protein of an antibiotic can decrease susceptibility to the antibiotic. Similarly, mutations due to insertion/deletion, especially due to transposons, can cause major alteration in the genes, either resulting in a non-functional gene, or greatly altered gene product. When such mutations occur in the genes encoding antibiotic targets, such as penicillin binding proteins, ribosomal RNA, etc., they confer resistance to the respective antibiotics, which are no longer able to bind the altered proteins. Often, a collection of mutations is required to develop resistance to most classes of antibiotics.

1.2.2 **Horizontal gene transfer**

The HGT between same or closely related species mainly occurs by the process of conjugation; transformation and transduction. Additionally, mobile DNA elements such as plasmids, transposons, conjugative transposons and integrons, which may carry antibiotic resistance genes, are involved in lateral gene exchange between same or related bacterial species, eventually leading to the spread of drug resistance among different bacteria.

A combination of mutational and HGT events are generally involved in the development of drug resistance, causing great difficulties in controlling such bacteria. Some key
illustrations include the emergence of extended spectrum β-lactamases (ESBLs) that have arisen due to random mutations in the plasmid encoded enzyme, such as the TEM or CTX-M, which was acquired from the environmental *Kluyvera* strains into the clinical strains, by HGT. These ESBLs confer resistance to the penicillins as well as other β-lactam antibiotics such as cephalosporins. The antibiotic class, fluoroquinolones, work by inhibition of DNA gyrase in bacteria. Mutations in the gyrase genes; efflux pumps to expel the antibiotic; the presence of aminoglycoside N-acetyltransferases, etc. has endowed bacteria with the capability to overcome the effects of fluoroquinolones. Moreover, these resistance genes are being transmitted by HGT, and limiting the effectiveness of the antibiotic (Davies & Davies 2010).

1.3 Different mechanisms of drug resistance

Various mechanisms of drug resistance have been identified in bacteria, such as drug inactivation, alteration in target molecules, reduction in the membrane permeability of the drug, elimination of drug through efflux pumps and existence as biofilms.

1.3.1 Drug inactivation

Many bacteria produce enzymes that convert the active drug into an inactive form; for example. β-lactamases that catalyze hydrolysis of the β-lactam ring of penicillin and other β-lactam antibiotics; which open up the ring, converting active penicillin into inactive penicilloic acid. Antibiotics such as aminoglycosides, chloramphenicol are inactivated by chemical modifications, such as acetylation, phosphorylation, etc.

1.3.2 Alteration in antibiotic target

Antibiotics such as streptomycin, an aminoglycoside, bind to bacterial ribosomes, leading to the inhibition of protein synthesis. Resistance to streptomycin has been achieved by modification in the protein of 30S subunit of the bacterial ribosome; which does not allow binding of the antibiotic. Overexpression of the target molecule is also one of the mechanisms to render the antibiotic ineffective. For example, sulphonamides, analogues of p-aminobenzoic acid (PABA), compete with PABA to bind and inactive the enzyme dihydropteroate synthetase. This enzyme catalyzes the synthesis of folate, which is
essential for nucleic acid synthesis. Overexpression of PABA, the enzyme substrate, overcomes enzyme inhibition by the sulphonamides.

1.3.3 Changes in membrane permeability of the drug
Mutation in the genes encoding membrane proteins can reduce the permeability of the drug, thus conferring resistance to the antibiotic. As in case of the organism, *Neisseria gonorrhoea*, mutation in the gene encoding the protein, porin, has resulted in resistance to tetracycline and penicillin.

1.3.4 Elimination of drug through efflux pumps
Many bacteria express drug efflux pumps, which expel the drug out of the cell, via energy driven, proton exchange mechanism. This does not allow the drug to accumulate up to its therapeutic concentration, inside the bacterial cell; thus preventing its inhibitory effect. Efflux pumps may act on single or many drugs; for example, the MexAB-OprM efflux pump in *P. aeruginosa* is known to expel many antibiotics such as tetracycline, chloramphenicol and fluoroquinolones (Piddock 2006).

1.3.5 Existence as biofilms
Some bacteria protect themselves by producing either single or mixed species biofilms, an assemblage of bacterial microcolonies which is enmeshed in an exopolysaccharide matrix. These biofilms are generally impermeable to many drugs, disinfectants, and various chemicals; or they may dilute the effect of these chemicals by the production of an excess of polysaccharide. Mixed species biofilms also provide for exchange of resistant genes among close or far related bacterial species, resulting in the spread of resistance among different bacteria.

1.4 Hospital scenario of drug resistant organisms
The phenomenal progress in the emergence of antibiotic resistance among the nosocomial bacterial pathogens has substantial consequences on the infected patients, relating to increased hospital stay, increased stay in intensive care unit (ICU) and high infection associated mortality (Wisplinghoff et al. 2004; Rosenthal et al. 2006, 2010;
Souli & Galani 2008). In comparison with the developed countries, the incidence rates of nosocomial infections have been higher in the developing countries, probably due to poor hygiene practices and inadequate amenities in the hospitals. Besides, the existence of drug resistant strains and their long persistence in the hospital environment has been observed all around the world (Rosenthal et al. 2006, 2010; Enoch et al. 2007; Mehta et al. 2007; Strateva et al. 2007; Bhattacharjee et al. 2008; Patwardhan et al. 2008; Akhtar 2010). Non fermentative Gram negative bacteria have been the major cause of nosocomial infections, followed by Enterobacteriaceae, S. aureus and K. pneumoniae. Among Gram negative bacteria, Pseudomonas aeruginosa and Acinetobacter baumannii pose the greatest threat to the medical system, owing to the profound intrinsic and acquired resistance mechanisms, biofilm persistence, high virulence potential, and extensive adaptability. These are aerobic bacilli or coccobacilli occurring ubiquitously in the environment, commonly in soil and water. Both of them are opportunistic pathogens causing infection in severely ill or immunocompromised patients and are generally not associated with healthy humans. P. aeruginosa is often associated with severe pneumonia in Cystic fibrosis (CF) patients, or hospitalized patients, urinary tract infection (UTI), surgical site infection (SSI), wound infection especially in burn patients, contact lens induced keratitis, and septicaemia (Strateva & Mitov 2011). A. baumannii generally causes device associated infections such as pneumonia, UTIs, SSIs, etc., as well as wound infections and bloodstream infections (Perez et al. 2007). In an extensive data compilation study by the International Nosocomial Infection Control Consortium (INICC), the nosocomial infection data for 173 ICUs from all over the developing world during the period 2003 to 2008 was collected and analyzed. P. aeruginosa and A. baumannii appeared to be the common isolates in pneumonia, UTI and bacteraemia; and often associated with high resistance rates (30 to 78 %) to the current treatment options such as fluoroquinolones, piperacillin, piperacillin/tazobactam, amikacin, carbapenems (imipenem or meropenem) and cefepime (Rosenthal et al. 2010). Similarly, high incidence rates of these organisms were also observed in the systematic analysis of the published studies of the developing countries between the period of 1995 to 2008 (Allegranzi et al. 2011). The developed parts of the world, such as Europe, have also observed the emergence of XDR strains of Gram negative bacilli, particularly in P.
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*P. aeruginosa* and *A. baumannii* (Souli & Galani 2008). With relevance to the Indian scenario, several epidemiological studies in the last decade have highlighted the prevalence of MDR strains of these organisms, particularly exhibiting resistance to ceftazidime, gentamicin, fluoroquinolones, cefepime and piperacillin/tazobactam (Mehta et al. 2007; Oberoi et al. 2009; Ramana & Chaudhury 2012; Durairajan et al. 2013; Juyal et al. 2013). For the rising incidence rates and emergence of drug resistance of *P. aeruginosa* and *A. baumannii*, the necessity of inventing new effective antibacterials against these organisms has arisen and needs to be dealt as an urgent issue.

1.5 Precautionary measures to control nosocomial infections and recommended antibiotic strategies for infection therapy

It is always better to prevent infection as far as possible, and this can be achieved by following the standard precautionary measures recommended by the CDC (Center for Disease Control and Prevention). These include the implementation of proper hand hygiene practices, precautions during contact with patients, judicial use of antibiotics, regular surveillance of MDR organisms, dumping of infected instruments in the environment using standard sterilization procedures, etc (Petrosillo et al. 2010). A surveillance study conducted in developing countries such as Argentina, Mexico, Salvador, and Tunisia looked into the effectiveness of infection control practices such as hand hygiene, disinfection of medical devices, employment of sterile dressing, and other sterility precautions. It was observed that the incidence rate of central line associated bloodstream infections reduced substantially, almost by 55 %, demonstrating the importance of hygiene and sterility in controlling nosocomial infections (Rosenthal et al. 2013). For the treatment and control of MDR infections, experts have suggested selecting the antibiotic therapy specifically based on the resistance pattern, severity of illness, minimum inhibitory concentration (MIC) of the drugs for the causative pathogen and by studying the pharmacokinetic aspects of the drug. The initial therapy should involve strong, broad spectrum antibiotics, which may be changed further, based on the antibiotic susceptibility of the causative organisms. In case of MDR infections, combination therapy may be prescribed to assure the effectiveness of at least one antibiotic (Petrosillo et al. 2010).
For an effective infection control, besides applying precautionary measures, regular surveillance on the trends of resistance to antibiotics and disinfectants needs to be undertaken, and based on this data, the modification in prevention and treatment procedures may be implemented. Such practices may assist in controlling the bacterial infection and increase the survival rate of patients. However, the problem of the increasing emergence of TDR strains still persists, and hence, the development of new infection therapies is imperative to control the resistant pathogens.

1.6 Application of novel treatment strategies to control infections

Diverse approaches are being followed to develop new antibacterial drugs. Antimicrobial peptides have been identified as potential drug candidates. These are small molecular weight peptides that form a part of the innate immunity in a majority of the living species, including animals and humans. These peptides have been active against a broad range of Gram positive and Gram negative bacteria at micromolar concentrations \textit{in vitro}. However, many peptides have failed to show efficacy at lower concentrations in preclinical and clinical studies. There are other limitations associated with the antimicrobial peptides, such as high cost of production, chances of resistance development and proteolysis (Giuliani et al. 2007). Natural products such as biosurfactants produced by various micro-organisms such as \textit{Bacillus} sp., \textit{Streptococcus} sp., \textit{Lactobacillus} sp., \textit{Candida antarctica}, etc. have demonstrated significant \textit{in vitro} antimicrobial, antiviral, immunomodulatory properties. However, the lack of sufficient studies on human cell lines, or animal studies and the associated expenditure in production, lack of toxicity information have limited their use in the medical field (Rodrigues et al. 2006). Various active principles produced by plants, such as alkaloids, flavonoids, coumarins, tannins, essential oils, have been discovered with significant antimicrobial activities. Some of these also find applications in treatment of infections by the general public or in some topical formulations, such as cranberry juice (\textit{Vaccinium macrocarpon}) in UTIs, tea tree essential oils in topical formulation for cutaneous infections, etc. Plant sources have also demonstrated efficacy as resistance modifying agents such as efflux pump inhibitors against Gram positive bacteria (piperine from \textit{Piper nigrum}, chalcone from \textit{Dalea versicolor}, etc.), or antibiotic coadjuvants such as...
phytochemicals that alter the membrane permeability (essential oil of *Thymus vulgaris*, Gallic acid from berry) (Cowan 1999; Abreu et al. 2013). In recent times, nanotechnology has gained widespread applications in the medical field, in diagnosis, disease mechanistic studies, and treatment. Silver nanoparticles have exhibited considerable antimicrobial activity and are also applicable in silver dressings, as coating on medical devices, etc. Although silver nanoparticles serve as important candidates for antimicrobials, some toxicity studies on human cell lines have depicted their cytotoxic effects, which augment with increasing concentration. Hence, more studies on the toxicity aspects of nanoparticles are needed before they can be developed as antimicrobial agents (Rai et al. 2009).

The traditional approach of combating infections operates by affecting bacterial cell viability. As a promising alternative to the tradition, interference of bacterial virulence is being considered for the development of new drugs. Such approach exerts lower selective pressure for the development of resistance, since virulence traits are not essential for bacterial survival (Rasko & Sperandio 2010).

### 1.7 Quorum sensing as a potential target of anti-virulence strategy

An anti-virulence approach for *Pseudomonas aeruginosa* and *Acinetobacter baumannii* is to interrupt their quorum sensing systems. Quorum sensing (QS) is a cell to cell signalling mechanism that enables the bacteria to control gene expression in response to population density. This mechanism involves the production, release, and detection of small signal molecules called as autoinducers. At low population density, basal-level expression of an autoinducer synthase by each bacterial cell results in the production of small amount of autoinducer that diffuse out of the cell and are immediately diluted in the surrounding environment. An increase in population density results in the gradual accumulation of autoinducers in and around the cells. When a threshold concentration of the autoinducers is achieved (the *quorate* level), it specifically binds and activates a transcriptional regulator protein. These activated regulator-autoinducer complexes then interact with target DNA sequences and enhance or block the transcription of QS regulated genes, further resulting in the synchronous activation of certain phenotypes in a
bacterial population. Traits under QS control include surface attachment, extracellular polymer production, biosurfactant synthesis, sporulation, competence, bioluminescence, pigment production and the secretion of nutrient sequestering compounds and production of virulence factors (Taga & Bassler 2003; González & Keshavan 2006).

1.7.1 Quorum sensing in Gram negative bacteria

The QS systems (Figure 1.1) occurring commonly in Gram negative bacteria, produce proteins homologous to the LuxI and LuxR proteins of *Vibrio fischeri*, a marine bioluminescent bacterium in which QS was initially discovered. The LuxI-type protein catalyzes the formation of a specific acyl-homoserine lactone (AHL or acyl-HSL), the autoinducer that can diffuse in and out of the cell and increases in concentration in proportion to the bacterial cell density. The LuxR-type protein binds its cognate AHL autoinducer when the concentration of autoinducer reaches a threshold level. The LuxR–AHL complexes activate transcription of target genes by recognizing and binding specific DNA sequences at quorum-sensing-regulated promoters. Some of the characteristics controlled by the LuxIR-type quorum-sensing systems include plasmid conjugation in *Agrobacterium tumefaciens*, antibiotic production in *Erwinia carotovora*, biofilm maturation, and virulence in *Pseudomonas aeruginosa*, and expression of factors necessary for symbiosis in *Sinorhizobium meliloti* (Taga & Bassler 2003)

![Figure 1.1 The general LuxR/I mechanism of QS in Gram negative bacteria](image)

*Figure 1.1 The general LuxR/I mechanism of QS in Gram negative bacteria; wherein acyl homoserine lactones (AHLs) are produced as autoinducers. The structure of AHLs and the QS pathway is given here.*
1.7.2 QS in *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

*P. aeruginosa* produces two types of AHLs, N-(3-oxododecanoyl)-L-homoserine lactone (3-oxo-C12-HSL) and N-butyryl-L-homoserine lactone (C4-HSL), that bind to specific transcription factors and regulate expression of many virulence factors such as cell adhesion factors (pili, non-pilus adhesions, lipopolysaccharide) and extracellular virulence factors (proteases, pyocyanin, exotoxin, rhamnolipids, etc.), which are responsible for the infection associated extensive tissue damage. AHLs also regulate maturation of biofilms in this organism, a prevalent feature on inanimate surfaces and inside the body of the host. Biofilm often form a major concern, when present on invasive medical devices such as catheters. Antibiotic resistance associated with biofilms, has been linked, in part, to the QS regulation of biofilm maturation. 3-oxo-C12-HSL is also known to modulate host immune system, to favour establishment of the infection (Telford et al. 1998).

In case of *A. baumannii*, 3-hydroxy-C12-HSL acts as its cognate AHL molecule and is synthesized by the catalytic activity of the AbaI synthase protein. This signal binds and activates a specific transcriptional regulator protein, AbaR, which then regulates gene expression responsible for surface motility and biofilm maturation of this pathogen (Niu et al. 2008; Clemmer et al. 2011). The mechanism of *A. baumannii* infections is not very clear at present; though some virulence factors have been noticed, such as pilus, lipopolysaccharide, OmpA and biofilms (Cerqueira & Peleg 2011). It is known that *A. baumannii* commonly occurs on invasive devices as well as inside the host in the form of biofilms. The QS system of this organism partly contributes to the biofilm related drug resistance, due to its important role in the maturation of biofilm and surface motility.

Thus, it can be understood that by inhibiting QS in *P. aeruginosa* and *A. baumannii*, it can be possible to restrain the virulence and biofilm development of these pathogens. The endeavour of the project, thus, was to inhibit quorum sensing of the opportunistic pathogens, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.
1.8 Natural compounds as medicine

Many synthetic drugs have been shown to alleviate treatment of many diseases, but they do not provide a permanent solution to the problem, especially in chronic diseases, and are often coupled with adverse side effects including decrease in immunity, or the overall well-being of the patient. Due to the problem of side effects on chronic exposure; unmet therapeutical needs and the lookout for novel therapeutics, a lot of interest has incurred in natural products research for the development of new bioactive pharmaceuticals.

Natural products are the compounds produced by living organisms, more commonly by microbes, marine plankton, higher plants. The secondary metabolites produced by the living organisms have been often recognized as potential bioactive molecules. Primary metabolites include the proteins, amino acids, sugars, lipids or fatty acids, etc., that are produced in primary metabolic processes. These metabolites group are common among all the living organisms and are essential for their life processes. Secondary metabolites are those compounds that are produced but not known to be essential to the living organisms. The type and structure of secondary metabolites depend on the species or a particular group of organisms. In nature, largely varied secondary metabolites are produced especially by the wide ranging plant species. Their structure is far more complex to be even imagined by the human mind.

The active principles of many drugs, till date, have been derived from natural sources, either directly isolated from natural sources, a derivative of natural product, or modelled from a natural compound. Noteworthy illustrations of such drugs include the antibiotics that have been enormously applied in treatment of infections. Various classes of antibiotics are obtained by microbial fermentation, for example, penicillins from *Penicillium* sp., aminoglycosides such as streptomycin from *Streptomyces griseus*, cephalosporin C from *Cephalosporium acremonium*, carbapenems such as imipenem is a derivative of thienamycin produced by *Streptomyces cattleya*, and many more. Drugs of natural origin have also been valuable in treatment of malaria (quinine from Cinchona bark, artemisinin from a Chinese herb, *Artemisia annua*); as antivirals (derivatives of spongouridine and spongorthymidine, isolated from marine sponges); as analgesics
(morphine and codeine, from the plant, *Papaver somniferum*; and their semisynthetic derivatives); anticancer drugs (Taxane diterpenoid of the plant, *Taxus brevifolia* as Taxol, derivatives of camptothecin from *Camptotheca acuminata* as topotecan and irinotecan), etc (Singh 2012).

### 1.9 Plants as medicinal sources

Since human civilization, plants have been used for management of various ailments; the most ancient systems of medicine being Indian Ayurvedic medicine, Traditional Chinese medicine and Egyptian Medicine. The traditional knowledge of various plants and its medicinal preparations, has been documented in the Indian Ayurveda (in about 1000 BC), Chinese Materia Medica (1100 BC), and in Egyptian Medicine (2900 BC). This traditional knowledge was then carried to other countries, through Greece in Europe, and to North, Central and South America. Traditional medicines focus on the overall mental, physical and emotional health of the patient, and treat with a holistic approach, by prescribing a mixture or decoction of plant drugs that have multiple effects on the body (Singh 2012).

Even today, traditional medicine is widely used for daily healthcare needs of humans. Also, a quarter of the pharmaceutical drugs are plant based formulations, wherein extracts of plants, or substances derived from plants are used as the active ingredients. According to WHO, about 80% of the world’s population, especially in developing countries, use plant based medicines for their illnesses (Gurib-Fakim 2006).

For 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.
1.10 Simplification and acceleration in pharmacognosy research with advanced technology

In earlier times, in spite of the immense knowledge of traditional medicine, research interest in medicinal plants was limited due to time consuming, tedious procedures and difficulties in identification and isolation of bioactive compounds. However, with the advancement in technology, the advent of modern techniques such as high pressure liquid chromatography (HPLC), mass spectrometry (MS), nuclear magnetic resonance (NMR) techniques; the development and application of hyphenated techniques in the field of medicinal chemistry, it has become feasible to identify the bioactive compound and determine its complex structure. Also, enormous progress in synthetic chemistry has facilitated synthesis of plant based compounds and their derivatives, which solves the issue of supply, since it is difficult to isolate and obtain huge quantities of natural products. It has also become easier to understand structure-activity relationship using computational chemistry and combinatorial chemistry (Sarker et al. 2006).

With such an opinion and interest in herbal medicine, the goal of the research project was designed to screen some medicinal plants for anti-quorum sensing activity with respect to *Pseudomonas aeruginosa* and *Acinetobacter baumannii* and further attempt to purify and identify the bioactive molecule/s in the plant extract. It was intended to take an initiative towards solving the crisis in the treatment of MDR nosocomial infections of *P. aeruginosa* and *A. baumannii*. 