INTRODUCTION

*Staphylococcus aureus* is defined as one of the most medically important bacterial pathogens. Its potential to cause wide spectrum of pyogenic lesions which involves several organs, hospital outbreaks and community-acquired infections are well recognized.

*Staphylococcus aureus* is a bacteria which most commonly colonizes the anterior nares, the rest of the respiratory tract are the potential site. Open wounds, intravenous catheters and the urinary tract are also potential sites for infection. They are Gram positive, non-spore forming bacteria, spherical in shape, aerobic or facultatively. *Staphylococcus aureus* is a catalase-positive as well as coagulase-positive.

*S. aureus* infections are often fatal in nature and they are associated resistance to several beta-lactam antibiotics used in hospitals. These strains are known as MRSA (methicillin resistant *S. aureus*).

Historically, *S. aureus* had drawn special attention since 1970 due to its association with several nosocomial outbreaks and cross infections.

The epidemiology of this organism has changed over years. The life-threatening infections which were limited only in hospitals are now becoming widespread in community.

High usage of antibiotics in the hospitals and selection pressure of these antibiotics has been implicated in the development of the multidrug resistance (MDR) in hospital acquired MRSA (HA-MRSA) strains. Likewise, increased use of antibiotics in the animal feed has resulted in emergence of a new MRSA strain (livestock associated MRSA or LA-MRSA) with multiple non-beta lactam drug resistance.

**Disease caused by Staphylococcus aureus**

Around 30% of individuals carry *S. aureus* in their nose, pharynx or even back of throat and on their skin.

Skin infection – *S. aureus* causes boils, furuncles, stye, impetigo and other superficial skin infections in humans.
Infection of surgical and trauma wounds — those with the chronic illness, diabetes, traumatic injury, burns or even the immunosuppression are susceptible to more severe skin deeper tissue infections and abscesses.
Urinary tract infection are also caused by *S. aureus*.
Food poisoning and gastrointestinal tracts infections may be caused by the consumption of food contaminated with *S. aureus*.
Infections of the organs include pneumonia (lung infection), osteomyelitis (bone infection), endocarditis (heart infection), phlebitis (infection of the veins and blood vessels), mastitis (infection of breast and formation of abscesses) and meningitis (brain infection). Infections from and on indwelling medical devices include infection of joint prostheses artificial heart valves.
Generalized life threatening blood infections or the Toxic shock syndrome (TSS).

**Diagnosis of *S. aureus***

Definitive diagnosis of *S. aureus* infection is by obtaining a culture from the area of suspected infection.
Suspect diagnosis is based up on the patient symptoms and the healthcare provider’s evaluation.

► Many humans carry strains of this bacteria on their skin, nose is also a site where humans carry stains and pharynx as harmless commensal bacteria. This makes diagnosis of *S. aureus* from an infection difficult.
► For diagnosis, the very first important step is isolation of the bacteria from appropriate specimens. This is followed up by the identification of *S. aureus* toxins or by the measurement of antibodies in the special cases, such as deep-seated infections or also in the food poisoning.

**Collection of specimens**

► This depends upon the part of the area of the body affected. For example, those with the skin infections or throat, nostrils and wound infections need to swabbed for the pus and other body discharge with the bacteria.
Those with a urinary tract infection need to provide a urine samples in the sterile containers and those with a generalized blood infection need to provide with the blood samples. Blood samples are then transferred to blood culture bottle.

**Identification of the bacteria:**

- This is done by staining with Gram stain or dyes like crystal violet and basic fuschin and viewed under the microscope. *S. aureus* is a Gram positive and stains blue or purple and appears as small round cocci or short chains and most are commonly as the grape-like clusters. Since *S. aureus* may be normally present on skin and mucous membranes, this test is not always confirmatory.

**Confirmation of diagnosis:**

- To confirm a diagnosis, the sample from the patient is placed onto a culture media. For *S. aureus*, the medium used contains blood and lactose. The commonly used medium is the mannitol salt agar (MSA), which is a selective medium with 7–8% of the salt or sodium chloride that allows *S. aureus* to be grown selectively. These media are then placed on petri dishes and swabbed with the sample. The petri dishes are then incubated in the incubator overnight at 37°C. After a set period of time the typical golden colonies of *S. aureus* are seen. These are then stained with the Gram stain for the confirmation and also undergo specific characteristic tests like the catalase test or the coagulase test for the diagnosis.

**Rapid diagnostic tests:**

- Rapid diagnostic tests help in the detection of the bacteria in the real-time. These techniques include Real-time PCR and Quantitative PCR.

**Identification of toxins:**

Toxins produced by *S. aureus*, such as enterotoxins A to D and TSST-1 may be identified by agglutination tests. Agglutination tests are determined by clumping of the latex particles by the toxins present in the sample.

**Antimicrobial assay studies**

These assay studies help determine the specific susceptibility to the particular antibiotics of
the infected strain. Antibiotics which are used like penicillin, amoxicillin, methicillin, first-generation cephalosporins, bacitracin and vancomycin are commonly tested.

**Treatment**

Staphylococcal infections are a common and one of the most significant clinical problem in medical practice. Many strains of the *Staphylococcus aureus* have now become resistant to penicillin, and the methicillin-resistant strains of *S. aureus* (MRSA) are common in the hospitals and are now emerging in the community.

Penicillinase-resistant penicillins (flucloxacillin, dicloxacillin) are the antibiotics of choice for the management of serious methicillin-susceptible *S. aureus* (MSSA) infections.

- First generation cephalosporins (cefazolin, cephalothin and cephalexin), clindamycin, lincomycin and erythromycin have the important therapeutic roles in less serious MSSA infections such as skin and soft tissue infections.
- Conventional anti-MRSA antibiotics like Vancomycin, Teicoplanin, Linezolid and Daptomycin are currently in clinical use.\(^5\)
- However, development of resistance to many of these drugs has been identified worldwide. Vancomycin resistant and the intermediate MRSA strains (VRSA and VISA) have been reported sporadically.
- Methicillin-resistant *S. aureus* (MRSA) was known to be first detected approximately 40 years ago and is still among the top three clinically important pathogens.\(^6,7\)
- The increase emergence of high levels of penicillin resistance followed by the development and spread of the strains resistant to the semisynthetic penicillins (methicillin, oxacillin, and nafcillin), macrolides, tetracycline, and aminoglycosides has made the therapy of the staphylococcal disease a global challenge.\(^8\)

The glycopeptide vancomycin was considered to be the best alternative for the treatment of the multi drug resistant MRSA.\(^9\). However, there are increasing numbers of reports which are indicating the emergence of vancomycin-resistant *S. aureus* (VRSA) strains exhibiting two different resistance mechanisms.
Initially vancomycin-resistant *S. aureus* (VISA) noted in Japan in 1996 and subsequently in United States in 1997, which was believed to be due to the thickened cell wall, where many vancomycin molecules were been trapped within the cell wall. The trapped molecules clog the peptidoglycan meshwork and finally form a physical barrier towards further incoming of the vancomycin molecules. The second, noted in United States in 2002 among *S. aureus*, was identical to the mechanism seen in the vancomycin-resistant *Enterococcus*. Vancomycin resistant *Enterococcus faecium* harbours the vanA operon, which contains five genes, VanS, -R, -H, -A and – X. But Tiwari et al., have reported a VRSA which is van gene-negative. Subsequent isolation of VISA and VRSA isolates from other countries including Brazil, France, United Kingdom, Germany, India, and Belgium has confirmed that the emergence of these strains is a global issue.

The second form of vancomycin resistance has resulted from the probable conjugal transfer of the vanA operon from a vancomycin-resistant *E. faecalis*. There is a possibility that this plasmid exchange will occur more frequently (due to the reason that there is ever increasing likelihood of patients being colonized with both MRSA and vancomycin-resistant enterococci), and resistance of these strains to both β-lactams and glycopeptides all increase the likelihood that VRSA strains will rapidly become more and more prevalent.

Furthermore, it has also shown an increase in the minimum inhibitory concentration (MIC) to the Glycopeptides over years indicating reduced susceptibility. With the emergence of resistance to these drugs along with the scarcity of newer anti-MRSA in the pipeline, the therapeutic options are likely to be further narrowed in future.

The lower effectiveness of antibiotics causes thousands of deaths worldwide (Allahverdiyev et al., 2011).

The worldwide increase of methicillin-resistant *Staphylococcus aureus* and the more recent emergence of the vancomycin-intermediate *S. aureus* and vancomycin resistant *S. aureus* strains had a major impact on antibiotic policies and also prompted an active reaction from the pharmaceutical industry which are concerning the discovery and development of new antibiotics to combat these strains (Cornaglia and Rossolini 2009).

So, the identification of an alternative and safer drug for the control of MRSA is necessary to combat this worldwide problem. Nature is the only source to provide a
A variety of chemical compounds that can be used for new drug discovery especially from mineral, plant and animal products.

- The control of major diseases by synthetic products is decreasing there is increased interest in the revival of herbal medicines leading to the current widespread belief that the “green medicine” is safe, more accessible and also more affordable (Parekh et al., 2006) than the costly synthetic drugs, many of which have the adverse side effects. [24] 60% of the total global population remains dependent on the traditional medicines for their health care system; whereas about 80% of the rural population of India depends on the wild varieties of plants for the treatment of various diseases (Shrestha and Dhillion, 2003) [25].

- Recently, pharmaceutical industries have started taking more interest in plant products to isolate active constituents from different plant parts and use them directly as a drug or design them as a pharmacologically active compounds with or without the addition of synthetic ones (Tiwari et al., 2008) [26]. Novel bioactive natural products have been identified to display an anti-MRSA activity. Current research suggests that these natural products have the prospect of being considered for treatment of MRSA infections.