ABSTRACT

Staphylococcus aureus is a gram-positive coccoid bacterium found in humans and animals, causing a wide range of infections from mild to life-threatening. It resides in the nasal membrane and skin, causing skin, wound, food poisoning, nosocomial infections, and bloodstream infections. Epidemiologic studies have reported the highest number of morbidity and mortality rates due to *S. aureus* infections. The highly toxic nature of the bacterium reduces the efficacy of antibiotics making it resistant to the wide spectrum antibiotics. Medicinal plants thereby, serve as an alternative for fighting against such multidrug resistant pathogens as they are known to possess vital pharmacologically active compounds that target such pathogens making them susceptible in nature.

Wound healing is a complex process involving stages like hemostasis, inflammation, proliferation, and remodeling. Bacteria colonization can delay the healing process especially, *S. aureus* due to formation of biofilm which aids the bacteria to strengthen and colonize thereby delaying the wound healing process. Natural antimicrobial agents isolated from plant essential oils can prevent bacterial growth and promote wound healing. Essential oils are volatile, lipophilic liquids produced by plants as secondary metabolites. Plants have significant potential for wound management and treatment, with many used in tribal and folklore for wound and burn treatment. Essential oils are highly valued in the industry for their antioxidant, anti-free radical, and metal chelating properties. They have anti-nociceptive, neuroprotective, anticonvulsant, and anti-inflammatory properties, and have been reported in preclinical studies as potential sources for drug development.

Kaempferia galanga L. is widely used folk medicine exhibiting anti-inflammatory, anti-oxidant, anti-tumorous, anti-bacterial, and anti-angiogenesis effects, closely linked to its numerous ethnomedicinal applications. The study evaluated the wound-healing capacity of *Kaempferia galanga* L. essential oil-based ointment in Wistar Albino rats, considering its biological properties to potentially enhance the wound healing process.

Chapter 1 cover in detail the Introduction of the problem of emergence of multidrug resistant *Staphylococcus aureus* and its strain Methicillin-Resistant *Staphylococcus aureus* (MRSA). The chapter also explains the requirement of new drugs and various approaches in the form of medicinal plants and essential oil to combat against the resistant strains as they are known to possess phytochemically rich compounds. This chapter also explains on how the

formulated drug from medicinal plants are being therapeutically used. The aim and research objectives are also highlighted in this chapter.

Chapter 2 is on Review of Literature and presents comprehensive review on the anti-staphylococcal drug discovery from medicinal plants. The review is divided into natural products and their use in drug discovery, MRSA resistance mechanism and its prevalence worldwide and in India, comorbidity. The Chapter also reviews various *in silico* approaches like docking, Adsorption Distribution Metabolism Excretion-Toxicity (ADMET) studies, molecular dynamics simulation studies and concludes with a final discussion on ointment formulation and its activity against wound healing study.

Chapter 3 details the selection of the plant species, *Kaempferia galang*a Linn, isolation of essential oil and characterization of the bioactive compounds, antimicrobial, biochemical, antioxidant analysis, *in-silico* approach to study the target biofilm forming proteins of *S. aureus*, ointment formulation and wound healing study on Wistar Albino rats was used.

Chapter 4 is on the Results and Discussions. The chapter presents a critical analysis of the results obtained in the studies. Firstly, eleven active compounds were characterized and identified from the essential oil of *K. galanga* L. The phytochemical analysis showed the presence of phenolics and flavonoid depicting the E.O's antioxidant activity. Secondly, essential oil also demonstrated anti-biofilm activity against *Staphylococcus aureus*. Thirdly, the *in-silico* study docking against two targets of biofilm-forming proteins in *S. aureus*, CrtM and SarA, by the identified molecules from the essential oil revealed the binding affinity of the compounds. Further molecular simulation demonstrated the stability and binding affinity of the molecules and the PCA analysis demonstrated the conformational stability and changes in the structure of the molecules. Finally, formulated ointment demonstrated better wound healing property.

Chapter 5 presents the conclusions of the work and proposes further future works.

The last part of the thesis contains the references cited in the thesis.