The present study was taken up to perform a detail analysis of the wound healing activity of specific *Garcinia* species through *in-vitro* and *in-silico* analysis. The wound healing activity of the four species, namely, *G.pedunculata*, *G.morella*, *G.xanthochymus* and *G.lancifolia*, were established prominently through microbiological species against three test organisms, that is, *P.aeruginosa*, *S.aureus coagulase positive* and *S.pyogenes β hemolytic*.

The present study on the patient population at referral hospital established that infection is encountered at all stages of a wound, as they invariably impair the first line of host defenses between environmental microbes and the host's internal millieu. When the bacteria breach this barrier it results in different types of wound infection. Surgical wound infections, better termed as Surgical Site Infections, are common and cannot be completely eliminated. But a reduction in the infection rate could have significant benefits like reduction in the postoperative morbidity and mortality, wastage of health care resources and finances. The general causes for increased predisposition to wound infections are pre-existing illness, prolonged operating time, the wound class and wound contamination. Technical problems with the operation, particularly bleeding, the amount of devitalized tissue generated, and the need for drains within the wound determine the risk of infection along with patient's general metabolic status which includes obesity and diabetes. Rigorous wound surveillance, a technically perfect operation along with the judicious use of prophylactic antibiotics would greatly aid in attaining minimum infection. Bacterial isolates were prominent in the SSI's under the current study as also in skin wounds and burn wound infections.

There has been a change in the bacterial etiology of surgical and burn wound infection from time to time. A century ago, the most feared and frequent pathogen was *Streptococcus*, twenty years ago the coagulase positive *Staphylococcus* was the principal
offender. In burn wounds the gram negative bacilli are now replacing *Staphylococcus*, the principle offender in SSIs. The present study shows the emergence of Gram negative *Pseudomonas* accounting as the principal offender in burn wound infection which supports the finding of Ekrami & Kalanter (2007).

*Garcinia* is one of the few genus whose almost all species has been found to have medicinal properties but little effort has been made to conserve these species. Due to their slow growth and reproduction, its species are facing extinction especially the *G. lancifolia*, *G. accuminata* and *G. pedunculata*. Except for some cultivated areas these species were not found in wild during collection of the species.

The *Garcinia* had rich source of flavonoids and phytochemicals for which they had been used as a nutrient source by the people as mentioned before. The bioactive and phytochemical constituents of *Garcinia* exhibit a wide range of biological activities one of which is their ability to scanvenge for hydroxyl radicals, and superoxide anion radicals, and thus health promoting in action (Ferguson, 2001). Flavonoids have exhibited anti-inflammatory, antiangionic, anti-allergic effects, analgesic and antioxidant properties (Hodek et al., 2002) while tannins, saponins and steroids have exhibited a wide range of antimicrobial activity in these species. Xanthones (Mahabusakaram et al., 2005) and benzophenones (Baggett et al., 2005) have been reportedly isolated from *Garcinia* species, and some of them have also been reported to have shown antibacterial activity (Rukachaisirikul et al., 2003). Flavonoids glycosides and cardiac glycosides found in the extracts are suggestive of their antioxidant property. Flavonoid glycosides are reported to be antioxidants and used as anti-inflammatories in the treatment of capillary fragility (Iwu, 1993). Their presence in the extracts is an indication of the plants' potent antioxidant and membrane-stabilizing properties.
The presence of flavonoids and tannins in all the plants is likely to be responsible for the free radical scavenging effects observed.

Thus it can be safely inferred from the current study that the rich constituents of secondary metabolites present in the tested *Garcinia* species are responsible for the antimicrobial activity as seen through the *in-vitro* studies.

A knowledge of the chemical constituents of plants are fairly desirable, not only for the discovery of therapeutic potent bioactive compounds but also because such information may be of high value in disclosing new sources of such economic tannins, oils, gums, precursors for the synthesis of complex chemical substances, etc. In addition, the knowledge of the chemical constituents of plants would further be valuable in discovering the actual value of folkloric remedies. The results of present research highlights the fact that the organic solvent extracts exhibited greater antimicrobial activity because the antimicrobial principles were either polar or non-polar and they were extracted only through the organic solvent medium. The present observation suggests that the organic solvent extraction was suitable to verify the antimicrobial properties of medicinal plants and they supported by many investigators.

The discovery and development of antibiotics are among the most powerful and successful achievements of modern science and technology for the control of infectious diseases. However, the rate of resistance of pathogenic microorganisms to conventionally used anti-microbial agents is increasing with an alarming frequency (Ge et al., 2002; Nair and Chanda, 2005; Neogi et al., 2008). Surveys have revealed that almost no group of antibiotics has been introduced to which resistance had not been observed (Eloff, 2000). In addition to this problem, antibiotics are sometimes associated with adverse side effects on the host, which include hypersensitivity, depletion of beneficial gut and mucosal microorganisms, immunosuppression and allergic reactions (Al-Jabri, 2005). The use of
higher plants and preparations made from them to treat infections is a longstanding practice in a large part of the population, especially in the developing countries, where there is dependence on traditional medicine for a variety of ailments (Ahmad and Mohammad, 1998). The present study justifies the claimed uses of *Garcinia* in the traditional system of medicine to treat various infectious diseases caused by the microbes which is comparable to the standard antibiotics.

It is well known that *Garcinia* is a rich source of oxygenated and prenylated xanthones. The present observation suggests that the organic solvent extractions of these plant parts are suitable to verify the antimicrobial properties of these plants. Based on this, further chemical and pharmacological investigations to isolate and identify minor chemical constituents in *G lancifolia* and *G.accuminata* and to screen other potential bioactivities may be recommended. Although, absence of certain phytochemicals in one sample and its presence in the other can be safely attributed to the various physiological and biothynthetic reactions taking place inside the plant, the effect of the environment too should not be neglected, as the environment always modify the things.

The preliminary screening assays for antimicrobial activity and phytochemical analysis can largely be considered as qualitative assays and are used for identifying the presence or absence of bioactive constituents in the extracts. However, these methods of assay offer little information on these compounds. Minimum zone of inhibition is a quantitative assay and provides more information on the potency of the compounds present in the extracts. Thus, the zone of inhibition (ZOI) values of crude extracts of the five *Garcinia* species were determined so as to demonstrate the potency of the extracts against the selected strains of bacteria. The methanol extract of *G.pedunculata* seeds showed antibacterial activity against all the clinically isolated bacterial strains and most of the standard bacterial strains which was comparable with that of investigated antibiotics. The extracts were found to contain various
phytochemical constituents. For example, *Garcinia pedunculata* which was active against all the test microorganisms had high concentration of tannin but were absent of steroids. It also had flavonoids and alkaloids and high amount of reducing sugar which supports the findings of Mudoi et al., (2012) on this plant. It also had saponin in moderate amounts but were absent of steroids. The present study also showed high content of total flavonoid in *Garcinia pedunculata*. The physiological effects of flavonoids include possible antioxidant activity, therefore, suggesting their role in prevention of coronary heart diseases including atherosclerosis (Seirens, 2002).

The results of the present study suggest that the *G.pedunculata* seed extract possess compounds with antibacterial properties that can be explored as a viable, alternative source to commercially available antibiotic drugs. Further studies are needed to isolate and characterize the major active constituent of methanolic extract of *G. pedunculata* seed and test it on other microorganisms and against various infections, where in the information procured would further serve as a strong evidence for the plant as potent antimicrobial agent. The present results support the facts that most of these plants are used traditionally to treat and manage infections caused by bacterial pathogens.

Emerging antimicrobial resistance trends in burn wound bacterial pathogens represent a serious therapeutic challenge for clinicians caring for burn patients. Antibiotic-resistant organisms such as MRSA, vancomycin-resistant enterococci, and multiply-resistant gram-negative rods, including *Pseudomonas aeruginosa*, *Acinetobacter* spp., and various members of the family *Enterobacteriaceae*, have been associated with infections of the burn wound and other anatomic sites in patients with major thermal injury, occasionally in the form of nosocomial outbreaks. Success results with the tested *Garcinia* species provides an insight to the knowledge that these species can be further recommend for finding new drugs to treat these abnormalities naturally.
Since all the plant extracts have exhibited their potency against bacterial isolates in the current study it is worth recommending that the extracts can be tested against a wide range of bacteria. Further study on the plant species can be done on the basis of analysis and isolation of the compounds present as well as determination of their bioactivity of the pure compounds. Such an effort could lead to identification of a new range of compounds for management of bacterial infections.

Bioassay of combinations of plant extracts that exhibited moderate and low activity can be carried out to establish any synergism between them. Traditionally medicine plants decoction are taken in combination and at a high dose. This may explain the low and moderate activity of some form of extracts of the species under study. Thus bioactivity on all parts of the plants for example, root, stem bark and leaves can be combined so as to report certain activity of a plant. The results validate the ethnobotanical use of the studied plant species by the people of NorthEast India.

A rational approach is needed to maximize the chances of finding new drugs, and to exploit the opportunities of potential new drug targets emerging from genomic and proteomic initiatives, and from the large libraries of small compounds now readily available through combinatorial chemistry through insilico process. The present research focuses on applications and protocols, with the main emphasis on critical analysis to study the effect (or non-effect) of docked natural molecules into protein receptors. Ligand protein docking has been developed and used in facilitating new drug discovery. In this approach, single or multiple small molecules are attempted to dock into a receptor site so as to find putative ligands. A number of studies have shown that docking algorithms are capable of finding ligands and binding conformations at a receptor site close to experimentally determined structures. These algorithms are expected to be equally applicable in identification of multiple proteins to which a small molecule can bind or weakly bind to. Application of this
approach can potentially facilitate the prediction of unknown and secondary therapeutic target proteins and those related to side effect and toxicity of a drug or drug lead.

Virtual screening techniques are applied early during the docking protocol to reduce the size of large compound libraries. Initially libraries are “pre-filtered” using a series of simple physicochemical descriptors to eliminate compounds not expected to be suitable drugs. Procedures like pharmacophore analysis, neural nets, similarity analysis, scaffold analysis, Lipinski’s rule of five and garbage filters are used to sort out molecules according to their ADME properties, among others. This procedure, which reduces the size of the library to a group of molecules more likely to bind the target receptor, is known as enrichment. In the current study out of a total of 98 ligands from *Garcinia* only 59 were selected after screening, in which only a 23 of them showed the credibility of inhibiting the target enzyme. Even within it the number varied on comparison between Total binding energy and the number of H-bond interaction with the amino acid pool of the enzyme complex as seen in table 4.20-table 4.24. Even the total binding energy of all the ligands of a single *Garcinia* species varied with the type of enzyme inhibited and the inhibition activity of the compounds of *G.xanthochymus* were seen to be the best in this case. In terms of enzyme inhibition, the multidrug resistant protein of *P.aeruginosa* exhibited the least resistance while the gamma hemolysin component of *S. aureus* was the most resistant of all the protein targets.

It is necessary to stress that the selection criteria used during the enrichment steps need to be carefully chosen, as application of too stringent filters may lead to early exclusion of potential leads. Similarly, drug-likeness of potential leads may be less important at the early stages than ease of the molecule experimental validation with in vitro assays. Similar compounds can be further grouped together and arranged in smaller assemblies to assist the screening process. The use of several small libraries is not only a more cost-effective
approach, but can usually provide a broader chemical diversity than a single large library. Also lead compounds have served as the basis for the synthesis of more specific ligands with fewer side effects.

The bioactivity assay of compounds reveals many important characteristics hitherto unknown. The study reveals many compounds functioning as GPCR ligands, ion channel inhibitors, protease inhibitors, enzyme inhibitors and nuclear receptors. Ion channels are involved in many, if not all, cellular functions and are altered in many pathological conditions either indirectly or directly, as in the channelopathies. It is not surprising, therefore, that drugs targeting ion channels constitute important therapeutic interventions for a number of diseases (Okuno et al., 2008). The compound as gambogenone and Assiguxanthone derivatives shows the possibility of functioning different ion-channel blockers. With the discovery of ion channelopathies, the therapeutic value of many basic drugs targeting ion channels has been confirmed. Also, further analysis of structural similarities of GPCRs and the lead compounds as ligands can give a deeper insight into the development of GPCR specific drugs that initiates signal transduction cascades. Many diseases involve the malfunction of these receptors, making them important drug targets. In human, the estimated number of GPCRs is approximately 948, corresponding to about 5% of the total number of human genes. However, more than 45% of all modern drugs target GPCRs; these represent around 25% of the 100 top-selling drugs worldwide (Zhang et al., 2006).

The three dimensional (3-D) structure of both ligand and protein are necessary for the application of docking techniques. While the manifold of conformational structures of small molecules may be relatively easy to predict, the lowest energy conformation obtained may not correspond to that of the bound ligand. Many proteins targeted for drug design do not have an experimentally determined structure and, therefore, docking studies cannot be
performed directly. In some cases, computational techniques can be used to predict the 3-D structure of a protein provided the structure of a closely related protein homolog is known. Homology modeling or sequence threading techniques may be used to generate models of protein structures which, although not as good as experimentally determined structures, can be used as docking targets. In summary, it is of great importance to carefully prepare the structure of the protein target before the docking process.

Creation of a virtual database in the last and the final step in cheminformatics and drug designing which makes the procedure complete. A database created as such ultimately provides the platform for all to input and gather all the information required on that source within that field.

While such information provided in the database can serve a wide variety of purposes, it is perhaps in the field of virtual screening that it may have its greatest impact. Structures either can be searched for their similarity to known active compounds or can be docked to receptors of particular molecular targets, providing new information on their therapeutic potential. Information on molecular drug targets (of wound infecting pathogens) of plant compounds has however also increased over the past few years. Again, this is of particular significance for virtual screening in that the information of a particular bioactive compound of a particular disease target present in the database can be used to identify other phytochemicals which may be expected to show similar behavior and affords the first opportunity to map the ligand-receptor space of plant compounds and their respective molecular targets.

In Assam or in North-east as a whole, no database has come up related to a particular disease or ailment. The particular database has been created with a view that the information regarding plants related to particular disease will be useful not only to the scientific community but en masse.
Many biological information systems rely on relational database management systems (RDBMS) to manage high-throughput biological data. With this view the database is aimed to enlist plants used locally in the treatment of various diseases along with their secondary drug targets. This will be however, the first database containing medicinal plants locally available only in Assam for treatment a particular disease. The database will find utility to the scientific community for a quick review on the number of plants and plant parts for different drug target sourced medicinal plant research and may serve as a platform for development of drugs.