6. CONCLUSION

Biomedical Product associated infections (BMPAI) in the day to day life has become life threatening to the patients in the hospitals. Even though several reasons are associated with nosocomial infections, BMPAI plays a critical role for the patients exposed to several biomedical products like implantable materials - catheters, stents, shunts, prosthesis, dental ligatures, joint ligaments, sutures and non-implantable materials - textile surgical gowns, patients’ uniforms, pillow cases, bed covers, blankets, drapes, etc. Major complications of the biomedical products were the failures of these implants in the patients, due to the formation of microbial biofilms on the implant surface; and surface colonization of pathogens and its transmission from the non-implantable materials. The medical practitioners prescribing the oral antibiotic prophylaxis to the patients over meet the complications like survival of multi drug resistant organisms and its pathogenicity. Mostly prescribed oral drugs by the medical practitioners, falls under the category of cephalosporin, penicillin derivatives, quinolones and fluoroquinolones. Several research articles have discussed the problems associated with the multi-drug resistant bacteria and its BMPAI.

Hence, in the present study instead of depending on a single type of antimicrobial drug, two different compounds having similar mode of action on the microbes were selected. Fluoroquinolone and nitroimidazole drugs combination plays a major role against aerobic, anaerobic bacterial and parasitic infections. The mode of action of these two drugs was almost similar, inhibiting the DNA replicative essential enzymes like topoisomerase, gyrase and polymerase. Furthermore, the above antibiotics possess specific anti-bacterial functions absolutely different from that of other formulations generally known at present. Also, there exist rare drug-resistant bacteria in relation to the above antibiotics because the antibiotics do not have anti-bacterial activity attained by plasmid. The synergistic antibiotics make DNA gyrase inactivate, which is an enzyme necessary to replicate DNA of bacteria for supercoiling such as joining DNA cut pieces with other DNA after cutting circular DNA, distortion, relaxation, and ATP hydrolysis, etc. Thus, such enzyme inactivation causes abnormal chromosome conditions.
which results in impossible division and growth of bacteria, thereby showing sterilization effect.

For Biomedical Product associated infections and surgical site infections, these synergistic drugs were mostly prescribed by the medical practitioners. The drugs were used only as oral prophylactic drugs at a very higher concentration ranging between 200-750 mg/day. In every oral dose of fluoroquinolone drug atleast 30-40% is absorbed and accumulated in various body fluids and tissues like prostate 2.5 µg/g, seminal fluid 2.7 µg/ml, testicle 1.6 µg/g, uterus/cervix 3.0 µg/g, vagina 4.3 µg/g, fallopian tube 1.9 µg/g bile 6.9 µg/g. Hence to prevent the accumulation of these two compounds, instead of using orally, if coated/treated onto the implantable and non-implantable materials, the organisms associated with BMPAI could be inhibited to a larger extend.

In the present research, the implantable and non-implantable biomedical products were coated/treated with these two drugs along with different biocompatible drug carriers. The drug-carrier selected in the study is made of food and medical grade biodegradable polymers. The main reason for grafting the carrier with the drugs was the coated materials release the drugs at a sustained rate. Due to the sustained release of drugs by the carriers the surface colonization or adhesion of bacteria and its proteins could be inhibited; also it increases the persistence rate of drugs on material surface.

Among the three different drug combinations [D₁ - norfloxacin-metronidazole, D₂ - ofloxacin-ornidazole and D₃ - ciprofloxacin-tinidazole (C+T)] selected in the study, the drug, D₂ - ofloxacin-ornidazole was found to be more effective for both implantable and non-implantable materials. For each implantable and non-implantable material, a specific drug-carrier combination was found to be effective. The efficacy was proved based on qualitative antibacterial activity, drug release analysis, bacterial adherence properties and persistence of drug or wash durability. The surface characteristics of drug-carrier coated material was analysed topographically by SEM and chemically by FTIR.

Carriers involved in sustained release of drugs provide more durability and persistence of the antibacterial compounds in the surface of biomedical products.
In the research, it was proved through *in vitro* challenge test that the drugs were persistent for more than 30 days (till 5th challenge dose) under controlled chamber conditions. The duration of drugs in the material surface was potent in inhibiting the biofilm formation. Under *in vivo* condition these analysis will be suitable for the patients who were implanted with biomedical products.

SEM analysis predicted the ultra-smoothness of material surface on the coated biomaterials. Also, it determined the size of the drug particles attached to material surface. FTIR analysis showed no chemical interactions/alterations in the biomedical materials after being coated with drugs and carriers. Biocompatibility of the *drug-carrier coated* material was checked by HET-CAM method. HET-CAM test was proportionally an accepted *in vivo* model. No described tissue reactions with endpoints were detected on CAM, instead well-developed blood vessels without inflammations were recorded. Since these results were obtained only in laboratory conditions, animal *in vivo* model should be thoroughly studied before applying on the human trials.

Since these drugs were commercially available at an affordable cost, commercial biomedical product manufacturers will not be affected with the overall cost of the materials. So, economically the materials coated with the synergistic drugs will be certainly less than that of the products coated with antimicrobial agents like triclosan, chitosan, poly DL-lactic acid, silver, titanium oxide, quaternary ammonium compounds and nano composites of heavy metals.

By using these controlled coating methods (dip-coating and microencapsulation), the selected drugs or any other new drugs which emerge in future could be used to coat implantable and non-implantable materials for the prevention of biomedical product-associated infections. If these results surpass the human trial without any side effects or tissue hypersensitivity reactions, it could be a terminology for making different antibacterial drug coated biomedical products and its applications for the patients based on their disease profile.

### Advantages of synergistic drug and carrier coated biomedical products

- The synergistic drugs selected in the study were already used as oral antibiotics at high concentration (200-500mg) to prevent biofilm formation after implantation.
Whereas, only 10-100 times lower than the oral dose was exposed at the implanted site when the drugs were surface coated on the implants.

- Fabricating the material with drugs and carriers by coating and encapsulation methods could be comparatively cheaper, reliable and economic than the other complicated/sophisticated methods like plasma technology and vibrating devices.

- Drugs and carriers are easily available at considerable cost so that the surface coated implantable and non-implantable materials could be commercialized at an affordable price. This could be a better alternative for the costlier antimicrobial biomedical products.

- Carriers used are of food and medical grade; already used in medical, food, pharmaceutical and cosmetic fields. Carriers have antibacterial and anti-oxidant properties, so it enhances the purpose of fabricating the materials to graft it with synergistic drugs, there is no risk of hypersensitive tissue reactions unlike the other antimicrobial biomedical products surface modified with different heavy metals, disinfectants and marine elements.

- Drug-carrier coated materials provide sustained release of drugs; hence persistence of drugs were more potent; prolonged antibacterial property will be well established from the surface; prevention of bacterial adhesion and biofilm formation could be significance.

**Future Perspectives**

Thus the fabricated implantable and non-implantable materials provided broad spectrum, prolonged antimicrobial durability, inhibited bacterial adherence. If these results can be confirmed in vivo, these antibacterial coatings on biomedical products could be of great interest to avoid cross infection by pathogenic microorganisms, to arrest metabolism in microbes in order to reduce the formation of odour, to safeguard the product from staining, discoloration and quality and over all to increase the standard of hygiene in hospitals and healthcare centres.