

CHAPTER 5

CONCLUSION

Though extremely concise, both on the worldwide developmental and mankind's history scales, the anti-infection agents have experienced many high points and low points, giving us significant lessons on numerous parts of how the microbial world around us behaves. The revelation and utilization of anti-infection agents, anti-infection resistance markers, and versatile components such as plasmids were at the establishment of hereditary designing and sub-atomic science that in the long run brought about fabulous achievements of the human genome and other sequencing ventures. Microorganisms, notwithstanding, utilize the extremely same (and most likely some extra yet at the same time unidentified) common systems to ensure themselves against the gigantic antibiotic ambushes ceaselessly propelled by the mankind from the season of disclosure of antibiotics. Examination of the microbial world around us for potential systems of anti-microbial resistance and dispersal may plan the early cautioning and preventive measures to support the viability of antimicrobials and chemotherapy.

Considering different discoveries of the present study, it can be inferred that extended range beta lactamases are slowly expanding in India with co-imperviousness to some different classes of antimicrobial agents is extremely disturbing. This study demonstrates that *K. pneumoniae* is basic for the incite acknowledgment of antimicrobial resistant organisms, as it is more resistant than *E. coli*. Infection control experts and clinicians require the clinical research center to quickly distinguish and describe diverse sorts of resistant microscopic organisms uniquely ESBLs effectively to minimize the spread of these microbes and select more fitting antibiotics. It is exceptionally hazardous for research center specialist that a few measures of ESBLs are available in 3GCs sensitive microscopic organisms. So ESBLs must be recognized by double disc diffusion test. The study of disease transmission of ESBL-producing microscopic organisms is turning out to be more unpredictable with progressively obscured limits amongst healing centers and the group. Additionally studies are required to explore MDR microorganisms and ESBL from different parts of India utilizing more detaches. Investigations of sub-atomic studies on molecular

epidemiology of these resistant types can likewise be utilized for examination with qualities officially secluded from different parts of the world.

Essentially, high pervasiveness of MRSA was additionally found in human patients in tertiary care clinics. Different variables are in charge of expanding patterns in MRSA infections in creating nations like India including self-drug, ignorance, non-reconnaissance framework, treatment slant from quacks, inconsiderateness by specialists with respect to remedy of anti-infection agents and neediness. MRSA is a disease causing bacteria that produce many muddled diseases in people. MRSA is a variation of *S. aureus* that has created imperviousness to beta-lactam anti-infection agents, which incorporate the penicillin's (methicillin, Oxacillin, and so on.) and the cephalosporin's. In different nations the pervasiveness of MRSA has shifted from doctor's facility to healing center. Everywhere throughout the world, expanded commonness and anti-microbial safe microscopic organisms are the developing issues, confronted by the clinics. MRSA infections have turned into a reason of vital ailments with now and then deadly outcomes. Transmission of MRSA happens by direct contact to a colonized transporter. The fundamental wellspring of spread is from patient to quiet on the hands of healing center staff. Post-surgical diseases represents around one-fourth of all doctor's facility gained contaminations. MRSA predominance rate from blaze wounds have additionally expanded around the world. The general pervasiveness of *S. aureus* in tests got from human injuries was observed to be 48.6%, the predominance of MRSA was observed to be 85.7%. All MRSA contains *mecA* quality which are in charge of imperviousness to beta-lactam anti-infection agents. All MRSA confines affirmed by latex agglutination with penicillin restricting protein 2a (PBP2a) were molecularly described to identify *mecA* quality utilizing polymerase chain reaction (PCR). The segregates were tried for the chromosomal qualities "nuc" encoding (thermo-nuclease particular for *S. aureus*) and *mecA* (methicillin safe particular quality). All detaches were discovered positive as *mecA* quality and *nuc* quality was found in all MRSA disconnects. Antimicrobial helplessness profile was performed on Mueller-Hinton agar plates against generally utilized antibiotics. All MRSA secludes demonstrated quality resistance against amoxicillin, ciprofloxacin, ampicillin and amoxicillin-Clavulanic acid. Transitional resistance was found against doxycycline (12%), oxacillin (4%) and levofloxacin (12%). More elevated amount of affectability was seen against vancomycin and linezolid. Vancomycin was considered

as the medication of decision against MRSA diseases however resistance against this medication have been created. Still it is the successful medication as vancomycin is not ordinarily utilized as a part of our healing facilities. Multi-site resistance is a critical finding in this study. As per present study vancomycin is the best medication against MRSA contaminations took after by linezolid and tigecycline. Considering different discoveries of the present study, it can be reasoned that extended spectrum beta lactamases and MRSA were slowly expanding with co-imperviousness to some different classes of anti-infection agents. There is a high commonness of ESBL and MRSA in our tertiary care healing facility thus it is fundamental to report the ESBL generation and MRSA alongside the normal affectability reports.

Anti-infection agents are critical class of medication valuable in various sorts of microbial infection. Numerous antimicrobial medications are hard to direct on account of their poor liquid-dissolvability, toxic effect to sound cells also quick corruption and clearance from the circulatory system. Since the revelation of liposomes in 1964, the field and applications thereof has widened impressively. The most utilized lipid segment is phosphatidyl choline, on account of its propensity to be nonpartisan and relatively low in cost. Cells get inactively focused on, especially the cells of mononuclear phagocytic framework (Antimonials, porphyrins, amphotericin B, immunizations, and immuno-modulators). Supported arrival of locally or systemically regulated medications is seen in liposomes stacked with Cytosine arabinoside, doxorubicin, cortisones, peptides or organic proteins e.g.: vasopressin. Doxorubicin and amphotericin B are cases of site-evasion instrument.

Multilamellar liposomes were prepared and encapsulated inside the liposomes and was coated with PEG. This was characterized using FTIR, UV-Vis Spectroscopy, AFM and TEM. Further we saw that the MLVs are bigger in diameter and presented greater integrity of encapsulation ability. Drug entrapment efficiency after 1 hr and 24hrs was calculated using the absorbance of the UV-Vis spectra. In case of ciprofloxacin encapsulated liposomes, the efficiency was calculated to be 16.45% in 1 hr and after 24 hrs the efficiency was found to be 76%. The result showed higher entrapment efficiency in ciprofloxacin encapsulated liposomes than PEG coated ciprofloxacin encapsulated liposomes after 24 hrs than 1 hr. Similarly in comparison with the coated and uncoated drug encapsulated liposomes was confirmed using AFM

and TEM. MLV liposomes produced a more suitable action due to the existence of several phospholipid two layers that free the antibiotic gradually over an extended period of time. Interpretation of liposomal drug activity depends on physicochemical properties of antibiotic and the area of the antimicrobial target in the microbes. *In vitro* Antimicrobial studies by liposomal antibiotic formulation with multidrug resistant bacteria showed higher rate of growth inhibition. The complete work proved that the *in vitro* antibacterial activity for the drug encapsulated liposomes significantly increased the zone of inhibition against the multidrug resistant bacteria. The obtained experimental findings of liposomal formulation of Cloxacillin and vancomycin significantly increased the zone of inhibition, against multidrug resistant gram negative bacteria due to fusion mechanism are encouraging and would justify to further research the utility of liposomal formulations containing antibiotics to enhance the action of various antimicrobial agents contrary to resistant bacteria.

Our liposomal formulation significantly increased the zone size against resistant strains used in this study. From these findings, it perhaps wrap up that entrapping ciprofloxacin, amikacin, cloxacillin and vancomycin into vesicles raise their antimicrobial action contrary to *E. coli*, *Klebsiella pneumonia*, *Acinetobacter baumannii* *Staph.aureus* and MRSA. *Escherichia coli* ATCC 25922, *K. pneumonia* ATCC 700603 and *Staph aureus* ATCC29213. This indicates that liposomal preparations perhaps an efficient substitute for curing infections produced by these microbes and an authentic way contrary to the advancement of microbial resistance. Moreover, liposomal drugs when coated with PEG, significantly increases their antibacterial activity by increasing the zone of inhibition (lowered the MICs) against multi drug resistant strains and ATCC strains utilized in this study.

5.1 Inference

- Liposome formation containing Amikacin remarkably increased the zone size towards resistant strain used in our research. Further presented sustained antibacterial action towards the highly drug resistant isolates by coating with PEG as determined by micro well diffusion assay. So, aforementioned formulations perhaps utilized in establishing more efficient antibacterial agents in the treatment of bacterial infection caused through multidrug resistant bacteria.

- Liposomal preparations described in this perhaps deliver a sufficient volume of amikacin in the direction of drug-impermeable microbes. Application of different technique proved liposome-plasma membrane integration as the molecular tool on this subject aspect.
- Liposome-encapsulated aminoglycosides offer possibilities for increasing the therapeutic index of this class of antibiotics. Local application of liposomes may provide a reservoir that prolongs therapeutic drug concentrations at the site of infection. Readily accessible infected tissues such as in the eye, wounds and lungs could benefit from this local administration. In order to optimize therapeutic efficacy it is important to balance drug release and for retention in the liposome. Specific liposome compositions may enhance bacterial killing by interacting with the infectious organism.
- Medication for intracellular diseases in the mononuclear phagocyte system tissues can profit by the immense measures of aminoglycosides so that perhaps conveyed inside the cell. Investigation is required for toxicity towards kidney and ears due to traditional liposomal preparations of aminoglycosides, concerning their drawn out nearness in the body. In that way, MiKasome has demonstrated an amazing security profile. The evaluated outcomes shows encouraging future for liposome-embodied aminoglycosides and assurance assist medical examinations concerning effective utilization of particular definitions for the management of extreme diseases-
- Our liposomal ciprofloxacin formulation significantly increased the zone size against resistant strain used in this study as a result of (i) a higher antibiotic infiltration in microbial tissues and (ii) conservation against adverse environmental surroundings. More sites in the body perhaps entered through fine-tune liposome diameter, phospholipid content, and surface charge.
- The liposomal formulations characterized in view of this research can develop in to a provocative weapon for the topical treatment of Gram-negative–constant infections, alike burnings, in that the particular types of microbes are normally seen. Contrarily, if a systemic use will be programmed in the boost of the liposome content would be needed, for example by coating the vesicle surface with applicable hydrophilic substance able to assure a lengthy durability time in the circulation.

5.2 Recommendations

5.2.1 The great pervasiveness of Methicillin resistant staph aureus and ESBL

- Seems to be associated to the huge antimicrobial utilization;
- Obtainability of antimicrobials at pharmacy stores without physicians instruction.
- Unwise use of antimicrobials in health care settings.
- Uncontrolled use in animal agriculture.

5.2.2 The problem of drug resistance is very alarming, as it appears to be increasing, particularly with the emergence of resistance to newer antibiotics such as ciprofloxacin among the clinically important bugs such as methicillin resistant staph aureus strains.

It is urgently required to:

- Ban the sale of antimicrobials without instruction,
- Use drugs more wisely in health care settings by in-depth teaching of the concept of the utilization of antimicrobials, and
- Organize effective control measures of hospital acquired infections.
- Control the consumption of antibiotics for both human being and animals.

With the existing achievement in this area, there is no question that liposome-based drug conveyance method will continue to revamp therapy to microbial infections, mainly in serious diseases like staphylococcus infections and tuberculosis.

Disregarding the considerable advances on nanoparticle-based antimicrobial medication conveyance, here we point out the need to join the mutual enthusiasm between nano engineers and microbiologists in creating novel nanotechnological methods focusing on a couple of major neglected difficulties on antimicrobial medication conveyance. Initially, procured microbial medication non-susceptible remains a noteworthy test for microbial remedy. Conceivable start is to consolidate various antibacterial medication to a liposome and after that simultaneously convey the medications to similar microorganisms. Combinatorial medication treatment is required to have notable strength as numerous medications perhaps accomplish collective impacts and overpower bacterial guard instruments. Potential medication discharge triggers incorporate pH esteem, enzyme and other one of a kind characters

of the disease microenvironment. It would be gainful for disease therapy if antibacterial nanoparticles could be altered through irresistible cell antigen particular ligands with antibodies, immune response pieces, aptamers and peptides.