# Chapter 7
# Summary & Future prospects

# Chapter 7 Summary and Future Prospects

The thesis is focused on amino-acid and peptide-modified Polyurethanes and their various biomedical applications, including drug delivery, anti-bacterial efficacy, as anti-oxidants, and mainly on targeted "Cancer treatment". Key findings of the thesis are summarized as follows:

- We report how different diisocyanates modulate the drug release kinetics of PU. PU made with aromatic diisocyanates exhibits less than 20% drug release in PBS (pH 7.4), while those made with aliphatic diisocyanates release approximately 80% of the drug, following a non-Fickian diffusion pattern. Contact angle measurements reveal that PU-I (IPDI-based PU) is more hydrophilic. However, drug release is sensitive to several factors, mainly including drug-polymer interactions, hydrophilicity, and the degree of branching in the polymer chain. FTIR analysis indicates that the presence of −NH– groups at the ends of the polymer chain increases hydrophilicity, with strong hydrogen bonding between chains that is disrupted upon reaction completion. This disruption enhances the interaction between the polymer and the drug, limiting drug exposure to the solvent. Concerning cell killing efficacy, the order of potency is PU-I > PU-H > PU-M > PU-T. Nevertheless, PU-I still possesses 55% cell viability at 3 days, while PU-T, at the same drug concentration, exhibits 76% cell viability over a comparable time course.
- We have successfully synthesized PU-TRP to enhance the biocompatibility of aromatic PU. TRP-grafted polyurethane 6% and 16% have been confirmed by NMR, and their fluorescence properties have been successfully integrated into the PU matrix. Drug release studies showed a 74% release over 24 hours for the TRP-modified PU compared to just 8%

for pure PU. Biocompatibility assessments through cell adhesion on two cell lines demonstrated that TRP modification enhances both the biocompatibility and selectivity of the material towards cancer cells. Cell viability in cancer cells, when combined with the drug, was 14% at 72 hours. The cellular uptake in healthy cells and the 3-day fluorescence study on SiHA cells confirm the theranostics approach of the material. *In-vivo* release kinetics, using both IV and IP, proved that the vehicle of the drug would produce a more sustained and controlled release compared with the pure drug. In gelation studies in mice, skin toxicity was excluded, and we found out that (by H&E staining) morphology is intact, and by TNFα, we see there is no amount of inflammation on the skin section, so the material is perfect for localized treatment.

- We report how CYS-modified aliphatic PU and explore its antibacterial and targeted cancer cell-killing efficacy. CYS-modified polyurethane (PU) showed increased porosity, hydrophilicity, and degradation characteristics, thus enhancing the drug release to as high as 89% within 48 hours compared to 58% by the prepolymer (PP) under the same conditions. The addition of cystine to the PU chains as a chain extender did not affect the SiHA (tumor) cells or 3T3 (normal muscle) cells. Importantly, the drug release from the carrier was sustained and controlled over three days, specifically to cancer cells, thus lessening the frequency of administration. In addition, CYS-modified PU exhibited antibacterial activity against S. aureus with a minimum inhibitory concentration (MIC) of 20 µg/ml. The antibacterial properties of cystine further enhance PU's performance and reduce ROS levels, addressing concerns related to oxidative stress.
- We have synthesized peptide-modified aromatic PU with homopeptides of Glycine. The PU-G2 system exhibits improved porosity, hydrophilicity, and degradation as compared with

pure polyurethane (PU). This indicates that the drug release is controlled and sustained in case of PU-G2 for more than 5 days. So, it reduces the administration of a huge amount of the drug regularly; hence, its dosage reduces as well as drug-related toxicity and the cost of treatment. Drug release for more than 24 hours has been recorded, i.e., 31% for PU-G2, while 9% for pure PU in 7 days. Both drug-loaded PU-G2 and PU-G3 presented over 90% cell viability at 100 µg/ml in 3T3 cells, while PU-G2 provided better drug release efficiency and a higher potential for killing cancer cells. The sustained release of drugs and good biocompatibility of PU-G2 make it a promising candidate for anti-cancer drug delivery.

## Future Prospects

Our work involves researching into the complex domain of biomedical applications, particularly regarding an *in-vitro* study about the modification of PU, variation with small bioactive segments with considerable potential in a multitude of medical applications. That, however, is still an area of study under work and development.

- The next phase of our research involves *in-vivo* studies by taking PU-TRP 16%, the drug delivery capabilities for killing cancer cells with minimal toxicity on internal organs will have to be checked this innovation is not merely confined to the laboratory; we envision this advancement becoming indispensable in clinical settings, reshaping the landscape of medical interventions.
- Our vision includes using PU-TRP 16% for diagnostic purposes in live imaging from mouse models to clinical settings.
- Moreover, our investigation into PU-CYS has shown promising results in drug delivery and antioxidant properties, as demonstrated by *in-vitro* studies and ROS assays. But this is only

an initiation to such advancements which, to be fully realized, need continued research, more importantly, *in-vivo* studies. Optimizing these materials requires them to behave inside the human body; therefore, thorough *in-vivo* studies will not only confirm our findings but also help ease the transition of these materials into their intended clinical applications. Imagine the potential of drug delivery systems that could target and work effectively in a laboratory setting but also demonstrate such excellent efficacy in the dynamic complexities of the human body.

- By checking the potential PU-G2 of ECM mimicking potential in *in-vivo*, we can reduce repeated dosage necessity and can achieve a more proficient DDS system.

Hence, in summary, our work is not only a discovery from science but also how we mold the future of health. This pathway, from synthesis to *in-vitro* studies, gives prominence to our pursuit of making greater strides in medical science. As we advance on a scale of what's achievable, the influence of our work has a ripple effect and spans beyond the laboratory environment foundation of healthcare practice ends.