Summary
7.0 Summary

- The growing resistance of microorganism to the drug molecule and the need for new small molecule to combat the disease like cancer is an emerging area of interest. Cancer cells gain their multidrug resistance by building extra P-glycoprotein, which continually ejects the anticancer drugs out of the cancer cells by efflux mechanism. Review of literature suggests that the fluorenyl compounds are found to have various therapeutic applications which are reported in the past. This chapter mainly emphasizes the drug applications of 9-fluorenyl compounds in the field of pharmaceutical chemistry.

- Chapter 2 describes the preparation of different 9-fluorenone ketimines using simple condensation or the acid catalyst promoted dehydration using high boiling solvent. Eight compounds were prepared and characterized using $^1$HNMR and mass spectra. Some of the heterocyclic and amino acid ester like 2-amino thiazole, 2-aminopyrazine, methyl anthranilate and L-valine methyl ester did not result in the desired ketimines formation using the acid catalyzed dehydration process in toluene solvent. The prepared 9-fluorenyl ketimines are further investigated for its antimicrobial and antibacterial activity.

- Chapter 3 focuses more on the preparation of N-9-fluorenyl amines derivatives using aliphatic, aromatic and heterocyclic amines and the aliphatic amines were resulting in the desired secondary amine derivatives in protic and aprotic solvent at high temperature. Aromatic and heterocyclic amine compounds such as 2,6 dimethyl aniline, 2,6 di isopropyl aniline, 2-amine pyrazine, 2-amine thiazole were not successful even after using variety of acid scavenger such as anhydrous...
sodium acetate, triethyl amine and Hunig’s base and this may be due to the higher base constant value of the aromatic and heterocyclic amine. Dimeric fluorene, bifluorenylidene was obtained as major product when sodium methoxide was used as scavenger during the aromatic and heterocyclic amine coupling reaction.

- Chapter 4 explains the preparation of novel N-9-fluorenyl amino acid methyl ester using 9-chlorofluorene, L-amino acid methyl ester and Hunig’s base in acetonitrile solvent which in turn facilitates the replacement hazardous lead nitrate as acid scavenger during the coupling reaction. The prepared library compounds were further investigated for its antibacterial and antimicrobial activity.

- Novel N-9-fluorenyl amino alcohols were prepared using the corresponding amino ester derivatives, lithium aluminium hydride in tetrahydrofuran solvent. The reduction reactions are temperature sensitive and the desired product formation was observed at -40°C with less side reactions.

- Chapter 5 detailing the antibacterial and antimicrobial activity of the library compounds derived from 9- fluorenone such as 9-fluorenyl ketimines, N-9-fluorenyl amine derivatives, N-9-Fluorenyl amino acid methyl ester and N-9-fluorenyl amino alcohol against the various microorganisms. Most of the library compounds showed better antibacterial activity against *Staphylococcus aureus* and *Proteus mirabilis* and also N-9-fluorenyl library compounds showed good antifungal activity against *Penicillium chrysogenum*, *Aspergillus Niger* and *Trametes vesicolor*.

- Docking study of the N-9-fluorenyl derivatives obtained from the synthesis exhibit good MDR property against the target protein P-glycoprotein. Amine compounds such as N-9-fluorenyl morpholine, N-9-fluorenyl imidazole, and
N-9-fluorenyl cyclopropyl amine compounds show more favorable binding with PHE and VAL residues in the active site of the protein. The prepared library compounds such as N,N'-bis-fluoren-9-ylidene-ethane-1,2-diamine, 2-(9H-fluoren-9-ylamino)-3-phenyl-propionic acid methyl ester, 2-(9H-fluoren-9-ylamino)-propionic acid methyl ester 2-(9H-fluoren-9-ylamino)-3-methyl-pentanol, 2-(9H-fluoren-9-ylamino)-3-phenyl-propanol have good dock score when compared with Olivacine and proved to be a potential drug candidate for the multidrug resistance in cancer caused by P-glycoprotein.

- The bioactive compounds in future can be used as drug candidate for treating the multidrug resistance in cancer caused by p-glycoprotein and further invitro and invivo studies should be carried out in future by comparing with Olivacine to prove the potency of the drug candidates.
List of Publications
8.0 List of Publication


List of Patents

✓ Novel N-2-(9H-fluorenyl)-amino acid derivatives

Application number 3584/CHE/2012

Conference participated

✓ Attended the conference during 04 & 05 Jan 2013

✓ Integrated Approach on Herbal technology at Triple Helix hall,

Central Leather Research Institute, Chennai