CHAPTER VI

CONCLUSION AND FUTURE PEREPECTIVES
1. CONCLUSION

In the present investigation, efforts have been made to combine two approaches, i) fragment based drug design approach and ii) computational modelling, for the identification of potential lead molecules of biological importance. The stepwise achievements of the present work are given below.

- Bioinspired diversity oriented / atom efficient synthesis has been developed for the preparation of an array of flavonoids and their partial methyl ethers (total 77 compounds). Methoxymethyl (MOM) protection was used extensively. An eco-friendly or green protocol for the deprotection of MOM group was developed using pTSA through solid phase reaction.
- Novel syntheses of rare (I-3,II-3)-biflavones have been developed using cerium ammonium nitrate for oxidative coupling and followed by double cyclodehydration.
- First synthesis of pachypodol and analogs have been developed from spiraeoside, obtained from onion peel waste. The spiraeoside was efficiently converted into bioactive compound, pachypodol and analogs through regio-specific methylation and deprotection.
- Phytochemical investigation of Berberis tinctoria was undertaken. Of the different parts, berberine was found in the stem and roots of Berberis tinctoria. A rapid and efficient method was developed for the isolation of berberine from Berberis tinctoria. Berberine quantity in Berberis tinctoria (3.5-4%) was comparable with the reported plant source (B. chitria; 5.20%) in the literature. From this study, we suggest that Berberis tinctoria can be an alternative source of commercially important berberine.
- Synthesised compounds were subjected for the various bioassays viz. inhibition of MMPs, NFkB and CA II activities. It was found that chrysoeriol, 5-deoxychrysoeriol, acacetin were found to be good inhibitor of NFkB. Biacacetin, pachypodol were found to be best for inhibition of MMP-2 and MMP-9. Kaempferide, apigenin, acacetin were found to be excellent inhibitor for CA II.
- Computational modelling studies were extremely useful for the identification of mode of binding in afore mentioned proteins. Using this study, we discovered some novel non-zinc binding inhibitors for CA II and MMPs.
2. FUTURE PERSPECTIVES

From the above studies, seven lesser known compounds are found to exhibit good inhibitory activities for MMPs, NFkB, COX-2 and CA II. In the listed compounds (figure 30), acacetin-a partially methylated flavone derivative showed promising effect in all the biomarkers such as MMPs, NFkB, COX-2 and CA II in micro molar ranges. Further, acacetin can be taken for different animal model experiments. For improving its potency, QSAR based studies can be performed.