CHAPTER – 6

SUMMARY AND SUGGESTIONS FOR FUTURE WORK

6.1 SUMMARY

Single crystals growth has an important role to play in the present era of rapid scientific and technological advancement, where the field of single crystal has so much to offer as prospect and potential for various applications in science and technology. The new materials which are synthesized in this field will form the lifeline of the solid state research and device technology. The fastest growing pharmaceutical crystal engineering will play a leading role in the development and improvement of pharmaceutical products. In the next few years, the field of crystal engineering will offer wide scope for drug development which will be widely accepted and entertained by the industry practitioners. The never ending research and development and propagation of new materials of pharmaceutical crystal engineering will pave the way for new frontiers being explored and conquered in fighting life threatening diseases and drug development.

The investigations carried out in this thesis reveal that 4-MAPS, ANPTFA and ANPTM crystals are valuable and applicable materials for potential applications in bio medicine. Initiatives were taken to grow these organic crystals with suitable solvents by slow evaporation technique at 30 °C using constant temperature bath.

The growth conditions were optimized for all the three organic crystals investigated in the present work. The 4-MAPS compound was synthesized by the reaction of equimolar ratio of 4-methyl aniline with phenolsulfonic acid and grown using methanol as solvent. Crystals of
size of 12 × 9 × 2 mm³ were harvested after 15 days. ANPTFA was synthesized by the chemical reaction of 2-amino-5-nitro pyridine and trifluoroacetic acid in the molar ratio of 1:2 and grown in water. The grown crystals were of size 8 × 6 × 3 mm³ and the period of growth was two weeks. AMPTM was synthesized by the reaction of equimolar ratio of 2-amino 4-methylpyridine with tartaric acid and the crystals were grown by using methanol as a solvent. After a period of four weeks, crystals of size 10 × 10 × 5 mm³ were grown. These grown crystals were subjected to various characterizations such as single crystal XRD, FT-IR, NMR, UV-Vis-NIR, photoluminescence, photoconductivity, thermal, microhardness, dielectric, SEM, AFM and Cytotoxicity studies.

Single crystal structure X-ray diffraction studies of the three organic crystals revealed that the 4-MAPS and ANPTFA crystals belong to monoclinic system with centrosymmetric space group P2₁/c. Whereas, the AMPTM material crystallized into triclinic system with non-centrosymmetric space group P1. The presence of various functional groups along with different types of protons and carbon atoms present in 4-MAPS, ANPTFA and ANPTM crystals were identified by FT-IR and NMR spectral analyses.

The UV-Vis-NIR transmittance spectra of 4-MAPS, ANPTFA and AMPTM crystals were recorded. The 4-MAPS crystal showed 50% transmittance with a lower cutoff value of 294 nm and the ANPTFA crystal possessed a lower cutoff of 414 nm. The AMPTM crystal had 65% transmittance in the entire visible region with a lower cut-off value of 344 nm and the optical band energy was found to be 3.44 eV. The photoluminescence spectra of 4-MAPS, ANPTFA and AMPTM were recorded. For 4-MAPS, the UV emission was centered around 4.02 eV. The photoluminescence emission spectrum of ANPTFA showed the broad emission spectrum at 436 nm corresponding to blue emission. In
the case of AMPTM, the broad emission spectrum with $\lambda_{\text{max}} = 414$ nm coincided with the violet emission centered at 3 eV.

Photoconductivity studies confirmed that 4-MAPS and ANPTFA crystals are negative photoconductive crystals, whereas AMPTM exhibited positive photoconductive nature.

The thermal behavior of 4-MAPS, ANPTFA and AMPTM were studied. From the thermal analysis, it was inferred that the 4-MAPS, ANPTFA and AMPTM crystals were stable up to 192 °C, 118 °C and 85 °C respectively. From TGA analyses, some of the kinetic parameters such as the activation energy ($E$), enthalpy of activation ($\Delta H$), entropy of activation ($\Delta S$), and Gibbs free energy change of decomposition ($\Delta G$) were estimated. These analyses show that 4-MAPS, ANPTFA and AMPTM crystals have the negative value of $\Delta S$ and positive values of $\Delta H$ and $\Delta G$.

Microhardness measurements were carried out on 4-MAPS, ANPTFA and AMPTM single crystals. The Meyer’s index value was determined as 2.02, 1.87 and 2.05 for 4-MAPS, ANPTFA and AMPTM single crystals respectively. Interestingly all the three materials were found to be soft. Dielectric studies were carried out for the grown crystals and all the three crystals showed normal dielectric behavior. By Arrhenius principle, the activation energy of 4-MAPS, ANPTFA and AMPTM crystals were estimated as 0.862 meV, 0.31 meV and 0.1 meV, respectively.

The growth morphology of the grown crystals was observed by SEM analyses at different magnifications. The crystals ANPTFA and AMPTM showed rod-shaped growth pattern. The surface morphology of all the three samples were studied by atomic force microscopy and
roughness parameters, skewness parameter \( (S_{sk}) \) and surface kurtosis \( (S_{ku}) \) were determined.

The material AMPTM crystallizes in triclinic system with non-centrosymmetric space group P1 which allows contribution of a molecular nonlinearity. The relative SHG conversion efficiency of the grown crystal was found to be 0.3 times that of the KDP crystal. Among the three crystals, AMPTM alone exhibited the SHG property as the other two crystals were centrosymmetric.

The cytotoxicity studies of 4-MAPS, ANPTFA and AMPTM crystals were carried out to determine the non-toxic dose. 4-MAPS had 53.2% cell viability at 62.5 µg/ml in normal Chang liver cell lines. The ANPTFM and AMPTM crystals showed 50% and 48% cell viabilities respectively at a concentration of 125 µg/ml in Vero cell lines. From the observed values, it is inferred that the grown crystals 4-MAPS would be suitable for pharmaceutical use with a concentration less than 62.5 µg/ml, whereas ANPTFM and AMPTM crystals would be useful at concentration less than 125 µg/ml. Among the three samples, 4-MAPS has substantial cytotoxic effect, which means it has potential for anticancer treatment. Further cytotoxic studies using different cancer cell lines could be done to ascertain this.

6.2 SUGGESTIONS FOR FUTURE WORK

The 4-MAPS, ANPTFA and AMPTM are new organic single crystals with ample scope for further research, because of their structural similarity with many reported compounds. The crystals have potential properties suitable for chemical, industrial and biomedical applications. Motivated by the significant properties displayed by organic crystals attempt can be made to grow bigger sized crystals by adapting the slow cooling method or by unidirectional crystal growth
method (Sankaranarayanan and Ramasamy method) for various applications. The growth of these crystals can be carried out in various solvents including the mixed solvents. The growth experiment can be further simplified by careful optimization of various parameters. Studies such as ESCA/AUGER near the phase transition temperature will be very useful in understanding the mechanism during the phase transition. The etching behavior of the crystal can be studied in order to investigate the perfection of the grown crystal. By etching studies, the imperfections are revealed by suitable etchants and solvents that differentially attack the material.

In order to test the crystalline quality of the grown crystal, the high resolution X-ray diffraction (HRXRD) analysis can be carried out. Though the microhardness studies have been carried out on the prominent orientation of the crystal, it will also be interesting to study the same for different orientations as well as varying conditions such as pH of the grown crystals, temperature and crystals grown with different solvents. Thermomechanical analysis (TMA) can be carried out in future to evaluate the coefficients of thermal expansions (linear and bulk expansion coefficient) to find the thermal stress produced on the crystal.

Three dimensional structure determination and conformational analysis of the grown crystals provide valuable information about the structure function relationship, which will be of use to identify the crystal as potential drugs to treat number of diseases.

Cytotoxicity studies, the screening test for cancer treatment has to be carried out to find out the suitability of the grown crystals for its use in cancer treatment. The investigation can also be extended for their usefulness in anti-viral, anti-bacterial and anti-fungal treatments.