Education is what survives when what has been learned has been forgotten.
- B. F. Skinner (US psychologist, 1904 - 1990)

Preface

Chemistry, the study of the formation and properties of molecules and materials, is central to the advancement of science and technology. Chemistry deals with the properties that distinguish one substance from another. In Chemistry, there are several different branches including organic chemistry, inorganic chemistry, physical chemistry, analytical chemistry and biochemistry. It’s a science in its own right that supports and interacts with other scientific disciplines. In connection with biology, physics, medicine, materials science and other core disciplines, it offers effective solutions to problems facing the world today and renders mankind the essentialities for tomorrow. By discovering the world of molecules and ways to synthesize them, chemists profoundly influence and enable science and technology and shape the world as we know it today. Chemistry can be broadly defined as the study of matter and the changes that it undergoes. Many people think of chemistry as the chemical changes in terms of mysterious experiments conducted in chemical laboratories with strange chemicals and complex apparatus. This is only one aspect of chemistry. Chemical changes are also natural processes and take place all about us. The burning of coal, gas, and wood; the cooking of meat and other foods; the rusting of a kitchen knife and the tarnishing of silver—all these things which we take for granted involve chemical changes. Life processes such as growth, digestion, and breathing are also examples of chemical change. Many of these changes, which take place in our bodies, are so complex that they cannot yet be duplicated in chemical laboratories.

The emergence of supramolecular chemistry is a great evolution of human knowledge and is an effort to understand and analyze the
supermolecules and their important scientific findings. Advancement of this field along with crystal engineering paves the way for the growth of X-ray crystallography in organic chemistry, a branch of chemistry. The crystal engineering approach is also used in the design of molecules prior to synthesis is more convenient, insightful and cost effective and useful in designing new candidates with desired physical and chemical properties. In recent years polymorphs, cocrystals, salts, eutectics and solid solutions have progressed into the direct applications in the pharmaceutical industry because they exhibit different properties i.e., stability, solubility, dissolution and bioavailability. These strategies are used to understand the very subtle but weak non-covalent interactions that guide many complex biological processes to design the drug molecules and solve the issues associated with marketed drugs. The present thesis work is such an attempt focusing on the designing of molecules for sulfa drugs, amphoteric drugs, fenamates, amino acids and fibrates.

Chapters 2, 3 and 4 are dealing with the polymorphism that exhibit different properties of bio-active sulfonamides, amphoteric molecules and N-acetyl-L-cysteine drug respectively. These sulfonamides with well analyzed crystal structures have been taken for the present study in order to compare the molecular conformations with solubility and dissolution trends of six sulfonamides. Therefore in chapter 2, the solubility properties of twisted molecular conformations are responsible for the high solubility behavior due to the less packing of molecules in the crystal lattice. Hence the functional group modification can be used to solve the solubility issues via chemical modification in the drug discovery step. Chapter 3 is just opposite to the above one, the functional group modification was done by using the crystal engineering strategy of optimizing the zwitterionic polymorphs for the better solubility and stability. We proved it through the structure-solubility relationship and apply the same trend in other drugs
without any more chemical modification. The chapter 4 is interesting one
that deals with identification of novel polymorphs of NAC and the
comparison of structure-stability relationship. The thermal stability and
thermodynamic stability of polymorphs were investigated in this chapter
and recommending the NAC form I as the suitable form for the formulation
from the comparison of hydrogen bonding and other noncovalent
interactions with stable modification.

Moving from polymorphs to designing molecules for drugs to
pharmaceutical materials, a complete understanding of the strong and weak
intermolecular interactions that stabilize the complex/ multi-component
systems is essential for me to expand the idea of understanding the
structure-property relationship studies into it. Realizing the promise these
studies have by leading to new idea for engineering novel cocrystals and salt
materials are the complex formation drugs substances with GRAS coformers
(chapter 5 and 6). A complete solid state characterization of all cocrystals
and salts is done in this thesis to understand the effect of these multi-
component systems on solubility and dissolution rate. The competencies of
salts and cocrystals towards solubility have been studied in chapter 5 and
found that salts are high soluble and stable compared to the cocrystals.
Therefore, salt formation techniques are extended to the chapter 6 for some
of the BCS class II drugs to address the solubility issues. Successfully, these
salts are well characterized in terms of improving the drug properties and
interestingly the solubility is 10 times more for all drug salts. The mineral
salt and molecular salts are of having equal advantage of solubility and
dissolution properties. Out of all these works, six papers have been
published and one more are in a ready to submit. The published results, after
minor modifications have been straight-away adapted as chapter 2, 3, 4 and
5. Chapter I describe the background of the several solid forms,
characterization and structure-property relationship, along with a brief note
on supramolecular synthons. Scope of the thesis is appended at the end of chapter 1 and 7. Description about polymorphs, cocrystals, salts and eutectics is avoided in the introduction section of every chapter since it has been discussed in the introduction of chapter 1. All crystallographic details related to polymorphs, salts and cocrystals are mentioned in the tables in the appendix at the end of the 7 chapters.

“Life is Chemistry: Dilute your Sorrow. Evaporate your Worries. Filter your Mistakes and Boil your Ego. "You will get the Crystal of Happiness"”

(ந. சுதலை குமார்)