CHAPTER 7

Conclusions and Scope for Future Work

Abstract

The present chapter outlines the conclusions of the present study as well as the scope of future work. The thesis is focused on research work about "chiral materials," as these materials have important applications in interdisciplinary domains of science, pharmaceuticals, and research. To study characteristic details of chiral molecules, one important method is to observe their interaction with linearly polarized light and circularly polarized light. A quarter wave plate is usually used to produce circularly polarized light. In this work, initially, we have unraveled a method to find fast and slow axes of QWP with the help of the Michel Levy Interference colour chart. The optical path difference developed by QWP was correlated to the interference colours observed. Observing the huge applications of chiral materials, work is concentrated on recognizing, observing, and differentiating the optical handedness of chiral materials, as they are very useful in research and for designing drug molecules.

We present a technique to observe the handedness of chiral materials by using Newton's rings experimental setup. Newton's rings experimental setup was modified, and enantiomers of chiral molecules were differentiated with the help of interference technique and refractive index measurements. We performed high pressure study on chirality-inducing compound under quasi-hydrostatic and non-hydrostatic pressure environments and probed it with Raman spectroscopy.

In the pharmaceutical industry, chiral compounds are used as active pharmaceutical ingredients (APIs) to make drugs. To observe the effect of pressure on drug molecules, *in-situ* high pressure Raman optical activity experiments were performed to obtain characteristic details of chiral molecules (both enantiomers) under non-hydrostatic pressure environment. Present investigation of chiral compounds is simple, novel, and inexpensive. Our investigation on enantiomers of chiral molecules indicate, a small compression of 0.08 GPa switches the chirality (racemization) of enantiomers. These findings are extremely beneficial for the pharmaceutical industry because pelletization of drug is carried out under pressure and it may change the chirality of the drug.

The appendix I of the thesis is focused on a review of negative refractive index metamaterials, and chiral metamaterials on which we did a literature survey. We found that negative refractive index metamaterials are artificial materials and have wide applications in making perfect lenses, invisibility cloaks, and antennas. Chiral metamaterials are artificially fabricated materials and exhibit the properties of chiral materials (optical activity and circular dichroism). A chiral metamaterial structure can lead to have properties of a negative refractive index metamaterial.

7.1 Conclusions

My research work presented in this thesis is summarized below. Our findings are significant, first of their kind and will be tremendously beneficial to students, researchers, pharmaceutical companies, and for the entire society.

7.1.1 Correlating Fast and Slow Axes of a Quarter Wave Plate to Interference Colours

Quarter wave plates (QWP) are made up of anisotropic materials due to their birefringent properties. QWP is an optical component that can convert linearly polarized light into circularly and elliptically polarized light. Its fast axis orientation with respect to polarized light determines the resulting polarization. When the fast axis of quarter wave plate is oriented at $\pm 45^\circ$ with respect to the polarization direction, circularly polarized light is generated. It is one of the essential components that is required to study chiral materials and minerals in the field of optical mineralogy and is used in petrographic microscopes. We investigated quarter-wave plates made of uniaxial (quartz) and biaxial (mica) crystals due to their wide applicability in physics, chemistry, geology, and mineralogy and attempted to understand the nature of interference colours observed when these plates are tilted about their fast and slow axes. An explanation has been given by using the Michel Levy interference colour chart. The interesting outcomes of the chapter are as follows:

An axes determination test was performed to find the fast and slow axes of a quarter wave plate made up of mica and quartz. Minimum resources were used to conduct the experiment. QWP, not marked with fast and slow axes, was kept between crossed polarizers and positioned to get the maximum amount of light. QWP kept between crossed polarizers was rotated about vertical direction (parallel to the polarizer's transmission axis) and different colours were observed. The colours observed are associated with the optical path difference of the interacting e and o rays. The chapter provides an explanation of why different interference colours are observed and explains it on the basis of the Michel Levy interference colour chart.

7.1.2 Insights on Optical Handedness of Chiral Materials using Newton's Rings

In this work, Newton’s rings experimental setup was modified to differentiate enantiomers of chiral molecules. The presented technique is simple, novel, and inexpensive and is able to observe the optical handedness of chiral materials. Interference rings and refractive indices (of both enantiomers) were used as an analytical tool. Linearly polarized light (at different polarizing angles) and circularly polarized light (both handed) were employed to measure refractive index of both enantiomers. Differentiating chiral enantiomers is essential, as these materials are used to make drugs in the pharmaceutical industry. These are the observed outcomes of the chapter:

Newton's interference rings setup available in undergraduate labs was modified, and the optical handedness of chiral materials was observed. An enantiomer was filled in the sample cavity, and the refractive index of each enantiomer was measured. We were able to distinguish enantiomers on the basis of refractive index, as enantiomers show different R.I values due to circular birefringence. The presented method requires only 40 µl sample of each enantiomer, which is very less compared to other known traditional methods. Our findings indicate that the number of chiral centers present in a chiral molecule affects the refractive index value. A number of enantiomers can be investigated using the modified Newton’s rings setup.

7.1.3 High Pressure Raman Spectroscopic Study on Chirality inducing agent: A Case Study of Sodium Dithionite ($Na_2S_2O_4$)

In this work, we investigated the effects of high pressure on the chirality-inducing agent Sodium dithionite ($Na_2S_2O_4$) under quasi-hydrostatic and non-hydrostatic pressure environments. It is extensively used as a powerful reducing agent and has a very long S-S bond. The important outcomes of the study are:

Sodium dithionite ($Na_2S_2O_4$) can provide chirality to the oxidized product. To verify chiral product formation, a solid state synthesis reaction of Sodium dithionite ($Na_2S_2O_4$) was performed under high pressure with 1-phenyl-1-one (acetophenone/ methyl phenyl ketone) and 1,2-diphenylethane-1,2-dione (benzil) (ketones). Solid state reactions between sodium dithionite and ketones under high pressure show a decrease in the carbonyl bond frequency, indicating the formation of a chiral center of particular carbon atom attached to ketones. Under extreme pressure the dynamics of sodium dithionite show that it can act as a chirality inducing agent.

Quasi-hydrostatic and non-hydrostatic pressure effects on sodium dithionite were investigated using Raman spectroscopy. It was conjectured that in quasi-hydrostatic pressure environment, reduction of the van der waals gap can lead to the formation of new structures of $Na_2S_2O_4$ molecules with different orientations, while under non-hydrostatic pressure, linear chains could be formed along the c axis due to the reduction of the van der waals gap and the slipping of S-S bonds against the neighbouring 'ac' plane.

With decompression, in a quasi-hydrostatic pressure environment, some hysteresis was observed as the old S-S bond broke. In non-hydrostatic pressure environment, due to the residual effects, significant memory effects on the lattice were observed. The findings of this work are significant for understanding the reactivity of disulphide-bridged systems, such as proteins, when they are under external stress.

7.1.4 Raman Optical Activity (ROA) Studies on Chiral Materials: BINAP (2,2′bis(diphenylphosphino)-1,1′-binaphthyl) ($C_{44}H_{32}P_2$)

In this work, Raman optical activity (ROA) experiments were performed on both enantiomers of chiral compounds under non-hydrostatic pressure environment. ROA spectroscopy is sensitive to optical activity and able to differentiate enantiomers. In the pharmaceutical industry, chiral compounds are used as active pharmaceutical ingredients (APIs) to prepare drugs. Pelletization of drug molecules is done under pressure. To probe pressure effects on drug molecules, *in-situ* Raman optical activity experiments were performed under non hydrostatic high pressure environment. High pressure analysis of chiral molecules is a simple, novel, and inexpensive technique. For ROA studies, our lab Raman setup was optimized by using a quarter wave plate and Lyot depolarizer. The ROA setup was validated by observing

Raman optical activity on both enantiomers of BINAP, tartaric acid, and BINOL. These are the observed outcomes of the chapter:

The effects of non-hydrostatic high pressure on both enantiomers of 2, 2'- bis (diphenyl phosphino) - 1,1' binaphthyl (BINAP) ($C_{44}H_{32}P_2$) were probed by *in-situ* Raman Optical Activity (ROA) and normal Raman Spectroscopy techniques. The chiroptical properties of both enantiomers were analysed to investigate pressure effects on both enantiomers. At ambient conditions, Raman Optical Activity (ROA) spectra were found to be mirror image (opposite) of each other. Our findings indicate that small compression of 0.08 GPa results in switching of the chirality (racemization) of both enantiomers.

Normal Raman spectra of both enantiomers overlap on each other at ambient conditions. Raman spectra show phase change at very small pressure 0.36 GPa and around 2 GPa for both enantiomers of BINAP. Few vibrational modes start splitting and some start merging at a very low pressure of 0.36 GPa, and major pressure induced changes are observed around 2 GPa for both enantiomers. Results indicate significant pressure induced changes in both enantiomers and the possibility that both of the enantiomers switch chirality under stress. On decompression, partial reversibility is observed, indicating that pressure has an irreversible impact on the chirality of both enantiomers. Compression causes significant changes in structure in both chiral enantiomers, along with chirality switching.

Our findings suggest that compression during the tableting process is a highly influential factor in determining a drug's chirality. Results are extremely beneficial to the pharmaceutical industry, as during the tableting process, pressure can alter the drug's chirality and either reduce the effectiveness of the chiral medicine or make it hazardous.

7.2 Scope for Future Work

The results that we obtained through our experimental work will definitely be helpful in understanding minerals, finding the optical handedness of chiral materials, and understand high pressure effects on chirality inducing agent. Effect of high pressure on active pharmaceutical ingredients and effects on chiral drugs. Present research work will definitely provide help in physics, mineralogy, research, pharmaceutical industry, manufacturing drug molecules, understanding protein reacting pathways, health and tableting etc. Based on the outcomes of our present work we have set targets and scopes for our future work. The entire thesis work will be beneficial in numerous future endeavours.

1. The patented setup for observing the optical handedness of chiral materials will be upgraded to collect data automatically and quickly. Will focus on its scalability as well as its commercialization. So, the setup can serve better in the research and stereoisomeric world.
2. High-pressure study on chirality inducing compound, will definitely attract the attention of future researchers to investigate in depth study of more chirality inducing materials.
3. Exploration of the S-S bond under pressure can provide a new reversible pathway to understand the reactivity of the S-S bond. This system is extremely useful in understanding protein-reacting pathways and will allow future researchers to investigate biological molecules as in all biological molecules such as proteins, nucleic acids, and vitamins, sulphur is present.
4. Research work can be initiated to study Raman optical activity (ROA) and high pressure ROA on more chiral materials in depth. A limited study has been reported; there is a need for more investigations, which gives an opportunity for further research.

Our findings have significant applicability in the biomedical sciences. Significant findings of our present research work on chiral materials will definitely add more information to the literature and benefit students, researchers, pharmaceutical companies, and society.