Chapter 7

Summary and conclusion

Heterocyclic compounds are of synthetic interest owing to their diverse applications in biology and medicine. These compounds are involved in the metabolism of living organisms. Most of the pharmacologically important compounds are composed of heterocyclic cores in their structure. The growing demand for these compounds in the medicinal field requires the development of new synthetic protocols for their synthesis.

In the present work, new synthetic methods for the synthesis of a number of heterocyclic compounds have been developed. The compounds that we have synthesised are thiocoumarins, 1,2-dithiole-3-thiones, dihydropyridine-2-thione, 3,4-diphenyl thiophene, triazoles and their fluorene derivatives. Characterisation of all the synthesised compounds has been carried out using FT-IR, ^{1}H NMR, ^{13}C NMR, mass spectroscopy and single crystal XRD analysis. The biological properties such as *in vitro* cytotoxicity and antibacterial activity of the synthesised compounds have been studied. The *in silico* molecular docking studies have been carried out which provided theoretical explanations for the cytotoxic and antibacterial activities of the synthesised compounds. The triazoles and fluorene derivatives are fluorescent compounds. The intensity of fluorescence and wavelength of maximum absorption of the compounds in the uncomplexed and complexed form with thorium (IV) ion have been studied quantitatively.

Chapter 1 of the thesis describes an overview of the thesis. We have used β-oxdithioesters as the synthon in majority of the synthetic protocols. So a comprehensive review of β-oxodithioesters has been depicted in **chapter 2**. Various synthetic methods and synthetic utilities of β-oxodithioesters have been reviewed.

Chapter 3 explains the synthesis of chromene-2-thiones from β-oxodithioesters. Its synthesis involves two steps. The first step is the reaction between ketone and dimethyl trithiocarbonate in the presence of sodium hydride in N,N-

dimethylformamide to afford β-oxodithioester. In the second step, the β-oxodithioester obtained is converted to chromene-2-thiones. For this, two methods have been devised: the first one is the conventional heating method and the second is the microwave irradiation strategy. Both methods furnished the chromene-2-thiones in good yields. But the microwave heating method was found to be more efficient that yielded the product within a few minutes. Characterisation of the chromene-2-thiones has been carried out using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR, mass spectroscopy and single crystal XRD analysis. The chromene-2-thiones were screened for cytotoxic activity. The *in vitro* cytotoxic studies showed that the chromene-2-thiones are selectively active against cancer cell lines and the activity increases with the increase in the concentration of the chromene-2-thiones. The cytotoxic activity was theoretically proved *via in silico* molecular docking studies.

Chapter 4 deals with the synthesis, characterisation and applications of 1,2-dithiole-3-thiones. These compounds have been synthesised from β-oxodithioesters. The synthesis involves two steps. The first step is the synthesis of β-oxodithioester. In the second step, a mixture of β-oxodithioester and Lawsson's reagent was irradiated under microwave conditions for 6-10 minutes to afford 1,2-dithiole-3-thiones in good yields. The characterisation of 1,2-dithiole-3-thiones has been carried out using FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopy. The *in vitro* cytotoxic studies showed that the1,2-dithiole-3-thiones are selectively active against cancer cell lines and the activity increases with the increase in the concentration of the 1,2-dithiole-3-thiones. The cytotoxic activity was theoretically proved *via in silico* molecular docking studies.

Chapter 5 describes the synthesis, characterisation and applications of dihydropyridine-2-thione and 3,4-diphenyl thiophene. β-Oxodithioesters are the synthons for both compounds. The reaction between thioamide derived from β-oxodithioester was treated with chalcone to furnish dihydropyridine-2-thione. Whereas the reaction between β-oxodithioester and phenacyl bromide afforded 3,4-diphenyl thiophene. The characterisation and biological applications of the synthesised compounds were discussed in this chapter. The dihydropyridine-2-thione was tested for antibacterial activity against two gram-positive (*Bacillus subtilis* and

Staphylococcus aureus) and two gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria using ampicillin as reference drug. The disc diffusion method was employed for the purpose. The study showed that the dihydropyridine-2-thione was only slightly active against the bacteria tested. *In silico* molecular docking studies were used for theoretically analysing the anticancer and antibacterial properties of dihydropyridine-2-thione and 3,4-diphenyl thiophene. The human DNA topoisomerase II alpha, human DNA topoisomerase II beta, FtsZ and DNA gyrase was selected as target proteins for molecular docking studies. The studies showed that these compounds exhibit moderate antibacterial and anticancer properties.

Chapter 6 describes the synthesis, characterisation and applications of triazoles and their fluorene derivatives. The triazoles have been synthesised by the reaction between an excess amount of alkyl halide, alkyne and sodium azide in the presence of the catalytic amount of copper supported polymer catalyst (CuPVPNNMBA) in a 1:3 mixture of distilled water and t- butyl alcohol. Triazole functionalized coumarin, triazole functionalized fluorine and thioamide functionalized fluorine have been synthesised. The characterisation and applications of the synthesised compounds were discussed in this chapter.

Antibacterial activity of these compounds against four bacterial strains- *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* have been carried out employing the disc diffusion method. It was found that the triazoles are active against all the bacterial strains whereas the fluorene derivatives exhibited only slight antibacterial activity. The antibacterial properties were theoretically studied using *in silico* molecular docking of some of the synthesised compounds with the bacterial proteins- FtsZ and DNA gyrase. The studies showed that these compounds exhibit good antibacterial properties.

The fluorescence properties of the compounds were studied using a UV inspection cabinet, UV-Visible spectrometer and spectrofluorometer. The compounds exhibited good fluorescence in UV light and the intensity of fluorescence increased upon complexation with thorium. It was found that the intensity of fluorescence increases with the increase in the concentration of thorium with a red shift in the wavelength of maximum absorption. The fluorescence studies showed that the triazole

functionalized fluorene derivative could be used as a fluorescence detector for thorium (IV) ions even at micromolar level.

The work presented in this dissertation includes development of new protocols for novel heterocyclic compounds, their experimental and theoretical studies in anticancer and antibacterial properties. Finally, an efficient method for sensing thorium, an environmental pollutant has been developed.