SUMMARY

The First chapter provides a brief discussion on thiadiazoles and thiazoles and their exploitation as anticancer agent, focusing particularly on their application in organic synthesis. Failures of cancer drugs are crucial in determining the future course of research in drug development for cancer. The task of discovering and developing safe and effective drugs is more promising as our knowledge about disease increases. Recent drug discovery efforts are highly focused towards design and modification in the structure of small molecules as anticancer agents.

Structural activity studies shows that a variation in the ring system or incorporation of different biologically active ring systems or minor group modifications imparts distinct pharmacological effects upon the drug molecules. At present among the new drugs available, more than 90% contain heterocycles. Among the heterocyclic molecules 2, 5-disubstituted-1, 3, 4-thiadiazole and C2, C4 substituted 1,3-thiazole derivatives are important pharmacophore of heterocyclic group as a anticancer drugs. Research on synthesis of 1,3,4 thiadiazole,1,3 thiazole continue to expand and provides superior methods for this heterocyclic compound. This results in the discovery of new drug candidates that are more active, specific and safer.

The chapter-2 deals with the synthesis of thiosemicarbazone from O-acylated acetophenone. O- acylation of 4-hydroxy acetophenone was synthesized with various acid chlorides in the presence of different bases and it carried out at various conditions such as conventional, microwave and ultra sonnication. The maximum yield of the product was achieved by using potassium carbonate as a base and reaction was completed within 5min in microwave condition when compared to the other bases and methods.

Further O-acylated acetophenone was condensed with thiosemicarbazide in ethanol and the reaction was carried out in various conditions to obtain the corresponding O-acylated
acetophenone thiosemicarbazones. The formation of product was completed within 20 minutes of reaction and the yield was 98% and the results suggest that promising yield and reaction time was achieved by our method when compared with literature report due to the selection of starting material. The spectroscopic data of the product confirms exhibit characteristic peaks of the expected functional groups.

The Chapter-3 discussed in the first time reports that borane catalyst used as synthesis of 1,3,4-Thiadiazole compounds from 0-acylated acetophenone thiosemicarbazone. Among the 10 catalyst screened (-)Diisopinocamphenyl chloro borane gave ee of 98.3% of (S) isomer with para toluyl thiosemicarbazone and selected as a best catalyst to perform chiral 1,3,4-Thiadiazole.

The enantiopurity is affected by substitutents on the aryl ring of the 1,3,4-TDZ is been illustrated using o,m,p-acylated acetophenones. The para substituent gave maximum 98.3% ee when compared to ortho and meta substitutions.

The synthesis of 1,3,4-TDZ reaction was carried out at various conditions such as conventional, microwave and ultra sonnication. Among this microwave conditions exhibits maximum yield as 95% of the product and the product formation was completed within 3-5min. The product chirality was studied by optical rotation and the purity was determined by chiral HPLC. The product structure was elucidated by NMR, Mass and IR spectroscopy.

The Chapter-4 discussed in the first time reports that borane catalyst used as synthesis of 1,3,4-Thiadiazole compounds from 0-acylated acetophenone thiosemicarbazone. This is modified method of Hantzsch synthesis. In this studied simple and facile synthesis(with in 20 mins) were carried out at room temperature by using cyclisation of the $O$-acylated acetophenone thiosemicarbazones compounds with $\alpha$-halo ketone like 2-chloro acetophenone. Phenyl
substituted 1,3-Thizole at C4 position of thiazole ring were synthesized with higher yield more than 92%.

The Fifth chapter deals with the synthesized molecules were screened for bioactivity studies like insilico and in-vitro anti cancer activities. 1,3,4-TDZ and 1,3-thiazoles are known to serve as a anti cancer agents. The synthesized 20 compounds were molecular docked against Tyrosine- protein kinase ABL1 and results showed that the derivatives of 1,3,4-Thiadiazole C9, C8, C7, C6, C3 and 1,3-Thiazone D10, D9, D8, D7, D6 showed higher docking score and glide energy. The in-vitro cytotoxicity analysis showed that the above molecules possess maximum cytotoxic activity against MCF-7, MDA-MB-231, A-549 and HT-29 cell lines which is comparable with the standard drug.

This study suggests that the synthesized scaffolds act as a good anticancer drug and the present work confirms that, synthesized drugs which exhibit greater bioavailability comparable with standard drug. Hence further studies may also find its commercial application as a therapeutic drug.
APPENDIX-I

Fig-195: IR spectrum of compound B1

Fig-196: IR spectrum of compound B2
Fig-197: IR spectrum of compound B6

Fig-198: IR spectrum of compound B7
Fig-199: IR spectrum of compound B8

Fig-200: IR spectrum of compound B10
Fig-201: IR spectrum of compound C1

Fig-202: IR spectrum of compound C4
Fig-203: IR spectrum of compound C6

Fig-204: IR spectrum of compound C7
Fig-205: IR spectrum of compound C8

Fig-206: IR spectrum of compound C10
Fig-207: IR spectrum of compound D1

Fig-208: IR spectrum of compound D5
Fig-209: IR spectrum of compound D6

Fig-210: IR spectrum of compound D8