The thesis describes the results of synthetic, structural and pharmacological activity studies of a number of thiourea and adamantyl derivatives. The objective of the work is to explore the effect of substituents on the spectral and structural parameters, pharmacological activities and on the pattern of hydrogen bonding in the compounds studied.

In recent years there has been an increasing interest in the synthesis of various sulfur containing compounds such as 1,3-disubstitued thioureas. Thiourea derivatives are extremely versatile building blocks for the synthesis of a variety of heterocyclic compounds and have been demonstrated to possess a wide spectrum of bioactivities. Acylthiourea derivatives have been patented as antidiabetic, antiarthritic, antineoplastic and anticoagulant agents and for treatment of cognitive problems and prostate disorder. Herbicidal, fungicidal, bactericidal, insecticidal and plant growth regulator activities have also been reported. N,N-Dialkyl-N-aryloyl thioureas are efficient ligands for the separation of platinum group metals. 1,3-Dialkyl or diaryl thioureas exhibit significant antifungal activity against plant pathogens, Pyricularia oryzae and Drechslera oryzae. N-Aryl-N-phenylthioureas have been developed as anion-binding sites in hydrogen-bonding receptors and calixarenes containing thioureas as neutral receptors towards α,α-dicarboxylate anions. 1-Benzoyl-3-(4,6-disubstituted-pyrimidinyl)thioureas have shown excellent herbicidal activity.

Thioureas have also been widely used in enantioselective synthesis, such as in nitro-Mannich reactions, aza-Henry reaction, and Michael Addition. Symmetrical and asymmetrical phenethyl thioureas, 5-halo-substituted thiophene pyridyl thioureas and heterocyclic thioureas are non-nucleoside inhibitors of HIV-1 reverse transcriptase. Synthesis and anion recognition of molecular tweezers receptors based on acyl thioureas and efficient colorimetric anion sensors have also been reported. Moreover, thiourea analogues are potent influenza virus neuraminidase inhibitors. Condensation of thiourea derivatives with carbonyl compounds have been used in the synthesis of N-alkyl-1,3-thiazol-2-amines and 3-alkyl-1,3-thiazolimines, 1-aryloyl-3-aryloyl-4-substitutedimidazole-2-thiones and 2-(arylimino)-3-aryloyl-4-methyl/phenyl-1,3-thiazolines. Cyclocondensation of unsymmetrical perfluoroalkyl substituted beta-
diketones with urea, thiourea and guanidine lead to various heterocycles. Thus thiourea and its derivatives have become increasingly important in research and technological application such as inhibitors in the corrosion field, catalysts in chemical reactions.

The chemistry of 1-adamantyl derivatives show distinct physical, chemical and biological properties. The presence of adamantane radicals in molecules of medicinal preparations enhances their activity and depresses the toxicity. They restore functional activities of nervous, hormonal and immune systems and also increase mental and physical capacities and resistance of organisms to viral and bacterial infections. Many adamantane derivatives show antiviral, antibacterial, antifungal, anti-inflammatory, central nervous and 11b-HSD1 inhibitory activities. Hence 1-adamantyl derivatives are of interest in synthetic and biological chemistry.

Thus as part of our studies on the effects of substituents on the structural and bond parameters of compounds of biological interests, a number of N-acetyl-N’-(substitutedphenyl)thioureas, i-XC₆H₄NHCSNHCOC₃H₃ (i-X = H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-CH₃, 3-CH₃, 4-CH₃ or 4-OCH₃) and i,j-X₂C₆H₃NHCSNHCOC₃H₃ (i,j-X₂ = 2,3-Cl₂, 2,4-Cl₂, 2,5-Cl₂, 2,6-Cl₂, 3,4-Cl₂, 3,5-Cl₂, 2,3-(CH₃)₂, 2,4-(CH₃)₂, 2,5-(CH₃)₂, 2,6-(CH₃)₂, 3,4-(CH₃)₂ or 3,5-(CH₃)₂) and 16 N-pivaloyl-N’-(substitutedphenyl)thioureas, i-XC₆H₄NHCSNHCOC(CH₃)₃ (i-X = H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-CH₃, 3-CH₃, 4-CH₃ or 4-OCH₃) and i,j-X₂C₆H₃NHCSNHCOC(CH₃)₃ (i,j-X₂ = 2,3-Cl₂, 2,3-(CH₃)₂, 2,4-(CH₃)₂, 2,5-(CH₃)₂, 2,6-(CH₃)₂, 3,4-(CH₃)₂ or 3,5-(CH₃)₂), N’-(substitutedphenyl-sulfonyl)adamantyl hydrazides of the general formula, i-XC₆H₂SO₂NHNHCOC₁₁H₁₅ (i-X = H, 4-CH₃, 4-Cl, 4-Br, 2-NO₂, 3-NO₂, 4-NO₂ or 4-NHCOCH₃), i,j-X₂C₆H₂SO₂NHNHCOC₁₁H₁₅ (i,j-X₂ = 2,4-(CH₃)₂, 2,4-Cl₂ or 3-CH₃-4-Cl), N’-(benzoyl)adamantyl hydrazides of the general formula, i-XC₆H₂CONHNHCOC₁₁H₁₅ (i-X = H, 4-Cl, 4-CH₃ or 4-NO₂) and N-(1,3-dioxo-1,3-dihydro-2H-isoinidol-2-yl)-adamantane-1-carboximide have been prepared, characterized and their infrared spectra in the solid state, ¹H and ¹³C NMR spectra in solution were measured and correlated. Single-crystal X-ray structures of several of these compounds have also been determined and analyzed to explore the effect of substituents on the geometrical parameters of these compounds.
Experimental Methods

The FT-IR spectra of the compounds were recorded on a Shimadzu FT-IR 157 spectrometer in the frequency range 400–4000 cm\(^{-1}\). The NMR spectra were recorded in DMSO-\(d_6\) on a BRUKER AVANCE II 400 MHz FT-NMR spectrometer using TMS as internal reference.

Small single crystals of the compounds used in the X-ray diffraction studies were grown from their DMF/Acetonitrile solutions by slow evaporation of the solvent. Single crystal X-ray studies were carried out at room temperature. The crystal structures were solved by direct methods and Fourier synthesis employing SHELXS-97 program and refined by full-matrix least-squares techniques on F2 using program SHELXL-97.

The results of these synthetic, spectral, structural and pharamacological studies are presented and discussed in the thesis. The thesis is broadly divided into SIX CHAPTERS with several sections in each chapter.

Chapter 1 gives an overview of the chemistry of thiourea and adamantyl derivatives, an introduction to the infrared (IR) and nuclear magnetic resonance (NMR) spectroscopic methods, crystal structure studies, hydrogen bonding phenomena and sketches the objectives and scope of the present work.

Chapter 2 describes the synthesis, infrared, \(^1\)H & \(^{13}\)C NMR spectral and biological studies of 21 \(N\)-acetyl-\(N'\)-(substitutedphenyl)thioureas of the general formulae, \(i-XC_6H_4NHCSNCH_3\) (\(i-X = H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-CH_3, 3-CH_3, 4-CH_3 or 4-OCH_3\)) and \(i,j-X_2C_6H_3NHCSNCH_3\) (\(i,j-X_2 = 2,3-Cl_2, 2,4-Cl_2, 2,5-Cl_2, 2,6-Cl_2, 3,4-Cl_2, 3,5-Cl_2, 2,3-(CH_3)_2, 2,4-(CH_3)_2, 2,5-(CH_3)_2, 2,6-(CH_3)_2, 3,4-(CH_3)_2, 3,5-(CH_3)_2\) or \(3,6-(CH_3)_2\)) and 16 \(N\)-pivaloyl-\(N'\)-(substitutedphenyl)thioureas, \(i-XC_6H_4NHCSNCHOCOC(CH_3)_3\) (\(i-X = H, 2-Cl, 3-Cl, 4-Cl, 4-F, 2-CH_3, 3-CH_3, 4-CH_3 or 4-OCH_3\)) and \(i,j-X_2C_6H_3NHCSNCHOCOC(CH_3)_3\) (\(i,j-X_2 = 2,3-Cl_2, 2,4-Cl_2, 2,5-Cl_2, 2,6-Cl_2, 3,4-Cl_2, 3,5-Cl_2, 2,3-(CH_3)_2, 2,4-(CH_3)_2, 2,5-(CH_3)_2, 2,6-(CH_3)_2, 3,4-(CH_3)_2, 3,5-(CH_3)_2\) or \(3,6-(CH_3)_2\)). The data have been measured, analyzed and correlated. These compounds were screened for their phytotoxicity, larvicidal and antifungal activities.

The general assignments of the frequencies to various important modes of vibrations in \(N\)-acetyl-\(N'\)-(substitutedphenyl)thioureas and \(N\)-pivaloyl-\(N'\)-
(substitutedphenyl)thioureas have been made. The C=O stretching vibrations appear as very strong absorptions in the ranges, 1696.4-1685.8 cm$^{-1}$, 1704.1-1677.1 cm$^{-1}$, 1685.8-1670.4 cm$^{-1}$ and 1685.7-1672.3 cm$^{-1}$ for N-acetyl-N’-(monosubstitutedphenyl)thioureas, N-acetyl-N’-(disubstitutedphenyl)thioureas, N-pivaloyl-N’-(monosubstitutedphenyl)thioureas and N-pivaloyl-N’-(disubstitutedphenyl)thioureas, respectively. The N-H stretching vibrations are in the ranges, 3299.4-3146.1 cm$^{-1}$, 3333.1-3282.9 cm$^{-1}$ and 3399.6-3296.3 cm$^{-1}$ for N-acetyl-N’-(monosubstitutedphenyl)thioureas, N-acetyl-N’-(disubstitutedphenyl)thioureas, N-pivaloyl-N’-(monosubstitutedphenyl)thioureas and N-pivaloyl-N’-(disubstitutedphenyl)thioureas, respectively. Similarly, the C=S stretching vibrations appear in the ranges, 1170.4-1116.0 cm$^{-1}$, 1165.0-1134.1 cm$^{-1}$ and 1161.2-1143.3 cm$^{-1}$ for N-acetyl-N’-(monosubstitutedphenyl)thioureas, N-acetyl-N’-(disubstitutedphenyl)thioureas, N-pivaloyl-N’-(monosubstitutedphenyl)thioureas and N-pivaloyl-N’-(disubstitutedphenyl)thioureas, respectively. Similarly, the C=S stretching vibrations appear in the ranges, 1170.4-1116.0 cm$^{-1}$, 1165.0-1134.1 cm$^{-1}$ and 1161.2-1143.3 cm$^{-1}$ for N-acetyl-N’-(monosubstitutedphenyl)thioureas, N-acetyl-N’-(disubstitutedphenyl)thioureas, N-pivaloyl-N’-(monosubstitutedphenyl)thioureas and N-pivaloyl-N’-(disubstitutedphenyl)thioureas, respectively. Similarly, the C=S stretching vibrations appear in the ranges, 1170.4-1116.0 cm$^{-1}$, 1165.0-1134.1 cm$^{-1}$ and 1161.2-1143.3 cm$^{-1}$ for N-acetyl-N’-(monosubstitutedphenyl)thioureas, N-acetyl-N’-(disubstitutedphenyl)thioureas, N-pivaloyl-N’-(monosubstitutedphenyl)thioureas and N-pivaloyl-N’-(disubstitutedphenyl)thioureas, respectively.

The $^1$H and $^{13}$C NMR chemical shifts of aromatic protons and carbons of all N-acetyl-N’-(substitutedphenyl)thioureas and N-pivaloyl-N’-(substitutedphenyl)-thioureas are analysed. Since the chemical shift is dependent on the electron density around the nucleus or associated with the atom to which it is bonded, the incremental shifts of the aromatic protons due to -NHCSNHCOCH$_3$ and -NHCSNHCOC(CH$_3$)$_3$ groups were computed by comparing the proton chemical shifts of N-acetyl-N’-phenylthiourea (C$_6$H$_5$NHCSNHCOCH$_3$) and N-pivaloyl-N’-phenylthiourea (C$_6$H$_5$NHCSNHCOC(CH$_3$)$_3$), with the benzene proton shift of 7.27 ppm. Further, the incremental chemical shifts due to -CSNHCOCH$_3$ and -CSNHCOC(CH$_3$)$_3$ groups were computed by comparing the proton chemical shifts of N-acetyl-N’-phenylthiourea and N-pivaloyl-N’-phenylthiourea with those of the corresponding aniline proton values of H-2,6 = 6.48 ppm, H-3,5 = 7.05 ppm and H-4 = 6.67 ppm.

Similarly, The incremental shifts of the aromatic carbons of the benzene ring due to -NHCSNHCOCH$_3$ and -NHCSNHCOC(CH$_3$)$_3$ groups were computed by comparing the $^{13}$C chemical shifts of N-acetyl-N’-phenylthiourea (C$_6$H$_5$NHCSNHCOCH$_3$) and N-pivaloyl-N’-phenylthiourea (C$_6$H$_5$NHCSNHCOC(CH$_3$)$_3$), with the benzene $^{13}$C value of 128.5 ppm. Further, the incremental chemical shifts due to -CSNHCOCH$_3$ and -CSNHCOC(CH$_3$)$_3$ groups were computed by comparing the $^{13}$C chemical shifts of N-acetyl-N’-phenylthiourea
and N-pivaloyl-N’-phenylthiourea with those of the corresponding aniline $^{13}$C values of C-1 = 146.2 ppm, C-2,6 = 114.6 ppm, C-3,5 = 128.8 ppm and C-4 = 117.8 ppm. The chemical shifts of the aromatic protons and carbons in N-acetyl-N’-(substitutedphenyl)thioureas and N-pivaloyl-N’-(substitutedphenyl)thioureas are then calculated in three ways as per the principle of substituent addition.

The variations of IR absorptions and the $^1$H and $^{13}$C NMR chemical shifts of N-H protons, C=O and C=S carbons with the substitution in the aniline ring are shown in terms of bar diagrams. The variations of absorptions with substitutions do not show particular trends. The comparison of the observed chemical shifts and the calculated values for both $^1$H and $^{13}$C NMR spectra revealed that the three procedures of calculations lead to almost the same values in most cases, signalling the validity of the principle of additivity of the substituent effects in these compounds. The variations of these chemical shifts with substitutions in the aniline ring do not show particular trends and hence the effect of substitution on these parameters could not be generalized.

The selected N-acetyl-N’-(substitutedphenyl)thioureas and N-pivaloyl-N’-(substitutedphenyl)thioureas exhibited moderate to significant phytotoxicity, larvicidal and antifungal activities.

Chapter 3 describes the effect of substituents on the crystal structures of N-acetyl-N’-(aryl)-thioureas of the general formulae, i-XC$_6$H$_4$NHCSNHCOCH$_3$ (i-X = 3-CH$_3$, 4-CH$_3$ or 4-Cl) and i,j-X$_2$C$_6$H$_3$NHCSNHCOCH$_3$ (i,j-X$_2$ = 2,3-(CH$_3$)$_2$, 2,4-(CH$_3$)$_2$, 2,5-(CH$_3$)$_2$, 2,6-(CH$_3$)$_2$, 3,4-(CH$_3$)$_2$, 3,5-(CH$_3$)$_2$, 2,3-Cl$_2$, 2,6-Cl$_2$ or 3,5-Cl$_2$) by determining the crystal structures of 12 N-acetyl-N’-(aryl)-thioureas and analyzing the data along with those reported in literature.

N-Acetyl-N’-(4-chlorophenyl)thiourea crystallized in orthorhombic crystal system with the P 2$_1$2$_1$2$_1$ space group with one molecule in the asymmetric unit and four molecules in the unit cell, in contrast to the parent N-acetyl-N’-(phenyl)thiourea which crystallized in monoclinic crystal system with the P 2$_1$/c space group with one molecule in the asymmetric unit and eight molecules in the unit cell, whereas all the three dichlorosubstituted compounds, N-acetyl-N’-(2,3-dichlorophenyl)thiourea, N-acetyl-N’-(2,6-dichlorophenyl)thiourea & N-acetyl-N’-(3,5-dichlorophenyl)thiourea
crystallized in triclinic crystal system with the P_1̅ space group, but with different numbers of molecules in their asymmetric units and in the unit cells.

C-C ring mean distances in the structures of substituted compounds are generally slightly higher than the mean distances observed in the parent compound. In all the compounds, C=S distances are smaller than the parent compound. The (O)C=N, N-C(S) and S(C)-N bonds are all shorter than the average C-N single bond distance of 1.472(5)Å. In general, the N-C(S) bonds are slightly shorter than both (O)C=N and S(C)-N bonds. The C9-C8 bond in these compounds is marginally longer than the corresponding bond in aroyl substituted thioureas, possibly indicating a degree of resonance between carbonyl group and aromatic group.

Torsion angles of N-acetyl-N'- (dichlorosubstitutedphenyl)thioureas which give an indication of different orientations of the carbonyl and thiocarbonyl groups relative to each other. In general, the conformations of the amide C=S and the C=O bonds are anti to each other. A similar observation is seen in N-acetyl-N'-phenyl-thioureas. Further, in all the compounds, the conformation of one of the N–H bonds is *anti* to the C=S and the other is *syn* and the adjacent N-H bonds are *anti* to the C=O. The conformations of the two N—H bonds are also *anti* to each other. In N-acetyl-N’-(2,3-dichlorophenyl)thiourea, the N–H bond adjacent to the 2,3-dichloro-phenyl ring is *syn* to the *ortho* - and *meta*-Cl atoms in one of the molecules and *anti* in the other molecule.

The central carbonyl-thiourea (S1/C7/N1/N2/C8/O1) moiety connecting the phenyl ring and acetyl group is slightly less planar in all the compounds, with the C2-C1-N1-C7 torsion angles ranging from 62.9(2)° to -133.6(2)° and the C6-C1-N1-C7 torsion angles ranging from -120.7(2)° to 68.6(7)°.

The hydrogen atom of the NH attached to the substituted phenyl ring and the amide oxygen exhibit a bifurcated hydrogen bonding by showing the simultaneous intra- and inter-molecular hydrogen bonding. The comparison of hydrogen bonds showed that the N-H…O hydrogen bonds connecting the amino-H atom of the aniline segment (N1) with the carbonyl O atom (O1) are stronger than the hydrogen bonds involving the amide-H atom (N2) and thiono S atom (S1). The N–H…O hydrogen
bonds are the shortest in the compound with 2,3-dichloro substituent. Further, the intramolecular N-H…-O hydrogen bond generates an S(6) ring motif.

The \(N\)-acetyl-\(N'\)-(3-methylphenyl)thiourea and \(N\)-acetyl-\(N'\)-(3,5-dimethylphenyl)thiourea have crystallized in monoclinic crystal system with the \(P 2_1/c\) space group, while 4-methyl, 2,3-dimethylphenyl, 2,4-dimethyl-phenyl, 2,5-dimethylphenyl, 2,6-dimethylphenyl & 3,4-dimethylphenyl substituted compounds crystallized in triclinic crystal system with \(P\overline{1}\) space group. Asymmetric unit of \(N\)-acetyl-\(N'\)-(4-methylphenyl)thiourea contained two molecules and four molecules in the unit cell, while all other compounds have one molecule each in the asymmetric units and two molecules in the unit cells, except in 3-methyl and 3,5-dimethylphenyl-substituted compounds, which contained four molecules each in their unit cells.

The crystal data revealed that all of the compounds exhibit cis–trans configuration with respect to the position of the carbonyl group and the benzene ring against the thione group across the C–N bonds. Such configuration allows the formation of intramolecular hydrogen bonds between the carbonyl oxygen atom and thioamide hydrogen atom. The C–N bonds such as C(7)–N(1), C(1)–N(1), C(7)–N(2) and C(8)–N(2) are shorter than the normal C–N bond (1.469 Å), indicating that the C–N bond has partial double bond character. The elongation of C(7)–N(2) relative to C(7)–N(1) is known from other thioureas, which is probably due to the electron withdrawing effect of the carbonyl group. The C-N bond lengths lie in the ranges, 1.316(4)-1.399(3), 1.331(3)-1.440(5), 1.383(4)-1.404(2) and 1.356(2)-1.388(3) Å, for C(7)–N(1), C(1)–N(1), C(7)–N(2) and C(8)–N(2), respectively. C-C ring mean distances in the structures of substituted compounds are generally slightly higher than the mean distances observed in the parent compound. But C=S distances are smaller than the parent compound. The hydrogen bonding interactions such as N(1)-H(1)...O(1) and N(2)-H(2N)...S(1) stabilize the molecule. The intramolecular hydrogen bond, N(1)-H(1)...O(1) forming pseudo-six membered rings.

**Chapter 4** discusses the effect of substituents on the crystal structures of \(N\)-pivaloyl-\(N'\)-(substitutedphenyl)thioureas of the general formulae, \(i\)-\(XC_6H_4NHCS-NHCOC(CH_3)_3\), where \(i = 2, 3\) or 4 & \(X = H, CH_3\) or Cl and \(i,j\)-\(X_2C_6H_3NHCS-NHCOC(CH_3)_3\), where \(i,j = 2,3; 2,4; 2,5; 2,6; 3,4\) or 3,5 and \(X = CH_3\) or Cl), by determining the crystal structures of 11 \(N\)-pivaloyl-\(N'\)-(substitutedphenyl)thioureas of
the formulae, i-XC₆H₄NHCSNHCOC(CH₃)₃ (i-X = H, 2-CH₃, 3-CH₃, 4-CH₃ or 4-Cl) and i,j-X₂C₆H₃NHCSNHCOC(CH₃)₃ (i,j-X₂ = 2,3-(CH₃)₂, 2,4-(CH₃)₂, 2,5-(CH₃)₂, 2,6-(CH₃)₂, 3,4-(CH₃)₂ or 3,5-(CH₃)₂), and analyzing the data along with the structures of chlorosubstituted compounds, reported earlier.

N-Pivaloyl-N’-phenylthiourea, N-pivaloyl-N’-(2,3-dimethylphenyl)thiourea, N-pivaloyl-N’-(3,4-dimethylphenyl)thiourea and N-pivaloyl-N’-(3,5-dimethylphenyl)thiourea have crystallized in monoclinic crystal system with P2₁/c space group with one molecule each in their asymmetric units and four molecules in the unit cells, except N-pivaloyl-N’-(3,5-dimethylphenyl)thiourea, which contains two molecules in its asymmetric unit and four molecules in the unit cell. N-Pivaloyl-N’-(3-methylphenyl)thiourea, N-pivaloyl-N’-(4-methylphenyl)thiourea and N-pivaloyl-N’-(2,5-dimethylphenyl)thiourea have crystallized in monoclinic crystal system with the C2/c space group with one molecule each in the asymmetric unit and eight molecules in their unit cells, except N-pivaloyl-N’-(4-methylphenyl)thiourea which contains three molecules in its asymmetric unit and 24 molecules in the unit cell. N-Pivaloyl-N’-(2-methylphenyl)thiourea and N-pivaloyl-N’-(2,6-dimethylphenyl)thiourea are crystallized in triclinic crystal system with P₁̅ space group with a molecule each in the asymmetric units and two molecules in their unit cells. N-Pivaloyl-N’-(4-chlorophenyl)thiourea has also crystallized in triclinic crystal system with the same space group but with two molecules in its asymmetric unit and four molecules in its unit cell. N-Pivaloyl-N’-(2,5-dimethylphenyl)thiourea crystallized in monoclinic crystal system with the P2₁/n space group with two molecules in its asymmetric unit and eight molecules in its unit cell.

The crystallographic data revealed that in all the compounds, the conformations of the two N—H bonds are anti to each other. Further, the conformations of the amide C=S and the C=O bonds are also anti to each other.

The C–N bonds such as C(7)–N(1), C(1)–N(1), C(7)–N(2) and C(8)–N(2) are shorter than the normal C–N bond (1.469 Å), indicating that the C–N bond has partial double bond character. The C-N bond lengths lie in the ranges, 1.323(2)-1.344(4), 1.415(4)-1.467(7), 1.382(8)-1.405(7) and 1.338(9)-1.395(2) Å, for C(7)–N(1), C(1)–N(1), C(7)–N(2) and C(8)–N(2) bonds, respectively. The short C–S distance clearly
shows its double-bond character and is very close to the unweighted mean value of 1.681 Å for the C=S distance in thioureas.

A significant intramolecular H-bond is N(2)–H⋯O(1), with the H⋯O(1) distance falling in the 1.86(2)–1.98(3) Å range and the angle N(2)–H⋯O(1) varying from 135(3)° to 146(3)° for N-pivaloyl-N’-(substitutedphenyl)thioureas. Extending the three-dimensional spatial orientation of the tertiary butyl group has weakened the intermolecular non-bonding interactions between the molecules. The intramolecular N-H….O hydrogen bonds which generated S(6) motifs stabilized the packing arrangement and the molecules form intermolecular N-H….S hydrogen bonds in many cases to generate chains and layered structures in a few cases.

Chapter 5 describes the synthesis and characterization of some N’-(substitutedphenylsulfonyl)adamantyl hydrazides of the general formulae, i-XC₆H₄SO₂NHNHCOC₁₁H₁₅ (i-X = H, 4-CH₃, 4-Cl, 4-Br, 2-NO₂, 3-NO₂, 4-NO₂ or 4-NHCOCH₃) and i,j-X₂C₆H₃SO₂NHNHCOC₁₁H₁₅ (i,j-X₂ = 2,4-(CH₃)₂, 2,4-Cl₂ or 3-CH₃-4-Cl), N’-(benzoyl) adamantyl hydrazides of the general formula, i-XC₆H₄-CONHNHCOC₁₁H₁₅ (i-X = H, 4-Cl, 4-CH₃ or 4-NO₂) and N-(1,3-dioxo-1,3-dihydro-2H-isooindol-2-yl)-adamantane-1-carbaximide. The compounds have been screened for their anti-inflammatory and antituberculosis activities.

The anti-inflammatory activities of sixteen newly synthesized compounds [4(a-k), 5(a-d) and 6] have been determined by carrageenan induced paw edema method. The tested compounds showed anti-inflammatory activity ranging from 36.96 - 84.16%, whereas standard drug diclofenac sodium showed 83.85% inhibition after 3 h. The anti-inflammatory activity of N’-(substitutedphenylsulfonyl) adamantyl hydrazide derived from adamantane carboxylic acid was in the range of 36.96 - 76.40% inhibition. It was observed that compound having 4-acetamidophenylsulfonyl (4h) and 2,4-dichlorophenylsulfonyl (4j) groups showed good activity, viz. 72.98% and 76.40%, respectively. When these groups were replaced by 4-nitrophenylsulfonyl, 2,4-dimethylphenylsulfonyl, 3-nitrophenylsulfonyl, 4-bromophenylsulfonyl, 4-chlorophenylsulfonyl, 2-nitrophenylsulfonyl and 4-methylphenylsulfonyl, the activity was found to be decreased.
The anti-inflammatory activity of N′-(substituted benzoyl) adamantyl hydrazides derived from adamantane carboxylic acid is in the range from 38.82 - 75.78%. It was observed that the adamantyl hydrazide containing 4-nitrobenzoyl (5d) moiety exhibited good activity. But when these groups were replaced by 4-chlorobenzoyl (5c), 4-methylbenzoyl (5b) and benzoyl (5) groups, there was sharp decrease in the activity. The compound 4-chlorobenzoyl (5a) moiety also showed moderate activity. Among the tested compounds N-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-adamantane-1-carbaxamide (6) showed highest activity of 84.16%, slightly higher than the standard.

The antimycobacterial activities of compounds [4(a-k), 5(a-d) and 6] were assessed against Mycobacterium tuberculosis (H37RV) strain using Microplate Alamar Blue Assay Method (MABA) to determine the minimum inhibitory concentration (MIC). The analysis of antimycobacterial screening data revealed that all the tested compounds showed good mycobacterial inhibition. The tested compounds showed activities against mycobacteria with MIC values ranging from 100.0 to 1.6 μL/mL. Compounds 4b, 4h and 4j exhibited good activity at MIC value of 6.25 μL/mL. The compound 4-bromophenylsulfonyl (4d) showed very good activity at MIC of 3.12 μL/mL. It has been observed that compounds 4f and 6 having a 3-nitrophenylsulfonyl and phthalimide groups respectively, showed highest antimycobacterial activity at a MIC of 1.16 μL/mL.

Chapter 6 discusses the effect of substituents on the crystal structures of five N′-(substituted phenylsulfonyl) adamantyl hydrazides of the general formula, i-XC₆H₄SO₂NHNHCOC₁₁H₁₅ (i-X = H, 4-Cl, 4-CH₃ or 4-NO₂), 3-CH₃-4-ClC₆H₃-SO₂NHNHCOC₁₁H₁₅ and 4 N′-(substituted benzoyl) adamantyl hydrazides of the formula, i-XC₆H₄CONHNHCOC₁₁H₁₅ (i-X = H, 4-Cl, 4-CH₃ or 4-NO₂).

The N′-(phenylsulfonyl)-, N′-(4-methylphenylsulfonyl)-, N′-(4-chlorophenylsulfonyl)- and N′-(4-nitrophenylsulfonyl)- adamantyl hydrazides have crystallized in monoclinic crystal system with P₂₁/c space group with one molecule each in their asymmetric units and four molecules each in their unit cells, while N′-(3-methyl-4-chloro-phenylsulfonyl) adamantyl hydrazide crystallized in triclinic system with Pñana space group and four molecules in its unit cell. It is evident from these that substitution at the para position in phenylsulfonyl ring did not affect either the crystal
system or the space group, irrespective of the nature of the substituent, while introduction of an additional substituent changed the crystal system from monoclinic to the triclinic with P\(\overline{1}\) space group. The effect of substituent on the molecule may be insignificant due to the presence of adamantyl fragment as part of the molecule.

The \(N'-(\text{substitutedphenylsulfonyl})\text{adamantyl hydrazide}\) molecules with rigid adamantyl cage at one end of the C\((\equiv O)\)NH–NH–SO\(_2\) chain and a planar phenyl ring at the other end, display extended zigzag configurations. The conformations of the amide N—H and C\(\equiv O\) bonds in the adamantyl ring side are anti to each other. The amide N—H bonds are also anti to each other. In general, in the central chain, the bonds such as N—H and C\(\equiv O\) bonds are anti to the adjacent N—H or C\(\equiv O\)/S=O bonds. The molecules of \(N'-(\text{substitutedphenylsulfonyl})\text{adamantyl hydrazides}\) are bent at the S atom. Further, the C-C ring mean distances are almost the same except in the \(N'-(3\text{-chboro-4-methylphenylsulfonyl})\text{adamantyl hydrazide}\).

The observed bond lengths of the compounds studied showed a clear distinction between single and double bonds in the central spacer unit. The C7–O3 [1.221(4)–1.225(5) Å] interatomic distances confirm that double bond character, whereas C7–N2 [1.353(5)–1.359(2) Å] distance is marginally shorter than the normal bond length reported for the amide C–N (1.469Å) single bonds. The slightly shorter bond distances compared to the reported value indicate a significant delocalization of \(\pi\)-electron density over the hydrazide portion of the molecule. The intramolecular the sulfonamide N-H…O-C bonds generate S(5) motifs leading to different H-bond patterns through weak intermolecular interactions.

The parent compound, \(N'-(\text{benzoyl})\text{adamantyl hydrazide dihydrate}\) crystallized in triclinic crystal system with P\(\overline{1}\) space group with its two molecules and two water molecules in the asymmetric unit, while \(N'-(4\text{-methylbenzoyl})\text{adamantyl hydrazide monohydrate}\) and \(N'-(4\text{-chlorobenzoyl})\text{adamantyl hydrazide monohydrate}\) crystallize in the monoclinic crystal system with P2\(_1/c\) space group with a molecule of the compound and one water molecule in the asymmetric unit and four molecules each in the unit cell. \(N'-(4\text{-Nitrobenzoyl})\text{adamantyl hydrazide crystallizes}\) in the monoclinic crystal system with C2 space group with one molecule in the asymmetric unit and four molecules in the unit cell.
The conformations of the N-H and C=O bonds are anti to each other. The O…H intermolecular H-bond distances and the N-H…O bond angles for all the compounds are in the range of 1.94–2.56 Å and 134.5–172°, respectively. The longest H-bond distance, 2.56 Å observed for 4-Cl derivative, confirms the lesser stability in presence of electron withdrawing substituent.

*N*’-(substitutedbenzoyl)adamantyl hydrazides except the 4-nitro derivative crystallized in the hydrated forms, in contrast to the non-hydrated forms of *N*’-(substitutedphenylsulfonyl)adamantyl hydrazides. Thus the H-bond patterns are different in the two sets of compounds, although all the para-substituted derivatives in both the sets crystallize in the monoclinic systems with almost the same space group and the same number of molecules in the asymmetric units and the unit cells.