CHAPTER 1: SYNTHESIS OF N, N'-DISUBSTITUTED UREA DERIVATIVES USING DIFFERENT CATALYSTS

Ureas are very significant compounds in organic synthesis. Urea is a functional moiety that is found in many natural products and Urea based organic compounds have great pharmacotherapeutic profiles. In particular, symmetric ureas have attracted attention due to their wide range of applications. Some urea derivatives are useful as active ingredients in antimicrobial, antifungal, algacides agents, HIV-1 protease inhibitor, as anti-tuberculosis agent, anti melanoma agents, anti-depressants etc.

Substituted urea derivatives of various anilines have been prepared by Curtius rearrangement, reductive alkylation of aromatic aldehydes from CS₂, palladium catalyzed reactions etc.

Synthesis of N, N'-disubstituted urea derivatives from urea and substituted amines using different catalysts

As the traditional methods mentioned above for the synthesis of symmetrically disubstituted ureas suffer from many drawbacks like lower yields, toxicity, longer reaction time, laborious work up etc. We aimed at developing new benign, eco-friendly methods under dry media conditions and in conjunction with microwave irradiation. Hence, N, N'-disubstituted urea derivatives has been synthesized by reacting urea with differently substituted amines under microwave irradiations. The reaction was carried in dry media under solvent free conditions. The effect of various catalysts on the reaction was investigated. A variety of environmentally benign catalysts have been explored such as p-Toulenesulphonic acid (TsOH.H₂O), Hydrochloric acid (HCl), Montmorillonite KSF, Montmorillonite K-10, Zirconyl Oxychloride (ZrOCl₂.8H₂O), Acidic alumina (Al₂O₃) and Sodium chloride (NaCl). The various amines investigated are: Aniline, 2-Methylaniline, 4-Methylaniline, 2-Methoxyaniline, 4-Meyhoxyaniline, 2-Nitroaniline, 4-Nitroaniline, 2-Chloroaniline, Phenylhydrazine and cyclohexylamine.
Synthesis of N, N'-disubstituted urea derivatives from biuret and substituted amines using different catalysts

We also envisaged the synthesis of the N, N'-disubstituted ureas from biuret and amines under solvent free condition using microwave irradiations. A variety of environmentally benign catalysts have been explored such as p-Toulenesulphonic acid (TsOH.H₂O), Hydrochloric acid (HCl), Montmorillonite KSF, Montmorillonite K-10, Zirconyl Oxychloride (ZrOCl₂.8H₂O), Acidic alumina (Al₂O₃) and Sodium chloride (NaCl). Various amines investigated are: Aniline, 2-Methylaniline, 4-Methylaniline, 2-Methoxyaniline, 4-Methoxyaniline, 2-Nitroaniline, 4-Nitroaniline, 2-Chloroaniline, Phenylhydrazine and cyclohexylamine.

CHAPTER 2: SYNTHESIS OF NEW UREA AND THIOUREA DERIVATIVES OF SACCHARIN BY REACTION OF SACCHARIN WITH DIFFERENTLY SUBSTITUTED UREAS AND THIOUREAS

Saccharin widely known over many years for its sweet taste, is a derivative of 1, 2-benzisothiazole. Saccharin i.e 1, 2-benzisothiazole-3(2H)-one 1, 1-dioxide is primarily used as an artificial sweetening agent but it has gained the attention of researchers because of its biological properties. Aryl sulphonyl urea derivatives of saccharin were found to be potent pesticides. Sachharin moeity has been used in drugs, pharmaceuticals, 5-HT1a receptors, serine proteases, human mast cell tryptase, human leukocyte inhibitors, analgesics, anti-inflammators and many more. Saccharin has been used in synthesis of schiff bases and other saccharin derivatives that posses antimicrobial properties. They recently have been utilised as key component in the synthesis of heterocyclic compounds and Sulphonephthaleins. Such diverse biological profile of saccharin prompted us to investigate the reaction of ureas and thioureas with saccharin. Hence new urea and thiourea derivatives of saccharin are synthesized.
by reaction of saccharin with different ureas and thioureas under solvent free conditions using microwave irradiations. Different type of ureas and thioureas used are: Urea, 1,3-Dimethyl urea, 1,3-Diethyl urea, n-Butyl urea, Trimethylsilyl urea, Cyclohexyl urea, Thiourea, 1,3-Dimethylthiourea and 1,3-Diethylthiourea.

CHAPTER 3: SYNTHESIS OF NEW SULFONIC ACID DERIVATIVES OF UREA AND THIOUREA BY REACTION OF DIVERSE UREAS WITH SULFANILIC ACID

Sulfonamide or sulfa drugs constitutes wide variety of chemotherapeutic agents, which are against a large number of bacterial infections in human beings. Sulfonamide group is present in synthetic antimicrobial agents. The sulfonylureas and thiazide diuretics are some notable drug groups which are based on the antibacterial sulfonamides. Sulfonamides are bacteriostatic as they act as competitive inhibitors of DHPS (enzyme which incorporates p-aminobenzoic acid (PABA) into folic acid (p-teroyl-glutamic acid, PGA). Sulfonamide moiety is present in medications used to treat allergies, malaria, cough, fungal and bacterial ailments. Sulfonamide is also present in non anti-microbial medications, such as thiazide diuretics, loop diuretics, sulfonylureas glipizide, glyburide and anti-inflammators like COX-2 inhibitors. Sulfasalazine is used as an antibiotic and in the treatment of inflammatory bowel disease as well. Such diverse biological profile of sulfonic acid derivatives prompted us to investigate the reaction of ureas and thioureas with sulfanilic acid. Hence new sulfonic acid derivatives of ureas and thioureas are synthesized by reaction of different ureas and thioureas with sulfanilic acid under solvent free conditions using microwave irradiations. Different type of ureas and thioureas used are: Urea, 1,3-Dimethyl urea, 1,3-Diethyl urea, n-Butyl urea, Trimethylsilyl urea, Cyclohexyl urea, Thiourea, 1,3-Dimethylthiourea and 1,3-Diethylthiourea.
CHAPTER 4: ANTIMICROBIAL ACTIVITY

While a countless number of antibiotics and chemotherapeutics are accessible for therapeutic use, the antimicrobial resistance created an extensive need of novel class of antibacterial agents in the preceding decades. The hastily escalating populace of immune conceded patients resulted in a consequent upsurge of diseases instigated by bacteria, fungi and other microbes. The prevalence of bacterial toxicities has amplified noticeably in recent times. The prevalent use of antibacterial and antifungal drugs and their resistance against bacterial and fungal contagions has steered to grave health threats. The resistance developed in a broad spectrum of antibacterial agents has impelled reform of prevailing drugs toward new antifungal and antibacterial remedies.

Literature review reveals that urea and thiourea derivatives exhibited a comprehensive spectrum of biological activities as anti-HIV, antiviral, HDL-fostering antibacterial, analgesic properties and many more. 1, 3-disubstituted urea derivatives synthesized by us were evaluated for their antibacterial and antifungal properties against different bacterial and fungal stains.

On similar lines urea and thiourea derivatives of saccharin and sulfonic acid derivatives of ureas and thioureas were also evaluated for their antibacterial and antifungal properties against different bacterial and fungal stains. Many synthesized compounds showed significant activity against different bacterial and fungal stains.