Summary

The work represented in the thesis entitled “Studies on Some Oxygen, Nitrogen and Sulfur Containing Heterocycles” is divided into three sections with seven chapters which can be summarized as below.

Section A deals with the potent antitumor DNA bifunctional alkylating agents and is further divided into three chapters.

Chapter 1 comprises of the general introduction of the DNA bifunctional alkylating agents. Initially, the naturally occurring antitumor Mitomycin C (MMC), which possess two reactive nucleophilic centers are capable of cross-linking with DNA. The other synthetic antitumor bifunctional alkylating agents, bis(hydroxymethyl)pyrrolizines derivatives were also able to induce DNA cross-linking via a similar mechanism of action of MMC. Based on the mechanism of action of these agents, in this chapter, we recently design several bis(hydroxymethyl) and bis(alkylcarbamates) pyrrolo derivatives.

In Chapter 2, planned to synthesize Target Molecules (TMs). A series of linear bis(hydroxymethyl)-5,10-dihydropyrrolo[1,2-b]isoquinolin-1-yl derivatives and their bis(alkylcarbamate) derivatives were prepared. In this chapter, 53 compounds enlisted which are newly synthesized and bioactive compounds for various antitumor activities.

Chapter 3, consists of antitumor activity of both bis(hydroxymethyl)pyrrolo[1,2-b]isoquinoline and their bis(alkylcarbamate) derivatives. All the prepared derivatives show potent antitumor activity in various human tumor xenografts in vitro. Among these analogues, we discovered compound 81a, which was selected for antitumor studies in animal models, exhibits potent therapeutic efficacy against human breast MX-1 xenograft in nude mice, as complete tumor remission was observed. This agent is also able to significantly suppress human ovarian tumors (SK-OV-3) implanted in nude mice. The results reported herein warrant further investigation to optimize the schedule and dosage to get greater suppression of other human tumor growth in animal models. Studies on the DNA interstrand cross-linking suggested that the newly synthesized derivatives are potent bifunctional DNA cross-linking agents. Furthermore, these agents induced substantial G2/M phase arrested of the cell cycle.
Section B encompasses the pyrano[3,2-c]quinolone derivatives and is further divided into two chapters.

Chapter 4 covers the history and background of pyrano[3,2-c]quinolone analogues. Various biological activities like Antibiotic, Anticancer, Anti-HIV, Calcium Channel Blockers, Antiallergic, Antimicrobial etc are summarized. Various synthetic procedures for the synthesis of pyrano[3,2-c]quinolone core structure are also shown. In Chapter 5, attempts were made to generate small library of pyrano[3,2-c]quinolone derivatives. The one-pot three-component Tendem Knoevenagel Michael addition reaction to furnish novel 4H,5H,6H,9H-pyrido[ij]pyrano[3,2-c]quinoline derivatives. The biological activity of newly synthesized compounds is under investigation.

Section C deals with the (1H-benzo[d]imidazol-2-yl)amino-pyrimidine derivatives and is further divided into two chapters.

Chapter 6 narrates the background and biological activity study of the Benzimidazole and Pyrimidine derivatives as well as in here including some recent synthetic strategies which have been employed to synthesize this class of compounds. The literature survey revealed that such class of which contains both heterocycles are show various biological activity. In Chapter 7, first time reported three component condensations of guanidines, orthoester and active methylene carbonyl compounds leading to several novels substituted-(1H-benzo[d]imidazol-2-yl)amino-pyrimidine derivatives. 22 new molecules are prepared and characterized in this chapter. The yield of these compounds is good to excellent.

In all 96 derivatives have been synthesized in current work which are characterized by spectral data. Some of the compounds were tested for preliminary antitumor activity and advanced study. Other mechanistic studies like DNA interstrand cross-linking, cell cycle inhibition and rat plasma stability was also performed in the current work. The remaining synthesized compounds are also under screening for Anticancer, Anti-tubercular as well as antimicrobial activity study, the results of which are awaited.