Preface

The present work personified in this thesis comprises the synthesis of podophyllotoxin derivative using a novel synthetic route and using the [4+2] cycloaddition reaction. The synthetic strategy employed here is to convert the 1,2-oxazine to tetralones which are then used for synthesis of podophyllotoxin derivatives. The podophyllotoxin derivatives are tested for biological activity. The thesis comprises of six chapters which are subdivided into sub-sections. Literature references are cited separately at the end of each chapter.

Chapter I is an introductory chapter, which is subdivided into two parts. Part I deals with the relevant literature survey regarding the synthesis, biological activity of podophyllotoxin derivatives. Part II deals with the literature survey pertaining to cycloaddition reactions and methods for the preparation and applications of 5,6-dihydro-4H-1,2-oxazines.

Chapter II is divided into two parts. Part I deals with synthetic plan adopted by us in this thesis for synthesizing the podophyllotoxin derivatives. The acetophenone oximes of benzene derivatives were prepared and then converted to the oxazines by the procedure followed by Rai et al. The 1,2-oxazines are then converted to γ-hydroxy ketones. The γ-hydroxy ketones which has electron donating groups on the benzene ring are cyclized to form the corresponding tetralones. The tetralones are then converted to a podophyllotoxin derivatives having a chalcone moiety and another derivative, a fused heterocycle having an amino-thiazole group attached to the aryl tetralin ring system and the podophyllotoxin derivative. Part–II deals with the methodology followed in synthesizing of new 5,6-dihydro-4H-1,2-oxazines employing the method developed by Rai et al.
In Chapter III, part I deals with the relevant literature survey regarding the formation and cleavage of N-O bonds, chemistry of $\gamma$-hydroxy ketones and reduction methodologies using zinc.

Part II describes the novel methods adopted in the thesis for the cleavage of N-O bonds of 5,6-dihydro-4H-1,2-oxazines to the respective $\gamma$-hydroxy ketones. Two new methodologies are described. One is using zinc and ammonium chloride and the other is using zinc and aqueous chelating ethers. Mechanism pertaining to the reduction using zinc and aqueous ethers is also proposed.

Chapter IV deals with the synthesis of podophyllotoxin derivatives from $\gamma$-hydroxy ketones via $\alpha$-tetralones. The methodology described here involves the cyclization of $\gamma$-hydroxy ketones to $\alpha$-tetralones using acid catalyst which are then converted to 2-bromoderivative. The 2-bromoderivative is then converted to 2-amino-thiazole moiety. The $\alpha$-tetralones are also converted to chalcone derivative and the podophyllotoxin derivative.

Chapter V describes the experimental details of the reactions discussed in the chapters II-part II and chapters III and IV. Physical characteristics yield and spectral data of all new compounds are included here.

Chapter VI deals with the biological activities of the synthesized podophyllotoxin derivatives, chalcone derivatives and the amino-thiazole derivative, for anti-bacterial and anti-fungal activity.