

**UNIVERSITI TEKNOLOGI MARA**

**SYNTHETIC STUDIES TOWARDS  
THE TOTAL SYNTHESIS OF (-)-CODONOPSININE,  
AN ANTI-HYPERTENSIVE COMPOUND FROM  
*Codonopsis clematidea***

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for the degree of  
Doctor of Philosophy**

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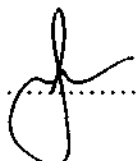
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## ABSTRACT

In this study (-)-codonopsinine was chosen as the synthetic target molecule due to its unique *trans pentasubstituted* pyrrolidine structure as well as remarkable antibiotic and hypotensive activity.

The synthetic approach towards the total synthesis of codonopsinine requires an appropriate diketo pyrrolidinone ring template, formed by Dieckmann cyclisation of an intermediate diester which provided the  $\beta,\beta$ -diketo pyrrolidinone or through condensation with ring closure *via* multicomponent reactions to yield different  $\beta,\gamma$ -diketo ring template. Performing series of successive functional groups modification on both ring templates, which include demethoxycarbonylation, keto reduction, *O*-protection and  $\beta$ -elimination, successfully furnished over 20 pyrrolidine type compounds in moderate to good yields. In this study, an important intermediate of olefin, **67** was successfully synthesised in 9 steps with an overall yield of 18%. Nevertheless, a different intermediate of acyloins, **82** with completed *N*-Me installation in the ring was also achieved in 3 steps (with an overall yield of 18%) *via* the multicomponent reactions. Biological studies conducted on some of the codonopsinine derivatives confirmed to exhibit from moderate to the most potent activity towards anti-MRSA and efflux pump inhibition.

In brief, two novel synthetic approaches towards the total synthesis of codonopsinine were devised which offer interesting new scientific knowledge and findings.

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## TABLE OF CONTENTS

|  | Page  |
|--|-------|
| TITLE PAGE   |       |
| AUTHOR'S DECLARATION   | ii    |
| ABSTRACT   | iii   |
| ACKNOWLEDGEMENT  | iv    |
| TABLE OF CONTENTS  | v     |
| LIST OF TABLES   | xv    |
| LIST OF FIGURES  | xvii  |
| LIST OF ABBREVIATIONS  | xviii |
| <br>   |       |
| <b>Chapter 1: INTRODUCTION</b>                                     |       |
| <br>   |       |
| 1.0 Introduction   | 1     |
| 1.1 Naturally Occuring Alkaloids and Sugar Mimicking Alkaloids     | 1     |
| 1.2 Polyhydroxylated Alkaloids with a Pyrrolidine Ring System      | 2     |
| 1.3 Codonopsinine: Stereochemistry, Activity and Synthetic Studies | 6     |
| Towards Total Synthesis  |       |
| 1.3.1 Iida's Synthetic Approach                                    | 7     |
| 1.3.2 Calabrese's Synthetic Approach                               | 9     |
| 1.3.3 Yoda's Synthetic Approach                                    | 11    |
| 1.3.4 Correia's Synthetic Approach                                 | 13    |
| 1.3.5 Goti's Synthetic Approach                                    | 15    |
| 1.3.6 Larcheveque's Synthetic Approach                             | 17    |
| 1.3.7 Rao's Synthetic Approach                                     | 20    |
| 1.4 Objectives of Research   | 23    |