

การศึกษาทางพฤษเคมีของ เปลือกต้นตุมกาขาว



นางปราณี ชาวลิตร่าง

วิทยานิพนธ์นี้ เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญา เกษตรศาสตรมหาบัณฑิต

ภาควิชา เกษตรพฤษศาสตร์

บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

พ.ศ. 2534

ISBN 974-578-469-9

ลิขสิทธิ์ของบัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

017677
117881171

PHYTOCHEMICAL STUDY OF STRYCHNOS NUX-BLANDA A.W. HILL BARK

Mrs. Pranee Chavalittumrong

A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science in Pharmacy

Department of Pharmaceutical Botany

Graduate School

Chulalongkorn University

1991

ISBN 974-578-469-9

Thesis Title PHYTOCHEMICAL STUDY OF STRYCHNOS NUX-BLANDA A.W.HILL

BARK

By Mrs. Pranee Chavalittumrong

Department Pharmaceutical Botany

Thesis Advisor Associate Professor Rapepol Bavovada, Ph.D.



Accepted by the Graduate School, Chulalongkorn University
in Partial Fulfillment of the Requirement for the Master's Degree

Thavorn Vajrabhaya
..... Dean of Graduate School
(Professor Thavorn Vajrabhaya, Ph.D.)

Thesis Committee

B. K. Laddawan
..... Chairman
(Associate Professor Laddawan Boonyaratanakornkit, M.Sc.)

Rapepol Bavovada
..... Thesis Advisor
(Associate Professor Rapepol Bavovada, Ph.D.)

Kalaya Phradai
..... Member
(Associate Professor Kalaya Phradai, M.Eng.)

Ekarin Saifah
..... Member
(Associate Professor Ekarin Saifah, Ph.D.)

Copyright of the Graduate School, Chulalongkorn University



| | |
|-------------------|--|
| หัวข้อวิทยานิพนธ์ | การศึกษาทางพฤกษเคมีของ เปลือกต้นตุมกาขาว |
| ชื่อผู้ผลิต | นางปราณี ชาลิตธำรง |
| อาจารย์ที่ปรึกษา | รองศาสตราจารย์ ดร. รพีพล ภาโววาท |
| ภาควิชา | เภสัชพฤกษศาสตร์ |
| ปีการศึกษา | 2533 |

บทคัดย่อ

จากการศึกษาทางพฤกษเคมีของเปลือกต้นตุมกาขาว (*Strychnos nux-blanda* A.W.Hill) ได้พบ indole alkaloids สองชนิด ชื่อ Strychnine และ Brucine และพิสูจน์เอกลักษณ์ของสารทั้งสองนี้โดยอาศัยข้อมูลทางสเปกโตรสโกปี

Thesis Title PHYTOCHEMICAL STUDY OF STRYCHNOS NUX-BLANDA A.W.
HILL BARK

Name Mrs. Pranee Chavalittumrong

Thesis Advisor Associate Professor Rapepol Bavovada, Ph.D.

Department Pharmaceutical Botany

Academic Year 1990

ABSTRACT

The two indole alkaloids, strychnine and brucine, were isolated from the stem bark of *Strychnos nux-blanda* A.W. Hill and their structure were identified by spectroscopy.



ACKNOWLEDGEMENTS

The author is deeply indebted and grateful to her advisor, Associate Professor Rapepol Bavovada of the Department of Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University for his kindness, helpful guidance, valuable advice, contiguous interest, and continual encouragements throughout the course of this work.

The author wishes to express her deepest appreciation to Miss Thawepol Dechatiwongse Na Ayudhya, Chief of Phytochemical Section, Division of Medicinal Plant Research and Development and Miss Yenchit Jewvachdumrongkul for her valuable suggestion during time of the study.

Special thanks are due to all of my colleagues in Division of Medicinal Plant Research and Development for their helpful discussion and their skilful recording of the UV and IR spectra, the Technical Staffs of the Sciences and Technological Research Equipment Center, Chulalongkorn University, for determining several 90 MHz ^1H NMR, ^{13}C NMR, and Mass Spectrometer



Contents

| | Page |
|--|------|
| Abstract (Thai)..... | iv |
| Abstract (English)..... | v |
| Acknowledgements..... | vi |
| Contents..... | vii |
| List of Figures..... | ix |
| List of Tables..... | xi |
| Abbreviations..... | xii |
| | |
| Chapter | |
| I Introduction | |
| General Introduction..... | 1 |
| Strychnos Species in Thailand..... | 12 |
| The strychnos alkloids..... | 15 |
| Biosynthesis of strychnos alkaloids..... | 40 |
| Pharmacology of strychnos alkaloids..... | 51 |
| Alkaloids with convulsant activity..... | 53 |
| Alkaloids with muscle-relaxant activity..... | 56 |
| Alkaloids with cytotoxic activity..... | 62 |
| Alkaloids with antimicrobial activity..... | 69 |
| Alkaloids with hypotensive activity..... | 73 |
| Alkaloids with other activities..... | 74 |

| | | |
|-----|--|-----|
| II | Introduction to | |
| | <i>Strychnos nux-blanda</i> A.W. Hill..... | 75 |
| | The Medicinal used of | |
| | <i>Strychnos nux-blanda</i> A.W. Hill..... | 79 |
| | Previous investigations..... | 80 |
| | Purpose of the Present Investigation..... | 89 |
| III | Experimental..... | 91 |
| IV | Discussion..... | 105 |
| V | Conclusion and Recommendation..... | 111 |
| | Reference..... | 112 |
| | Appendix..... | 122 |
| | Vita..... | 134 |

List of Figures

| Figure | Page |
|--|------|
| 1. Biosynthetic diagram of alkaloids and closely related compounds..... | 12 |
| 2. Structural features of simple indole together with precursors of the second class indole alkaloids..... | 16 |
| 3. The skeletal types with corresponding examples of alkaloids..... | 17 |
| 4. Overall view of the biosynthesis of Strychnos alkaloids..... | 44 |
| 5. Transformation of 4,21-Dehydrogeissoschizine to Dehydropreakuammicine..... | 45 |
| 6. Alkaloids derived from Dehydropreakuammicine..... | 46 |
| 7. Alkaloids derived from Nor-F-fluorocurarine..... | 47 |
| 8. Formation of Strychnine from Wieland-Gumlich aldehyde and acetate unit..... | 48 |
| 9. The final stage in the biosynthesis pathway of Strychnine..... | 50 |
| 10. <i>Strychnos nux-blanda</i> A.W. Hill..... | 77 |
| 11. Details of flower of <i>Strychnos nux-vomica</i> Linn..... | 78 |
| 12. Details of flower of <i>Strychnos nux-blanda</i> A.W. Hill..... | 78 |
| 13. Ultra violet absorption spectrum of PC 3 in ethanol..... | 123 |

List of Figures (Continued)

| Figure | Page |
|---|------|
| 14. Infrared absorption spectrum of PC 3 in KBr disc..... | 124 |
| 15. ^1H -Nuclear Magnetic Resonance spectrum (90 MHz) of PC 3 in CDCl_3 | 125 |
| 16. ^{13}C -Nuclear Magnetic Resonance spectrum (90 MHz) of PC 3 in CDCl_3 | 126 |
| 17. Mass spectrum (150 ° C) of PC 3..... | 127 |
| 18. Ultra violet absorption spectrum of PC 4-1 in ethanol..... | 128 |
| 19. Infrared absorption spectrum of PC 4-1 in KBr disc..... | 129 |
| 20. ^1H -Nuclear Magnetic Resonance spectrum (90 MHz) of PC 4-1 in CDCl_3 | 130 |
| 21. ^{13}C -Nuclear Magnetic Resonance spectrum (90 MHz) of PC 4-1 in CDCl_3 | 131 |
| 22. Mass spectrum (200 °C) of PC 4-1..... | 132 |
| 23. Thin layer chromatogram of <i>S. nux-vomica</i> L. and <i>S. nux-blanda</i> A.W.Hill alcoholic extracts..... | 133 |

List of Tables

| Table | Page |
|--|------|
| 1. Taxonomic Position of the Genus <i>Strychnos</i> within the Family Loganiaceae..... | 2 |
| 2. The Known Geographical Distribution of the Asian Species of <i>Strychnos</i> | 3 |
| 3. <i>Strychnos</i> Species Growing in Thailand..... | 13 |
| 4. Subdivision of the Main Types of <i>Strychnos</i> Alkaloids..... | 20 |
| 5. Sample data and results of alkaloid screening procedure for <i>Strychnos nux-blanda</i> A.W.Hill..... | 82 |
| 6. Alkaloids identified by thin-layer chromatographic (T), gas-liquid chromatographic (G), and mass spectrometric (M) techniques in various collections of <i>Strychnos nux-blanda</i> A.W. Hill..... | 86 |
| 7. The alkaloids previously found in <i>Strychnos nux-blanda</i> A.W.Hill..... | 88 |

Abbreviations

| | |
|------------------------|---------------------------------------|
| $^{\circ}\text{C}$ | degree celsius |
| ^{13}C NMR | Carbon-13 Nuclear Magnetic Resonance |
| ^1H NMR | Proton Nuclear Magnetic Resonance |
| g | gram |
| kg | kilogram |
| mg | milligram |
| MHz | Mega Hertz |
| min | minute |
| ml | millilitre |
| MW | Molecular weight |
| m/z | mass to charge ratio |
| nm | nanometre |
| ppm | part per million |
| UV | Ultra violet |
| λ_{max} | the wave length at maximum absorption |
| ν | wave number |
| Δ | unsaturated double bond |
| amu | atomic mass unit |
| R_t | retention time |
| J | coupling constant in Hertz |
| s | singlet |
| d | doublet |
| t | triplet |
| m | multiplet |
| δ | chemical shift |