UNIVERSITI TEKNOLOGI MARA

BIOTRANSFORMATION OF SELECTED NATURAL PRODUCTS AND PHYTOCHEMISTRY OF FERMENTED *Alnus sieboldiana* AND LIVERWORT *Conocephalum conicum*

NURUNAJAH BINTI AB GHANI

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Nurunajah binti Ab Ghani
Student I.D. No	:	2011186911
Programme	:	Doctor of Philosophy (Science) –AS950
Faculty	:	Applied Sciences
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Signature of Student	:	.....
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ABSTRACT

Biotransformation is a process by which organic compounds are transformed into its derivatives, aided by organisms such as fungi, bacteria and enzymes. Biotransformations are used as a valuable strategy to diversify chemistry of compounds particularly natural products. The aim of this work is to explore biotransformation on natural products using several concepts, in order to obtain varieties of natural entities. This thesis presents biotransformation studies on two classes of bioactive natural products represented by an anthraquinone and chalcones, followed by *in-situ* transformation of chemical constituents of male flowers by fungus, and changes in biosynthetic pathways when Japanese liverwort is grown under stressed condition. Small scale biotransformation of the bioactive anthraquinone nordamnacanthal **8** using 19 selected strains revealed its sturdy nature where only *Absidia coerulea* managed to convert the compound into lucidin **143**. Then, *in-labo* biotransformation was pursued with microbial transformation of hydroxychalcones; 4′-hydroxychalcone **145** and 4-hydroxychalcone **146** by *Aspergillus niger*. After 7 days of fermentation, four dihydrochalcone derivatives were obtained. Isolated products were identified as 4′-hydroxydihydrochalcone **147**, 4-hydroxydihydrochalcone **149**, 3′,4′-dihydroxydihydrochalcone **148** and 3,4-dihydroxydihydrochalcone **150**, resulting from bioreduction at α,β-unsaturated double bond of hydroxychalcone and hydrogenation reaction at the activated phenyl rings. On the other hand, *in-situ* transformation of *Alnus sieboldiana* male flowers by fungus *Penicillium* sp. is of interest due to the common infection causing significant change in the smell. Infected male flowers were allowed to ferment for six months. Analysis of the volatile components of the fermented male flowers revealed β-phenylethyl cinnamate **174** (10%) as a major component followed by 2-phenylethanol **170** (8.7%). The level of 2-phenylethanol **170** in the fermented male flowers is three times higher as compared to the fresh male flowers (2.7%) which explained the unpleasant odor of fermented male flowers. Yashabushidiol A **72**, yashabushidiol B **73** and naringenin **69**, which were known to be original constituents of the fresh male flowers, were successfully isolated from the ethyl acetate extract of fermented male flowers. Additional transformation products isolated includes six flavonoids kaempferol **195**, quercetin **196**, pinocembrin dimethyl ether **197**, *trans*-3-hydroxy-5,7-dimethoxyflavanone **198**, galangin-5,7-dimethyl ether **199** and 5-methoxy-3,6,7-trihydroxyflavanone **200**. Detailed analysis of the metabolic pathways of isolated compounds suggested flavanone-3-hydroxylase, flavonoid-3′-hydroxylase and plant-*O*-methyl-transferases enzymes were released due to the enzymatic action of fungus *Penicillium* sp. When Japanese liverwort *Conocephalum conicum* was grown under stressed condition, the biosynthesis pathways taking place in the plant seem to be affected resulting in confusions from chemotype perspective. Under normal growth conditions, (+)-bornyl acetate **94** is the major component in the type-II *C. conicum* while *cis*-methyl cinnamate **204** and *trans*-methyl cinnamate **87** should not be present. However, when grown under stressed conditions, *trans*-methyl cinnamate **87** was found to be present as the major component instead of (+)-bornyl acetate **94**, indicating activation of shikimate pathway along with mevalonic acid pathway. Thus, it is suggested that the stress *C. conicum* to be categorized under '*trans*-methyl cinnamate > bornyl acetate' subtype, since there were dual biogenetic pathways present at stressed condition.

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TABLE OF CONTENTS