

## CHEMICAL AND PHARMACOLOGICAL STUDIES OF ANTI-MICROBIAL, ANTI-VIRAL AND ANTI-TUMOUR COMPOUNDS FROM SELECTED MALAYSIAN PLANTS (*MORINDA*, *HEDYOTIS*, *GARCINIA* AND *JUNIPER SPP.*)

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### Introduction

There is strong interest lately in the search for new drug from the tropical rain forest. This is partly due to the high potential of discovering new pharmacologically important molecules from the vast and diverse flora and fauna of the tropics. The diversity of flora and fauna enhance the chances of discovery resulted from the unlimited number of sample variety available for pharmacological screenings. University Putra Malaysia has established several screening programmes to study the cytotoxic, anti-microbial, anti-viral and anti-oxidative activities in biological extracts and pure samples. This project was aimed at discovering new bio-active compounds from our natural biological resources based on our available assay systems.

### Materials and Methods

Plants are collected from several areas of Peninsular Malaysia and extracted various organic solvents and water. Plants with relevant medicinal claims are primarily of higher interest to our study. The extracts were then subjected to several bioassay systems and the activity was measured. Plants showing high activity from the assays were selected for detail investigation to isolate and purify the constituents and finally identified spectroscopically. The activity of each isolate was measured and the bio-activity-structure relationship was established. Structures showing high activity were synthesised or production using alternative methods was pursued, including cell culture approach.

### Results and Discussion

Twelve anthraquinone compounds from the roots *Morinda elliptica*. They have been characterised based on their spectroscopic data and identified as derivatives of 9,10-anthraquinones. One of the compounds isolated was new. The results of this chemical work have been reported (Ismail et al. 1997). Three of the compounds showed strong cytotoxic activity toward T-lymphoblastic leukemia and Melanoma cell-lines, in addition to being anti-microbial and anti-HIV virus. Several of these isolates also showed anti-oxidative activity. The synthesis of selected 2-formyl-1-hydroxy-9,10-anthraquinone, the new compound isolated from this species was completed with good yield and synthesis of further derivatives is currently pursued. A large-scale synthesis is now being planned. Synthesis of other structurally modified anthraquinones with potential bio-activities is also being planned. The structure-activity relationship with regards to anti-microbial, cytotoxicity and anti-oxidative activities will be pursued. The work on the compounds pro-

duced by the cell culture callus has led to the isolation of 11 pure compounds. Several of the isolates are those that occur in the plant, but some of them are not. Further isolation from the polar components is continued. The isolation of bio-active compounds from *Juniperus chinensis* have been conducted to result in the identification of a cytotoxic compound, deoxypodophyllotoxin which caused up to 100% cell reduction on HeLa cells. It was also active against chronic myelogenous leukemia, renal carcinoma, melanoma as well as T-Lymphoblastic leukemia cell-lines. The compound also showed anti-microbial activity. The results of this work have been published (Mackeen et al. 1997) The work on isolation of bioactive compounds from the fruits of *Garcinia artoviridis* was accomplished. The active compounds identified as the dibutyl methyl ester of hydroxycitric acid and the respective beta-lactone were found to act strongly against *Cladosporium herbarum* a common agricultural fungus. Extraction of the chemical components from the roots and stem bark of *G. artoviridis* has been completed and bio-activity test showed that several fractions are very active against bacteria and strong anti-oxidative. Further isolation and structure determination is initiated. Isolation and purification of a *Hedyotis herbacea* var. was conducted and two flavonoid-glycosides characterised as quercetin-glucoside and quercetin-rutinoside were isolated along with three two irridoid compounds and two triterpenoids. The study on the constituents of *Hedyotis* species has been continued. New anthraquinones were isolated from *H. dichotoma* (Hamza et al. 1997). The isolation of components from the virus/fungus-infected plant was continued and seven compounds were isolated, sent for NMR and characterised. Four of the compounds are quinonoids with two of them being new. The new 1,4-anthraquinones were found to be strongly cytotoxic. In addition a flavonoid-glycoside, kaempferol rutinoside and two triterpenoids were also isolated.

### Conclusion

Several anthraquinones were isolated and identified from *Morinda elliptica*. Biological activities shown by these compounds include cytotoxicity, anti-microbial and anti-viral activities. The new compound isolated from this study was synthesised. An approach to alternative production anthraquinones was also pursued using cell culture technique resulted in the useful information on the product profile from the process. The cytotoxic component of *Juniperus chinensis* was established as deoxypodophyllotoxin. The yield are however very low. Investigation on *Garcinia artoviridis* resulted in the isolation of anti-*Cladosporium* compound identified as hydroxycitric acid butyl ester and its lactone derivative. Several new anthraquinones were also isolated from *Hedyotis* species, some of which are strongly cytotoxic.

### References

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