ANTIMICROBIAL COMPOUNDS FROM ZANTHOXYLUM, CALOPHYLLUM, PITURANTHOS AND PHAGNALON SPECIES

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Keywords: murraya, zanthoxylum, carbazole alkaloid, flavonoid, antimicrobial.

Introduction

Malaysia has about 15000 species of plant that are known to possess medicinal properties (Latif, 1988). Tropical plants have been acknowledged to be source of forest product substances such as pharmaceuticals, natural insecticides and flavours. As part of our interest in the phytochemistry of Rutaceae plants, several medicinal plant species including *Murraya paniculata, M. keonigii, Zanthoxylum myriacanthum, Z. acanthopodium* and *Aegle marmelos* were selected for investigation. *M. paniculata* is a shrub and naturally distributed on limestone hill. Its leaves and barks are widely used for the treatment of stomach and toothache, and for stimulant (Burkill, 1966). Previous reports on the extracts of *M. paniculata* have revealed the presence of flavonoids and coumarins (Kiroshita and Firman, 1977) whereas *M. koenigii* contained mostly carbazole alkoloids (Mukherjee et al. 1983). The objectives of this project were to isolate and elucidate the structure of the bioactive constituents of the plants and to assess their biological acitivity.

Materials and Methods

This study involved extraction with various solvents, separation using chromatographic techniques and elucidation of the products using spectroscopic methods such as UV, IR, MS and 2D-NMR. The bioassays of the crude extracts and isolated pure compounds against some pathogenic microbes (bacteria, virus, amoeba) and cytotoxic tests against cancer cell lines were also carried out.

Melting points were determined on Kohfler hot stage melting point apparatus and were incorrected. The IR spectra were recorded using KBr disc on Perkin Elmer FT-IR spectrophotometer model 1650. ^{1}H and ^{13}C NMR spectra were obtained on JEOL spectrometer at 500 and 125 MHz, respectively. MS were obtained on Finnigen MAT 710 and HP 5989A instruments at 70 eV. The plant species were collected from around Peninsular Malaysia and were air-dried prior being used. The plant material (leaves, roots, stem barks) were soaked continuously with petroleum ether, chloroform and methanol. Each of the extract was subjected to the flash column chromatography separation; the products obtained were purified and analysed using various spectroscopic methods. Several pathogenic microbial strains such as *Bacillius cereus, Pseudomonas aeruginosa* and *Candida lipolytica* were used for antimicrobial activity evaluation, whereas T-lymphoblastic leukaemia cell line was used for cytotoxic test.

Results and Discussion

The structure of the compounds were elucidated based on their spectroscopic data and also by comparison with the literatures. From the petroleum ether, chlorofrom and methanol extracts of leaves and stem bark of *M. paniculata,* several polysubstituted flavonoids, coumarins and triterpenes were characterized. Bioassay procedures have shown that these compounds exhibited mild activity against several microbes employed in the test. Work-up procedures on the extracts of *M. koenigii* have afforded various products, mostly carbozole alkaloids, which were established especially through long range NMR coupling assignments. Some of these alkaloids have showed strong activity against amoeba, *Acanthamoeba castellani.* Gininimbine and mahanimbine were calculated to have IC_{50} values of 3.04 ppm and 1.18 ppm, respectively. At the same time, girinimbine had also exhibited substantial anti-tumor promoting activity.

Further investigations on other Rutaceous plant, *Z. myriacanthum* have resulted in the isolation of a new phenanthridine alkaloid, 7,9-dimethoxy-2,3-methylene-dioxybenzophenantiridine, together with its known isomer, *N*-nortidine and some triterpenes.

Conclusions

Investigation on some Rutaceae plants used in this tudy have afforded several new and known compounds, including indole and phenanthridine alkaloids, flavonoids, triterpenes and volatile constituents. Bioassays evaluation indicated that some of the compounds exhibited strong and moderate activity against pathogenic microbes and were cytotoxic against cancer cell lines.

References

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Supported by IRPA Grant 09-02-04-0024