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CHEMICAL STUDIES ON BIOLOGICALLY ACTIVE NATURAL PRODUCT FROM MEDICINAL PLANTS IN SABAH

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ABSTRACT. *A concerted effort has been undertaken to study the abundant biological resources of Sabah especially those with medicinal values in order to discover new drugs for the treatment of diseases. Important source of new drug are those derived from natural products, and among naturally derived products, plants have proven to be a major source for new pharmacological agents especially in treating cancer and AIDS. More then 600 medicinal plants used by various ethnic groups have been documented. Phytochemical studies on some of the selected plants showed interesting results. Studies on* Goniothalamus boorneensis *resulted in the isolation of goniothalenol, goniotriol, goniothalamin, goniobutenolide A, goniofufurone goniothalesdiol, goniothalactam and aristolactam A-III, all with interesting biological activity and studies on* G. velutinus *resulted in the isolation of aristololactam-BII and velutinam with cytotoxic activity. Alstophyline and vilastonine have been isolated from* Alstonia scholaris *while studies on* Litsea pallidifolia *resulted in the isolation of oxycanthine and obaberine all with antimalarial activity. Uses and phytochemical information on some of the plants will be discussed.*

KEYWORDS. Bioactivity, drug discovery, ethnopharmacology, phytochemistry, secondary metabolites

INTRODUCTION

Tropical rainforest are rich in various bioactive compounds and many important drugs such as quinine, quinidine, reserpine, pilocarpine, vinblastine, vincristine, atropine and quabain are derived from tropical forest. Some interesting finding from tropical rainforest includes calanolide A from *Calaphyllum lanigerum* with anti-HIV activity (Kashman *et al.*, 1991), taxol from *Taxus brevifolia* for the treatment of ovarian cancer (Kingston, 1993), michellamines A & B alkaloids from *Ancistrocladus abbreviatus* (Manfredi *et al.*, 1991) and castanospermine from *Castanospermum australe* with anti-HIV activities (Duke, 1989) and camptothesin from *Camptotheca acuminata* as antitumour agent (Lee, 1993).

Natural products studies especially in the drug discovery requires a highly integrated and multidisciplinary approach. Researchers in this area are usually presented with several options with respect to the investigative approach and methodology to select and screen plants for bioactive compounds. This entails either random, taxonomic, chemotaxonomic or ethnobotanical approach. Ethnic folklore uses of plants material can always be used an early indication of the possibility to discover some pharmacologically active components. Plants are collected with the helps of traditional medical practitioner among the local communities. Plants collected are then extracted to identify and elucidate the properties of any possible bioactive ingredients or novel chemical compounds. The biological activity of each extract is determined against a variety of diseases. Extract which show biological activities are further subjected to in-depth investigation and undergo bioassay-directed fractionation procedures for the isolation and identification of the active principles.

MEDICINAL PLANTS OF SABAH

The uses of more then 600 medicinal plants from 150 species by various ethnic groups in Sabah have been documented (Fasihuddin and Hasmah, 1992; Fasihuddin, 1993; Fasihuddin and Holdsworth, 1994, 1995; Fasihuddin *et al.*, 1995; Fasihuddin 1995a, 1995b; Fasihuddin 2000; Fasihuddin and Holdsworth 2001). Most of the plants are used to treat common diseases such as cuts and wounds (*Blumea balsamifera, Elephantopus scaber, Eupotarium odoratum, Jatropha excelsa*), stomachache (*Psidium guajava, Annona muricata, Brucea javanica, Phylanthus niluri, Merrimia gracilis*), cough (*Costus speciosus, Dinochloa scabrida, Elusisne indica, Drynaria sparciosa, Centella asiatica*), fever (*Centella asiatica, Cinnamomum iners, Polytalthia insignis, Vitex pubescen*), hypertension and diabetes (*Allium sativum, Alstonia scholaris, Andrographis panniculata, Centella asiatica, Eurycoma longifolia, Physalis minima, Rauvolfia serpentina*), malaria (*Alstonia scholaris, Brucea javanica, Eurycoma longifolia, Pyhlanthus niruri, Tinospora crispa*) and fungal infection (*Cassia alata, Hoya latifolia, Mollatus macrostachyus* (Fasihuddin and Hasmah, 1992; Fasihuddin, 1993; Fasihuddin and Holdsworth, 1994,1995; Fasihuddin *et al.*, 1995; Fasihuddin 1995a, 1995b; Fasihuddin 2000; Fasihuddin and Holdsworth 2001). The chemical and biological characteristics of these plants were assayed by phytochemical screening, phytochemical studies and pharmacological screening. Most of the plants used in treating wounds and stomachache showed strong antibacterial properties indicating the effectiveness of the plants in treating those diseases. Information on some medicinal plants, biological activities and ethnopharmacological uses are presented in Table 1.

PHYTOCHEMICAL STUDIES

Based on phytochemical screening and bioassay information, plants have been selected for further chemical investigation for the sole purpose of finding new biologically active component. The plants investigated include *Goniothalamus* spp., *Phaeanthus crassipetalus*, *Kopsia dasyrachis*, *Tinomischium petiolare*, *Alstonia scholaris* and *Litsea pallidifolia*. The

secondary metabolites isolated from the mentioned plants are listed in Table 2 (Fasihuddin *et al.*,1991a,1991b; Siraj *et al.*, 1992; Fasihuddin *et al.*, 1995; Fasihuddin, 1995; Fasihuddin *et al.* 1996; Cao *et al.*, 1998).

Table 1: Uses and biological activity of some selected medicinal plants in Sabah.

Plants species/Family	Bioactivity	Ethnopharmacologial uses
Alstonia scholaris (Apocynaceae)	Hypoglycemic, hypotensive, antimalarial, antidiarrheal, antimicrobial.	Antidiabetic, antimalarial, antitussive, febrifuge, treatment for asthma, treatment for boils, skin ulcer and rheumatic pains, antipyretic.
Andrographis paniculata (Acanthaceae)	Antibacterial, antidiarrheal, antimicrobial, febrifuge, hypotensive.	Analgesic, antipyretic, antidiabetic, skin diseases, diarrhoea, remedy for snake-bite.
Blumea balsamifera (Compositae)	Antihistamine, antispasmodic, antitumour, diuretic, hypotensive, tranquillizing, vasodilator.	Antihelmintic, expectorant, vermifuge, antipyretic, antidiarrheal, sore throat, promote blood circulation, antifungal.
Carica papaya (Caricaceae)	Cardiac depressent, CNS depressent, hypotensive.	Abortifacient, antihypertensive, antimalarial, cardiotonic, expectorant, laxative, treatment of asthma, vermifuge, skin problem.
Centella asiatica (Umbelliferae)	Antimicrobial, antiinflammatory, antipyretic, CNS depressent, hypotensive, insecticidal.	Anti-allergic, antidiarrheic, antidiabetic, antidysentric, antimalarial, hypotensive, stimulant, diuretic and tonic.
Eurycoma longifolia (Simaroubaceae)	Antihistaminic, antimalarial, antitumour, antiulser, antiviral, cytotoxic.	Antidotal, antihypertensive, antipyretic, antituberculotic and antivinous, used to cure indegestion, lumbago and vermifuge, used as febrifuge, tonic after childbirth, treatment of joundice, fever, dropsy and diarrhoea.
Rauvolfia serpentina (Apocynaceae)	Antiarrhytmic, antidepressant, antihypertensive, antiviral.	Antihypertensive, febrifuge, laxative, antidiarrheal, antidote, transquillizer.

Table 2: Secondary metabolites from some selected medicinal plants in Sabah

Plants species	Compounds isolated
Alstonia scholaris (Apocynaceae)	Alstonerine, alstophyline, vilastonine, pleiocarpamine.
Andrographis panniculata (Acanthaceae)	Andrograpanin, paniculide A,B, and C, andro-grapholide, myristic acid, euginol, caffeic acid.
Blumea balsamifera (Compositae)	Blumealactones, camphor, cryptomeridiol, quercetin, flavone, flavonone, alkaloids.
Carica papaya (Caricaceae)	Carpaine, carpaine glycoside, carposide, dehydrocarpamine, 6,7-epoxylinalool, lycopene, pseudocarpaine.
Centella asiatica (Umbelliferae)	Asiatic acid, asiaticoside, brahminoside, centellic acid, centelloside, hydrocotyline, indocentelloside, kaempferol, madasiatic acid, madecassoside, alkaloids and polyphenolic compounds.
Eurycoma longifolia (Simaroubaceae)	Dihydroeurycomalactone, eurycomalactone, eurycomanol, laurylcolactone, longilactone, pasakbumin, piscidinol A, scopoletin, alkaloids, quassinoids.
Goniothalamus borneensis (Annonaceae)	Goniothalenol, goniotriol, goniothalamin, goniofufurone, goniothalesdiol, goniothalactam, and pinocembrine.
G. uvaroides (Annonaceae)	Goniothalamin, 5-acetoxygoniothalamin, goniotriol, velutinam alkaloids.
G. velutinus (Annonaceae)	Aristololactam -BII, velutinam
G. woodii (Annonaceae)	Goniothalamin, 5-acetoxygoniothalamin, goniotriol, 5-hydroxygoniothalamin.
G. clemesii (Annonaceae)	Goniothalamin, 5-hydroxygoniothalamin, 5-acetoxy-goniothalamin, pinocembrin, goniotriol and goniofufurone.
Litsea pallidifolia (Lauraceae)	Oxycanthine, obaberine.
Phaeanthus crassipetalus (Annonaceae)	Pheanthine, limacine, lanuginosine, triterpenoid.
Kopsia dasyrachis (Apocynaceae)	Indole alkaloids kopsinine, kopsoffine.
Tinomischium petiolare (Menispermaceae)	5-hydroxypalmitine, jatrorrhizine, oxypalmitine.

Studies on *G. borneensis* resulted in the isolation of various goniothalamin derivatives and alkaloids with interesting biological properties (Cao *et al.*, 1998). Some of the compounds isolated include goniothalenol, goniofufurone, goniotriol, goniothalediol, goniothalactam and aristolactam A-III. . Goniothalenol, goniotriol and aristolactam A-III showed strong cytotoxic activity. Goniothalenol, goniotriol, goniopypyrone and goniofufurone were also reported from *G. giganteus* by various workers (El-Zayat *et al.*, 1985; Alkofahi *et al.*, 1989; Fang *et al.*, 1990). Goniothalamin is biologically active styryldihydropyrone with embryotoxic and teratogenic properties has been reported from various *Goniothalamin* spp. (Jewers *et al.*, 1972; Sam *et al.*, 1987; Fasihuddin *et al.*, 1991a). 5-acetylgoniothalamin, a novel compound was first isolated from *G. uvaroides* besides other styryl-lactone, alkaloids and flavonoids (Fasihuddin *et al.*, 1991a). Studies on *G. velutinus* which is well known as 'kayu-tas' or 'limpanas', a plant endemic to Borneo, resulted in the isolation of various alkaloids especially velutinam I, velutinam II and aristololactam-BII. All alkaloids isolated from *G. velutinus* exhibited interesting cytotoxic properties against leukemia cell lines such as HeLa and HL-60 (Siraj *et al.*, 1992). Alkaloids isolated from *P. crassipetalus* showed strong activity against several bacteria and also cytotoxic to the human leukemia cell line CEMC7 (Fasihuddin *et al.*,1991b). Studies on *Kopsia dasyrachis*, a plant endemic to Borneo resulted in the isolation of various indole alkaloid such as kopsinine and kopsoffine. Similar alkaloids have been previously reported from *K. officinalis* with strong antibacterial activities (Feng *et al.*, 1984). Studies on *Alstonia scholaris* and *Litsea pallidifolia* resulted in various alkaloid such as vilastonine, oxycanthine and obaberine with strong antimalarial activities. Other plants that are commonly used by various ethnic groups being investigated for their biological activities and phytochemical studies in order to obtain new drugs to treat various diseases.

CONCLUSION

It is clear that there is a wealth of potential drugs in tropical rainforest. The studies of plants used in traditional medicine by various ethnic groups resulted in the isolation of important drugs that are critical to modern medicine. Synthetic analogues are not as effective as their natural counterparts or the cost for synthetic drugs are much higher or in some cases the drugs with complex structures may be totally impossible to synthesize. Therefore the plants especially medicinal plants will always play important role in our life. While new compounds are being discovered from medicinal plants, one can only wonder about potential drugs that have not been discovered yet especially in treating various diseases such as viral diseases, AIDS and cancer; diseases of unknown etiology such as arthritis, muscular dystrophy and Parkinson; self inflicted diseases and also genetic diseases. In view to the fact that only small proportion of tropical forest has been investigated for their chemical compounds and medical potential, the direction should be to do more integrated research in order to find important drugs from new plants sources. We also should preserve and protect these precious resources as our natural heritage.

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