BIOASSAY-GUIDED ISOLATION OF ANTIPLASMODIAL COMPOUNDS FROM TWO MALAYSIAN *KOPSIA* SPECIES

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Prof. Madya Dr. Nor Hadiani Binti Ismail
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Puan,

KELULUSAN PERUNTUKAN BAGI MEMBIAYAI PROJEK-PROJEK SCIENCEFUND DI BAWAH RMKe-9 *CYCLE* 1/2006

Dengan hormatnya perkara di atas adalah dirujuk.

Dimaklumkan Jawatankuasa Kelulusan MOSTI telah mempertimbangkan permohonan Puan untuk membiayai projek penyelidikan di bawah dana ScienceFund *Cycle* 1/2006 pada 20 Oktober 2006.

Sukacita dimaklumkan bahawa projek penyelidikan Puan telah pun diluluskan oleh Jawatankuasa tersebut. Walaubagaimanapun Puan diminta untuk mengambil perhatian atas ulasan yang diberikan oleh Jawatankuasa dalam bahagian Catatan.

Puan juga dikehendaki untuk mengemukakan *Research Agreement* (RA) atau *Memorandum of Understanding* (MoU), yang mana berkenaan, yang telah ditanda tangani kepada IRDC dalam tempoh 3 hari dari tarikh terima surat ini. Dokumen RA / MoU boleh dimuat turun dari laman web eScienceFund.

Pembiayaan keseluruhan yang diluluskan adalah seperti berikut:

Kod Projek	Tajuk	Ketua Projek	Tempoh Projek (Bulan)	Peruntukan Keseluruhan (RM)	Catatan
02-01-01-SF0028	Bioassay-Guided Isolation Of Antiplasmodial Compounds From Two Malaysian Kopsia Species.	Nor Hadiani Binti Ismail	24	150,000	The proposal project is recommended for funding.

Sehubungan dengan itu juga kami mengucapkan tahniah kepada Puan kerana berjaya mendapatkan peruntukan E-Science ini dan semoga berjaya menyiapkan projek penyelidikan ini dengan cemerlang.

5.2 Enhanced Executive Summary

In our search for antiplasmodial compounds from Malaysian plants, two plants from genus *Kopsia* (family Annonaceae) that are *Kopsia terengganensis* and *Kopsia teoi* were investigated. Based on the traditional use of this plant for treating fever, we had carried out the study on the antiplasmodial effect of *Kopsia terengganensis*. This study was undertaken to investigate the possibility of antimalarial activity of *K. terengganensis* and *K. teoi.* by isolating of the phytochemicals from the extracts and active fractions of *K. terengganensis* and *K. teoi*, identifying the structures of the purified phytochemicals using spectroscopic methods and determining the antiplasmodial activity. Chromatographic separation and isolation procedures on *K. terenganensis* yielded the alkaloids larutensine (**1**), eburnamine (**2**), akuammidine (**3**), eburnaminol (**4**), rhazidigenine (**5**), quebrachamine (**6**), isoeburnamine (**7**) and eburnamonine (**8**). From *Kopsia teoi*, rhazimol (**9**), kopsinginol (**10**), kopsigine (**11**), eburnamenine (**12**), akuammiline (**13**), isoeburnamine (**7**) and kopsinol (**14**) were obtained. Compounds coded *5011-14 CRYS, 3P2, RJ-18* and *5035* H_2O showed strong inhibition with IC_{50} values below 5 μg/mL. The strongest inhibition was shown by compound *5011-14 CRYS* with IC_{50} 0.11 μg/mL. Compounds *RAW1* and *5035 H CRYS* showed moderate inhibition with IC_{50} values of 10.09 and 16.72 μg/ml, respectively. Further work on these compounds is being pursued based on the promising activities shown. This data suggests that *K. terengganensis* and *K. teoi* are potential source of antimalarial agents.

5.3 Introduction

New incidences of malaria annually are in the order of 500 million with 1.5 to 2.7 million deaths. The majority of death cases are children (Phillipson, 2001). Resistance of malaria to chloroquine and to other drugs triggers the search for alternative drugs with novel modes of action. Much of the world's population living in areas of endemicity relies almost solely upon traditional herbal remedies and these must be considered as a potential source of new drugs (Kirby, 1996). The prospect of drugs and medicines from plant sources cannot be denied. The first effective anti malarial drug, quinine was isolated from the *Chincona* bark. More recently, the discovery of artemissinin, an unusual sesquiterpene endoperoxide from Chinese anti malarial herb *Artemisia annua* is indeed incentive for further research into plants.

The family Apocynaceae represents about 250 genera and 2000 species of mostly tropical, often poisonous trees, shrubs, woody climbers or herbs producing abundant milky latex. Leaves simple, exstipulate, opposite, spiral or whorled. Secondary nerves often straight, parallel and conspicuous. Flowers showy, often pure white, ornamental, regular and slightly fragrant. Calyx tubes 5-lobed, corolla tubular with 5 typical contorted lobes. Inflorescences: cymes or cymose panicles. Stamens 4 to 5, epipetalous. Ovary superior 2-celled and surrounded by a nectar disc. Fruits: characteristic pairs of berries, drupes or follicles. Seeds sometimes winged or tufted in splitting fruits. Common examples of Apocynaceae are *Plumieria* spp. (frangipani); *Nerium oleander* (oleander), and *Allamanda cathartica* (yellow allamanda) which are widely cultivated as garden or street ornamentals in the tropical world.

Plants in Apocynaceae family have long been known for their medicinal uses. *Aganosma* spp. Are mainly used internally as tonic, diuretic and febrifuge medicines. In Malaysia, decoctions of *Aganosma marginata* roots are taken for the treatment of fever, irregular menses, urinary disorders and after parturition. The bark of *Alstonia scholaris* is widely used as bitter tonic, antidysentry, antidiarrhoeal, antimalarial remedies. *Catharanthus roseus* is mainly used in Southeast Asia, India, South Africa and Queensland as an antidiabetic remedy. In Malaysia, a decoction of the plant is taken for diabetes, dysentery, menstrual pains, hypertension, insomnia and cancer. Crushed leaves are applied to scalds, burns, sores, mumps, swollen neck, tonsillitis and insect bites. In Vietnam, the stalks and leaves are more specifically used for irregular menses, and the roots of the white variety for diabetes and malaria. The