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## **ABSTRACTS**

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Name : Che Puteh Osman

Title : Antiplasmodial Phytochemicals From *Rennellia Elliptica* Korth. And Their Synthetic Analogues

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*Rennellia elliptica* or commonly known as 'segemuk' is popularly dubbed as Malaysian Ginseng probably due to the appearance of its yellow root as well as its many medicinal uses. Preliminary study revealed that its root extract is rich in phenolic compounds and is a potential antioxidant. Thus, the root extract of *R. elliptica* was subjected to extensive chemical and biological studies in order to evaluate its potential as a new botanical drug. The dichloromethane extract showed potent antiplasmodial activity against *Plasmodium falciparum* (3D7) with an IC<sub>50</sub> value of 4.04 µg/ml. When evaluated against *P. berghei* in animal model, the dichloromethane extract gave an ED<sub>50</sub> value of 1.23 µg/ml BW. HPLC analysis of dichloromethane extract showed the presence of 15 compounds and many of them are *Rubia anthraquinones* similar to those reported from genera *Morinda* and *Prismatomeris*. Two new pyranoanthraquinones, rennellianone 115 and 4'-ethyl-2,3-pyrano-1-hydroxy-9,10-anthraquinone 116 and one new 9,10-anthraquinone, 1,2-dimethoxy-6-methyl-9,10-anthraquinone 113 were identified from the root extract of *R. elliptica* along with eleven known anthraquinones. Eleven anthraquinones were later screened for antiplasmodial activity and four anthraquinones displayed potent activity with IC<sub>50</sub> values of less than 2 µM. The new anthraquinone 113 showed strong activity with an IC<sub>50</sub> value of 1.10 µM. Due to the structural significance of 9,10-anthraquinone towards their antiplasmodial activity, a series of 9,10-anthraquinones resembling those from *R. elliptica* were synthesized and structure-activity relationship (SAR) analysis was performed to analyze structural requirement for potent antiplasmodial activity. Thirty two anthraquinones were synthesized using Friedel Craft and O-alkylation reactions. It was found

that symmetrical arrangement of substituents, availability of free carbonyl and free hydroxyl are essential for strong antiplasmodial activity. The new synthetic anthraquinone, 1,3-dihydroxy-6-methyl-9,10-anthraquinone 125 was the most potent anthraquinone with an IC<sub>50</sub> value of 20nM. Some of the potent antiplasmodial anthraquinones showed mild cytotoxicity when evaluated against 3T3 fibroblast cell line, thus they are highly potential for further antiplasmodial study. Two dimensional quantitative SAR (2D-QSAR) study was also performed to examine physico-chemical properties which are essential for antiplasmodial activity of 9,10-anthraquinones. 2D-QSAR analysis was conducted using Vlife MDS 3.5 software. Multiple linear regression and stepwise forward selection method were used to build QSAR model. Dipole moment and SaaCHE-index descriptors gave negative contribution towards the antiplasmodial activity of 9,10-anthraquinones. The present data suggests that *Rennellia elliptica* is a new promising herbal drug for the treatment of malaria and the activity is due to the 9,10-anthraquinones present in the root of the plant.