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PHYTOCHEMICAL STUDY OF SELECTED SPECIES FROM (*RUBIACEAE* AND *GUTTIFERAE*) FAMILIES AND BIOLOGICAL STUDY OF ISOLATED COMPOUNDS AS WELL AS SYNTHETIC SCHIFF BASES COMPOUNDS

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ABSTRACT

A series consisting of 30 novel imidazo [4,5-b]pyridine benzohydrazones derivatives have been synthesized and evaluated for antiglycation and antioxidative activities. Result obtained showed that di and tri-hydroxy substituted compounds showed good activity with compound 25 (140.16 ± 0.36 lM), which is twice lower than Rutin. The results also showed certain correlation between antiglycation and antioxidant activities. Dried leaves of *Garcinia griffithii* and stem bark of *Garcinia malaccensis* (Guttiferae) were extracted under reflux with MeOH and fractionated through vacuum liquid chromatography (VLC) technique using different polarity. Phytochemical investigations have revealed two known xanthones derivatives, 1,3,5,6-Tetrahydroxy-7-(3-methylbut-2enyl) xanthone (**1**) and Rubraxanthone (**2**) and four compounds 5-Hydroxyflavone (**3**), 2'-Hydroxyflavanone (**4**), Paeonol (**5**) and Bergenin (**6**). All spectroscopic data were showed excellent agreement with the previously published results. All those compounds were determined for their ability to inhibit platelet aggregation induced by arachidonic acid (AA), collagen and adenosine diphosphate (ADP). Were showed strong antiplatelet aggregation activities at 100 µg/ml in human whole blood in *vitro*. Both 1,3,5,6-Tetrahydroxy-7-(3-methylbut-2-enyl) xanthone, Rubraxanthone, 5-Hydroxyflavone, Paeonol (**5**) and Bergenin (**6**) showed marked inhibitory effect on platelet aggregation caused by the three inducers. 2'-Hydroxyflavanone (**4**) showed inhibitory effect on platelet aggregation caused by two inducers AA and ADP. The IC_{50} value of all the compounds shows inhibition higher than that of aspirin. The compounds isolated from *Prismatomeris glabra* were determined for cytotoxicity and antiinflammatory activities using THP-1 macrophage cell line. Cell viability was determined using the (MTS) assay. Cells were treated with amentoflavone, 5,7,4'-hydroxyflavonoid and stigmasterol, with various concentration (0- 30 µg/mL) on THP-1 cells for (24, 48 and 72 h) incubation , $\bar{x} \pm$ S.D. (n=3), and then incubated with MTS reagent for 2 h. shows the cell viability at (0-30 µg/mL) of compounds amentoflavone, 5,7,4'- hydroxyflavonoid and stigmasterol. After 24 h of incubation, IC_{50} values for amentoflavone was (21 µg/mL ≡ 38 M), 5,7,4'-hydroxyflavonoid was (18 µg/mL ≡ 66 M) and stigmasterol was (20 µg/mL ≡ 48.5 M). The effects of the compounds (5,7,4'-hydroxyflavonoid, amentoflavone and stigmasterol) on PGE_2, TNF-α and IL-6 expression in human THP-1 derived macrophages cells were pretreated with different concentration (0-30 µg/mL) for 24h. Compounds significantly reduced the production of TNF-α, IL-6 and PGE_2, in dose-dependent manner.

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CHAPTER ONE
INTRODUCTION

1.1 General Background

The plant kingdom has served as one of man's oldest sources of useful drugs. They are remarkable in their ability to produce a vast number of diverse secondary metabolites ranging in chemical complexity and pharmacological activities. The practice of using of traditional medicine since ancient time, but the uses has increased rapidly lately. Southeast Asia region especially Malaysia, Indonesia and Thailand are well known with their traditional herbal medicines. Herbal medicines can be defined as the use of plant that can give benefit in healing and maintaining of human body and source of molecules with therapeutically potential (Atanas *et al.*, 2015). Phytochemicals are very effective and alternative in the management of human infections and diseases e.g. malaria and inflammation. Thus, in recent years, there has been a significant rise in the interest of scientific community to explore the pharmacological activities of medicinal plants and to confirm the claims made about them in folklore medicines (Chah *et al*., 2006). Plant secondary metabolites are a group of naturally occurring compounds classes biosynthesized by differing biochemical pathways whose plant content and regulation is strongly susceptible to environmental influences and to potential herbal predators. From ancient to modern times, herbs and plant have been used as medicinal agents, first only on a folkloric basis and later developed on a scientific basis. Natural products of plant origin offer a wide variety of bioactive compounds that could meet the demand for base compounds of drugs (Kumar *et al*., 2013).

A large production of the drugs used in modern medicine were either directly isolated from plants or synthetically modified from lead compounds of natural origin. Drug discovery is an iterative process of lead discovery (i.e. isolation of bioactive lead compounds from these natural sources) coupled with lead improvement (rational design and synthesis of new analogues to improve pharmacological profiles) and natural products play an important role in drug development programs of pharmaceutical industry. Over 50% of all modern clinical drugs are of natural product origin and higher plants as source of