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Title : PHYTOCHEMICAL STUDIES OF GNETUM MICROCARPUM, GNETUM CUSPIDATUM, CYNOMETRA CAULIFLORA, BOUEA OPPOSITIFOLIA AND THEIR BIOLOGICAL ACTIVITIES

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In the present work, phytochemical and pharmacological studies were conducted on four species of plants from three different families. The studied plant samples were the air-dried lianas of two species from Gnetaceae family which are Gnetum microcarpum Blume and Gnetum cuspidatum Blume and the twigs of Cynometra cauliflora Linn from the family of Fabacaeae and Bouea oppositifolia (Roxb.) Meisn from the family of Anacardiaceae. The aims of this study are to isolate the secondary metabolites from the plants, to propose biogenetic pathway of the new isolated compounds, to determine their DPPH scavenging, PGE2 inhibitory and cytotoxic activities and to study the Structure-Activity Relationship (SAR). The isolation process was done by conventional method of maceration, fractionation, separation and purification using several chromatographic techniques and structural elucidation was based on the spectroscopic data evidences and comparison with reported authentic data. Phytochemicals investigation on the lianas of the two Gnetum species yielded 11 known stilbenoid compounds; resveratrol (1), isorhapontigenin (3), gnetol (10), gnetifolin P (18), gnetofuran C (20), gnetucleistol C (21), cuspidan B (24), ε-viniferin (31), parvifolol D (44), gnemonol M (48) and malaysianol D (388), two new compounds from G. microcarpum characterized as malaysianol E (25), malaysianol F (389) and one new compound from G. cuspidatum, namely malaysianol G (399). Phytochemicals investigation on C. cauliflora and B. oppositifolia gave 16 known flavonoid compounds; naringenin (263) and eriodictyol (262) were obtained from both species; flavone apigenin, acacetin, luteolin, luteolin 3',5 dimethyl ether, 3',4',7-trihydroxyflavone, 4',7-dihydroxyflavone (392-397) and 5,7-dihydroxychromone (391) from C. cauliflora; chalcone isoliquiritigenin (398), flavanone liquiritigenin and butin (399-400), flavanol taxifolin (260), fustin, garbanzol (401-402) and aurone sulfuretin (403) from B. oppositifolia. Both flavonoids and stilbenoids were derived from the combination of shikimate pathway and acetate pathway from a cinnamoyl-CoA starter unit and three molecule of malonyl-CoA extender unit to form intermediate polyketide. The enzyme stilbene synthase (STS) gave resveratrol which then undergo polymerization to produce larger stilbenoid, while chalcone synthase (CS) gave chalcone which then act as precursor for a vast range of flavonoid derivatives. In the DPPH assay, gnemonol M (48) and fustin (260) displayed good scavenging activity with IC50 of 30.07 and 23.93 μM, respectively, higher than that of standard trolox (IC50 83.22 μM). In the PGE2 inhibition assay, gnemonol M (48) and 4',7-dihydroxyflavone (397) exhibited significant activity with IC50 of 1.15 and 3.39 μM, respectively, comparable to the standard, indomethacin (IC50 1.29 μM). For cytotoxicity, all the tested compounds were found to be, either moderate, weak or not cytotoxic against HCT116 cancer cell line. In the SAR study of DPPH scavenging, the number of hydroxyl groups and the presence of an electron donating group are essential for stilbenoids, while the catechol moeity is in the top priority to exert flavonoids activity. Meanwhile, both type of compounds required the substituents which will contribute to their hydrophobicity and balance number of hydroxyl group in their structure in order to exert better PGE2 inhibitory activity.