UNIVERSITI TEKNOLOGI MARA

THE DOCTORAL RESEARCH ABSTRACTS

Volume: 10, Issue 10 October 2016

TENTH ISSUE

INSTITUTE of GRADUATE STUDIES

IGS Biannual Publication

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Title : HPLC METHOD DEVELOPMENT & STRUCTURAL ELUCIDATION OF ANTI-PROLIFERATIVE QUASSINOIDS FROM *Quassia borneensis* NOOT. (SIMAROUBACEAE)

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Bitter quassinoids have been reported to possess numerous biological activities. They are degraded triterpenoids classified according to their basic skeletons; C_{18}, C_{19}, C_{20}, C_{22}, C_{25}. Currently, more than 200 quassinoids have been isolated from genus *Quassia, Brucea, Soulamea, Eurycoma, Picrolemnia* and others. A study on *Quassia borneensis* Noot. (Simaroubaceae) (Qb) for its anti-proliferative active quassinoids using a developed and validated high performance liquid chromatography (HPLC) isolation method is appropriate for data gathering. In addition, a total synthesis exploration of canthin-6-one would provide information regarding its mechanism and influential factors for viability study. The study was accomplished by extracting powdered bark and root Qb by cold maceration and soxhlet in methanol for yield comparison. The methanol extracts were partitioned to acquire n-hexane, chloroform and aqueous fractions. They were tested for their anti-proliferative activity based on MTS assay using HL-60 cell line. Later, chloroform and aqueous fractions were subjected to isolation and purification with HPLC. Then, pure isolates were structurally elucidated with liquid chromatography-mass spectroscopy (LC-MS) and nuclear magnetic resonance (NMR). In addition, the mass profile of active fractions was measured using liquid chromatography-mass spectrometer triple quadrupole time of flight (LC-MSQTOF). Lastly, pure quassinoid compounds were subjected to MTT assay. In a biomimetic total synthesis attempt, canthin-6-one of Simaroubaceae was pursued through carboxyl-mediated approach following the method of Czerwinski et al. (2003). The positively identified sample was collected at Tawai Forest Reserve, Telupid, Sabah, Malaysia. Qb was successfully extracted and partitioned. Later, the anti-proliferative activity of hexane (Q_1-Q_4), chloroform (Q_5-Q_8) and aqueous (Q_9-Q_{12}) fractions were found active except Q_2 while Q_8 was found to be most active at 0.2 µg/mL. HPLC isolation method was developed and validated in a chromatographic system consists of Zorbax SB C-18 250 mm x 4.6 mm, 5 µm stationary phase with H_2O:ACN as its mobile phase flowing at 0.6 mL/min in step gradient elution mode of 0-100-0 % ACN with 10 % increment in an interval of five-minute for 50 minutes and 50% decrement twice in 10 minutes as post equilibration. The acquired values of selectivity factor (α), retention factor (k'), number of theoretical plates (N) and resolution (R) are at optimum indicating good separation and column performance. A peak at retention time of 21.7 minute was chosen which gives standard deviation of σ=0.04 at N=5, indicating chromatographic system usability. Thus, Q_8 was fractionated due to its best HPLC profile and anti-proliferative activity. Five quassinoids and one canthin-6-one were successfully structurally elucidated and identified as glaucarubolone (**10**), chaparrinone (**8**), holacanthone (**9**), glaucarubinone (**11**), ailanthinone (**102**) and canthin-6-one (**7**) in reference to past reports. The mass profile of chloroform fractions implied that the root part contains more quassinoids while soxhlet procedure would yield more extract. Glaucarubolone, chaparrinone, holacanthone and ailanthinone were found to be significantly active at IC_{50} of 6.8, 7.2, 5.6 and 2.8 µM respectively. As new data, ailanthinone was found to be comparably active to doxorubicin which was tested to be active at 0.9 µM. The synthesis work of canthin-6-one yielded 64.51%, 67.05%, 48.86%, 33.56% and 0.6% of Nb, Nbb, Nbc, Nbd and Nbe respectively. A schematic mechanism of PSR in carboxyl-mediated synthesis of canthin-6-one and its influential factors were discussed. It is suggested that further isolation should be performed to Qb as more quassinoids might be found.