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Name : **Fatimah Binti Salim**
Title : **Phytochemicals From Malaysian *Uncaria Longiflora* Var. *Pteropoda* (Miq.) Ridsd. And Their Activities Against The Human Neuroblastoma Sh-Sy5y Cell Line**
Faculty : **Applied Science**
Supervisor : **Associate Prof. Dr. Rohaya Ahmad (MS)**

Phytochemical investigation on the methanolic extract of the stems and leaves of Malaysian *Uncaria longiflora* var. *pteropoda* (Miq.) Ridsd. was carried out with the aim of isolating and identifying their chemical constituents. The extract of the stems was subjected to acid-base extraction, while the leaf extract was successively triturated with hexane, CHCl3, EtOAc and MeOH. The crude extracts were then further fractionated and purified using extensive chromatographic techniques. Structural elucidation of the phytochemicals was based on spectroscopic evidence and comparison with literature values. The absolute configurations of the new chiral compounds were established by comparing the CEs of the experimental ECD spectra to the simulated ECD values, as well as to the ECD spectra of the known related chiral compounds in hand. A total of thirty-two phytochemicals were isolated of which six are new and nine are common to the leaves and stems. Phytochemicals isolated from the stem extract include two new pentacyclic oxindole alkaloids (POAs) deduced as rauniticine-*allo*-oxindole B **ULS1** and rauniticinic-*allo* acid B **ULS2**, five known POAs (isopteropodine **ULS3**, pteropodine **ULS4**, isopteropodic acid **ULS5**, uncarine F **ULS6** and speciophylline **ULS7**), two coumarins (scopoletin **ULS8** and 4-hydroxy-3,7-dimethoxycoumarin **ULS10**), one phenyl compound (4-hydroxybenzoic acid methyl ester **ULS9**) and three terpenes (stigmasterol **ULS11**, β-sitosterol **ULS12** and β-sitostenone **ULS13**). Phytochemistry on the leaf extract successfully afforded three new alkaloids named as 2-oxosecologanine **ULL5**, isoformosaninol **ULL6** and formosaninol **ULL7**, one new flavonoid deduced as uncariechin **ULL14**, four known POAs (isopteropodine **ULL1**, pteropodine **ULL2**, uncarine F **ULL3** and isopteropodic acid **ULL4**), two flavonoids [(-)-*epi*-afzalechin **ULL12** and (-)-*epi*-catechin **ULL13**], two coumarins (scopoletin **ULL8** and 3,4-dihydroxy-7-methoxycoumarin **ULL11**), two phenyl compounds (4-hydroxybenzoic acid methyl ester **ULL9** and 4-hydroxy-benzaldehyde **ULL10**) and five terpenes (β-tocopherol **ULL15**, 6,10,14-trimethyl-2-pentadecanone **ULL16**, stigmasterol **ULL17**, β-sitosterol **ULL18** and β-sitostenone **ULL19**). Seven phytochemicals of sufficient quantities, comprising five alkaloids (isopteropodine, pteropodine, isopteropodic acid, uncarine F and rauniticine-*allo*-oxindole B) and two flavonoids [(-)-*epi*-afzalechin and (-)-*epi*-catechin] were further tested for their cytotoxic, neurotoxic, as well as neuroprotective activities against human neuroblastoma SH-SY5Y cell line. The alkaloid uncarine F was found to be both cytotoxic and neurotoxic against the cancer and normal human neuroblastoma SH-SY5Y cell lines, while the alkaloid pteropodine was found to be neurotoxic, both at a high concentrations. As antioxidants, the flavan-3-ols, (-)-*Epi*-afzalechin and (-)-*epi*-catechin possessed neuroprotective properties against the H2O2-induced toxicity on normal cell line with cell viabilities ranging from 75-88% compared to 50-60% cell viability following treatment with H2O2 alone. The alkaloids isopteropodine and isopteropodic acid, and the new alkaloid rauniticine-*allo*-oxindole B also consistently showed even higher protective properties with cell viabilities of 83-96%, thus suggesting their potential as an anti-neurodegenerative agent. With respect to the cytotoxic, neurotoxic and neuroprotective activities of the pure compounds tested, it may be suggested that the toxic properties of both the stem and leaf extracts of the plant at the maximum concentration against the cancer and normal human neuroblastoma SH-SY5Y cell lines may be due to the alkaloid uncarine F, and not the synergistic effect among the constituents.