Novel cytotoxic benzophenones from Garcinia paucinervis identified by UPLC-QTOF-MSE

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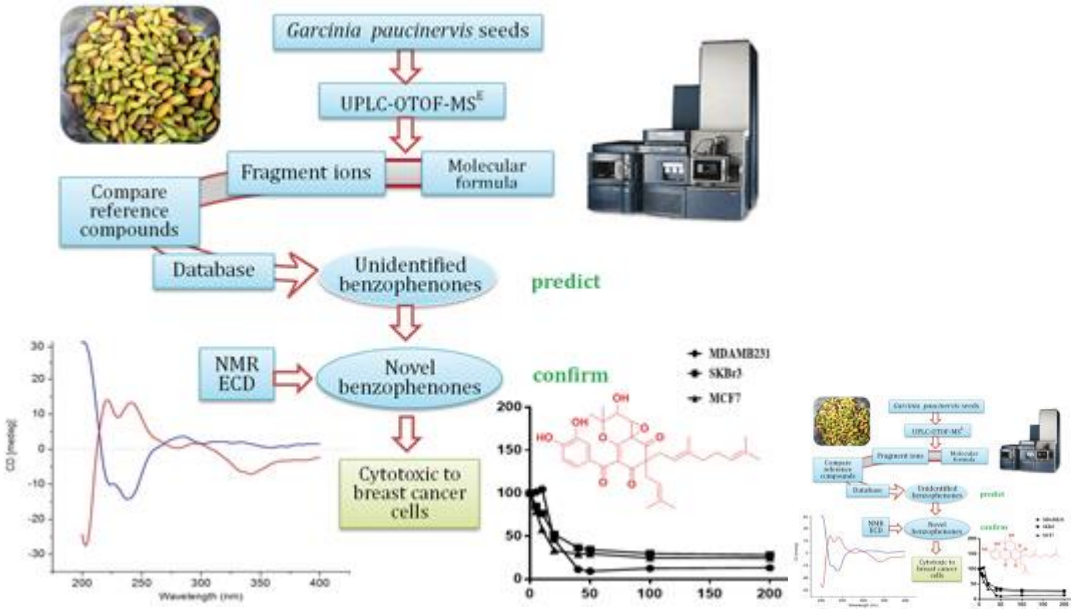
Most of benzophenones from *Garcinia* species are two classes of compounds, mainly including polyisoprenylated benzophenones (PIBs) and polycyclic polyprenylated acylphloroglucinols (PPAPs), and their structures usually couple with a number of prenyl or geranyl groups, hydroxyl groups, and complex ring systems [1]. The PIBs and PPAPs have exhibited important biological activities including cytotoxic effects on human cancer cell lines, antibacterial, anti-HIV, anti-inflammatory, and antioxidant activities [2]. Benzophenone derivatives from*Garcinia* species are recognized for their structural diversity and significant bioactivity, leading to the discovery of many new compounds [3].

Garcinia paucinervis (Clusiaceae) is endemic to China. It is a valuable hardwood among *Garcinia* species, and the roots, leaves and bark can also used as a traditional medicine for the treatment of carbuncles, bruises and burns [4]. In the past decade, our ethnobotanical team has isolated and identified a number of *Garcinia*prenylated benzophenones with cytotoxic activity [5, 6]. We continue to be interested in cytotoxic benzophenones from other *Garcinia* species, to better understand structure activity relationships (SAR) of benzophenones. In this paper, an UPLC-QTOF-MS^E strategy was used to identify novel benzophenone derivatives from the fractions of *G*. *paucinervis*.



Thirty-one peaks containing benzophenone derivatives, and 12 of these peaks contain compounds with unidentified. Based on UPLC-QTOF-MS^E fragment ions analysis on the peaks of nine *G. paucinervis* fractions, six target peaks were considered unknowns of interest. They were separated by semi-preparative HPLC to obtain five novel benzophenones, named as paucinones E-I. Their structures are assigned by the means of NMR, MS, IR, and ECD spectroscopy. The novel benzophenones were evaluated for cytotoxicity against human breast cancer cells using the WST assay. Paucinone G and H were the most cytotoxic against breast cancer cell lines (MDA-MB-231, SKBR3, and MCF7), with the IC_{50} values in the range of 15.70 – 23.23 μM and 10.34 – 19.02 μM, respectively, suggesting they should be further explored as potential drugs for treating breast cancer. This new technique, UPLC-QTOF-MS^E-based dereplication, could be a powerful tool for discovering bioactivity of natural products.

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