Design, Synthesis and Cytotoxic Effects of Curcumin Derivatives on K562, MCF-7 and MDA-MB-231 Cancer Cell Lines

Muhammad Nadeem Akhtar[*1], Siti Noor Hajar Zamrus[1], Swee Keong Yeap[2], Noorjahan Banu Alitheen[3], Seema Zareen[1]

[1]Faculty of Industrial Sciences & Technology, University Malaysia Pahang, 26300 Gambang, Malaysia
[2]Institute of Bioscience, Universiti Putra Malaysia, UPM Serdang 43400, Selangor Darul Ehsan, Malaysia
[3]Faculty of Biotechnology and Bimolecular Sciences, Universiti Putra Malaysia, Serdang, Selangor Darul Ehsan, Malaysia

*Corresponding author: nadeemupm@gmail.com

Curcumin is one of the leading compound extracted from the dry powder of *Curcuma longa* (Zingiberaceae family), which possess several pharmacological properties. However, *in vivo* administration exhibited limited applications in cancer therapies. Twenty four curcumin derivatives were synthesized, comprising cyclohexanone **1-10**, acetone **11-17** and cyclopentanone **18-24** series. All the curcuminoids were synthesized by acid or base catalysed Claisen Schmidt reactions in which the β-diketone moiety of curcumin was modified with mono-ketone. These curcuminoids **1-24** were screened against HeLa, K562, MCF-7 (an estrogen-dependent) and MDA-MB-231 (an estrogen-independent) cancer cell lines. Among them, acetone series **11-17** were found to be more selective and potential cytotoxic agents. Compound **14** exhibited activity (IC_{50} = 3.02±1.20 and 1.52±0.60) against MCF-7 and MDA-MB-231 breast cancer cell lines. Among the cyclohexanone series, compound **4** exhibited potential cytotoxicity (IC_{50} = 11.04±2.80, 6.50±01.80, 8.70±3.10 and 2.30±1.60) against four proposed cancer cell lines, respectively. In addition, the spectral data of (2*E*,6*E*)-2,6-*bis*(2-methoxybenzylidene)cyclohexanone (**1**) was reported for the first time. Curcuminoids with diferuloyl (4-hydroxy-3-methoxycinnamoyl) moiety with mono carbonyl group exhibited potential cytotoxic properties.

Keywords: curcuminoids synthesis; breast cancer cell lines; SARs; (2*E*,6*E*)-2,6-*bis*(2-methoxybenzylidene)cyclohexanone