Design, synthesis and cytotoxic effects of curcuminoids on HeLa, K562, MCF-7 and MDA-MB-231 cancer cell lines

ABSTRACT

Background

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.

Results

Twenty-four curcumin derivatives have synthesized, which comprises cyclohexanone 1–10, acetone 11–17 and cyclopentanone 18–24 series. All the curcuminoids were synthesized by the acid or base catalyzed Claisen Schmidt condenstion reactions, in which 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. The compound 14 was exhibited ($IC50 = 3.02 \pm 1.20$ and 1.52 ± 0.60 μg/mL) against MCF-7 and MDA-MB-231 breast cancer cell lines. Among the cyclohexanone series, the compound 4 exhibited ($IC50 = 11.04 \pm 2.80$, 6.50 ± 01.80, 8.70 ± 3.10 and 2.30 ± 1.60 μg/mL) potential cytotoxicity against four proposed cancer cell lines, respectively. All the curcucminoids were characterized with the detailed 1H NMR, IR, UV–Vis, and mass spectroscopic techniques. The structure of compound 4 was confirmed by using the single X-ray crystallography. Additionally, we are going to report the first time spectral data of (2E,6E)-2,6-bis(2-methoxybenzylidene)cyclohexanone (1). Structure–activity relationships revealed that the mono-carbonyl with 2,5-dimethoxy substituted curcuminoids could be an essential for the future drugs against cancer diseases.

Conclusions

Curcuminoids with diferuloyl(4-hydroxy-3-methoxycinnamoyl) moiety with mono carbonyl exhibiting potential cytotoxic properties. The compound 14 was exhibited ($IC50 = 3.02 \pm 1.20$ and 1.52 ± 0.60 μg/mL) against MCF-7 and MDA-MB-231 breast cancer cell lines.

Keyword: Curcuminoids synthesis; Breast cancer cell lines; SARs; (2E, 6E)-2,6-bis(2-methoxybenzylidene) cyclohexanone