A phenylbutenoid dimer, cis-3-(3′,4′-dimethoxyphenyl)-4-[(E)-3′′′,4′′′-dimethoxystyryl] cyclohex-1-ene, exhibits apoptogenic properties in T-acute lymphoblastic leukemia cells via induction of p53-independent mitochondrial signalling pathway

ABSTRACT

The current study was designed to evaluate the in vitro cytotoxicity effect of a phenylbutenoid dimer, cis-3-(3′,4′-dimethoxyphenyl)-4-[(E)- 3‴,4‴-dimethoxystyryl]cyclohex-1-ene (ZC-B11) isolated from the rhizome of Zingiber cassumunar on various cancer cell line, and normal human blood mononuclear cells, and to further investigate the involvement of apoptosis-related proteins that leads, to the probable pathway in which apoptosis is triggered. Cytotoxicity test using MTT assay showed selective inhibition of ZC-B11 towards T-acute lymphoblastic leukemia cells, CEMss, with an ICvalue of 7.11 ± 0.240 g/mL, which did not reveal cytotoxic effects towards normal human blood mononuclear cells (IC> 50 g/mL). Morphology assessments demonstrated distinctive morphological changes corresponding to a typical apoptosis. ZC-B11 also arrested cell cycle progression at S phase and causes DNA fragmentation in CEMss cells. Decline of mitochondrial membrane potential was also determined qualitatively. In the apoptosis-related protein determination, ZC-B11 was found to significantly upregulate Bax, caspase 3/7, caspase 9, cytochrome c, and SMAC and downregulate Bcl-2, HSP70, and XIAP, but did not affect caspase 8, p53, and BID. These results demonstrated for the first time the apoptogenic property of ZC-B11 on CEMss cell line, leading to the programmed cell death via intrinsic mitochondrial pathway of apoptosis induction.

Keyword: Phenylbutenoid dimer; Acute lymphoblastic leukemia; Antileukemic agent.