**INTRODUCTION**

Osteosarcoma is a malignant bone tumor prevalent in adolescents. Although chemotherapy is effective in improvement of patient survival, the prognosis is poor. *Toona sinensis* Roem. (Meliaceae) is a deciduous tree of unusual form and texture, which grows mostly in Asia, especially in China. *T. sinensis* is the only Toona species in which the leaflet margins can be serrated to become serrulate. Our previous studies indicated that *Toona Sinensis* leaf aqueous extracts (TSLs) showed potent anti-proliferation effect on many types of cancer, including lung, melatonin, ovarian, oral, colon and liver. We preliminarily found that TSL showed a potential anti-survival effect on osteosarcoma cells while the mechanism remains well investigated. In this study, the effects of TSL and its mechanism were examined.

**METHODS**

Three osteosarcoma cell lines, SaOs-2, U2Os and MG-63, were used in this study. Normal primary human osteoblasts (hOBs) were also used in this study for comparison. Cell viability, cytotoxicity, apoptosis/necrosis staining and apoptosis related protein levels were examined by using MTT assay, lactate dehydrogenase (LDH) leakage, flow cytometry and Western blot, respectively.

**RESULTS**

The results showed that treatment of fraction of *Toona sinensis* (TSL-1) for 24 hrs resulted in significant inhibition of cell viability in MG-63, SaoS-2 and U2OS osteosarcoma cell lines (Fig. 1A), while that did not significantly cause the suppression of normal hOB cell viability (Fig. 1B). We further found that treatment of TSL-1 for 24 and 48 hrs significantly elevated the LDH leakage, and induced apoptosis and necrosis in MG-63 cells. Furthermore, the treatment of TSL-1 increased PARP cleavage in MG-63 cells. Most importantly, our results showed that TSL-1 up-regulated Bax/Bcl-2 protein ratio in MG-63 cells.

**DISCUSSION**

In conclusion, our study indicates that TSL-1 inhibited cell viability in osteosarcoma cell lines, but not in normal osteoblasts. Furthermore, our results showed that TSL-1 increased PARP cleavage and Bax/Bcl-2 protein ratio, indicating that the anti-survival mechanism might highly relate to apoptosis induction. In conclusion, our result indicates that TSL-1 inhibited cell survival of osteosarcoma, but not normal osteoblasts, suggesting that TSL-1 could be used as anticancer drug for alleviating osteosarcoma survival, but not affect normal osteoblast functions. The effect of TSL-1 on human osteosarcoma Xenografts will be further investigated.

**Figure 1**

A. 

B. 

**Figure 2**

A. 

B. 

**Figure 3**

A. 

B.