Selective pro-apoptotic and anti-proliferative effects of nisin ZP against MG-63 osteosarcoma cells

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ABSTRACT

Osteosarcoma (OS), the most common primary bone cancer, has been explored for novel therapy due to its difficult-to-treat nature. Nisin, a known bacteriocin used as a food preservative, has shown promising anticancer effects in several in vitro and animal cancer studies. However, data on its OS cell selective killing effect is scarce. Aim: This study investigates the selectivity of nisin ZP (NZP) as a potential anticancer agent against MG-63 OS cells. Method: Monolayered culture of MG-63 OS and hFOB1.19 osteoblast cells at 37°C, 5% CO2 were treated with 543.8 µg/ml NZP followed by annexin and cell death assay, BAX and BCL-2 protein expression analysis via ELISA, and cell cycle assay analysis. Results: At 48 hours, the annexin assay revealed 59.18±2.56% live cells in NZP-treated MG-63, which is significantly lower compared to hFOB1.19 (85.25±1.02%) (p=0.04). In contrast, 38.73±1.51% of early apoptotic cells were recorded in NZP-treated MG-63, which is significantly more abundant than hFOB1.19 cells (14.00±5.80%) (p=0.002). ELISA showed significantly higher expression of BAX protein in NZP-treated MG-63 compared to non-treated MG-63 (p=0.005) and NZP-treated hFOB1.19 (p=0.016). However, no significant difference in the expression of BCL-2 between NZP-treated MG-63 and hFOB1.19 (p=0.665), as well as between the NZP-treated MG-63 and control. The percentage of MG-63 cells in the G2/M phase of the cell cycle is significantly higher when treated with NZP (33.50±1.35%) compared to control (15.8±2.31) (p<0.001) and NZP-treated hFOB1.19 (10.30±6.88%) (p=0.005). Conclusion: Higher abundance of early apoptotic cells in NZP-treated MG-63 is supported by the significant co-expression of pro-apoptotic protein, BAX and low anti-apoptotic protein, BCL-2. Increased cell cycle arrest at G2/M phase in NZP-treated MG-63 reduces cancer cell proliferation. This study demonstrates the selectivity of nisin as a pro-apoptotic and anti-proliferative agent for OS, thus offering potential as an anticancer.

Keywords: Osteosarcoma, nisin, apoptosis, cell cycle, BAX, BCL-2, MG-63