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Pharmacological evaluation of an advanced formulation of curcumin to prevent breast cancer bone metastasis

Iram Irshad[1], Ramin Rohanizadeh[2] and Pegah Varamini[1]
[1]The University of Sydney, Australia
[2]MacGill University, Canada

This study aims to investigate the preventative effects of breast cancer bone metastasis by curcumin nanoparticles modified with bisphosphonate. We formulated alendronate conjugated curcumin nanoparticles (Aln-Cur-NPs) and curcumin nanoparticles (Cur-NPs) without alendronate. The loading capacity was determined and was shown to be consistent in different batches of Aln-Cur-NPs and Cur-NPs prepared at different times and were found to be 4% and 5.7%, respectively. *In vitro* antitumor activity of the curcumin nanoparticles with/without alendronate was evaluated in three different breast cancer cells (as IC50 values). A significantly higher antitumor activity was observed for Aln-Cur-NP compared to Cur-NP with IC50 values of 13.9, and 7.7 μg/mL for MCF-7, MDA-MB-231 and SKBR, respectively. This study indicated the enhanced anticancer activity of curcumin nanoparticles with the addition of alendronate to curcumin, which strongly supports the synergistic effect of curcumin/bisphosphonates combination considering the similar amount up-taken by the cancer cells for both nanoparticle formulations. The impact of nanoparticles on the viability of MDA-MB-231 cells was also investigated using recording time lapse image technology by IncuCyte over two days. It was demonstrated that the uptake of raw curcumin was much less and it precipitated outside the cells while, curcumin encapsulated in nanoparticles was effectively up-taken by the cancer cells. In the same experiment, we observed that Aln-Cur-NPs affected the viability of the cells more effectively than Cur-NPs and raw curcumin. The uptake of Aln-Cur-NPs and Cur-NPs in nucleus and cytoplasm in MDA-MB-231after 24 hours of treatment was revealed by Confocal Scanning Laser Microscopy. The qualitative analysis of confocal images showed higher uptake for alendronate-modified nanoparticles (Aln-Cur-NPs) compared to raw curcumin and no uptake for the untreated (PBS) control was observed. The effect of our nanoparticles on the release of Parathyroid Hormone Related Protein (PTHrP) by MDA-MB-231 cell lines was determined by PTHrP ELISA assay for quantitative measurement of human PTHrP concentration released by MDA-MB-231 cells. PTHrP release is increased by cancer cells in bone microenvironment and promotes osteoclastic activity and contributes to osteolytic bone metastases. Its role in primary tumor development is not clear yet but normally it contributes to the development of breast. MDA-MB-231 cells were treated with alendronate-modified and non-modified curcumin nanoparticles. Results clearly showed reduction in the release of PTHrP by MDA-MB-231 cell lines and hence there is possibility of reducing the chances of metastases to the bone. The results demonstrated that Aln-Cur-NPs have more reducing effect on the release of PTHrP compared to both raw curcumin and Cur-NPs. These preliminary data suggest Aln-Cur-NPs can offer promises in preventing and treating breast cancer bone metastases.

Biography

Iram Irshad is a researcher in The University of Sydney, Australia. His research interest focuses on breast cancer.

iirs9221@uni.sydney.edu.au

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