

## Postbiotic metabolites produced by *Lactobacillus plantarum* strains exert selective cytotoxicity effects on cancer cells

### ABSTRACT

**Background:** *Lactobacillus plantarum*, a major species of Lactic Acid Bacteria (LAB), are capable of producing postbiotic metabolites (PM) with prominent probiotic effects that have been documented extensively for rats, poultry and pigs. Despite the emerging evidence of anticancer properties of LAB, very limited information is available on cytotoxic and antiproliferative activity of PM produced by *L. plantarum*. Therefore, the cytotoxicity of PM produced by six strains of *L. plantarum* on various cancer and normal cells are yet to be evaluated. **Methods:** Postbiotic metabolites (PM) produced by six strains of *L. plantarum* were determined for their antiproliferative and cytotoxic effects on normal human primary cells, breast, colorectal, cervical, liver and leukemia cancer cell lines via MTT assay, trypan blue exclusion method and BrdU assay. The toxicity of PM was determined for human and various animal red blood cells via haemolytic assay. The cytotoxicity mode was subsequently determined for selected UL4 PM on MCF-7 cells due to its pronounced cytotoxic effect by fluorescent microscopic observation using AO/PI dye reagents and flow cytometric analyses. **Results:** UL4 PM exhibited the lowest IC<sub>50</sub> value on MCF-7, RG14 PM on HT29 and RG11 and RI11 PM on HL60 cell lines, respectively from MTT assay. Moreover, all tested PM did not cause haemolysis of human, dog, rabbit and chicken red blood cells and demonstrated no cytotoxicity on normal breast MCF-10A cells and primary cultured cells including human peripheral blood mononuclear cells, mice splenocytes and thymocytes. Antiproliferation of MCF-7 and HT-29 cells was potently induced by UL4 and RG 14 PM respectively after 72 h of incubation at the concentration of 30% (v/v). Fluorescent microscopic observation and flow cytometric analyses showed that the pronounced cytotoxic effect of UL4 PM on MCF-7 cells was mediated through apoptosis. **Conclusion:** In conclusion, PM produced by the six strains of *L. plantarum* exhibited selective cytotoxic via antiproliferative effect and induction of apoptosis against malignant cancer cells in a strain-specific and cancer cell type-specific manner whilst sparing the normal cells. This reveals the vast potentials of PM from *L. plantarum* as functional supplement and as an adjunctive treatment for cancer.

**Keyword:** *Lactobacillus plantarum*; Postbiotic metabolites; Cytotoxicity; Antiproliferation; Haemolysis; Apoptosis