

Prophylactic Effects of Dairy *Kluyveromyces marxianus* YAS through Overexpression of BAX, CASP 3, CASP 8 and CASP 9 on Human Colon Cancer Cell Lines

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Abstract : Colorectal cancer (CRC) is one of the most prevalent cancers and intestinal microbial community plays an important role in colorectal tumorigenesis. Probiotics have recently been assessed as effective anti-proliferative agents and thus this study was performed to examine whether CRC undergo apoptosis by treating with isolated Iranian native dairy yeast, *Kluyveromyces marxianus* YAS, secretion metabolites. The cytotoxicity assessments on cells (HT-29, Caco-2) were accomplished through 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay as well as qualitative DAPI (4',6-diamidino-2-phenylindole staining) and quantitative (flow cytometry assessments) evaluations of apoptosis. To evaluate the main mechanism of apoptosis, Real time PCR method was applied. *Kluyveromyces marxianus* YAS secretions (IC₅₀) showed significant cytotoxicity against HT-29 and Caco-2 cancer cell lines (66.57 % and 66.34 % apoptosis) similar to 5-Fluorouracil (5-FU) while apoptosis only was developed in 27.57 % of KDR normal cells. The prophylactic effects of *Kluyveromyces marxianus* (PTCC 5195), as a reference yeast, was not similar to *Kluyveromyces marxianus* YAS indicating strain dependency of bioactivities on CRC disease prevention. Based on real time PCR results, the main cytotoxicity is related to apoptosis phenomenon and the core related mechanism is depended on the overexpression of BAX, CASP 9, CASP 8 and CASP 3 inducing apoptosis genes. However, several investigations should be conducted to precisely determine the effective compounds to be used as anticancer therapeutics in the future.

Keywords : anticancer, anti-proliferative, apoptosis, cytotoxicity, yeast

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