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Evaluation of the potential application of recombinant frutalin in cancer therapeutics

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Keywords: Cytotoxicity, Human breast cancer (T47D cell line), Human cervical cancer (HeLa cell line), Lectin, Recombinant frutalin

Abstract

Frutalin is the alpha-D-galactose-binding jacalin-related lectin expressed in breadfruit seeds (*Artocarpus incisa*). This lectin may be used in cancer diagnostics/therapeutics due to its potential ability to recognise specific carbohydrates expressed in cancer cells membranes and/or cells surface receptors. However, the extraction of frutalin from its natural source has several disadvantages, as it is a time-consuming process, with relative low yields, and typically results in a heterogeneous mixture of different natural isoforms. Frutalin isoforms may have distinct biological properties leading to undesired results variability when applied in cancer diagnosis and therapy. In order to overcome these limitations frutalin was expressed and produced in the *Pichia pastoris* expression system [1]. The ability of recombinant frutalin to recognise human tumour cells has already been demonstrated in immunohistochemical studies conducted with human prostate tissues removed from patients by surgery. Moreover, it showed higher capacity than native frutalin to differentiate malign from benign prostate diseases, highlighting its potential diagnostic application, namely as a bio-marker of prostate cancer [2]. In this work, the ability of recombinant and native frutalin to inhibit cancer cells proliferation was studied *in vitro* and the results obtained for each lectin were compared. Recombinant and native frutalin demonstrated a similar considerable potential therapeutic application, as both lectins strongly reduced cancer cells growth and induced their death. Native frutalin inhibited irreversibly the proliferation of HeLa (human breast cancer) and T47D cells (human cervical cancer) in a time- and dose-dependent manner. Recombinant frutalin, which has less carbohydrate-binding affinity than native frutalin, performed identical cytotoxicity on these cells, at similar concentrations. The two lectins also promoted visible morphological changes in cancer cells. These results indicate that the anti-cancer activity of frutalin is not dependent on its sugar-binding affinity. Therefore, recombinant frutalin might be used as a potential anti-cancer agent, in alternative to native frutalin.

[1] Oliveira C, Felix W, Moreira RA, Teixeira JA, Domingues L. (2008). Protein Expr Purif 60: 188-193.
[2] Oliveira C, Teixeira JA, Schmitt F, Domingues L. (2009). Submitted.