mechanism of action. HepG2 cells were treated with ginsenoside Rd at different concentrations. Scratch wound and Boyden chamber assays were used to determine the effects of ginsenoside Rd on the migration and invasiveness of HepG2 cells, respectively. The molecular mechanisms by which ginsenoside Rd inhibits the invasion and migration of HepG2 cells were investigated by RT-PCR, Western blotting, gelatin zymography, and treatment with inhibitors of MAPK signaling. Immunofluorescence analysis was carried out to evaluate the effect of ginsenoside Rd on focal adhesion formation in HepG2 cells. Treatment with ginsenoside Rd dose- and time-dependently inhibited the migration and invasion of HepG2 cells. It was achieved by reducing the expression of MMP-1, MMP-2, and MMP-7, by blocking MAPK signaling by inhibiting the phosphorylation of ERK and p38 MAPK, and by inducing focal adhesion formation and modulating vinculin localization and expression. Treatment of HepG2 cells with ginsenoside Rd significantly inhibited metastasis, most likely by blocking MMP activation and MAPK signaling pathways involved in cancer cell migration. This study may be useful for the development of novel chemotherapeutic agents for the treatment of malignant cancers. [This work was supported by the Priority Research Centers Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (Project No. 2010-0020141) to S-G Lee].

Keywords: Ginsenoside Rd, Anti-metastasis, MMP, Vinculin

doi:10.1016/j.ejphar.2011.09.233

Quercetin synergistically induces sensitivity to 5-fluorouracil through p53 modulation in colorectal cancer cells

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Colorectal tumors (CRC) with microsatellite instability (MSI) show resistance to chemotherapy with 5-fluorouracil (5-FU), the most widely used pharmacological drug for CRC treatment. The aims of this study were to identify compounds that increase sensitivity of MSI CRC cells to 5-FU and characterize their dependence on the p53 status of the cells.

Two MSI human CRC derived cell lines were used: CO115 wild-type for p53 and HCT15 that harbors a p53 mutation. The sensitivity of these cells to 5-FU was evaluated by TUNEL assay and the effects on apoptosis induction of co-incubation of the flavonoids, quercetin (Q) or luteolin (L), with 5-FU were characterized. The mechanisms of apoptosis induction were assessed by western blot and p53 mediated effects confirmed by small interference RNA (siRNA) in CO115 and in HCT116 wt and p53 knockout cells.

Our results demonstrate that CO115 is more sensitive to 5-FU than the p53 mutated HCT15. Additive effects on apoptosis were shown for L (in both cell lines) and Q (in HCT15). In CO115 Q synergistically induced apoptosis with 5-FU. Apoptosis induction was caspase dependent in CO115 cells but not in HCT15 cells. Both flavonoids increased p53 expression in both cell lines, an effect particularly remarkable for Q. The synergistic effect of Q and 5-FU in CO115 involved the activation of the mitochondrial pathway with an increase in the expression of cleaved caspase 9 and 3 and PARP, as well as a decrease in Bcl-2 expression. Importantly, knockdown of p53 by siRNA in CO115 cells and p53 knockout in HCT116 cells totally abrogated apoptosis induction, demonstrating the dependence on p53 modulation of apoptosis induction by Q.

This study suggests the potential applicability of these phytochemicals for enhancement 5-FU efficiency in CRC therapy, especially Q in p53 wild-type tumors.

Keywords: Quercetin, 5-Fluorouracil, Colorectal cancer, p53

doi:10.1016/j.ejphar.2011.09.234

Evaluation of cactus pear (Opuntia spp.) extracts as promising bioactive ingredients for colon cancer therapy

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Cancer is one of the most causes of death worldwide. In particular, colorectal cancer is the second most frequent malignant disease in Europe. Treatments for recurrent and metastatic diseases remain a centre of clinical attention. While continuing efforts have been made for discovering new molecular target-based molecules, there is an emerging interest in chemotherapeutic application of natural substances.

Epidemiological data suggests that the ingestion of phytochemicals from fruits and vegetables may contribute to reduce the incidence of cancer in humans. The mechanisms by which these compounds inhibit tumourgenesis include inhibition of tumour cell mediated protease activity, attenuation of tumour angiogenesis, induction of cell cycle arrest and promotion of apoptosis.

Cactus (Opuntia spp.) fruits and cladodes have been widely used as food and in folk medicine. Nutraceutical benefits of fruits are believed to be related to the presence of ascorbic acid, flavonoids, betaxanthin and betacyanin. Recently, several studies demonstrated that cactus pear juices inhibit the proliferation of human cancer cell lines suggesting that cactus compounds could be considered as promising ingredients for chemoprevention and chemotherapy.

Within this context, the main aim of this study was to develop natural ingredients from cactus pear and evaluate their potential use as natural chemotherapeutic agents on colon cancer.

Different varieties of cactus pear were screened for their antiproliferative effect on HT29 cells. The phenolic content was determined using HPLC technique in order to understand which compounds are responsible for the anticancer activity. The most promising varieties were selected and further processed using macroporous resin, aiming to develop polyphenol-rich concentrates.

The anticancer activity of final products was evaluated by quantifying the effective dose values and analysing cell cycle arrest on HT29. The results obtained were compared with doxorubicin, a conventional drug used in cancer treatment. Additionally, the development of a drug-resistant HT29 cell culture was performed aiming to evaluate the bioproducts' potential in overcoming the main drawback of chemotherapy.

Keywords: Opuntia, Natural ingredients, Colon cancer

doi:10.1016/j.ejphar.2011.09.235

Aloe vera and honey solution modulates the oxidative stress, calpain activity and survival in tumour-bearing rats

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Oxidative stress is linked to several tumorigenic events and host-waste, and also to senescence and apoptosis, the major mechanisms in