Biomedical Papers

OF THE FACULTY OF MEDICINE AND DENTISTRY
OF PALACKÝ UNIVERSITY, OLOMOUC
CZECH REPUBLIC

VOLUME 156, SUPPLEMENT 1

PALACKÝ UNIVERSITY PRESS, OLOMOUC
2012

BIOMEDICAL PAPERS

Volume 156, Supplement 1

Published quarterly
MK ČR E 12793

Published and printed by Palacký University Press, Olomouc
Křížkovského 8, 771 47 Olomouc, IČO 61989592

Olomouc 2012

ISSN 1213-8118
eISSN 1804-7521

International Congress

Natural Anticancer Drugs

Olomouc, Czech Republic, June 30 – July 4, 2012

GUEST EDITORS

Jiri Gruz
Vladimir Krystof

monitored by measuring their cytotoxic effects on malignant human cancer cell lines. The root extracts displayed the highest cytotoxicity of the tested extracts, for which IC50 values against the CEM cell line were less than 0.4 mg/mL (70% ethanol extract) and 0.9 mg/mL (methanol:tetrahydrofuran extract), respectively. The root extracts exhibited strong cell cycle inhibitory activity and induced caspase-dependent apoptosis.

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Cinnamic acid as a novel inhibitor of COX-2 expression

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Inflammation is considered a cancer-promoting factor. Cyclooxygenase-2 (COX-2), the inducible form of the family of cyclooxygenases is an important mediator of inflammation, which has been found to be constitutively expressed in many forms of cancer including breast, colon or prostate. A number of studies show that COX-2 is stably expressed since the early pre-neoplastic stages. This encourages us to consider COX-2 as a potential target in chemoprevention as well as in the treatment of cancer. Synthetic inhibitors of COX-2, which target its enzymatic activity, are the only clinical strategy to counteract COX-2. However, these compounds present severe side effects, a fact that limits their prolonged intake, like requested in chemoprevention or during anti-cancer treatment. An alternative strategy to target COX-2 functions is at the level of its gene expression. A number of studies show that several natural compounds including curcumin, resveratrol or apigenin preferentially target COX-2 expression without showing toxicity. Our study analyses of the effect of cinnamic acid, a natural compound derived from *Cinnamonium cassia* on COX-2 expression during carcinogenesis, with the final perspective to evaluate its potential in chemoprevention. For our chemopreventive purposes, we have used the non-carcinogenic breast cell line MCF10A, stimulated with the phorbol ester 12-phorbol myristate 13-acetate (PMA), which typically induces COX-2. We show a reduction of induced COX-2 expression after treatment with different concentrations of cinnamic acid (1-50 mM). This regulation takes place at both mRNA and protein levels. The results show that cinnamic acid is efficient in reducing the stability of COX-2 mRNA even when used at the lowest concentration tested (1mM). Moreover, an impact on p38 and Akt activation was observed. The concentrations used do not show any toxicity. This encourages us to further investigate the potential of cinnamic acid as a new COX-2 targeting agent and to evaluate its impact on cancer cell models that stably express this enzyme.

ACKNOWLEDGEMENTS

Research at the Laboratoire de Biologie Moleculaire et Cellulaire du Cancer (LBMCC) is financially supported by "Recherche Cancer et Sang" foundation, by «Recherches Scientifiques Luxembourg» asbl, by «Een Haerz fir Kriibskrank Kanner» association, the Action Lions "Vaincre le Cancer" Luxembourg, The Fonds National de la Recherche Luxembourg, Televie Luxembourg and the Foundation for Scientific Cooperation between Germany and Luxemburg for additional support. Further support was received from the European Union (ITN "RedCat" 215009 and Interreg IVa project "Corena"). LNS Print costs were covered by the Fonds National de la Recherche (FNR) Luxembourg.

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Diet supplemented with UA or EGCG confer protection against DNA damage in colonocytes

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Diet is an important factor in colorectal cancer. High fat diets are considered a risk factor for the development of colon cancer as they increase the content of bile acids in the colon. Bile acids have shown to induce the formation of reactive oxygen and nitrogen species, and these, in turn, induce DNA damage. On the other hand, diets rich in fruits and vegetables have shown preventive effects on colon cancer. A recent study from our lab showed chemopreventive effects of natural compounds *in vitro* by protection against oxidative DNA damage and stimulation of DNA repair. In this study, we evaluated the effects of *in vivo* consumption of two natural compounds, (ursolic acid (UA) and epigallocatechin gallate (EGCG)), and a bile acid, deoxycholic acid (DCA), on DNA damage in colonocytes and lymphocytes isolated from Fischer 344 rats. These compounds were provided in the diet and administered daily for two weeks. Endogenous DNA damage (strand breaks, oxidized and alkylated bases) was evaluated using the Comet assay. Also, H2O2 and MMS were used, *ex vivo*, to investigate the potential of our natural compounds to protect against oxidative and alkylating damage, respectively. This study demonstrated that endogenous DNA damage in colonocytes was slightly higher than in lymphocytes. UA and EGCG decreased the levels of endogenous DNA damage in colonocytes, while

in lymphocytes, only UA had preventive effects. There was a significant increase of DNA damage with H2O2 treatment when compared with endogenous DNA damage in colonocytes, while treatment with MMS showed a tendency to increase DNA damage but was not significant. UA protected against both types of induced DNA damage, while EGCG only protected against H2O2-induced damage. According to the literature, DCA induces DNA damage *in vitro*, however after two weeks of *in vivo* DCA treatment, increase of endogenous DNA damage in colonocytes or lymphocytes was not observed in this study. UA and EGCG protected colonocytes and lymphocytes against DNA damage. These results suggest that UA can protect DNA from both endogenous and induced DNA damage in both cell types. EGCG was found to protect only against endogenous and H2O2-induced DNA damage in colonocytes. Further studies are undergoing to verify the potential of these compounds on induction of DNA repair systems, specifically base excision repair, mismatch repair, and direct repair by O^6-methylguanine DNA methyltransferase.

ACKNOWLEDGEMENTS

AR and DP are supported by the FCT grants SFRH/BD/35672/2007 and SFRH/BD/64817/2009.

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Lysophosphatidic acid increased cell proliferation and colony formation in human prostate cancer PC-3 cells

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Prostate cancer is the most common form of cancer in men and the second leading cause of cancer deaths in men. Several chemotherapeutic drugs have been shown to be potentially effective in the patient with prostate cancer. Docetaxel, estramustine and mitoxantrone are used for prostate cancer treatment. Recently, many phospholipid mediators have received much attention because of their various biological activities. Lysophosphatidic acid (LPA) (1- or 2-acyl-sn-glycerol 3-phosphate) is one of the most interesting phospholipid mediator with multiple biological functions in various human diseases. In spite of its simple structure, it evokes various cellular responses including cellular proliferation, prevention of apoptosis, cell migration, cytokine and chemokine secretion, smooth muscle contraction and neurite retraction in various cell types. Prostate cancer cells as the other cancer cells are able to secrete LPA and to use it to regulate cell proliferation and migration. In the present study, we investigated the effects of LPA, docetaxel, estramustine and mitoxantrone on proliferation, colony formation and apoptosis of PC-3 cells. In this study, PC-3 cells were treated with LPA, docetaxel, estramustine, mitoxantrone, docetaxel + LPA, estramustine + LPA, and mitoxantrone + LPA. We chose 24 h incubation time, which is the most increased population of PC-3 cells. Cell proliferation assay kit was used to determine the cell proliferation of all groups. Colonies were fixed in absolute methanol and stained with 1% crystal violet and colony formation observed in these PC-3 cells. Apoptosis was detected by flow cytometric annexin V binding assay. Lysophosphatidic acid treatment increased cell proliferation of PC-3 cells compared to control group. Treated cells with docetaxel + LPA, estramustine + LPA and mitoxantrone + LPA increased cell proliferation of PC-3 cells compared to docetaxel, estramustine and mitoxantrone groups respectively. Lysophosphatidic acid increased colony formation. Docetaxel, estramustine and mitoxantrone decreased colony formation. Docetaxel + LPA, estramustine + LPA and mitoxantrone + LPA increased colony formation compared to docetaxel, estramustine and mitoxantrone groups respectively. Lysophosphatidic acid inhibited docetaxel, estramustine and mitoxantrone induced apoptosis. The data demonstrated that LPA increased the percentage of cell viability. Treating PC-3 cells with docetaxel, estramustine and mitoxantrone increased the percentage of apoptotic cells. In conclusion, LPA significantly increased cell proliferation and colony formation of PC-3 cells. Treated PC-3 cells with docetaxel, estramustine and mitoxantrone decreased cell proliferation, colony formation, and induced apoptosis. The combination of LPA with docetaxel, estramustine and mitoxantrone can promote the proliferation, colony formation of PC-3 cells. Lysophosphatidic acid protects PC-3 cells against docetaxel, estramustine and mitoxantrone induced apoptosis.

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Antiproliferative effects of the *Holodiscus discolor* (Pursh) Maxim. leaves and flowers infusions

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Holodiscus discolor (Pursh) Maxim., (Rosaceae), called cream bush or ocean spray, have had a wide fulfillment in traditional medicine of indigenous peoples in Pacific Northwest, particularly in treatment of viral and skin diseases. Seeds have been used in the treatment of black measles, smallpox, chicken pox and as a blood purifier.