1. Ottelione A inhibited proliferation of Ehrlich ascites carcinoma cells in mice

El-Missiry, MA (El-Missiry, M. A.)[1]; Othman, AI (Othman, A. I.)[1]; Amer, MA (Amer, M. A.)[1]; Mohamed, E (Mohamed, E.)[1]

[1] Zoology Department, Faculty of Science, Mansoura University, Egypt

E-mail Address: maelmissiry@yahoo.com

Abstract

While the main target of chemotherapy in cancer treatment is the induction of apoptosis and cell death, natural products provide a wealth to medicine and are considered great sources of new drugs for cancer treatment. We aimed to determine the antitumor effect of ottelione A (OTTE) on the growth and proliferation of Ehrlich ascites carcinoma cells (EACs) implanted i.p. in female mice. Animals were inoculated with EAC cells to serve as the control group. In the OTTE group, animals were implanted with EAC followed by i.p. administration of OTTE. Antitumor activity was evaluated 15 days after tumor implantation. The administration of OTTE significantly reduced ascetic volume, viability of EAC cells and increased the survival of tumor-bearing animals. Flow cytometric analysis indicated that OTTE induced G(0)/G(1), cell cycle arrest and apoptosis. These findings were associated with an alteration of redox state of EAC cells, which might impact cascade effects leading to cell cycle arrest at G(0)/G(1) phase. These effects include a decreased expression of cyclin D1, increased p53 expression and down-regulation of rRNA level, stimulation of CD8+ infiltrating T-lymphocytes. In addition, OTTE normalized oxidative stress in the liver of mice-bearing EAC cells evidenced by increased the levels of glutathione, superoxide dismutase, and catalase. In conclusion, the differential expression of p53, cyclin D1, and rRNA in EAC cells as well as the infiltration of CD8+ after OTTE treatment may play critical roles in the G(0)/G(1) cell cycle arrest that blocks cell proliferation and induce apoptosis of cancer cells. The potent antitumor property of the ottelione A can be exploited further to develop therapeutic protocols for treatment of cancer. (c) 2012 Elsevier Ireland Ltd.

Keywords: Cell cycle; Apoptosis; rRNA; p53; CD8+; Cyclin D1

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2. Alfa-Lipoic acid protects testosterone secretion pathway and sperm quality against 4-tert-octylphenol induced reproductive toxicity

Othman, AI (Othman, Azza I.)[1]; El-Missiry, MA (El-Missiry, Mohamed A.)[1]; Koriem, KM (Koriem, Khaled M.)[2]; El-Sayed, AA (El-Sayed, Aml A.)[1]

[1] Mansoura Univ, Fac Sci, Dept Zool, Mansoura 35516, Egypt
[2] Univ Sains Malaysia, Adv Med & Dent Inst, NRC, Dept Med Physiol, Kuala Lumpur, Malaysia

E-mail Address: maelmissiry@yahoo.com

Abstract

The protective effect of a-lipoic acid (LA) (50 mg/kg bw) against 4-tert-octylphenol (OP) (50 mg/kg bw) induced reproductive toxicity in male rats was studied. LA was injected 1 h prior to OP administration three times a week. OP caused significant increase in oxidative stress in hypothalamus and epididymal sperm, disturbed hormonal levels in serum, decreased sperm quality, increased DNA fragmentation and loss of 35 and 95 kDa proteins in sperm, as well as elevated proliferating index in testis. LA protected against oxidative stress through promoting the levels of glutathione and glutathione-S-transferase in hypothalamus and sperm. In addition, LA prevented the decrease in testosterone, dehydroepiandrosterone sulfate, 3 P-hydroxysteroid dehydrogenase, and inhibited the elevations in sex-hormone-binding globulin levels and showed normal sperm quality. LA modulated proliferation of germ cell, protected against DNA fragmentation and maintained membrane protein organization in the sperm. In conclusion, LA normalized oxidative stress and protected testosterone synthesis pathway across hypothalamus-testicular axis and sperm quality indicating its defensive influence against OP-induced oxidative reproductive dysfunction in male rats

Keywords: Alkylphenols; Antioxidants; Sperm quality; Testis; Proliferating index; DNA; Hormones; Pollution

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3. Assessment of biological changes of continuous whole body exposure to static magnetic field and extremely low frequency electromagnetic fields in mice

Hashish, AH (Hashish, A. H.)[2,3]; El-Missiry , MA (El-Missiry, M. A.)[1]; Abdelkader, HI (Abdelkader, H. I.)[2]; Abou-Saleh, RH (Abou-Saleh, R. H.)[2]

[1] Univ Mansoura, Fac Sci, Dept Zool, Mansoura 35516, Egypt
[2] Univ Mansoura, Fac Sci, Dept Phys, Mansoura 35516, Egypt
[3] United Arab Emirates Univ, Fac Sci, Dept Phys, Al Ain, U Arab Emirates

E-mail Address: maelmissiry@yahoo.com

Abstract

The question whether static magnetic fields (SMFs) and extremely low frequency electromagnetic fields (ELF-EMF) cause biological effects is of special interest. We investigated the effects of continuous whole body exposure to both fields for 30 days on some liver and blood parameters in mice. Two exposure systems were designed; the first produced a gradient SMF while the second generated uniform 50Hz ELF-EMF. The results showed a gradual body weight loss when mice were exposed to either field. This is coupled with a significant decrease ($P<0.05$) in the levels of glucose, total protein and the activity of alkaline phosphatase in serum. A significant increase in lactate dehydrogenase activity was demonstrated in serum and liver paralleled with a significant elevation in hepatic gamma-glutamyl transferase activity. The glutathione-S-transferase activity and lipid peroxidation level in the liver were significantly increased while a significant decrease in hepatic gluthathione content was recorded. A significant decrease in the Counts of monocytes, platelets, peripheral lymphocytes as well as splenic total, T and B lymphocytes levels was observed for SMF and ELF-EMF exposed groups. The granulocytes percentage was significantly increased. The results indicate that there is a relation between the exposure to SMF or ELF-EMF and the oxidative stress through distressing redox balance leading to physiological disturbances

Keywords: Electromagnetic fields; Antioxidants; Liver; Enzymes

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4. Melatonin controls oxidative stress and modulates iron, ferritin, and transferrin levels in adriamycin treated rats

Othman, AI (Othman, Azza I.)[1] ; El-Missiry, MA (El-Missiry, Mohammed A.)[1] ; Amer, MA (Amer, Maher A.)[1] ; Arafa, M (Arafa, Magada)[1]

[1] Mansoura Univ, Fac Sci, Dept Zool, Mansoura 35516, Egypt

E-mail Address: maelmissiry@yahoo.com

Abstract

Chemotherapy with adriamycin (ADR) is limited by its iron-mediated pro-oxidant toxicity. Because melatonin (MIT) is a broad spectrum antioxidant, we investigated the ability of MIT to control iron, its binding proteins, and the oxidative damage induced by ADR. Main methods: ADR was given as single i.p. dose of 10 mg kg(-1) body weight into male rats. MLT at a dose of 15 mg kg(-1) was injected daily for 5 days before ADR treatment followed by another injection for 5 days. Biochemical methods were used for this investigation. Key findings: ADR injection caused elevations in plasma creatine kinase isoenzyme, lactic dehydrogenase, and aminotransferases, iron, ferritin, and transferrin. These changes were associated with increases in lipid peroxidation and protein oxidation as well as decreases in glutathione (GSH) levels and glutathione-S-transferase (GST) activity, while glutathione peroxidase (GSH-Px), and catalase (CAT) activity were elevated in the heart and liver of ADR treated rats. In the MLT+ADR group, the cardiac and hepatic function parameters and the levels of iron, transferrin and ferritin in plasma were normalized to control levels. The rats that were subjected to MLT+ADR had normalized CAT and GSH-Px activity and decreased TBARS and protein carbonyl levels compared the group only treated with ADR. GST activity and GSH concentration in the heart and liver were normalized when MLT accompanied ADR treatment. Significance: MLT ameliorated oxidative stress by controlling iron, and binding protein levels in ADR treated rats demonstrating the usefulness of adriamycin in cancer chemotherapy and allowing a better management of iron levels.

Keywords: Adriamycin; Oxidative stress; Antioxidants; Melatonin; Heart; Liver; Iron; Ferritin; Transferritin; Iron binding proteins

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5. Mn-complex-based superoxide diamutase mimic ameliorates oxidative stress in alloxan-induced experimental diabetes Mellitus

El-Missiry, MA (El-Missiry, Mohammed A.); Othman, AI (Othman, Azza I.); Salem, TA (Salem, Tarek A.); El-Sayed, FH (El-Sayed, Fbrahim H.)

[1] Mansoura Univ, Fac Sci, Dept Zool, Mansoura 35516, Egypt
[2] Minoufiya Univ, Dept Mol Biol, Genet Engn & Biotechnol Inst, Menoufia, Egypt

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6. Role of melatonin in ameliorating lead induced haematotoxicity

A.I Othman[a], S Al Sharawy[b], M.A El-Missiry[a,]

[a] Zoology Department, Faculty of Science and Clinical Pathology, Mansoura University, Mansoura 35516, Egypt

[b] Clinical Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt

E-mail Address: maelmissiry@yahoo.com

Abstract

Owing to the risks of heavy metals-induced severe haematopoietic disorders, it is important to investigate these chemicals for their haematotoxicity and the possible ways to ameliorate their toxicity. The effects of melatonin on lead-induced haematotoxicity have, therefore, been examined in rat blood and bone marrow. When adult male rats were injected intramuscularly with lead acetate (10 mg kg^{-1}) daily for 7 days, the erthrocytic count, haematocrite value and haemoglobin content were significantly decreased. The counts of platelets, total leucocytes and lymphocytes in the peripheral blood were also significantly lower in lead-treated rats than in control animals. The total granulocyte count was significantly elevated in the peripheral blood of the same lead-treated rats. Significant decreases in polychromatic and pyknotic erythroid series as well as lymphocytes in bone marrow of the lead-intoxicated rats were also demonstrated. Meanwhile, the neutrophiles were increased in the same treated rats. The erythropoietin level was significantly decreased and the lead concentration was increased in the plasma of the lead-treated rats compared with the control rats. Bone marrow examination of the rats treated with lead for 7 days showed erythroid hyperplasia with a sign of dyserythropoiesis and demonstrated ringed sideroblasts in varying proportions. Daily pretreatment with melatonin (30 mg kg^{-1}) intragastricaly, concurrently with lead injection for 7 days significantly prevented the changes recorded in the peripheral blood parameters. The changes observed in the bone marrow polychromatic erythroid, lymphocytes and the neutrophiles were significantly ameliorated by coadministration of melatonin and lead compared with lead-treated rats, while the pyknotic erythroid series was still significantly low. The

levels of erythropoietin and lead in plasma were not changed in melatonin+lead-treated group compared with lead only treated rats. In addition, melatonin administration ameliorated the decrease in erythroid cell count in bone marrow. Less dyserythropoiesis and megaloblastic changes were observed in bone marrow film when melatonin was concurrently administered with lead. In the same animals, iron staining of the bone marrow cells showed absence of ringed sideroblasts. In conclusion, the present results indicate that melatonin has the ability to protect the haematopoietic cells from the damaging effects of exposure to lead. This protection might be attributed to the antioxidative power of melatonin.

Keywords: Melatonin; Heavy metals; Bone marrow; Erythropoietin

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