The protective action of melatonin on indomethacin-induced gastric and testicular oxidative stress in rats.

Reactive oxygen species and lipid peroxidation play a role in the pathogenesis induced by the nonsteroidal anti-inflammatory drug indomethacin. Melatonin (MLT) protection against indomethacin-induced oxidative tissue injury was investigated in gastric mucosa and testis of rats. MLT was administered intragastrically (i.g.) 30 min before the administration to fasted rats of 20 mg indomethacin/kg rat given i.g.. The area of gastric lesion as well as thiobarbituric acid substances (TBARS) and lactate dehydrogenase (LDH) activity were found to be significantly increased 4 h after administration of indomethacin in rat gastric mucosa and testis indicating acute oxidative injury. MLT pretreatment reduced gastric lesion area to 80% of the indomethacin-treated rats and reduced the rise in TBARS concentration. MLT treatment reduced the LDH activity increase in testis but not in gastric mucosa. In indomethacin-treated rats, both the cytosolic Cu,Zn superoxide dismutase (Cu,Zn-SOD) and mitochondrial Mn-SOD activities were significantly diminished in gastric mucosa as well as the total SOD activity in testis. In addition, glutathione (GSH) content in both tissues was markedly decreased following indomethacin treatment. Pretreatment with MLT significantly ameliorated both the inhibition of SOD activity and the decreased GSH content in both tissues. Thus, these results show the effective antiperoxidative and preventive actions of MLT against indomethacin-induced gastric mucosal damage and testicular oxidative injury and we propose that this action might be relevant for its use with other free radical generating drugs.

Assessment of Biological Changes of Continuous Whole Body Exposure to Static Magnetic Field and Extremely Low Frequency Electromagnetic Fields in Mice

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...
50 Hz 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 glutathione-S-transferase activity. The glutathione-S-transferase activity and lipid peroxidation level in the liver were significantly increased while a significant decrease in hepatic glutathione 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.

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

Aim
Chemotherapy with adriamycin (ADR) is limited by its iron-mediated pro-oxidant toxicity. Because melatonin (MLT) is a broad spectrum antioxidant, we investigated the ability of MLT 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.
4-

Ameliorative effect of melatonin against gamma-irradiation-induced oxidative stress and tissue injury

While radiation hazards, due to free radical generation, present an enormous challenge for biological and medical safety, melatonin is a potent scavenger of a variety of free radicals. The aim of this study was to investigate the radioprotective effect of melatonin against oxidative stress and tissue injury induced by gamma radiation. Rats were subjected to two doses of 2 and 4 Gy from cesium-137 source. Four days prior to irradiation, animals received melatonin daily (10 mg/kg body weight i.p.). In the irradiated animals, the oxidative stress markers malondialdehyde (MDA) and protein carbonyl were significantly increased in the liver, while a marked decrease in hepatic contents of DNA, RNA, and glutathione (GSH) as well as activity of glutathione-S-transferase (GST) was demonstrated. In addition, catalase (CAT) activity was increased in the liver 5 days after irradiation. The levels of total lipids, cholesterol, triglyceride (TG), low-density lipoprotein (LDL), urea, and creatinine, as well as activities of aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT), were significantly increased in sera of the irradiated rats. This is coupled with decreased serum levels of high-density lipoprotein (HDL), total protein and albumin, and total globulins by irradiation. The administration of melatonin alone daily for 4 days caused significant decreases in MDA and protein carbonyl content and produced significant elevations of GSH content and GST activity in the liver. Moreover, significant decreases in total lipids, cholesterol, and TG without change in LDL or HDL levels in serum were demonstrated. Treatment with melatonin for 4 days before acute irradiation significantly abolished radiation induced elevations in MDA and protein carbonyl levels in the liver and significantly maintained hepatic GSH content, GST, and CAT activities close to the control values. Preirradiation treatment with melatonin showed significantly higher hepatic DNA and RNA contents than irradiated rats. The levels of total lipids, cholesterol, TG, HDL, LDL, total proteins, albumin, total globulins, creatinine, and urea, as well as the activities of AST, ALT, and GGT in serum were significantly ameliorated when melatonin was injected before irradiation. In conclusion, the increase in oxidative stress markers and the concomitant change in antioxidant levels indicate the role of oxidative stress in radiation-induced tissue damage. Moreover, melatonin shows a radioprotective impact against ionizing-radiation induced oxidative stress and organ injury.

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Role of melatonin in ameliorating lead induced haematotoxicity
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 erythrocyte count, haematocrit 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) intragastrically, 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.

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L-Arginine ameliorates oxidative stress in alloxan-induced experimental diabetes mellitus.

Oxidative stress occurs in diabetic patients and experimental models of diabetes. The ability of L-arginine to ameliorate the oxidative stress and metabolic changes after treatment with alloxan was investigated in rats. Adult male rats were injected intraperitoneally with 100 mg kg⁻¹ of alloxan to produce
experimental oxidative stress characteristic of diabetes mellitus. Hyperglycaemia and hypercholesterolaemia were observed in serum after 7 days of alloxan treatment. This was associated with a depression of glutathione (GSH) concentration as well as superoxide dismutase (SOD) and catalase (CAT) activities in the liver and brain. In addition, the thiobarbituric acid-reactive substances (TBARS) were significantly elevated, indicating increased lipid peroxidation and oxidative stress in the same tissues. Administration of 100 mg kg\(^{-1}\) L-arginine for 7 days either before or after alloxan injection significantly ameliorated the oxidative stress evidenced by a lower TBARS and a higher level of the endogenous GSH concentration and SOD and CAT activities than alloxan-treated rats. These effects were paralleled by marked protection and partial prophylaxis against alloxan-induced hyperglycaemia and cholesterololemia. Thus, these results showed that exogenously administered L-arginine might improve the clinical manifestation of diabetes mellitus and decrease the oxidative stress in the liver and brain. In addition, the study supports the beneficial effect of L-arginine, which might be attributed to its direct, NO-dependent antioxidant capacity and/or NO-independent pathways. Copyright 2004 © John Wiley & Sons, Ltd.

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**Attenuation of the acute adriamycin-induced cardiac and hepatic oxidative toxicity by N-(2-mercaptopropionyl) glycine in rats**

The protective effect of the synthetic aminothiol, N-(2-mercaptopropionyl) glycine (MPG) on adriamycin (ADR) induced acute cardiac and hepatic oxidative toxicity was evaluated in rats. ADR toxicity, induced by a single intraperitoneal injection (15 mg/kg), was indicated by an elevation in the level of serum glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), creatine kinase isoenzyme (CK-MB), and lactic dehydrogenase (LDH). ADR produced significant elevation in thiobarbituric acid reactive substances (TBARS), indicating lipid peroxidation, and significantly inhibited the activity of superoxide dismutase (SOD) in heart and liver tissues. In contrast, a single injection of ADR did not affect the cardiac or hepatic glutathione (GSH) content and cardiac catalase (CAT) activity but elevated hepatic
CAT. Pretreatment with MPG, (2.5 mg/kg) intragastrically, significantly reduced TBARS concentration in both heart and liver and ameliorated the inhibition of cardiac and hepatic SOD activity. In addition, MPG significantly decreased the serum level of GOT, GPT, CK-MB, and LDH of ADR treated rats. These results suggest that MPG exhibited antioxidative potentials that may protect heart and liver against ADR-induced acute oxidative toxicity. This protective effect might be mediated, at least in part, by the high redox potential of sulfhydryl groups that limit the activity of free radicals generated by ADR.

Potential protective role of angiotensin-converting enzyme inhibitors captopril and enalapril against adriamycin-induced acute cardiac and hepatic toxicity in rats

Captopril and enalapril—angiotensin-converting enzyme (ACE) inhibitors—were evaluated for their antioxidative protective action against adriamycin-induced cardiac and hepatic toxicity. Rats were treated with either captopril (10 mg kg?1) or enalapril (2 mg kg?1) intragastrically (i.g.) daily for 7 days before single intraperitoneal (i.p.) injection with adriamycin (15 mg kg?1). The animals were killed 30 h after adriamycin administration. Adriamycin produced significant elevation in thiobarbituric acid reactive substances (TBARS), which is an indicator of lipid peroxidation, and significantly inhibited the activity of superoxide dismutase (SOD) in heart and liver tissues, with a significant rise in the serum levels of glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), creatine kinase isoenzyme (CK-MB) and lactic dehydrogenase (LDH), indicating acute cardiac toxicity. A single injection of adriamycin did not affect the cardiac or hepatic glutathione (GSH) content or cardiac catalase (CAT) activity, but hepatic CAT activity was elevated. Pretreatment with ACE inhibitors significantly reduced the TBARS concentration in both heart and liver and ameliorated the inhibition of cardiac and hepatic SOD activity. In addition, the ACE inhibitors significantly improved the serum levels of GOT, GPT, CK-MB and LDH in adriamycin-treated rats. Thus, these results suggest that captopril and enalapril possess antioxidative potential that may protect the heart against adriamycin-induced acute oxidative toxicity. This protective effect might be mediated, at
least in part, by the limitation of culprit free radicals and the amelioration of oxidative stress. Copyright © 2001 John Wiley & Sons, Ltd.

**Protection by metal complexes with SOD-mimetic activity against oxidative gastric injury induced by indomethacin and ethanol in rats**

We have investigated the protective effect of oral administration of copper and manganese complexes with superoxide dismutase (SOD)-mimetic activity against oxidative gastric mucosal injury induced by the non-steroidal anti-inflammatory drug indomethacin with ethanol in the rat. The total area of the gastric lesions and lipid peroxidation were significantly increased 1 h after oral administration of indomethacin (15 mg/kg) and ethanol, indicating an acute oxidative injury. The activities of SOD, catalase (CAT), glutathione-S-transferase (GST) and glutathione content were significantly decreased in the gastric mucosa by indomethacin plus ethanol. Manganese or copper complexes showed SOD-mimetic activity. Pretreatment with these complexes protected against gastric mucosal lesions and decreased lipid peroxides, as well as attenuating the decrease in the activities of SOD, CAT and GST in gastric mucosa. These findings suggest that active oxygen species and lipid peroxidation play an important role in the pathogenesis of gastric mucosal injury induced by indomethacin. In addition, we have shown that Mn and Cu complexes have gastroprotective properties against ulceration induced by indomethacin plus ethanol. The present results suggest that appropriate copper or manganese complex supplementation may potentially provide prophylaxis or therapy for some pathologies associated with excessive free radical production and inhibited SOD activity.

**Photosensitization induced reactive oxygen species and oxidative damage in human erythrocytes**

Generation of reactive oxygen species by photosensitization is the cornerstone of photodynamic therapy of tumors. Cell damage may be mediated by free radical species and lipid peroxidation of their membranes. The effects of oxygen active species (\(\cdot\)OH and \(O_2^-\) radicals) photogenerated by the novel photosensitizer m-chloroperbenzoic acid (m-CPBA) on human erythrocyte integrity and stability were studied. The biological toxicity of the reactive oxygen species on human red blood cells (RBCs) was evident by increased osmotic fragility, spherocytosis and haemolysis. The haemolysis was increased in concentration and time dependent manner. The lipid peroxidation product thiobarbituric acid reactive substances (TBARS) was elevated in m-CPBA photosensitized RBCs indicating increased oxidative stress. This was accompanied with a depletion of erythrocyte glutathione (GSH). These effects were blunted by hydroxyl radical scavengers, thiourea and mannitol, which might indicate the production of \(\cdot\)OH radical by photosensitization with m-CPBA. The antioxidant enzyme activities
such as superoxide dismutase (SOD), catalase (CAT), peroxidase (Px) and glutathione peroxidase (GSH-Px) were elevated in RBCs treated with m-CPBA in the presence and absence of hydroxyl radical scavengers, mannitol and thiourea. These results suggested that the main oxygen radical photogenerated from m-CPBA is O₂·₂ radical, which is transformed to ·OH radical probably by hydrogen abstraction. This is probably the main damaging oxygen species and played an essential role in oxidative haemolysis mediated by peroxidation of membrane lipids of human erythrocytes. This study provides an investigational promising data for photodynamic therapy. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

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**Influence of melatonin on proliferation and antioxidant system in Ehrlich ascites carcinoma cells**

The effects of oral supplementation of melatonin on growth of Ehrlich ascites carcinoma (EAC) cells implanted intraperitoneally in female mice were studied. Melatonin at 50 mg/kg body wt. reduced the viability and volume of Ehrlich ascites carcinoma cells and increased the survival of the treated mice. No significant change in intracellular reduced glutathione (GSH) content in EAC cells was observed indicating that GSH was not involved in the inhibitory effect of melatonin. The activity of glutathione-S-transferase in EAC cells was significantly increased. Flow cytometric studies showed that melatonin not only delayed the progression of cells from G0/G1 phase to S-phase of the cell cycle but also reduced DNA synthesis during cell cycle. In addition, the aneuploidy status was depressed in melatonin treated mice. Based on these data and the reduced viability in both in vitro and in vivo, it is suggested that melatonin might induce apoptosis in EAC cells. ©2000 Elsevier Science Ireland Ltd. All rights reserved.

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**Enhanced testicular antioxidant system by ascorbic acid in alloxan diabetic rats**

The diabetic subject is at significantly increased risk of developing testicular changes. Its etiology may involve oxidative damage by free radicals and protection against such damage can be offered by antioxidant supplementation. Alloxan elicited significant inhibition of antioxidants including superoxide dismutase, catalase and glutathione reductase activities and decreased glutathione content in testis. These effects were accompanied by significant elevation of testicular lipid peroxidation, decreased plasma testosterone level and a drop in copper and zinc concentrations in testis. The administration of ascorbic acid after alloxan treatment interfered and prevented alloxan action. Ascorbic acid blunted the increased
testicular lipid peroxidation and the decreased plasma testosterone level probably by protecting antioxidants and the loss of copper and zinc from testes. The data suggested that ascorbic acid has a protective effect on alloxan-induced damage by maintaining the activity of cellular antioxidants.

Amelioration of alloxan induced diabetes mellitus and oxidative stress in rats by oil of Eruca sativa seeds

Clinical research has confirmed the efficacy of several plant extracts in the modulation of oxidative stress associated with diabetes mellitus (DM). Oil of Eruca sativa seeds (ESS) is tried for prevention and treatment of DM induced experimentally by alloxan injection. A single dose of alloxan (100 mg/kg) produced a decrease in insulin level, hyperglycemia, elevated total lipids, triglycerides and cholesterol, decreased high-density lipoprotein and hepatic glycogen contents and elevated hepatic glucose-6-phosphatase activity. Concurrent with these changes, there was an increase in the concentration of malondialdehyde and 4-hydroxynonenal in the liver. This oxidative stress was related to a decreased glutathione (GSH) content and superoxide dismutase activity in the liver of alloxan-diabetic rats. ESS oil (0.06 ml/kg) on its own increased significantly hepatic GSH. Daily oral administration of ESS oil 2 weeks before or after diabetes induction ameliorated hyperglycemia, improved lipid profile, blunted the increase in malondialdehyde and 4-hydroxynonenal and stimulated the GSH production in the liver of alloxan-treated rats. We suggested that ESS oil could be used as antidiabetic complement in case of DM. This may be related to its antioxidative properties and to the increase in hepatic GSH.

Role of beta-carotene in ameliorating the cadmium-induced oxidative stress in rat brain and testis

The role of oxidative stress in chronic cadmium (Cd) toxicity and its prevention by cotreatment with b-carotene was investigated. Adult male rats were intragastrically administered 2mg CdCl2/kg body weight three times a week intragastrically for 3 and 6 weeks. Brain and testicular thiobarbituric acid reactive substances (TBARS) was elevated after 3 and 6 weeks of Cd administration, indicating increased lipid peroxidation (LPO) and oxidative stress. Cellular damage
was indicated by inhibition of adenosine triphosphatase (ATPase) activity and increased lactate dehydrogenase (LDH) activity in brain and testicular tissues. Chronic Cd administration resulted in a decline in glutathione (GSH) content and a decrease of superoxide dismutase (SOD) and glutathione S-transferase (GST) activity in both organs. Administration of b-carotene (250 IU/kg i.g.) concurrent with Cd ameliorated Cd-induced LPO. The brain and testicular antioxidants, SOD, GST, and GSH, decreased by Cd alone, were restored by b-carotene cotreatment. Concurrent treatment with b-carotene also ameliorated the decrease in ATPase activity and the increase in LDH activity in brain and testis of Cd-treated rats, indicating a prophylactic action of b-carotene on Cd toxicity. Therefore, the results indicate that the nutritional antioxidant b-carotene ameliorated oxidative stress and the loss of cellular antioxidants and suggest that b-carotene may control Cd-induced brain and testicular toxicity.

**Prophylactic effect of melatonin on lead-induced inhibition of heme biosynthesis and deterioration of antioxidant systems in male rats**

We studied the protective role of the pineal hormone melatonin on lead-induced suppression of the heme synthesis pathway as a consequence of reduced antioxidant systems in rat. We injected rats intramuscularly with lead acetate (10 mg/kg body weight) daily for 7 days, which significantly abolished heme synthesis as evidenced by decreased blood hemoglobin, liver d-aminolevulinic acid synthetase, erythrocytic d-aminolevulinic acid dehydratase, and hepatic iron content. These effects were accompanied with marked elevation of hepatic lipid peroxidation and decreased enzymatic antioxidants such as glutathione reductase, glutathione-S-transferase, superoxide dismutase, and catalase, as well as nonenzymatic antioxidants such as total sulfhydryl groups and glutathione. Furthermore, lead treatment caused hepatic deficiency in copper and zinc accompanied by a significant elevation of lead concentration in both plasma and liver. Daily pretreatment with melatonin (30 mg/kg body weight) intragastrically prevented the suppressive effects of lead on heme-synthesizing enzymes and iron deficiency. In addition, preadministration of
melatonin reduced the inhibitory effect of lead on both enzymatic and nonenzymatic antioxidants. This was accompanied by marked normalization of lipid peroxidation and modulation of copper and zinc levels in liver. The action of melatonin on lead-induced changes was attributed to protection of the antioxidant capacity in cells in addition to the ability of melatonin to scavenge free radicals. q 1999 John Wiley & Sons, Inc. J Biochem Toxicol 14: 57â€“62, 2000

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**Role of selenium against lead toxicity in male rats**

Male albino rats were intramuscularly administered a single dose of lead acetate (100 l mol/kg b.wt). Another group of rats were injected with sodium selenite (10 l mol/kg b.wt) before lead intoxication. After 3 and 24 hours, lead treatment resulted in significant increases in acid and alkaline phosphatases, GOT and GPT, total proteins, and cholesterol in serum. The total triglycerides in serum was decreased after 24 hours of intoxication. Lead treatment also produced significant elevation of lipid peroxidation in liver and kidney. The antioxidant capacity of hepatic and renal cells in terms of the activities of superoxide dismutase, glutathione reductase, and glutathione content was diminished. It appears from these results that lead may exert its toxic effect via peroxidative damage to renal and hepatic cell membranes after 24 hours. Selenium administration prior to lead injection produced pronounced prophylactic action against lead effects, and it is observed that selenium enhances the endogenous antioxidant capacity of the cells by increasing the activities of the superoxide dismutase and glutathione reductase and the glutathione content. As a result, the lipid peroxidation was decreased in both liver and kidney. q 1998 John Wiley & Sons, Inc. J Biochem Mol Toxicol 12: 345â€“349, 1998

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

LA protected against OP induced oxidative injury in both the hypothalamus and epididymal sperm by augmenting the endogenous antioxidants, particularly GSH and GST. This led to the maintenance of steroidogenesis that in turn maintained regular germ cell proliferation and production of normal sperm count, motility and morphology. Furthermore, LA
showed the potential to protect DNA and protein organization in sperm against OP-induced oxidative stress. It is anticipated that LA supplementation not only protects male fertility but also may assist normal fertilization and prevents the transfer of defective paternal DNA to the progeny.

**Current Topics in Ionizing Radiation Research**

Radiations exist ubiquitously in the environment since the Earth’s creation in soil, water and plants. Radiation exposure is a concern in the health industry and other occupations in the world. Apart from diagnostic, therapeutic and industrial purposes, humans also are exposed to ionizing radiations during air and space travel and exploration, background radiation, nuclear accidents, and nuclear terror attacks. Elevated radiation levels have been detected following Chernobyl on April 1986 at Ukraine, and recently Fukushima Daiichi Nuclear Power Plants on March 2011 at Japan. This raised the need for finding out efficient and reliable radioprotectors especially when a whole nation is exposed at high or even low levels for a prolonged period. The fallout and radioactivity cause concern during the weeks and months after the accidents. In addition, radiations are commonly used in a number of medical and industrial situations; however, their pro-oxidative effects limit their applications. Therefore, it is essential to protect humans from ionizing radiations by efficient pharmacological intervention. A valid approach to halt normal tissue radiotoxicity is the use of radioprotectors that when present prior to radiation exposure protect normal tissues from radiation effects. This view has also been used as a successful preventative measure for possible nuclear/radiological situation. From a practical point of view radioprotectors should perfectly have several criteria that relate to the ability of the agent to improve the therapeutic outcome. Ionizing radiation causes oxidative damage to tissues within an extremely short period, and possible protection against it would require the rapid transfer of smart antioxidants to the sensitive sites in cells. At this point, melatonin (N-acetyl-5-methoxytryptamine; MW= 232), an innate antioxidant produced mainly by the pineal gland, seems unique among antioxidants because of its multiple properties and reactions which reviewed and documented in several publications and summarised herein.

While ionizing radiation exposures, due to free radical generation, present an enormous challenge for biological and medical safety, melatonin is a potent radioprotector. In several investigations, melatonin has been recognized for successful amelioration of oxidative injury and illness due to direct and indirect effects of ionizing radiation and against oxidative stress in several experimental and clinical settings. Furthermore, numerous studies have established that melatonin is a highly efficient free radical scavenger, broad antioxidant and stimulator of several antioxidants in biological systems. Because of its unique characteristics; melatonin has effects not only at the cell level but also within subcellular organelles and structures. The antioxidant and prophylactic properties of melatonin allow the use of radiation during radiotherapy to get better therapeutic outcomes. Several published articles documented that melatonin’s anticaner and oncostatic effects make melatonin an excellent candidate and good choice to be used in routine radiotherapies, occupational settings where accidental exposure may occur, and space travel and following nuclear accidents This article will review antioxidant features that put melatonin on top of potentially efficient pharmacological
radioprotectors.