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Review article

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ANTIOXIDANT PROTECTION AGAINST COSMIC RADIATION-INDUCED OXIDATIVE STRESS AT COMMERCIAL FLIGHT ALTITUDE

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It is proposed that at the commercial flight altitude the cosmic radiation affects the human body and induces the oxidative stress. This review presents data to support this idea and also cumulates the information to provide the basis for antioxidant supplementation in persons that travel by plane at high altitudes. The conclusion is that the heterogeneity of cosmic radiation can produce different effects on human body through different mechanisms and the prophylactic treatment with antioxidants can reduce the oxidative stress generated by the radiation exposure.

Key words: *cosmic radiation, commercial flights, magnetosphere, antioxidants, oxidative stress, reactive oxygen species, plant extracts*

INTRODUCTION

The Earth is protected against the cosmic radiation by magnetosphere (magnetic field) and atmosphere. The measurements of the Earth magnetic field made by European Space Agency using three satellites launched in November 2013 showed modifications in the intensity of the magnetosphere: decreases were recorded over the Western hemisphere, increases over the Indian Ocean (1).

Previous studies, with different methods, showed a decrease in the magnetosphere intensity with 10% in the last 150 years. The intensity of the magnetic field varies between 0.3 Gauss at the equator and 0.6 Gauss at the poles (2). The decrease of the magnetosphere intensity permits the solar particles and cosmic radiation to reach the inner layers of the atmosphere, being able to affect the people who are at high altitudes. The ionized particles are reflected back into the space by the strong magnetosphere and atmosphere, but since the intensity of the magnetosphere decreases and the atmosphere layers are affected, in time, the Earth surface can be exposed to the cosmic and solar radiation.

The number of commercial flights using the routes over North Pole region has been multiplied during the last decades (3). At the polar region, the minimum protection ensured by the magnetosphere exposes the pilots and the passengers at high levels of cosmic radiation (4).

In this review, an overview of the ionized particles that can cause different types of illnesses in human beings is presented.

The antioxidant beneficial effects on human body are known and this study is focused on finding of an efficient protection against the radiation that can affect the people who travel by planes at high altitudes, especially over polar area.

EARTH PROTECTION AGAINST COSMIC RADIATION

The Earth magnetosphere acts as a shield against the solar flares that contain X-rays and against the solar wind that transports electrons, protons, alpha particles, and heavier particles. These solar particles can penetrate the magnetosphere to the low altitudes in the polar region. The Sun coronal mass ejections (containing ionized atomic matter with high kinetic energy) can create a shock wave that will enable the fast-flowing particle to collide with the Earth magnetosphere, initiating the magnetic storms, through which, energetic ions and electrons can enter deep into the magnetic field, creating a new electric current that will generate a different new magnetic field that can interfere with the Earth magnetic field (5).

The magnetosphere can also provide protection against galactic cosmic rays -source of highly energetic particles with origin outside the solar system. These cosmic particles consist of different chemical elements, fully ionized. During the intense solar activity, these cosmic particles are scattered by the solar wind, but when the Sun activity is reduced (during the solar cycle), the galactic cosmic particles that travel with a really high velocity can enter the atmosphere and react with the atmospheric particles generating secondary particles that can reach the ground. The Earth magnetic field can block the entering of these particles into the atmosphere especially at the equatorial areas, but near the polar regions, the protection is insignificant, affecting the passengers that fly at high latitudes and altitudes (6).

Inside the atmosphere, ionization occurs through solar radiation (UV), cosmic ray fluxes, X-ray solar flare, and surface radioactivity (effective at altitude lower than 3000 m). The lower atmosphere presents an excess of charged particles. At high latitude, middle atmosphere, ionization is intensified by aurora

X-rays, solar events (that increase the number of protons that are sent on Earth), and geomagnetic storms (that lead to the entering of electrons to the atmosphere in high concentration at mid latitude) (7). The maximum ion production rate is between 15,000 m and 20,000 m altitudes (1000/cm^3) (8). Below 15,000 m, the ion production is realized by secondary particles (9), and lower than 5000 m altitude ion production is in principal produced by the surface radioactivity (10). The ionization rate increases with latitude. Near the ground, ionization is with 20% higher at high latitudes than at equator (11).

COSMIC RADIATION

There are two types of cosmic radiation: primary and secondary. The primary cosmic radiation has its origin from outside of our solar system, contains particle of extremely high energy: protons (~89%), helium nuclei (~10%) and other heavier particles (~1%) (12), which do not reach the sea level in the geographical areas that are protected by the strong magnetic field. The secondary cosmic radiation results from the interaction of the primary cosmic rays with the atmosphere particles and provides new particles of low energy (photons, electrons, neutrons, muons) (13). At high mountain altitude (above 3000 meters), the secondary cosmic rays showers affect the people (14, 15) with different doses, depending on the altitude, geographic area and sun activity (16-21).

The cosmic rays (CR) continuously enter the atmosphere at high altitudes and have a periodicity of ~17 years (22). The magnetic field inclination is zero at the equator so it can block the entering of most charged particles at high altitudes of the atmosphere. The magnetic field inclination is perpendicular to Earth's surface at the poles, consequently, it is not able to block the charged cosmic particles so they will enter the lower layers of the atmosphere, where they can interact with gas molecules (23). The intensity of cosmic radiation and the energy spectra depend on longitude, latitude and azimuth angle, and have variations with ~27 days periodicity, according to the solar rotation (24). As the cosmic rays enter the atmosphere, they produce ionization that increases with the increasing of latitude. During solar storms, the cosmic radiation that enters the atmosphere is decreased (the solar wind blocks the cosmic rays) and the ionization produced by cosmic radiation is at a lower rate (25). When the cosmic rays enter the biosphere, the cells' metabolism can be affected (DNA mutations, chromosome alterations, carcinogenesis, apoptosis) and the body's functioning can be modified (blood pressure and heart rate variations, *etc*.).

FACTORS THAT AFFECT COSMIC RAY EXPOSURE

There are many factors that affect the CR exposure: altitude (cosmic radiation is increased at high altitudes), latitude (CR intensity is minimum at equator and is maximum at poles, increasing with latitude), outdoor activity, solar storms (alter the magnetosphere's protection against CR), sun rotation (cosmic radiation has a periodicity of 27 days) (26), solar flares (the source for protons that can enter into the atmosphere), mean solar activity (11-year variation), barometric pressure modification (modifies the muons, pions penetration inside the atmosphere), diurnal variations of CR (27).

COMMERCIAL FLIGHTS

On polar flight plan, the pilots and the passengers are exposed at a higher equivalent dose than those that fly along the equator: 0.0986 mSv/flight (28, 29). Radiation received by flight members is very heterogeneous, depending on the factors already mentioned. Over the years, the received dose during the same flight increased (*Figs*. *1* and *2*) (30). Air crew is exposed to ionizing radiation, mostly from galactic source. The cosmic radiation (protons and α-particles) enter the atmosphere where they collide with atmospheric particles generating nuclei of oxygen, nitrogen, other air atoms. In this way, the particles shower provides nuclei that can generate multiple other ionizing particles. Crew and passengers from commercial flights (6000 – 12000 meters altitude), at all latitudes are exposed at radiation, in which 88 – 97% of effective dose rate consists of: neutrons (33 – 52%), protons (21 – 28%), electrons and photons (17 – 41%), muons (2 – 11%) and charged pions (< 1%). At high latitude, the mean effective dose rate of CR is 2 – 2.7 times much higher, according to the altitude (31). A crewmember receives a higher dose (~6.1 mSv/y) than a person that works on the ground (3.0 mSv/y) (32), and the cosmic radiation can affect pregnant crewmembers (after only 4 – 5 months spent at high altitude, the recommended maximum dose of 2 mSv is reached) (33).

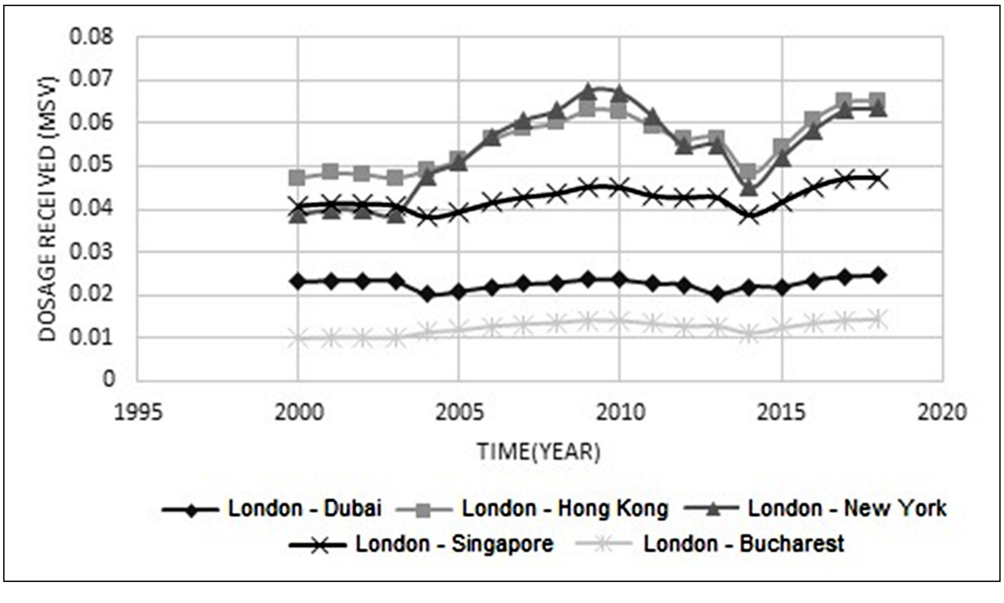

Fig. *1*. Radiation received by the flight members during transcontinental and intercontinental routes.

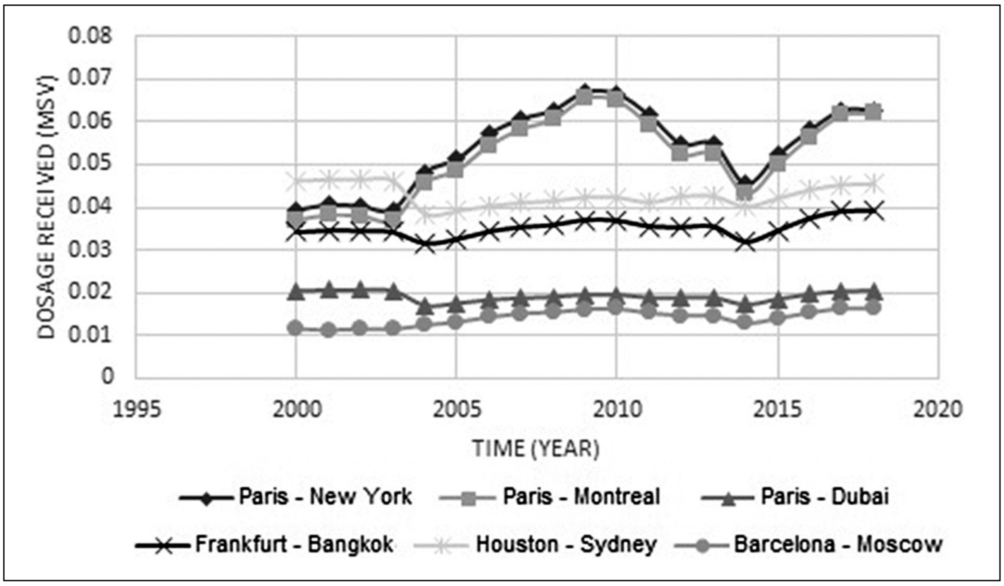

Fig. 2. Radiation received by the flight members during transcontinental and intercontinental routes.

COSMIC RADIATION EFFECTS

The radiation spectrum of cosmic radiation contains different particles with a broad range of energies that can produce different effects on the human body.

Radiation produces immediate effects (DNA damage, signal transduction responses, redox activation), early radiation effects (DNA repair, mutation, genomic instability, induced gene expression, cell cycle perturbation, apoptosis) and late radiation effects (fibrosis, altered functions of the body's systems, cataract, cancer).

Radiation effects on the body's cells can be caused by direct action (directly on DNA) and indirect action (through the reactive oxygen and nitrogen species that are produced by the water radiolysis or by the alterations of other cellular molecules) (34). The oxidative stress initiated by the ionizing radiation is responsible for two-thirds of DNA damages (35).

- Photons action on the tissues consists in a broad energy distribution with a maximum dose located close to the tissue surface (36). Photons with energy lower than 1.02 MeV can generate new electrons. The low-energy photons of cosmic origin affect the whole body: 5400 photons/second shower the body and the absorbed dose is stored inside the body for 132 seconds. The absorbed dose is 0.015 mGy/y and represents 5.5 % of effective annual dose of 0.27 mSv/y (37).

- Protons are able to produce nuclear interactions and to induce oxidative stress in cells (38). The whole porcine body irradiation with protons reduces the leukocytes number (39), and in mice even after two months post-irradiation, the oxidative stress altered the hematopoietic stem cells in bone marrow (40).

- Neutrons can transfer their energy to the hydrogen atoms located in the tissues and produce the recoil protons that can damage the tissue (41).

- Alpha-particles are particles with low-penetration depth so they remain blocked in the skin where they can produce an indirect ionization that leads to a persistent oxidative stress (42).

- X-rays cause DNA alterations but also cellular atoms ionization that releases electrons with energy capable to ionize further the tissue. The total body irradiation with X-rays decreases the level of vitamin C and vitamin E in the tissues (43).

- Gamma-radiation stimulates the nitric oxide synthesis in the cells, especially in the brain, liver, small intestine and colon (44). Nitric oxide causes proteins nitration that alters the protein functionality and signal transduction (45). Fang *et al*. showed that gamma-irradiation increases the lipids, proteins, vitamin C and folate oxidation (46).

- High-energy electrons produce water radiolysis in the tissue cells with the release of the reactive oxygen species that interact with macromolecules, leading to the protein damages (47). The low-energy electrons of cosmic origin are absorbed only within human skin: epidermis and partially within dermis. At latitude 45°N, longitude 20°E, 80 m altitude, the effective dose for uncovered skin is 0.83 mGy/y (48).

- Ionizing radiation causes DNA lesions by direct action but mostly by indirect action, through the increased concentration of reactive species (49) that are generated and that persist for weeks after radiation exposure (50, 51). Ionizing radiation activates nuclear factor κB (NF-κB), the protein that controls the post-irradiation inflammation (52). The quantity of reactive species that are produced by the ionizing radiation is in direct relationship with the total dose received by the tissue. Water radiolysis is the indirect mechanism that produces the most of the radiation damages. The reactive species that are produced can be neutralized by the scavengers, but superoxide (O_2^-) and hydrogen peroxide (H_2O_2) are relatively stable so they persist in the tissue for longer periods of time and they can diffuse and continue the oxidative stress into the distant tissues (53), causing DNA damages (54), protein oxidation and lipid peroxidation (55, 56). The irradiated cells produce reactive oxygen species, cytokines, RNAs or calcium ions, molecules that are released and received by the distant cells, cells that were not irradiated, realizing an intercellular communication that continues the damages into the body (57).

Very radiosensitive cells are the foetus cells that develop between 8 – 25 weeks. In adult, bone marrow, colon and stomach are very radiosensitive and the most resistant tissues are nerves and muscles (58, 59). The brain is very sensitive to ROS because of its decreased antioxidant capacity (vitamin E, superoxide dismutase (SOD)) (60), its increased oxidative reactions, its high iron concentration and its polyunsaturated fatty acids (61). Parihar *et al*. (62) demonstrated in their study made on rodents that CNS is sensitive to cosmic radiation. They exposed the animals to low realistic doses of charged particles and observed persistent dose-independent changes in functional connectivity between cortex and hippocampus with modifications of structure, number and distribution of specific synaptic proteins and neuroinflammation in prelimbic layer of medial prefrontal cortex, structural alterations that can explain the observed impaired recent memory (62). In a recent study, Parihar *et al*. observed that mice exposure at low realistic doses of helium ions produced modifications in perirhinal cortex: the resting membrane potential was changed in the principal cells and the number of activated microglia was increased, with persistent effects on cognition, anxiety and depression (63).

McCraty *et al*. suggested in their study performed in volunteers that increased CR exposure can stimulate the activity of parasympathetic system (64). Monthly studies made by the researchers presented the effects of cosmic radiation on the cardiovascular system and the directly proportional relationship between cosmic radiation activity and monthly deaths number (65, 66). The increased activity of CR affects the electrical activity of the heart and can disturb the lipid metabolism in artery wall. Neutrons enter the body and are converted to protons in the tissues with a high content of H^+ ions (including atheroma). The protons can destroy the cells leading to fatal arrhythmia in ischaemic cardiomyopathy, acute myocardial infaretion and can produce atheroma ruptures (67).

The oxidative stress induced by high energy iron ion radiation produces endothelial dysfunction, effect that was demonstrated by Soucy *at al*. in their study performed in rats (68). Grabham *et al*. studied the effect of charged particles on endothelial cells culture and observed vasculogenesis inhibition that depended on particles type: the low LET protons inhibited the motility of filopodia, while the high LET iron ions blocked the formation of the lumen (69).

The cosmic rays exposure affects the visual system. In the eye, cosmic radiation initiates a chain reaction that generates different reactive species and photons, mechanisms that can explain the light flashes upon dark-adaptation (70).

Each radiation type produces different effects in induction of gene expression (71). Different ionized particles activate in a specific manner the tissue proteins or the transforming growth factor β (TGF-β), in accordance to their dose and type (72). X-irradiation stimulates the oxidative stress in testicular (73) and ovary tissues, but the cosmic radiation contains also charged iron particles that affect the ovaries, inducing oxidative stress and apoptosis in ovarian follicles, with decreased ovarian negative feedback to the hypothalamus and anterior pituitary (74).

Eken *et al*. showed in their study that chronic low dose-radiation increases the antioxidant capacity of the body (75), but the broad spectrum of cosmic radiation encountered at high altitudes can initiate the oxidative stress through many other mechanisms overriding this enhanced antioxidant protection.

ANTIOXIDANT PROTECTION AGAINST COSMIC RADIATION DURING COMMERCIAL FLIGHTS

In persons that travel at high altitudes for a long time, especially through the polar routes, the radiation-induced oxidative stress can be reduced by the prophylactic administration of antioxidants. Because the antioxidant capacity of the body decreases with aging (76), in older persons, especially in those that travel through the polar routes, the administration of antioxidants is necessary.

Burns *et al*. showed that in rats, vitamin A inhibited the acute inflammation by inhibiting the expression of 80% of the inflammation-related genes induced by the ^{56}Fe ion radiation (77). Levenson *at al*. suggested that vitamin A may have prophylactic and therapeutic effects in rats exposed to whole-body gamma irradiation. Precocious administration of vitamin A after whole-body irradiation blocks leukopenia, thrombocytopenia and adrenal growth (78). The study made by Ben-Amotz *et al*. suggested that β-carotene administration in rats before the whole-body irradiation can protect against the oxidative stress produced by radiation, scavenging the free radicals (79).

Valko *et al*. presented in their review the role of vitamin C supplementation in reduction of DNA damages, in the protein and the lipid oxidation (80). Vitamin C (L-ascorbic acid) directly interacts with hydroxyl ($HO^{\bullet}$) resulted during oxidative stress and form less toxic free radicals (81). Ascorbic acid levels significantly decrease after irradiation in liver, brain and spleen (82) that is why a supplementation with this antioxidant helps in protection against oxidative stress produced by ionizing radiation.

Vitamin E supplementation with doses lower than 200 IU/day is considered beneficial (83) and protects the cell membranes against lipid peroxidation induced by radiation (84). Anwar *et al*. showed in their study that vitamin E may protect the rats' intestinal mucosa during the whole body gamma-irradiation, vitamin E supplementation being administered 15 minutes before the irradiation and for 13 days after irradiation (85). The mechanisms that lead to oxidative stress during exposure to cosmic radiation can be inhibited by the administration of vitamins E and C, to block the DNA damage, lipid peroxidation, and proteins oxidation (86, 87) and to inhibit the oxidative stress in testicular tissue (88). Trolox, a water-soluble derivative of vitamin E, can prevent the X-ray-induced apoptosis in irradiated lymphocytes (89). Kulkarni *et al*. demonstrated in their study that γ-tocotrienol, an analogue of vitamin E, protected the hematopoietic tissue in whole-body irradiated mice: hematopoietic stem cells and progenitor cells were preserved and DNA damages were repaired almost completely (90). The radioprotective effects of γ-tocotrienol on intestinal cells were demonstrated by Suman *et al*. in their study performed in mice with total-body gamma irradiation. The prophylactic administration of γ-tocotrienol increases the expression of anti-apoptoic genes, protecting the gastrointestinal cells from radiation effects (91).

Selenium can increase the concentration of antioxidant enzymes (92) and can protect the fibroblasts (93). Rostami *et al*. confirmed in their study that selenium and vitamin E have synergic effects and their simultaneous administration before the exposure to X-rays provides a much more efficient protection than their separated use (94).

Vitamin B_{12} and folic acid supplementation in rats may protect against the radiation-induced oxidative stress and leukopenia (95).

Lipoic acid is a lipid and water-soluble vitamin-like compound that can react with: singlet oxygen ($^1O_2^{\bullet}$), hydroxyl ($HO^{\bullet}$), peroxyl radical ($RO_2^{\bullet}$), and hypochlorous acid (HOCl). Lipoic acid is a potent antioxidant that can protect the cell membranes, especially when it interacts with vitamin C and glutathione (96, 97). Lipoic acid can protect against oxidative stress produced by radiation (98) in ovary and testicular cells (99), or in the hematopoietic tissue (100). Dihydrolipoic acid (DHLA), the reduced form of lipoic acid, is a much more potent antioxidant, being able to regenerate other endogenous antioxidants from their radical form (101).

N-acetyl-cysteine (NAC), precursor of glutathione (endogenous antioxidant), proved protective effects in rats, in the whole body gamma-irradiation. Mansour *et al*. reported that NAC administration for 7 days, 1 g NAC/kg body weight, previous to irradiation, decreased the lipid peroxidation, nitric oxide formation, DNA fragmentation and increased significantly the antioxidant activity in gamma-irradiated rats (102). NAC reduces NO synthesis, production of free radicals and the release of cytokines, modulating NF-κB activity (103). Reliene *et al*. demonstrated that N-acetyl-cysteine inhibits oxidative stress and DNA fragmentation (104). The ovary tissue can be protected by N-acetyl-cysteine against the effects of ionizing radiation, NAC being able to restore the ovarian function by inhibiting the initiated oxidative stress (105). N-acetyl-cysteine provides protection against oxidative stress in liver, decreasing lipid peroxidation and nitric oxide concentration (106).

The study made *in vitro* by Kojima *et al*. on human blood lymphocytes suggested that cimetidine, an antagonist of histamine type II receptors, inhibits apoptosis, by acting as a scavenger of $HO^{\bullet}$ (107), a free oxygen species that is produced by ionizing radiation through water radiolysis. Mozdarani *et al*. showed in their study made *in vivo*, that cimetidine protected the lympho-hematopoietic system and increased the survival rate in the whole body gamma irradiated mice (108). The radioprotective effects of cimetidine at low LET and high LET exposure were also presented by Jiang *et al*. in their research on long-term irradiated rats. In irradiated rats, cimetidine inhibited lipid peroxidation, increased the activity of SOD and GSH-Px, increased the number of leukocytes and DNA content of bone marrow cells (109).

The researches made *in vivo* and *in vitro* on plant extracts showed that their content (polyphenols, flavones, catechins, procyanidins) has inhibitory effects on the mechanisms initiated by the X-ray and gamma-irradiation (110).

The study made by Farag and Darwish on water extract of Theobroma Cacao showed that the daily administration of cocoa powder has antioxidant effects: the late radiation effects after whole body gamma-radiation in rats were inhibited by increasing the activity of antioxidant enzymes (111). The ROS scavenging properties of cocoa powder were also seen in a study made by Noori *et al*. during which, significant increases of SOD, GSH and CAT were recorded in the liver of the rats that received 1 g cocoa powder/kg for 21 days (112).

Rabin *et al*. showed that strawberries can have a protective effect against the heavy ion particles (113), and the dietary supplementation with these fruits can improve the protection against cosmic radiation.

The study made on grapes by Singha *et al*. suggested that grape seed extract administered in high concentration, may be a potent protector through its antioxidant effects against low dose of ionizing radiation (114). Grape seed extract contains phenols that initiate the synthesis of liver antioxidants. The study made on rats that received grape seed extract before and after total-body irradiation, showed the protective effects of this extract against oxidative stress, with reduced lipid peroxidation and protein oxidation in the tissues (115).

The extract of *Olea europaea* L. leaves contains polyphenols with important antioxidant effects: oleuropein, hydroxytyrosol, verbascoside that are able to inhibit, *in vivo* and *in vitro*, the lipid peroxidation (116). Oleuropein and hydroxytyrosol reduce the oxidation of low-density lipoproteins and decrease the total, free and esterified cholesterol (117). Benavente-Garcia *at al*. showed in their study made in mice exposed to X-radiation that *Olea europaea* L. leaves extract is a potent radioprotective mixture of polyphenols (118).

The ferulic acid (hydroxycinnamic acid) is found in wheat, broccoli and rice bran and has an important antioxidant activity, neutralizing the nitric oxide, hydroxyl radical (119) and maintaining the antioxidant enzymes activity. Das *et al*. showed that the administration of ferulic acid before irradiation preserves the antioxidant enzymes (120). Ferulic acid can be an efficient protective substance in the treatment of the early period of low-dose radiation (121), for example, after an exposure to an increased cosmic radiation. The inhibitory effects of the ferulic acid on DNA damages after the exposure to gamma-radiation, its activity on initiation of the repair processes recommend this antioxidant as a treatment after an accidental exposure to an ionizing radiation. Ferulic acid promotes nuclear translocation of Nrf2 reducing the oxidative stress by scavenging reactive oxygen species (122). The nuclear factor erythroid 2-related factor 2, Nrf2, is a transcription factor that regulates the expression of antioxidant proteins, playing an important key role in ROS scavenging, even in radiation exposure (123).

The radioprotective effects of sulphoraphane, an Nrf2 inducer identified in cruciferous vegetables (broccoli, Brussels sprouts, cabbages), were studied by Mathew *et al*. on human skin fibroblasts. The study showed that sulphoraphane has dose-dependent effects and may protect against ionizing radiation damages if it is administered repeatedly before the fibroblast exposure (124).

Lycopene, an Nrf2 enhancer, is a carotenoid found in tomatoes, carrots, watermelon, gac and papayas that showed radioprotective effects in the study made by Srinivasan *et al*. in cultured human lymphocytes, in administration before irradiation. The prophylactic administration of lycopene reduced the number of micronuclei, dicentric and translocation frequency, protecting the normal lymphocytes against γ-radiation effects (125).

The administration of green tea extract (EGCG; epigallocatechin-3-gallate) has many beneficial effects. Stepien *et al*. studied the effects of green tea extract oral administration in NaCl-induced hypertensive rats and observed, in serum, significant decreases of LDL and total cholesterol (126), molecules that can be the sources for reactive species synthesis in CR exposure. Topical treatment with green tea extract can be used to reduce the alpha-particles effects on human skin, because this polyphenol has antioxidant effects (127) blocking the DNA methylation (128).

Recent studies proved that saffron has protective effects against ionizing radiation. Koul and Abraham showed that saffron administration in mice inhibited the gamma-radiation-induced oxidative stress and DNA damages (129). Crocin, picrocrocin and safranal are the active compounds of saffron. In a recent study, crocin and safranal prevented the DNA damages and the testicular cells damages induced by the gamma-radiation and crocin also showed significant antioxidant effects, scavenging the hydroxyl radical (130).

Since the CR exposure affects the immune system, the photodynamic therapy (PDT) can be an alternative treatment for the infections that may occur. Davies *et al*. presented in their study the favourable effects of photodynamic therapy with porphyrin as photosensitizer (PS), and pointed out the importance of combined use of PDT with natural compounds, like curcumin as PS (131). The antioxidant effects of curcumin, a polyphenol identified in turmeric, were evaluated by Scrobota *et al*. in experimental oral cancer. Their study showed that curcumin administration reduced in serum and in malignant oral mucosa the concentration of malondialdehyde, a lipid peroxidation end-product (132). Jelveh *et al*. established in their study that curcumin decreased the lipid peroxidation in fibroblasts membrane after gamma-irradiation, in mice (133).

Saada *et al*. evaluated the effects of omega-3 fatty acids in rats' brain and found that this substance may reduce the oxidative stress produced by the whole-body gamma irradiation, study that suggests the protective effects of omega-3 fatty acids on the ROS that are produced in the brain, before and during the exposure to radiation (134).

The oxidative stress in rat lens is enhanced by the exposure to gamma-radiation and the antioxidant capacity can be increased by the administration of melatonin, as Taysi *et al*. established in their study (135). Melatonin can be a good protector against cataract that develops in pilots.

In summary, the heterogeneity of the cosmic radiation can produce different effects on the human body through different mechanisms. The antioxidant supplementation can aid in increasing the protection against the cosmic radiation in persons that travel by plane at high altitudes, but the type and the dose of the antioxidants must be adjusted according to age, sex, time spent at high altitudes and conditions related to the variations of the magnetosphere intensity and solar activity. A healthy diet helps in the immunity processes and the oral administration of antioxidants before and during the travel by plane reduces the cosmic radiation-induced oxidative stress. The exposed tegument can be protected with topical treatment containing Green tea extract and the melatonin administration can prevent the cataract development. The further studies on antioxidants will complete the information required for a better protection against cosmic radiation-induced oxidative stress.

Abbreviations: CR, cosmic rays; CNS, central nervous system; ROS, reactive oxygen species; SOD, superoxide dismutase; CAT, catalase; GSH, glutathione; GSH-Px, glutathione peroxidase; NAC, N-acetyl-cysteine; LDL, low-density lipoproteins; LET, linear energy transfer; Nrf2, nuclear factor erythroid 2-related factor 2; PDT, photodynamic therapy; PS, photosensitizer

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