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Radioprotectors and Medicine

R. R. Baymuradov
Bukhara state medical institute

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ABSTRACT

Radioprotectors are very essential for treating various diseases which related with ionization.

At the moment, radiotherapy is in great demand for the treatment of various oncological diseases. But sometimes the radiation dose exceeds the norm and there is a need for the use of radioprotectors [1-18].

The following mechanisms of action of radioprotectors are possible [19, 20]:

- ✓ reduction of oxidants and free active radicals formed during tissue irradiation;
- ✓ an increase in the content of endogenous thiol compounds in tissues;
- ✓ formation of mixed disulfides and their temporary reversible bond;
- ✓ formation of temporary reversible bonds with radiosensitive groups of vital enzymes or other protein molecules, which ensures their protection at the time of irradiation;
- ✓ formation of compounds with heavy metals, providing an accelerated chain reaction of oxidation;
- ✓ migration of excess energy from the macromolecule to the radioprotector;
- ✓ inhibition of chain reactions of oxidation;
- ✓ absorption of secondary ultraviolet radiation;
- ✓ increase the stability and mobility of the body's defense mechanisms;
- ✓ inhibition of metabolism;
- ✓ detoxification or accelerated elimination of toxic products from the irradiated body.

Natural radioprotectors are plant compounds that protect the body's cells from damage by

radiation therapy. Natural herbal products are non-toxic, have proven therapeutic benefits and are used to treat various diseases. Of the 1,144 new medicines developed over the past 25 years, about 60% are derived from natural resources. To date, about 74 plant products have been tested for their radioprotective potential in various in vitro and in vivo studies.

Also, protective and therapeutic effects of ozone therapy (OT) were revealed in radiation therapy-induced testicular damage. OT performed before and after irradiation significantly increased the levels of glutathione, superoxide dismutase, catalase and GPx and reduced the level of thiobarbituric acid. In addition, testicular weight and Johnson scale score were increased after OT [21].

Treatment of hormonal suppression with gonadotropin-releasing hormone (GnRH) analogues restored spermatogenesis in irradiated rats [22], but such attempts were unsuccessful in irradiated mice, monkeys and humans. Also, it was tested a stronger hormonal suppression regimen (GnRH antagonist, acilin and plus Flutamide) for effectiveness both in restoring endogenous spermatogenesis and in enhancing colonization of transplanted stem spermatogonia. 4- and 11-week hormonal suppression also increased the spermatogenic development of transplanted stem spermatogonia in irradiated recipient mice by 3.1 and 4.8 times, respectively. Moreover, a 10-week hormonal suppression regimen restored the fertility of some 13.5-gy irradiated recipient mice from donor spermatogonial stem cells.

Polytadine has an antioxidant and anti-inflammatory effect, so scientists have studied [30] its potential use in radiation protection. They demonstrated that polydatin effectively reduces testicular damage and preserves sperm viability. It was also found that polytadine reduces the concentration of oxidative products of malonaldehyde and 8-hydroxy-2'-deoxyguanosine, inhibits apoptosis-related proteins such as Bax and caspase 3. Thus, polydatin effectively alleviates testicular damage after irradiation, mainly by reducing ROS and oxidative stress.

Another antioxidant substance N-acetyl-L-cysteine (NAC) at a dose of 125 mg/kg significantly weakens the pathological effects of synchrotron X-rays. This was proved after irradiating the male gonads with increasing doses of X-ray radiation and studying them 1, 10 and 20 days after irradiation [23].

Diallyl disulfide (DAD), the main organosulfur compound obtained from garlic, also has radioprotective properties that have been studied from the outside [24]. Interestingly, pretreatment with DAP weakened morphological damage and cell apoptosis caused by carbon ion irradiation. In addition, DAP increased radiation-induced expression of p53 and P21, suggesting that p53 may be involved in inhibiting cell cycle progression through increased regulation of P21.

It has been proven [25], the radioprotective effect of rolipram, a specific type IV phosphodiesterase inhibitor, which is known to increase the expression and phosphorylation of the cyclic adenosine monophosphate response element-binding protein, a key factor in spermatogenesis. Rolipram protected germ cells from radiation-induced apoptosis 12 hours after irradiation and significantly increased testicular mass compared to the control after 35 days. Rolipram also improved radiation-induced morphological changes in the testicles, such as changes in the diameter of the seminal tubules and the height of the epithelium. In addition, the rates of seminal tubule repopulation and stem cell survival were higher in the group receiving rolipram than in the irradiation group.

Ang II AT1 receptor antagonists telmisartan and losartan also have a weak radioprotective effect [26]. Scientists after irradiation of rats (5Gy) injected them with telmisartan (12 mg / kg/day) or losartan (34 mg /kg / twice / day) for 60 days. Among the damaged tubules in the testes of the treated animals, several seminal tubules were found in the process of recovery. This gonadal

rearrangement and restoration of spermatogenesis in treated animals reflect a partial attenuation of radiation-induced damage and a potential start of recovery.

In the following experiment, daily subcutaneous injections of medroxyprogesterone acetate (8 mg/kg) plus testosterone (1 mg/kg) (MT group) were used for 55 days before irradiation of rats. The data significantly show that MT in pretreatment completely excludes qualitative damage to spermatozoa and changes in spermatogenesis, and there are also no genetic damage in germ cells.

It was found that hydrogen-containing saline solution (HRSS) and WR-2721 can be used against radiation-induced testicular damage [27]. The animals were intraperitoneally injected with HRSS (5 ml/kg) and WR-2721 (200 mg/kg) for 15 minutes before the start of gamma irradiation. Testicular weight, testicular size, sperm count, sperm motility, apoptosis index, and biochemical assays were evaluated after 4-day initiation of irradiation. All these indicators were improved in the experimental groups in relation to rats that received only radiation.

[28] proved global changes in the expression of testicular cell genes caused by estradiol (E2) treatment. By minimizing changes in other hormones and using parallel data on the regulation of genes by these hormones, they were able to analyze the effect of estrogen on gene expression, regardless of changes in gonadotropin or testosterone. E2 promotes the restoration of spermatogenesis after gonadotoxic exposure to ionizing radiation.

Since it was impossible to obtain more effective and less toxic radioprotective substances from synthetic molecules, researchers have to focus on studying the radioprotective potential of natural products. Based on the above, radioprotective drugs are being studied all over the world, which do not cause cumulative or irreversible toxicity, provide effective long-term protection, remain stable for many years with a long shelf life and have all the necessary properties of an ideal radioprotective drug [29].

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