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The contribution of radioprotectors to minimize acute and deleterious damage caused by radiation.

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1. Introduction

Historically, radioprotectors are agents used to protect cells and minimize radiation-induced damage and can be applied before or at the time of exposure. These agents can extend from the tissue and organ level to the cellular and molecular levels. Radioprotectants can eliminate the formation of reactive compounds, detoxify radiation-induced species, and boost the stabilization of vital biomolecules. Thus, they can be classified as chemical or prophylactic radioprotectors, mitigators and therapeutic preparations [1 and 2].

Many techniques have been developed to establish the best methods for radioprotection, these techniques are based on the replacement of endogenous antioxidant levels, induction of DNA repair pathways, suppression of reactive oxygen species occasionally formed from radiation, in addition to the postponement of cell division. An ideal radioprotectant should have low toxicity at therapeutic concentrations, be readily available, be affordable, and can be administered orally. In addition, it must promote an absence of cumulative effects, as well as be effective for different types of radiation 3, 4 and 5]

With free radicals being responsible for reproducing a considerable part of the damage caused by ionizing radiation, radioprotective compounds can suppress these free radicals in addition to removing them, inducing the production of natural radioprotection, increasing DNA repair, reducing the post-radiation inflammatory response [6 and 7]. The presence and concentration of the protective agent against the primary damage of ionizing radiation in cells needs to be sufficient in such a way as to act in a compensatory way against the produced radicals, that is, promoting an antioxidant defense that reduces the oxidative stress generated by both free radicals, as by the non-radical reactive species formed [7 and 14].

The aim of this research was to review in the literature the radioprotective properties that have been discovered over the last few years with benefits to humans to minimize the acute damage and deleteriousness caused by radiation

2. Methodology

This is documentary research through a descriptive review of the literature and explanatory indirect approach. From June to August 2021, articles were collected from the main search engines academics: Scopus, Capes Journal Portal, Academic Google and PUBMED in the selection, more than ten thousand articles were found, since those denoting the behavior of radioprotectors and their mechanisms of action in the human body were irrelevant, in addition to verifying evidence that reduced the damage caused by radiation, so around thirty articles were selected according to the authors' readings, in which at least 35% were of direct interest to this review and the other 25% of indirect nature (Contained general information on the subject).

Articles from recent years that demonstrate advances, innovations and perspectives on the research and use of radioprotectors were selected, and the following keywords were used for the research: Radioprotectors. Radiological protection. Radioprotective effect. Natural radioprotectors.

3. Results and Discussion

According to Mun [5], the mechanisms of action of radioprotectors can be classified as: antioxidant and anti-inflammatory activity, enabling DNA repair processes and cell recovery and regeneration of hematopoietic and immunostimulant cells. It is known that exposure to ionizing radiation (IR) causes cell damage arising from the formation of free radicals and reactive compounds, the use of radioprotectors helps to mitigate the formation of these damages by destroying or not forming these radicals. From this, radioprotectors are used in such a way that they promote an antioxidant defense in cells at the time of exposure to radiation. The anti-inflammatory character consists of blocking the side effects from radiation, as IR indirectly activates an immune response, which is often expressed through generalized inflammation.

Also based on the study by Mun [5], DNA damage caused by free radicals, such as single-stranded breakage (SSB), double-stranded breakage (DSB) and base damage, can be recovered through recovery pathways. of the DNA itself. These repair pathways can also be improved by radioprotectors from the stimulation of DNA precursors synthesizing enzymes, which in a beneficial metabolic pool provide an effective radioprotective environment. The lymphoid and hematopoietic systems are also affected by exposure to IR, here it causes a dysfunction called hematopoietic syndrome which can be fatal. Thus, it is interesting that there is a maintenance of the regeneration of hematopoietic compounds, as well as the stimulation of the immune system mediated by the use of radioprotectors [15 and 16]

Mishra [8], in their study, shows that many antioxidant enzymes aim to attenuate the cellular load of reactive oxygen species (ROS), formed from the interaction of water with radiation (indirect action). These radioprotective antioxidants catalyze free radicals from these reactive species, aiming to balance redox reactions, and may also act to increase the expression of antioxidant genes. This mechanism confers the modulation of redox-sensitive genes, consisting of one more way of repairing cell damage. According to the present study, ROS can also generate mitochondrial depolarization, where there will be the release of cytochrome C that forms the apoptosome complex (APAF-1, cytochrome C), resulting in the activation of caspase 9 and caspase 3, starting a process of cell death. Some radioprotectors enter this context by inhibiting the apoptosis process, without interfering with the DNA repair mechanism, they may confer this inhibition through binding with the apoptosome complex, or through the inhibition of caspase 3.

Transferring genes and directing them to tissues is an option to rescue cells or promote their growth, in addition to increasing the detoxification of free radicals and inhibiting apoptosis by their respective genes, which can be applied after exposure to radiation. In addition, stem cell therapies have demonstrated a role in the recovery of tissues exposed to IR from a therapeutic approach derived from regenerative medicine, using mesenchymal stem cells in addition to progenitor cells, which was found to reduce radiation-induced xerostomia, fibronecrosis , osteoradionecrosis and organ damage, for example. From the secreted interleukins, stem cells play a mechanical role in cell repair and recovery. All this still needs to be deepened so that these therapy possibilities can be used in people exposed to radiation [8, 15 and 16].

A preliminary study evaluated the radioprotective effect of Brazilian propolis in CHO-K1 cells irradiated with Co60 through the biodosimeter micronucleus assay. CHO-K1 cells were incubated for 1 h at different concentrations of propolis (3 – 33 mg/ml and 3.2 mg/ml), as reported in the study, before irradiation with various doses of gamma radiation (0.5; 1; 2 and 4 Gy) (0.722 Gy/min). The results obtained showed a tendency to reduce the amount of radioinduced damage in cells previously treated with propolis, at the concentrations tested. The radioprotective effect was predominantly more effective in cells previously treated with concentrations of 16 and 33 mg/ml, before irradiation. However, at the highest concentration of 3.2 mg/ml, there was a smaller reduction in the amount of radioinduced damage in the form of MN compared to concentrations of 8, 16 and 33 mg/ml. The preliminary results obtained suggest the existence of an optimal concentration of propolis for radioprotection in irradiated cells [9].

The investigation by Brand and collaborators [10] determined the efficacy of the radioprotective aminothiol PrC-210 against X-ray induced DNA damage in normal human cells and observation of dose and time effect models for future use of PrC-210 in humans, through the γ-H2AX test, to determine if the possible radioprotector would be able to reduce the damage induced by radiation, thus, several parameters were visualized observing a reduction in many aspects such as 80% reduction of γ-H2AX foci induced by X-rays in Blood lymphocytes, after irradiation with 10, 50 and 100 mGy, according to the authors, a reduction of 8-

oxo-deoxyguanosine (a marker of ROS-mediated DNA damage) was also seen. PrC-210 also eliminated radiation-induced cell death in colony formation assays after 1 Gy irradiation. The protective efficacy of PrC-210 in each of these test systems supports the authors that its development as a radioprotectant for humans in multiple radiation exposure environments is soon possible.

The radioprotective effect of sodium diclofenac was investigated by Alok and Agrawala [11] the widely used non-steroidal anti-inflammatory drug was tested in a human model simulating pre and post irradiation scenario using human peripheral blood culture as a model. Both pre- and post-irradiation drug treatments reduced gamma radiation-induced formation of dicentric chromosomes, cytochalasin-blocked micronuclei, and γ-H2AX foci in human peripheral blood lymphocytes.

Amani, assessed the effects of radiological protection with oleuropein in order to find an effective radioprotector, with this pre-treatment of oleuropein (25, 50, 75, 100, 200, 400 and 800 nM, and 1, 5 , 10, 15, 20, 25, 30, 40, 50, 75, 100, 125, 150, 175 and 200 μM) significantly increased the percentage of cell viability compared to the irradiated group ($p<0.001$). But only the concentration of 100 μM was considered ideal, considering that treatment with human mononuclear cells with Oleuropein (100 μM) before 2 Gy gamma rays significantly decreased apoptosis, genomic damage and the occurrence of micronuclei in mononuclear humans caused by gamma radiation ($p<0.001$). Furthermore, treatment with Oleuropein (100 μM) without radiation did not lead to apoptosis, genotoxicity or clastogenic effects caused by Oleuropein in human mononuclear cells [12].

In a recent study by Moshafi and collaborators [13]. It showed that Ferulago angulata is a possible radioprotective agent because the plant extract reduced the frequency of IR-induced micronuclei in exposed cells. At the concentration of 200μM of F. angulata, a maximum reduction in the frequency of micronuclei (63.11%) was observed, which demonstrated a high degree of radioprotection. Subsequently, pre-treatment at a concentration of 200μM of F. angulata inhibited oxidative stress in irradiated lymphocytes, leading to a reduction in the frequency of Micronuclei and levels of malondialdehyde, while Superoxide desmutase activity was increased in exposed cells.

4. Conclusions

As these agents have the property of reducing the damage caused by radiation, the increase in research in the search for new compounds or radiopotentiating substances is notorious, which is very good when looking at a future perspective, considering that radiation is increasingly being used to the benefit of man in various places, which also increases the risk of accidental exposure. Making evident the search for substances that protect the human body from radiation.

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