Review Article Open Access

Preventive and therapeutic effects of natural antioxidants against damage caused by X-rays

Qaswaa Yousif Jameel[1], Thowiba Yousif Jameel[2], Nameer Khairullah Mohammed[3]

[1]Department of Food Science, Colleges of Agricultural and Forestry, University of Mosul, Mosul, Iraq, [2]Graduate School of Natural and Applied Science, Erciyes University, Kayseri, Turkey, [3]Department of Food Science, College of Agriculture, Tikrit University 3400, Tikrit, Iraq.

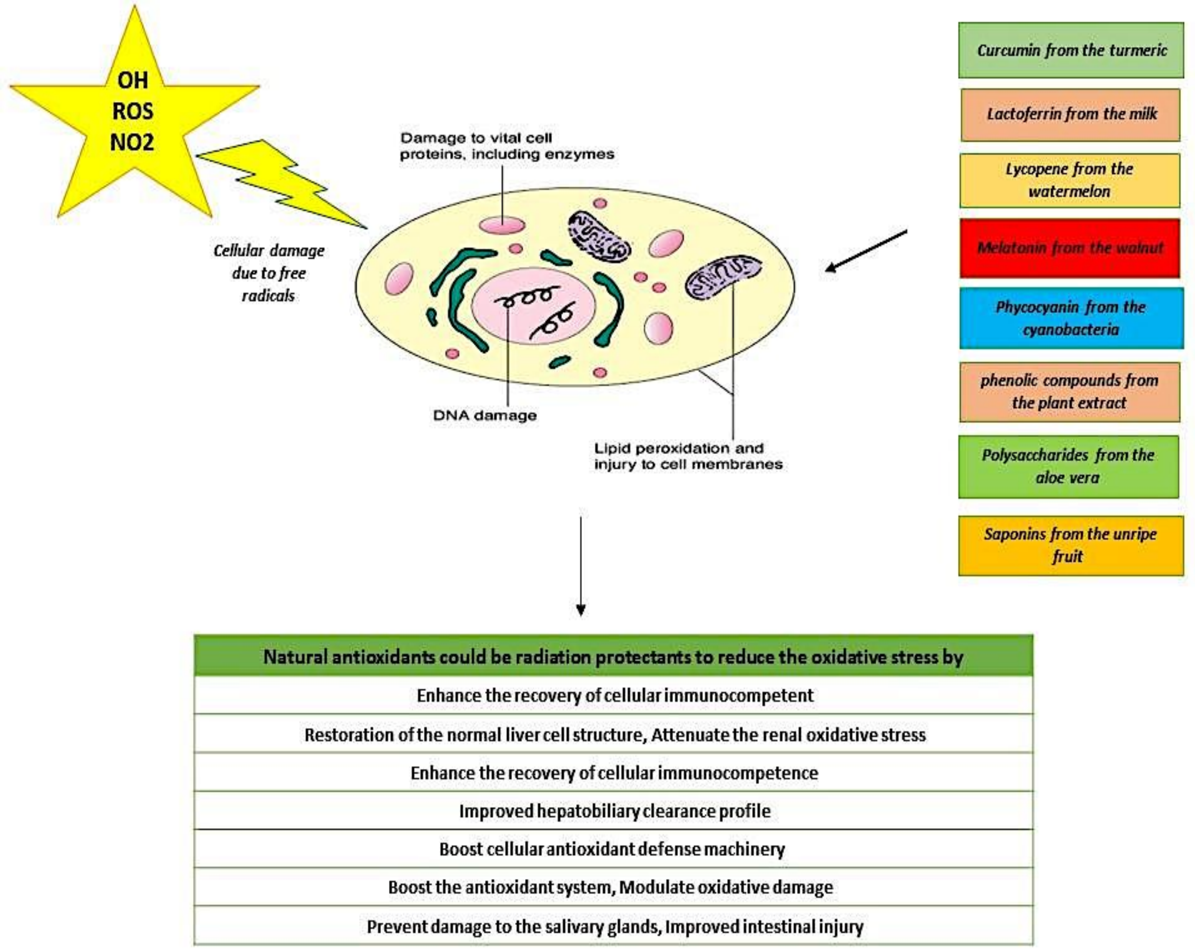
***Corresponding author:** Dr. Qaswaa Yousif Jamee, Department of Food Science, College of Agricultural and Forestry, University of Mosul, 94QJ+XWG, 80, Mosul, Nineveh Governorate, Iraq

Please cite this article as: Jameel Q. Y., Jameel T. Y., Mohammed N. K. Preventive and therapeutic effects of natural antioxidants against damage caused by X-rays-A review. *Bioactive Compounds in Health and Disease* 2025; 8(1): 1-20. DOI: https://www.doi.org/10.31989/bchd.87i1.1530

ABSTRACT

Plants and organic foods inherently contain bioactive compounds that combat oxidative stress effectively. A pharmacological overview of the activity and action of the active compounds against X-ray damage is provided, along with a review of the chemistry, functionality, and application aspects of active compounds derived from natural sources that may mitigate the harmful effects of X-ray radiation and shield biological systems from oxidative stress. The findings revealed that natural antioxidants such as natural compounds (lactoferrin, curcumin, melatonin, phycocyanin, and saponin) and phenolic compounds in plant extracts could be preventive and therapeutic agents against X-ray-induced toxicity. Natural antioxidants function as radiation protectants, mitigating oxidative stress induced by X-ray exposure. Given the non-toxic nature of the active compounds examined in this study, we suggest using them to produce a nutraceutical beverage that can be consumed or included in a daily diet to minimize oxidative stress.

Keywords: Active compounds, Antioxidant enzymes, Lactoferrin, Oxidative stress, Saponin, Watermelon juice



Graphical Abstract: Preventive and therapeutic effects of natural antioxidants against damage caused by X-rays

INTRODUCTION

X-rays are high-energy electromagnetic waves extensively utilized in materials science and medical diagnostics [1–2]. Healthcare providers, radiotherapy patients, and workers in sectors such as oil and gas frequently encounter X-ray radiation. [3–4]. Chronic exposure to X-ray radiation generates free radicals in healthy tissues, including the liver and surrounding tissues, within the human body. When X-rays interact with biological tissues, they can ionize atoms and molecules, forming free radicals such as reactive oxygen species (ROS). These free radicals have unpaired electrons, making them highly reactive and capable of causing damage to cellular components, including DNA [4–7]. The interaction of free radicals with cellular constituents, such as water and fat, can lead to the production of various reactive oxygen species, including hydrogen peroxide (H2O2), superoxide radical ($O_2^{\bullet-}$), and hydroxyl radical (•OH) [8–11]. These reactive oxygen species can further react with cellular molecules, including lipids, proteins, and nucleic acids, leading to oxidative damage; in particular, the production of lipid peroxides is a consequence of oxidative stress induced by reactive oxygen species [2–12]. Lipid peroxidation involves the oxidation of polyunsaturated fatty acids in cell membranes, generating lipid hydroperoxides and other reactive lipid species. This process can disrupt cell membrane integrity, impair cellular function, and contribute to tissue damage and inflammation [13]. The liver, a vital organ responsible for detoxification and metabolism, is particularly susceptible to oxidative stress from free radicals generated by X-ray radiation [14]. Oxidative damage to liver tissues can impair hepatic function and contribute to the developing of various liver diseases, including inflammation, fibrosis, and cirrhosis [15]. Overall, the production of free radicals and reactive oxygen species due to X-ray radiation exposure underscores the importance of mitigating oxidative stress and protecting cellular components from damage [16]. Enhancing antioxidant defenses and mitigating oxidative damage are key strategies for minimizing the harmful effects of prolonged X-ray exposure on human health [17]. There is a linear correlation between X-ray exposure and carcinogenesis (formation of cancer), such as skin cancer, liver cancer, cervical cancer, colon cancer, and lung cancer [18]. Other previous studies have indicated that free radicals generated by X-rays can reduce the levels of antioxidant enzymes, such as superoxide dismutase, catalase, and glutathione, thereby compromising immune functions [19–20]. They can also lead to decreased monoamine levels in the stomach and small intestine [21–24]. Therefore, protecting healthy body tissues from genotoxicity caused by free radicals is critical.

Natural antioxidants in plant extracts have been demonstrated to protect human cells against free radicals with no side effects[25 –26]. As we are frequently exposed to X-rays daily, antioxidants from foods are essential for reducing the risk of free radicals caused by X-rays [27]. Compared with synthetic compounds, natural antioxidants in plants and organic foods have received significant attention [28]. Various review articles and studies have emphasized the effectiveness of active compounds in protecting against oxidative stress caused by free radicals and their associated human health risks [29]. However, there is a notable gap in methodological evaluation concerning the efficacy of antioxidants against the harmful effects of X-radiation. While antioxidants have been extensively studied for their potential to mitigate oxidative stress and damage caused by various environmental factors and diseases, research specifically focused on their effectiveness against the harmful effects of ionizing radiation, such as X-rays, is relatively limited, mixed, and often inconclusive. Therefore, this review aims (1) to evaluate the scientific evidence relevant to the chemistry of natural compounds and their potential health-promoting role in human/our diet, (2) to identify gaps in the current literature, and (3) to suggest potential opportunities for future research and development related to the therapeutic and protective functions of the active compounds while addressing their roles in countering the harmful effects of X-radiation.

Oxidative stress induced by X-radiation: The term oxidative stress involves both a disruption of the cell's redox balance and an imbalance in the production of reactive oxygen species (free radicals) and antioxidant defenses [30–32]. Superoxide anion radicals, hydroxyl, alkoxyl, lipid peroxyl radicals, nitric oxide, and peroxynitrite are examples of reactive oxygenated/nitrogenated species [33–34]. Oxidative stress can be described by a decreased ability of endogenous systems to fight oxidative attacks on target biomolecules, which results from either an increased formation of ROS/RNS or a decrease in antioxidant protective ability [35–36]. Free radicals interact with cellular constituents inside cells, such as water and fat. The interaction of free radicals with biological systems produces reactive oxygen species such as hydrogen peroxide, superoxide radicals, and hydroxyl radicals, which produce lipid peroxides [31–32]. These findings clarify how reactive oxygenated/nitrogenated species play a role in disease development. Specific factors that cause oxidative damage in cells, such as the overexpression of oncogene genes, the generation of mutagen compounds, the stimulation of atherogenic activity, the occurrence of senile plaque, or inflammation, can be triggered by an imbalance between oxidant species and the antioxidant defense system, the consequences of which are cancer, neurodegeneration, cardiovascular disease, diabetes, and kidney disease [36–37]. Exposure to X-radiation has caused liver and kidney tissue damage, DNA damage, enzyme dysfunction, enhanced cell apoptosis, lipid peroxidation, and damage to the central nervous system (Figure 1) [25]. There is a linear correlation between X-ray exposure and carcinogenesis (formation of cancer), such as skin cancer, liver cancer, cervical cancer, colon cancer, and lung cancer [19]. There is a linear correlation between X-ray exposure and DNA impairments, which are caused primarily by indirect impacts comprising crosslinks, base damage, single-strand breaks, and double-strand breaks, resulting in complex DNA impairment. It may cause mutations (noncancerous) and consequent carcinogenesis depending on the dose ratio and time, mode of delivery, intensity, field size, and overall cumulative dose after radiation exposure [38]. The continuous manufacture of free radicals in the human body plays a key role in increased cell apoptosis [39], dysfunction of enzymes [24], and DNA damage [19]. Malondialdehyde and 4-hydroxynonenal, as well as isoprostanes from unsaturated fatty acids, are produced when lipids undergo oxidative collapse [25].

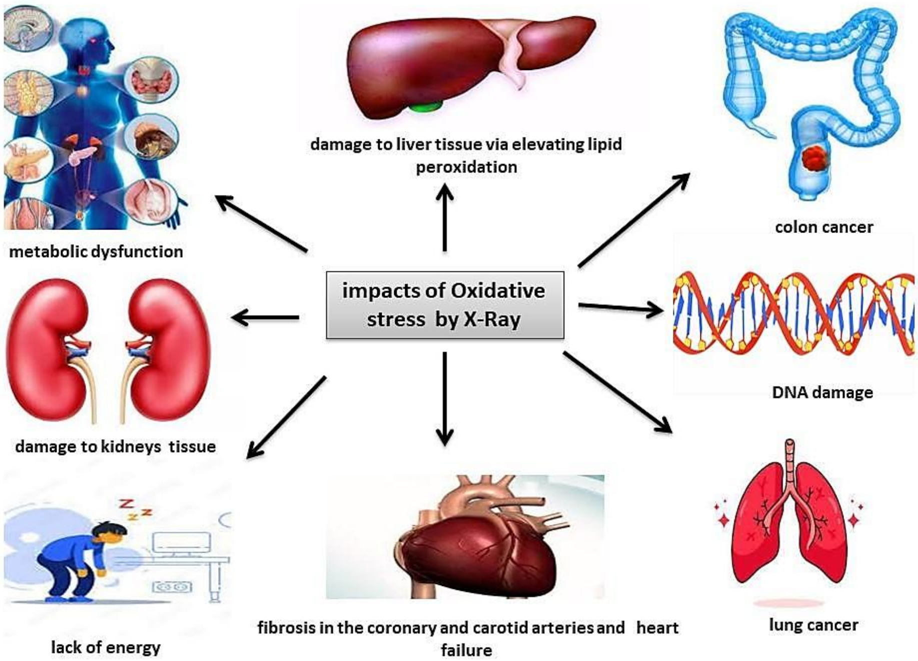


Figure 1: Effects of X-ray irradiation on oxidative stress

Role of natural antioxidants in preventing oxidative stress: Natural antioxidants primarily act as chain breakers, donating hydrogen to neutralize free radicals. Some secondary antioxidants are singlet oxygen quenchers, peroxide decomposers, metal chelators, oxidative enzyme inhibitors, and X-ray absorbers [40– 41]. Antioxidant functions imply a decrease in oxidative stress, DNA mutations, malignant transformation, and other parameters associated with cell damage. Epidemiological studies have shown the ability of antioxidants to affect reactive oxygen species activity [42–43]. Natural antioxidants are found in functional foods and several fruits and vegetables; they can be added as natural food preservatives [45] to prevent and cure various chronic ailments [44]. As we are frequently exposed to X-rays in daily life, we must take antioxidants from food to reduce the risk of free radicals caused by X-rays [46]. Compared with synthetic compounds, natural antioxidants in plants and foods have received significant attention [47–48]. Therefore, they must consume natural antioxidants in plants and foods instead of synthetic antioxidants [39]. Natural antioxidants help improve pathological conditions by slowing disease progression (Figure 2) [49–50]. Frequent X-ray exposure generates free radicals that interact with proteins, lipids, and DNA, leading to cellular dysfunction [51–53]. Endogenous enzymes, such as CAT, SOD, and GSHPx, may inhibit the oxidative damage caused by free radicals in human cells [36]. During oxidative injury, the levels of these enzymes within the cells increase to protect them. The SOD enzyme converts $O2–$ into $H2O2$, whereas CAT converts H_2O_2 into H_2O and O_2 [51–55]. Catalase transforms H_2O_2 to H_2O and O_2 [53], whereas GSHPx converts H_2O_2 to H_2O, preventing the oxidation and interlacement of thiol groups in proteins [56]. Effective defense and repair processes are present in natural antioxidants to safeguard against oxidant species. During the reduction in oxidative stress, energy is shifted from free radicals to antioxidant molecules, resulting in a state of energy-rich triplet. The trapping of other OH, ROS, NO_2, or peroxynitrite results in the oxidative decomposition of the molecules of antioxidants. Therefore, antioxidants may safeguard against DNA, protein, and lipid oxidation in vivo [57–59].

Figure 2. Targets of natural antioxidants

Biological activities of active compounds, which are found naturally against X-ray-induced damage in vivo: Choosing active compounds with minimal side effects that are readily available is crucial when considering potential radioprotective agents. Several compounds have been studied for their biological activities against oxidative stress induced by X-radiation, with varying degrees of effectiveness and safety profiles. In this review, these active compounds were selected based on their demonstrated antioxidant, anti-inflammatory, and radioprotective properties and their relatively low risk of side effects and availability.

Effects of lactoferrin against X-ray radiation: Lactoferrin is a crucial component of the mammalian innate immune system. It is an 80 kDa iron-binding multifunctional glycoprotein found in various biological fluids, including milk [60–62]. Lactoferrin is vital in host defense against pathogens and modulating immune responses [63–66].

Table 1 summarizes the antioxidant effects of lactoferrin in vivo and its ability to modify biochemical indicators of oxidative stress. According to a study by Feng *et al.* [64], lactoferrin at a concentration of 15.30 mg/kg was administered to male BALB/c mice for 30 days after radiation exposure at a 7 Gy X-ray dose. This reduced radiation-induced damage to DNA in hepatocytes. Leukocyte, erythrocyte, and platelet counts are the laboratory indicators of rapid recovery. The superoxide dismutase (SOD) level increased significantly, whereas the malondialdehyde (MDA) level significantly decreased. A review published by Sakai *et al.* [65] showed that administering 4 mg/kg body weight lactoferrin to male mice after they were exposed to 9 Gy of whole-body X-irradiation prevented damage to the salivary glands and regulated submandibular salivary gland branching morphogenesis. It also induced cell proliferation and improved the recovery rate of acinar cells after irradiation, especially regarding the restoration of the salivary gland percentage. In a different study by Wei *et al.* [66], lactoferrin was given to male BALB/c mice at doses of 2, 4, and 6 mg/kg bw before they were exposed to doses of 5 or 8 Gy of radiation, which decreased DNA damage in the mice after X-ray irradiation, increased cell viability, activated SOD and GST enzymes, and reduced cell death.

Regarding intestinal histology, there was a notable improvement in radiation-induced injury. There was also a significant increase in villus length and its ratio to crypt depth, a considerable decrease in the serum levels of IL-6 and TNF-α, a reduction in the radiation-induced expression of IKKα/β and NF-κB, and an improvement in intestinal injury through the downregulation of NF-κB expression and a decrease in inflammatory cytokines. Following a report by Nishimura *et al*. [67], male C3H/He mice were intraperitoneally administered lactoferrin at a dose of 4 mg/kg body weight after 30 consecutive days of 6.8 Gy whole-body X-ray exposure. This resulted in increased hemoglobin and hematocrit values and lactoferrin, demonstrating hydroxyl radical scavenger activity in vivo and decreasing glutathione depletion in the liver, kidney, and intestine. According to a study by Feng *et al*. [67], a high dose of lactoferrin (15.30 mg/kg) significantly decreased DNA damage caused by exposure to 7 Gy of X-rays. These findings indicate that lactoferrin, by scavenging free radicals and enhancing DNA repair processes, can protect cells from damage caused by radiation. Sakai *et al.* [64]. focused on the effects of a moderate lactoferrin dose (4 mg/kg) on radiation-induced damage to the salivary glands of animal models. These findings demonstrated that lactoferrin was an excellent defense against damage caused by 9 Gy of X-rays to the salivary glands. After radiation exposure, lactoferrin affects the structure and function of acinar cells. It also prevents damage to the salivary glands, regulates the morphogenesis of submandibular salivary gland branches, increases the expression of phosphorylated ERK1/2 and AKT proteins, and induces cell proliferation. As reported in a study by Wei *et al*. [65], intestinal damage from 5.8 Gy of radiation exposure decreased after low doses of lactoferrin (2, 4, and 6 mg/kg) were applied. The protective effects of lactoferrin are linked to a decrease in inflammatory cytokine levels, which decreases intestinal inflammation. A low dose of lactoferrin (4 mg/kg) significantly reduced glutathione depletion in the liver, kidney, and intestine caused by oxidative stress induced by 6.8 Gy of radiation, according to an additional research study by Nishimura *et al*. [66]. A crucial antioxidant that is essential for preventing cell damage is glutathione.

Effects of natural pigments against X-ray radiation: Several plant pigments have demonstrated remarkable efficacy in mitigating the harmful effects of X-ray exposure. These include lycopene, which is abundant in watermelons [68]; curcumin, the primary bioactive compound in turmeric [69]; and phycocyanin, which is derived from blue–green algae [70]. Lycopene, curcumin, and phycocyanin might help protect cells from damage (**Figure 3**). Lycopene is a type of organic pigment called a carotenoid; it is related to beta-carotene and gives some fruits, such as watermelon, a color; Lycopene, a potent antioxidant, protects cells from oxidative damage [71–72].

Table 1 summarizes the antioxidant effects of lycopene, found in watermelon juice in vivo, and its ability to modify the biochemical indicators of oxidative stress. Based on a study by Mohammad *et al*. [73], when male ICR mice were given 50 mg/kg bw of lycopene orally for 28 days before exposure to 100 Gy/min X-rays, lycopene in watermelon juice restored their intracellular antioxidant activities by significantly increasing the levels of glutathione and superoxide dismutase (SOD), decreasing malondialdehyde in liver tissues, helping reduce reactive oxygen species (ROS) and hydrogen peroxide (H2O2) in the serum, decreasing hydroxyl radical activity while increasing the serum levels of superoxide dismutase, glutathione-s-transferase, and catalase enzyme activity, and finally effectively attenuating apoptosis. Curcumin, a yellow-orange pigment, serves as the primary bioactive component of turmeric [73]. The compound is a diarylheptanoid, a family of natural phenols responsible for the yellow color of some plants[75]. Table 1 summarizes the antioxidant effects of curcumin in vivo and its ability to decrease the harmful effects of X-rays by reducing oxidative stress. According to a study by Cervelli *et al*. [76], male Wistar albino rats presented reduced levels of hydrogen peroxide, blood urea nitrogen, and malondialdehyde when given 10 mg/kg body weight curcumin for fourteen days after exposure to radiation at 0.25 Gy/min. In addition, it decreased lipid peroxidation and the expression of apoptotic and inflammatory markers, decreased renal dysfunction, balanced changes in renal morphology, and preserved the tissue structure of the kidneys. It also increased glutathione and total antioxidant levels.

Phycocyanin is a pigment-protein complex from the light-harvesting phycobiliprotein family [77]. Phycocyanin is a characteristic light blue color and is an accessory pigment to chlorophyll [78]. Phycocyanin is often found in cyanobacteria that thrive around hot springs; phycocyanin is used in the food and beverage industry as a natural coloring agent and in sweets and ice cream [79]. Phycocyanin has been shown to have anti-inflammatory and antioxidant properties, inhibit lipid peroxidation, and prevent hepatotoxicity in rats [78–79]. Table 1 summarizes the antioxidant effect of phycocyanin in vivo and its ability to decrease the adverse effects of X-rays by reducing oxidative stress. Based on research by Liu *et al*. [80], in mice given 200 mg/kg phycocyanin before being exposed to 0.47 Gy/min for seven consecutive days, phycocyanin treatment markedly upregulated radiation-induced oxidative stress damage by reducing the levels of malondialdehyde alanine aminotransferase, aspartate aminotransferase, lipid peroxidation, and apoptotic and inflammation markers; preserving the liver tissue structure; decreasing the level of ROS in the liver; and reducing DNA damage. Moreover, it increased glutathione and total antioxidants in the serum and liver. Notably, Mohammad *et al.* [73] reported that a dose (50mg/kg bw) of lycopene given orally to male ICR mice effectively modulates oxidative damage resulting from a 100 Gy/min dose. Lycopene given orally to male ICR mice effectively modulates oxidative activity, restoring intracellular antioxidant activity, reducing malondialdehyde levels in liver tissues, reducing hydroxyl radical activity, and increasing superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in the serum. It was reported that a dose (200 mg/kg) of phycocyanin has strong effectiveness in suppressing the harmful effects caused by a dose of 0.47 Gy/min X-rays through reduced malondialdehyde, alanine aminotransferase, aspartate aminotransferase, lipid peroxidation, and apoptotic and inflammatory markers; preserving the liver tissue structure; decreasing the level of ROS in the liver; and reducing DNA damage. Moreover, it increased glutathione and total antioxidants in the serum and liver tissue.

Effects of melatonin on X-ray radiation: Melatonin is found in many foods, such as walnuts [81]. Melatonin was first reported as a potent antioxidant and free radical scavenger in vivo [82]. Melatonin enhances cytokine production and promotes T-cell expansion, counteracting acquired immunodeficiencies [85] and anti-inflammatory effects [83]. Table 1 summarizes the antioxidant effects of melatonin in vivo and its ability to decrease the adverse effects of oxidative stress. A study by Zhu et al. [84] showed that when melatonin was administered intraperitoneally to mice at a dose of 100 mg/kg before irradiation at 1.5 Gy/min for 30 min, melatonin pretreatment significantly inhibited radiation-induced DNA strand breaks and lipid peroxidation. The inhibition of apoptotic proteins and radiation-induced sperm abnormalities in cauda-epididymes were reduced considerably. Another study by Musa et al. [85] revealed that administering 50,100 mg/kg melatonin to male Wistar rats for 30 min before exposure to 8 Gy X-ray radiation reduced malondialdehyde levels, induced cell proliferation, delayed the onset of mortality; reduced hydroxyl radical activity; increased superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in the liver and kidney tissue; and restored normal liver and kidney cell structure in pretreated animals. The increase in superoxide dismutase activity protected liver tissues.

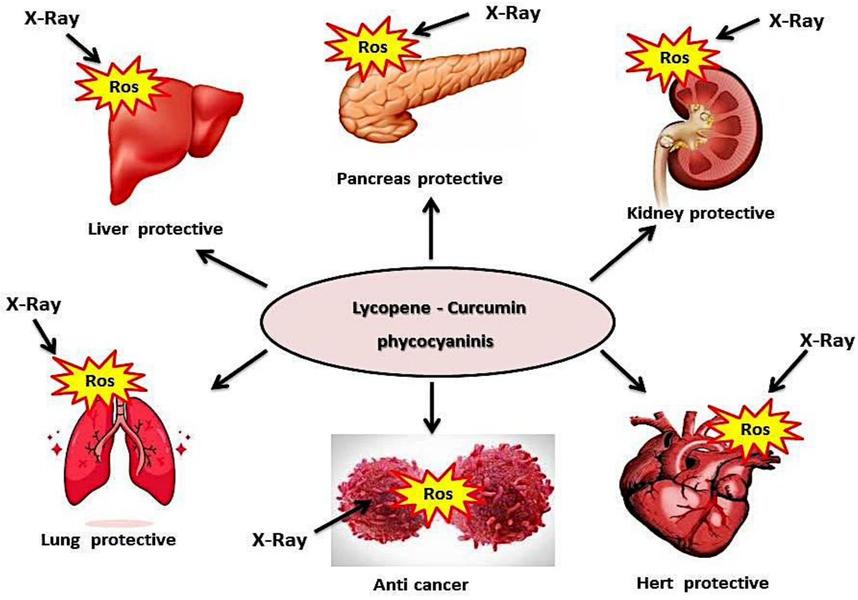


Figure 3. Effects of natural pigments on oxidation

In a different report by Carrillo *et al.* [86], the administration of 200 mg/kg melatonin to female C57BL/6 N mice intraperitoneally daily for 2 weeks before exposure to 3,12 Gy X-rays led to reduced hydroxyl radical activity with increased superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in liver and lung tissue. It restored normal liver and lung cell structure in pretreated animals, with decreased malondialdehyde levels. Zhu *et al.* [84] reported that a dose of melatonin (100 mg/kg) has a positive effect on reducing oxidative stress and increasing antioxidant enzymes via the inhibition of radiation-induced DNA strand breaks and lipid peroxidation, the inhibition of apoptotic proteins, and radiation-induced sperm abnormalities in cauda-epididymes, which are significantly affected by irradiation of the bodies of the animals at a dose of 1 or 5 Gy/min for 30 min (X-rays). The results of the study by Musa *et al.* [85] revealed that a dose (50,100 mg/kg) of melatonin was sufficient to increase the recovery of cellular immunocompetence in experimental animals that were subjected to oxidative stress because 8 Gy X-ray radiation was used for 30 minutes to delay the onset of mortality; reduce hydroxyl radical activity; increase superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in liver and kidney tissue; and restore the normal liver and kidney cell structure in the pretreated animals, improve superoxide dismutase activities, and protect liver tissues. Carrillo *et al.* [86] reported that a dose of melatonin (200 mg/kg) positively reduced the oxidative stress caused by X-ray radiation at a dose of 3.12 Gy through the protected male reproductive system.

Effects of polysaccharides against X-ray radiation: Polysaccharides are natural biomacromolecules found in plants, fungi, algae, animals, and bacteria [87]. Owing to their nontoxicity, stability, biodegradability, biocompatibility, and excellent antioxidant activity, polysaccharides have potential value in treating or preventing disease caused by oxidative stress [88]. Polysaccharides can reduce damage to the cell structure, regulate the signaling pathways related to antioxidation, improve the intracellular antioxidant enzyme system, reduce the substances that efficiently produce ROS, and protect the body tissue from ROS-induced damage through free radical scavenging activity and immunomodulatory activity [89]. Polysaccharides, found in aloe vera and ganoderma lucidum karst, have potential value in treating or preventing diseases caused by oxidative stress induced by X-rays [90]. Table 1 lists the antioxidant properties of polysaccharides in aloe vera gel tested in male BALB/c mice by Bala *et al.* [91]. A study used 50 mg/kg body weight aloe vera gel extract with X-ray radiation at 2 Gy/min for 30 consecutive days, and aloe vera gel extract helped scavenge hydroxyl free radicals, thereby eliminating chromosomal abnormalities. A minute increase in total antioxidants, thus protecting against hepatic and renal damage, improved hepatic and renal function parameters, which were associated with a reduction in ROS levels compared with those of their irradiated counterparts. Another review by Bala *et al.* [92] reported that administering aloe vera gel 50 mg/kg to male BALB/c mice via gavages after whole-body X-irradiation at 0.258 Gray for 30 days induced cell proliferation, reduced ROS activity, reduced hydroxyl radical activity; increased superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in testicular tissue; and restored standard testicular cell structure in pretreated animals. Another review by Bala *et al.* [93] reported that aloe vera extract (50 mg/kg) can be administered to male BALB/c mice after whole-body X-irradiation with 2 Gray; aloe vera gel extract helps to inhibit lipid peroxides and scavenge ROS, and a minute increase in the glutathione content in the lungs, along with significantly improved bone mineral density and the hepatobiliary clearance profile, was detected. Ganoderma Lucidum Karst is a feathery fungus widely found in China and Japan and has bioactive substances such as polysaccharides [94].

Ganoderma lucidum has antihepatotoxic and free radical scavenging properties, influences the cell cycle and cellular signal transduction, reduces lipid peroxidation, inhibits leukemic cell growth, and induces the differentiation of leukemic cells into mature monocytes. Furthermore, it may inhibit platelet aggregation, impede complex viral interactions with cell plasma membranes, inhibit tumor growth, and reduce other ailments, such as sleeping problems, headaches, glomerulonephritis, and tumors [95]. Table 1 summarizes the effects of polysaccharides in Ganoderma lucidum in vivo and their ability to decrease the harmful effects of oxidative stress. A review of the literature by Kubo *et al.* [94] revealed that when ganoderma lucidum extract was administered orally at doses of 1.25, 2.5, or 5 mg/kg bw to male B6C3F1 (Crj:B6C3FI) mice, for 1 week before irradiation at 2, 4, 7, 8, 10, or 12 Gy/min, animals treated with Ganoderma lucidum extract before irradiation exhibited a significant time-dependent increase in the studied hematological parameters, reduced hydroxyl radical activity, and increased survival rates and recovery of the seminiferous tubules [93]. The concentration (50 mg/kg body weight) of polysaccharides present in aloe vera gel has proven to be enormously effective against the damaging effects that occur when X-rays are used at a dose of 2 Gy/min through the scavenging of hydroxyl free radicals, thereby eliminating chromosomal abnormalities, providing protection against hepatic and renal damage, and improving hepatic and renal function parameters, which are associated with a reduction in reactive oxygen species (ROS) levels in male BALB/c mice [92]. Bala *et al.* [91] reported that a concentration of 50 mg/kg polysaccharide isolated from Aloe vera has a strong positive effect on the harmful damage caused by a dose of 0.258 Gray for 30 days through the induction of cell proliferation, a notable reduction in ROS activity, a reduction in hydroxyl radical activity with increases in superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in testicular tissue, and the restoration of the standard testicular cell structure in male BALB/c mice. A study conducted by Bala *et al.* [92] revealed that a concentration (50 mg/kg) of polysaccharides isolated from aloe vera leaves intensely effectively suppressed the harmful effects caused by a dose of 2 Gray X-rays. By helping to inhibit lipid peroxides and scavenge ROS, a minute increase in the glutathione content in the lung occurred, along with a significant improvement in the bone mineral density and the hepatobiliary clearance profile in male BALB/c mice. A study conducted by Kubo *et al.* [93] revealed that the concentrations (1.25, 2.5, and 5 mg/kg bw) of polysaccharides isolated from Ganoderma lucidum demonstrated strong effectiveness against the damaging effects resulting from X-ray doses (2, 4, 7, 8, 10, and 12 Gy/min) by increasingincreasing the studied hematological parameters, reducing hydroxyl radical activity, and increasing the survival rate and recovery of the seminiferous tubules in male B6C3F1 (Crj:B6C3FI) mice.

Effects of phenolic compounds against X-ray radiation: Phenolic compounds are important plant constituents with redox properties responsible for antioxidant activity, and the hydroxyl groups in plant extracts facilitate free radical scavenging [95]. Many studies have shown that phenolic compounds, such as those found in Polyalthia longifolia leaf extract, costus afer leaf extract, *Olea europaea* L. leaves, and Pycnanthus angolensis seed extract, have inhibitory effects on damage resulting from X-rays [96–97]. Polyalthia longifolia is a famous medicinal plant grown in India and Pakistan and contains bioactive substances such as phenolic compounds [98]. The literature indicates that polyalthia longifolia reduces lipid peroxidation, antioxidant, anti-inflammatory, and antimicrobial activities; protects DNA and other cellular macromolecules from oxidative stress; and preserves biological processes [99]. Table 1 lists the antioxidant properties of phenolic compounds from Polyalthia longifolia leaf extract tested in male Swiss albino mice by Jothy *et al.* (2016) [100]. A study used 250 or 500 mg/kg BW Polyalthia longifolia leaf extract for 30 consecutive days after exposure to 1.33 Gy/min and 6 MV/min X-ray radiation for one hour. Polyalthia longifolia leaf extract helps scavenge hydroxyl free radicals and has anti-inflammatory and antimicrobial activity; increases superoxide dismutase and catalase activity in both the liver and intestine; reduces hydroxyl radical activity; increases superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in liver tissue; and restores the normal liver cell structure in pretreated animals. Cooper is a famous plant grown in tropical Africa with bioactive substances such as phenols [101]. Many studies have shown that it has antioxidant, anti-inflammatory, and antibacterial properties and is also an antidote against poison [102]. Table 1 summarizes the antioxidant effects of phenolic compounds in Costus after leaf extraction against damage caused by X-rays, A study by Akomolafe. and Chetty. (2021) [103] used 250 mg/kg BW 6 days after exposure to 3,6 Gy/min X-ray radiation. Costus combined with leaf extract helped reduce the elevated levels of ALT and AST, increase superoxide dismutase activity and catalase activity in the liver, restore the normal numbers of red blood cells, platelet counts, and white blood cells; and restore the normal liver cell structure in animals pretreated with leaf extract [104]. Another review by Aguayo Torrez [26] revealed that the administration of costus after leaf extract (250 mg/kg body weight) to male and female Swiss albino mice via gavage after whole-body X-irradiation (3, 4, 6, or 8 Gy/min) for 36 days induced cell proliferation; delayed the onset of mortality; reduced hydroxyl radical activity; increased superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in the liver and kidney tissues; and restored normal liver and kidney cell structure in the animals pretreated with leaf extract. Olea europaea is a famous medicinal plant grown in Australia and southern Africa and contains bioactive substances such as phenolic compounds [105]. The literature indicates that olive leaf extract reduces lipid peroxidation, antioxidant, anti-inflammatory, and antimicrobial activities[106] and reduces other ailments, such as colds, sleeping problems, leprosy, and tumors[107]. Table 1 summarizes the effects of phenolic compounds extracted from Olea europaea L. leaves in vivo and their ability to decrease the negative effects of X-rays by reducing oxidative stress. A review of the literature revealed that administering Olea europaea L. leaves extracted orally at doses of 24.20 and 30.30 mg/kg bw to male Swiss mice before irradiation at 2 cGy/min reduced DNA damage; reduced hydroxyl radical activity; increased superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in liver and kidney tissues; and restored normal liver and kidney cell structure in pretreated animals, facilitating DNA repair and restoring the lymphocyte percentage[108]. Pycnanthus angolensis is a plant that is widely grown in West Central Africa and contains bioactive substances [109]. Many studies have shown that it has anti-inflammatory, anti-inflammatory, and antibacterial properties and is also an antidote against poison [110]. Several studies have reported that Pycnanthus angolensis seed extract has various health benefits, such as antihyperlipidemic, antiobesity, antibacterial, and fat deposition-inhibiting effects, and that the water extract of Pycnanthus angolensis has in vivo antioxidant activity [111]. Table 1 lists the antioxidant properties of phenolic compounds in pycnanthus angolensis warb seed extract tested in human blood samples by Achel *et al.* [112]. A study used 0.2 mg/kg BW pycnanthus angolensis warb seed extract to prevent the structural and molecular transformation of human serum albumin irradiated with X-ray radiation at 4, 6, 8, and 10 Gy per hour, which protects human serum albumin against damage to its secondary structure after exposure to 4, 6, 8, and 10 Gy per hour X-ray radiation. Pycnanthus angolensis warb seed extract helped scavenge hydroxyl free radicals, thereby eliminating an increase in bityrosine; there was a minute increase in the protein configuration rate. The concentration (250, 500 mg/kg body weight) of the phenolic compounds present in the Polyalthia longifolia leaf extract has proven to be strongly effective against the negative effects that occur at doses of 1.33 Gy/min and 6 MV/min from X-ray radiation for one hour. By increasing superoxide dismutase and catalase activity in both the liver and intestine, hydroxyl radical activity is reduced, superoxide dismutase, glutathione-s-transferase, and catalase enzyme activity are increased in liver tissue, and the normal liver cell structure is restored in male Swiss albino mice [100]. The concentration (250 mg/kg BW) of phenolic compounds present (costs after leaf extract) effectively suppressed the harmful effects resulting from an X-ray dose of 3.6 Gy/min through increasing superoxide dismutase and catalase activity in the liver, restoring normal numbers of red blood cells, platelet counts, and white blood cells; and restoring the normal liver cell structure in male BALB/c mice [103]. On the other hand, [16] reported that the concentration (250 mg/kg of body weight) of phenolic compounds found in (costus after leaf extract) effectively curbed the harmful effects resulting from a dose of (3, 4, 6, 8 Gy/min) radiation. x reduces hydroxyl radical activity; increases superoxide dismutase, glutathione-s-transferase, and catalase enzyme activity in liver and kidney tissue; and restores normal liver and kidney cell structure in male and female Swiss albino mice. Benavente-García *et al.* [104] reported that the concentration (24.20, 30.30 mg/kg bw) of phenolic compounds isolated from Olea europaea L. leaf extract has a new effect on inhibiting damage caused by a dose of 2 cGy/min, which is accomplished by reducing hydroxyl radical activity; increasing superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in liver and kidney tissue; and restoring the normal liver and kidney cell structure in male Swiss mice. For the phenolic compounds isolated from Pycnanthus angolensis warb seed extract, 0.2 mg/kg BW had a high efficiency in suppressing the negative effects of the dose (4, 6, 8, and 10 Gy per hour). X-rays protect human serum albumin from damage to its secondary structure and help scavenge hydroxyl free radicals, eliminating increased bityrosine [108].

Effects of saponins against X-ray radiation: Saponins are organic chemical compounds with a bitter taste because they contain various triterpenoidal and steroidal aglycons. Saponins are widely distributed in many plants, unripe fruits, and marine organisms and are used in medicines, dietary supplements, and soft and alcoholic beverages[113]. The consumer demand for natural products coupled with their physicochemical (surfactant) properties and increasing evidence of their biological activity (such as anticancer and anti-cholesterol activity) has led to the emergence of saponins as commercially significant compounds with expanding applications in the food, cosmetics, and pharmaceutical sectors[114]. Saponins are used as natural stabilizers, foaming agents, and emulsifiers in food applications. They have possible health benefits, such as decreasing cholesterol and having anticancer effects, and they help give food products their texture and solidity. In the pharmaceutical sector, saponins are valued for their extra bioactivities, which include anti-inflammatory, antibacterial, antiviral, and antiparasitic properties. In addition to their ability to act as adjuvants and exhibit cytotoxic activity against cancer cell lines, saponins can also increase the immune system's response to vaccinations. The promise of these materials in drug delivery systems is further enhanced by their ability to form stable complexes with medicines. However, for saponins to be effectively used in foods and related applications, issues such as bitterness, cytotoxicity, and instability under specific conditions must be resolved [115]. Table 1 summarizes the antioxidant*oxidant effects of saponins* in vivo and their ability to decrease the negative effects of X-rays by reducing oxidative stress. A previous study demonstrated that the oral administration of saponins at 25.50 mg/kg body weight over 14 days before irradiation and 7 days after the exposure of male Wistar albino rats to 5 or 10 Gy/min increased the survival rate, protected the hematopoietic system by decreasing reactive oxygen species levels; elevated the activities of superoxide dismutase, catalase, and glutathione peroxidase in the liver; and decreased DNA damage [116]. Drymaria cordata is a famous plant grown in India and contains bioactive substances such as saponins and tannins [117]. The literature indicates that dry milk reduces lipid peroxidation, antioxidant, anti-inflammatory, and antimicrobial activities, in addition to reducing other ailments, such as colds, sleeping problems, headache, glomerulonephritis, coryza, bronchitis, leprosy, and tumors[118]. Table 1 summarizes the effects of saponins isolated from drymaria Cordata extract in vivo and their ability to reduce the negative effects of X-rays. A review of the literature by Akomolafe. Chetty [9] reported that administering saponins orally at doses of 250 mg/kg to female BALB/c mice for thirteen consecutive days before exposure to X-ray radiation to the whole body at rates of 4 and 8 Gy/min increased superoxide dismutase and catalase activity in the liver, increased mouse survival, and restored normal red blood cell and platelet counts [119]. Another review by Aguayo Torrez[120] revealed that administering saponins isolated from drymaria cordata extract at 250 mg/kg body weight to male and female Swiss albino mice through gavages after whole-body X-irradiation (3, 4, 6, or 8 Gy/min) for 36 days induced cell proliferation; delayed the onset of mortality; reduced hydroxyl radical activity; increased superoxide dismutase, glutathione-s-transferase and catalase enzyme activity in liver and kidney tissue; and restored normal liver and kidney cell structure in pretreated animals. In a study by Yalinkilic, O., & Enginar, H. [116], the concentration (25, 50 mg/kg body weight) of saponin found in many unripe fruits has proven its strong effectiveness against the negative effects that occur due to a dose of 5 and 10 Gy/min from X-ray radiation) through the protection of the hematopoietic system by decreasing the reactive oxygen species levels, increasing the activities of superoxide dismutase, catalase, and glutathione peroxidase in the liver, and decreasing DNA damage in male Wistar albino rats [120]. A review of the literature revealed by Akomolafe. and Chetty [119] that the concentration (250 mg/kg body weight) of saponin found in (drymaria Cordata extract) had strong effectiveness against the negative effects that occur due to a dose of 4 and 8 Gy/min from X-ray radiation) through increasing superoxide dismutase and catalase activity in the liver, increasing mouse survival, and restoring normal red blood cell and platelet counts in female BALB/c mice[120]. A study conducted by Aguayo Torrez [116] revealed that a concentration (250 mg/kg body weight of saponin isolated from drymaria cordata extract) has strong effectiveness against the negative effects that occur at doses of 3, 4, 6, and 8 Gy/min of -ray radiation) and reduces hydroxyl radical activity; increases superoxide dismutase, glutathione-s-transferase, and catalase enzyme activity in liver and kidney tissue; and restores the normal liver and kidney cell structure in female Swiss albino mice[119].

Table 1. Applications of active compounds in clinical trials

Active compounds	Dose of X-ray	Dose of active compounds	Outcome	In vivo test models	R.F
Lactoferrin	7 Gy/min	15,30 mg/kg bw	Reduced radiation-induced DNA injury	male BALB/c mice	[64]
	9 Gy/min	4 mg/kg bw	Prevent damage to the salivary glands	male C3H/He mice	[65]
	5,8 Gy/min	2,4,6 mg/kg bw	Improved intestinal injury	male BALB/c mice	[66]
	6.8 Gy/min	4 mg/kg bw	Inhibit radiation damage	male C3H/He mice	[67]
Lycopene	100 μGy\min	50 mg/kg bw	Modulate oxidative damage	male ICR mice	[73]
Curcumin	0.25 Gy/min	10 mg/kg bw	Attenuate the renal oxidative stress	male wistar albino rats	[76]
Phycocyanin	0.47 Gy/min	200 mg/kg bw	Reduced liver damage	male C57BL/6 mice	[80]
Melatonin	8 Gy/min	50,100 mg/kg bw	Decreasing oxidative stress and increasing antioxidant enzymes.	male wistar rats	[84]
	3,12 Gy/min	200 mg/kg bw	Enhance the recovery of cellular immunocompetence	Female C57BL/6 N mice	[85]
	1,5 Gy/min	100 mg/kg bw	Protected male reproductive system	male C57BL/6 mice	[86]
Polysaccharides in aloe vera gel	2 Gy/min	50 mg/kg bw	Boost the antioxidant system	male BALB/c mice	[91]
	0.258 Gy/min	50 mg/kg bw	Boost cellular antioxidant defense machinery.	male BALB/c mice	[92]
	2 Gy/min	50 mg/kg bw	Improved hepatobiliary clearance profile	male BALB/c mice	[93]
Polysaccharides in Ganoderma Lucidum Spore	2, 4, 7, 8, 10, 12 Gy/min	1.25, 2.5, 5 mg/kg bw	Enhance the recovery of cellular immunocompetence	male B6C3F1 (Crj:B6C3FI) mice	[94]
Phenolic compounds in Polyalthia *longifolia* leaf extract	1.33 Gy/min; 6MV/min	250,500 mg/kg bw	Restoration of the normal liver cell structure	male Swiss albino mice	[100]
Phenolic compounds in Costus afer leaf extract	3,6 Gy/min	250 mg/kg bw	Protection hematological alterations	male BALB/c mice	[103]
	3,4,6,8 Gy/min	250 mg/kg bw	Increasing the mice's survival rate	male and female Swiss albino mice	[104]
Phenolic compounds in Olea europaea L. Leaves	2 cGy/min	24.20, 30.30 mg/kg bw	Inhibiting the pro-inflammatory cytokines	male Swiss mice	[108]
Phenolic compounds in Pycnanthus angolensisWarb Seed Extract	4, 6, 8, and 10 Gy/min	0.2 mg/kg bw	Stabilization of molecular structure of human serum albumin	human blood samples	[112]
Saponins in many unripe fruit	5,10 Gy/min	25.0, 50.0 mg/kg bw	Reinforce the antioxidant systems	male wistar albino rats	[116]
Saponins in Drymaria Cordata extract	4,8 Gy/min	250 mg/kg bw	Reduce radiation-induced damage and increase the survival rate	female BALB/c mice	[119]
	3,4,6,8 Gy/min	250 mg/kg bw	Increasing the mice's survival rate	male and female Swiss albino mice	[120]

CONCLUSION

The main focus of the current study was the therapeutic use of organically active chemicals from plants and other organic foods against oxidative stress caused by X-rays. According to the experimental findings, the materials under consideration offer X-ray protection. As a result, those operating in radiation therapy needs to be given antioxidants from organic food sources to reduce the harm caused by X-rays. This will decrease the need for more medication and enhance quality of life. We examined the associations between the oxidative stress caused by X-rays and the active chemicals found in plants and other organic foods. It has been demonstrated that natural materials can increase the quality of life. In addition to being used in food, it has been proposed that natural antioxidants could be applied as radiation protectants to reduce the oxidative stress generated by X-rays. Since the active compounds in the study had no toxic effects, we suggest the use of these active compounds to produce a nutraceutical beverage that can be consumed or included in a daily diet to minimize oxidative stress.

ABBREVIATIONS

ROS: Reactive oxygen species, H2O2: Hydrogen peroxide, O2•−: Superoxide radical, OH: hydroxyl radical, RNS: Reactive Nitrogen species, CAT: Catalase, SOD: Superoxide dismutase, GSHPx: Glutathione, MDA: Malondialdehyde, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, IL-6: Interleukin 6, TNF-α: Tumor necrosis factor alpha, Gy/min: Gray/min, z BW: Body weight

Author Contributions: Conceptualization, Qaswaa Yousif Jameel; methodology, Thowiba Yousif Jameel, and Nameer Khairullah Mohammed; validation, Nameer Khairullah Mohammed; data curation, Thowiba Yousif Jameel and Nameer Khairullah Mohammed; writing—original draft preparation, Qaswaa Yousif Jameel; writing—review and editing, Qaswaa Yousif Jameel; visualization, Qaswaa Yousif Jameel, Nameer Khairullah Mohammed, and Thowiba Yousif Jameel; supervision, Qaswaa Yousif Jameel; project administration, Qaswaa Yousif Jameel.

Funding: This research received no external funding.

Data availability statement: No new data were created or analyzed in this study. Data sharing does not apply to this article.

Conflicts of interest: The authors declare no conflicts of interest.

REFERENCES

1. Amendola R, Cervelli M, Tempera G, Fratini E, Varesio L, Mariottini P, et al. Spermine metabolism and radiation-derived reactive oxygen species for future therapeutic implications in cancer: An additive or adaptive response. Amino Acids 2014; 46: 487–98. DOI: https://doi.org/10.1007/s00726-013-1579-9
2. Chen YR and Zweier JL. Cardiac mitochondria and reactive oxygen species generation. Circulation Research 2014; 114: 524–537. DOI: https://doi.org/10.1161/CIRCRESAHA.114.300559
3. Gassert FT, Urban T, Frank M, Willer K, Noichl W, Buchberger P, et al. X-ray dark-field chest imaging: Qualitative and quantitative results in healthy humans. Radiology 2021; 301: 389–395. DOI: https://doi.org/10.1148/radiol.2021210963
4. Hashemi SA, Mousavi SM, Faghihi R, Arjmand M, Rahsepar M, Bahrani S, et al. Superior X-ray radiation shielding effectiveness of biocompatible polyaniline reinforced with hybrid graphene oxide-iron tungsten nitride flakes. Polymers 2020; 12: 1–21. DOI: https://doi.org/10.3390/polym12061407
5. Nosrati H, Seidi F, Hosseinmirzaei A, Mousazadeh N, Mohammadi A, Ghaffarlou M, et al. Prodrug Polymeric Nanoconjugates Encapsulating Gold Nanoparticles for Enhanced X-Ray Radiation Therapy in Breast Cancer. Advanced Healthcare Materials 2022; 11: 1–9. DOI: https://doi.org/10.1002/adhm.202102321
6. Klebowski B, Stec M, Depciuch J, Panek A, Krzempek D, Komenda W, et al. Improving the Effect of Cancer Cells Irradiation with X-rays and High-Energy Protons Using Bimetallic Palladium-Platinum Nanoparticles with Various Nanostructures. Cancers 2022; 14: 1–17. DOI: https://doi.org/10.3390/cancers14235899
7. Oakley PA and Harrison DE. X-Ray Hesitancy: Patients' Radiophobic Concerns Over Medical X-rays. Dose-Response 2020; 18: 1–11. DOI: https://doi.org/10.1177/1559325820959542
8. Jameel QY, Ajeel MA, and Mohammed NK. Nutritional and anti-gastro ulcerative role of the gum Arabic (Acacia senegal L.) compared to a reference drug. Functional Foods in Health and Disease. 2022; 12: 294–307. DOI: https://doi.org/10.31989/ffhd.v12i6.929
9. Jameel QY, Mohammed NK, and Ajeel MA. Fabrication of Nutraceutical Beverage from Saffron (Crocus sativus L .) Extract and Studying Its Health Effects. 2023; 12: 442–454. DOI: https://doi.org/10.31989/ffhd.v12i8.972
10. Abdulrazak EA and Jameel QY. Effect of spinach-derived glutathione against carbon tetrachloride-induced stress in rats. Functional Foods in Health and Disease 2022; 12: 442–454. DOI: https://doi.org/10.31989/ffhd.v12i8.972
11. Ali RTM and Jameel QY. Red beetroot betalains as a novel source of colorant in ice-cream as compared with red dye 40 (E129). Functional Foods in Health and Disease 2023; 13: 225–239. DOI: https://doi.org/10.31989/ffhd.v13i4.1096
12. Mortensen MS, Ruiz J, and Watts JL. Polyunsaturated Fatty Acids Drive Lipid Peroxidation during Ferroptosis. Cells 2023; 12. DOI: https://doi.org/10.3390/cells12050804

13. Gładysz AK, Stępniak J, and Karbownik-Lewińska M. Exogenous Melatonin Protects against Oxidative Damage to Membrane Lipids Caused by Some Sodium/Iodide Symporter Inhibitors in the Thyroid. Antioxidants 2023; 12. DOI: https://doi.org/10.3390/antiox12091688
14. Wali AF, Ali S, Rashid S, Alsaffar RM, Arafah A, Qamar W, et al. Attenuation of oxidative damage-associated hepatotoxicity by piperine in CCl4-induced liver fibrosis. Journal of King Saud University - Science 2021; 33: 101629.
DOI: https://doi.org/10.1016/j.jksus.2021.101629
15. Akbari B, Baghaei-Yazdi N, Bahmaie M, and Mahdavi Abhari F. The role of plant-derived natural antioxidants in reduction of oxidative stress. BioFactors 2022; 48: 611–633. DOI: https://doi.org/10.1002/biof.1831
16. Jideani AIO, Silungwe H, Takalani T, Omolola AO, Udeh HO, and Anyasi TA. Antioxidant-rich natural fruit and vegetable products and human health. International Journal of Food Properties 2021; 24: 41–67.
DOI: https://doi.org/10.1080/10942912.2020.1866597
17. Shore RE, Moseson M, Xue X, Tse Y, Harley N, and Pasternack BS. Skin cancer after X-ray treatment for scalp ringworm. Radiation Research 2002; 157: 410–418. DOI: https://doi.org/10.1667/0033-7587(2002)157[0410:SCAXRT]2.0.CO;2
18. Follen M, Levenback CF, Iyer RB, Grigsby PW, Boss EA, Delpassand ES, et al. Imaging in Cervical Cancer. Cancer 2003; 98: 2028–2038.
DOI: https://doi.org/10.1002/cncr.11679
19. Li Z, Lai X, Fu S, Ren L, Cai H, Zhang H, et al. Immunogenic Cell Death Activates the Tumor Immune Microenvironment to Boost the Immunotherapy Efficiency. Advanced Science 2022; 9: 1–37.
DOI: https://doi.org/10.1002/advs.202201734
20. Jin F, Liu D, Xu X, Ji J, and Du Y. Nanomaterials-based photodynamic therapy with combined treatment improves antitumor efficacy through boosting immunogenic cell death. International Journal of Nanomedicine 2021; 16: 4693–4712.
DOI: https://doi.org/10.2147/IJN.S314506
21. Lima F, Swift JM, Greene ES, Allen MR, Cunningham DA, Braby LA, et al. Exposure to Low-Dose X-Ray Radiation Alters Bone Progenitor Cells and Bone Microarchitecture. Radiation Research 2017; 188: 433–442.
DOI: https://doi.org/10.1667/RR14414.1
22. Whipple GH. Primary Injury of the Epithelium of the Small Intestine. 1923 Nov 30;38(6):731–739
DOI: https://doi.org/101084/jem386731 1922; 187–202.
23. Yuasa H, Inada KI, Watanabe H, and Tatematsu M. A phenotypic shift from gastric-intestinal to solely intestinal cell types in intestinal metaplasia in rat stomach following treatment with X-rays. Journal of Toxicologic Pathology 2002; 15: 85–93. DOI: https://doi.org/10.1293/tox.15.85
24. Radioprotective E, Oligopeptides W, Zhu N, Liu R, He L, Mao R, et al. molecules Against Gamma Radiation-Induced Splenocyte. 2019.
25. Deng S, Shanmugam MK, Kumar AP, Yap CT, Sethi G, and Bishayee A. Targeting autophagy using natural compounds for cancer prevention and therapy. Cancer 2019; 125: 1228–1246.
DOI: https://doi.org/10.1002/cncr.31978
26. Noor A, Gunasekaran S, and Vijayalakshmi MA. Article in Pharmacognosy Research. October 2017. Pharmacognosy Research 2018; 10: 24–30.
DOI: https://doi.org/10.4103/pr.pr
27. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, et al. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Springer Berlin Heidelberg, 2023.
DOI: https://doi.org/10.1007/s00204-023-03562-9
28. Hajam YA, Rani R, Ganie SY, Sheikh TA, Javaid D, Qadri SS, et al. Oxidative Stress in Human Pathology and Aging: Molecular Mechanisms and Perspectives. Cells 2022; 11. DOI: https://doi.org/10.3390/cells11030552
29. Reignier J, Méchin F, and Sarbu A. Jo ur na l P re of. Polymer Testing 2020; 106972.
30. Liu Q, Li W, and Qin S. Therapeutic effect of phycocyanin on acute liver oxidative damage caused by X-ray. Biomedicine and Pharmacotherapy 2020; 130: 110553. DOI: https://doi.org/10.1016/j.biopha.2020.110553
31. Mendes F, Sales T, Domingues C, Schugk S, Abrantes AM, Gonçalves AC, et al. Effects of X-radiation on lung cancer cells: the interplay between oxidative stress and P53 levels. Medical Oncology 2015; 32: 1–9.
DOI: https://doi.org/10.1007/s12032-015-0712-x
32. Yalinkilic O and Enginar H. Effect of X-radiation on lipid peroxidation and antioxidant systems in rats treated with saponin-containing compounds. Photochemistry and Photobiology 2008; 84: 236–242.
DOI: https://doi.org/10.1111/j.1751-1097.2007.00240.x
33. Abdelrazzak AB, El-Missiry MA, Ahmed MT, and Elnady BF. Effect of low-dose X-rays on the liver of whole-body irradiated rats. International Journal of Radiation Biology 2018; 95: 264–273.
DOI: https://doi.org/10.1080/09553002.2019.1554925
34. Klaus R, Niyazi M, and Lange-Sperandio B. Radiation-induced kidney toxicity: molecular and cellular pathogenesis. Radiation Oncology 2021; 16: 1–11.
DOI: https://doi.org/10.1186/s13014-021-01764-y
35. Zhao H, Zhuang Y, Li R, Liu Y, Mei Z, He Z, et al. Effects of different doses of X-ray irradiation on cell apoptosis, cell

cycle, DNA damage repair and glycolysis in HeLa cells. Oncology Letters 2019; 17: 42–54.
DOI: https://doi.org/10.3892/ol.2018.9566

36. Institute EM and JLP. DNA damage and repair dependencies of ionising radiation modalities. Bioscience Reports 2023; 43: 1–15.
DOI: https://doi.org/10.1042/BSR20222586

37. Farhood B, Goradel NH, Mortezaee K, Khanlarkhani N, Salehi E, Nashtaei MS, et al. Intercellular communications-redox interactions in radiation toxicity; potential targets for radiation mitigation. Journal of Cell Communication and Signaling 2019; 13: 3–16.
DOI: https://doi.org/10.1007/s12079-018-0473-3

38. Baulch JE. Radiation-induced genomic instability, epigenetic mechanisms and the mitochondria: a dysfunctional ménage a trois? International Journal of Radiation Biology 2019; 95: 516–525.
DOI: https://doi.org/10.1080/09553002.2018.1549757

39. El Bakary NM, Alsharkawy AZ, Shouaib ZA, and Barakat EMS. Role of Bee Venom and Melittin on Restraining Angiogenesis and Metastasis in γ-Irradiated Solid Ehrlich Carcinoma-Bearing Mice. Integrative Cancer Therapies 2020; 19.
DOI: https://doi.org/10.1177/1534735420944476

40. Rahaman MM, Hossain R, Herrera-Bravo J, Islam MT, Atolani O, Adeyemi OS, et al. Natural antioxidants from some fruits, seeds, foods, natural products, and associated health benefits: An update. Food Science and Nutrition 2023; 11: 1657–1670.
DOI: https://doi.org/10.1002/fsn3.3217

41. Bouzroud S, El Maaiden E, Sobeh M, Merghoub N, Boukcim H, Kouisni L, et al. Biotechnological Approaches to Producing Natural Antioxidants: Anti-Ageing and Skin Longevity Prospects. International Journal of Molecular Sciences 2023; 24.
DOI: https://doi.org/10.3390/ijms24021397

42. Sun W and Shahrajabian MH. Potencial terapêutico de compostos fenólicos em plantas medicinais – produtos naturais de saúde para a saúde humana. Molecules 2023; 28.

43. Roy NK, Parama D, Banik K, Bordoloi D, Devi AK, Thakur KK, et al. An update on pharmacological potential of boswellic acids against chronic diseases. International Journal of Molecular Sciences 2019; 20.
DOI: https://doi.org/10.3390/ijms20174101

44. Das L, Bhaumik E, Raychaudhuri U, and Chakraborty R. Role of nutraceuticals in human health. Journal of Food Science and Technology 2012; 49: 173–83.
DOI: https://doi.org/10.1007/s13197-011-0269-4

45. Sorenson J. Cu, Fe, Mn, and Zn Chelates Offer a Medicinal Chemistry Approach to Overcoming Radiation Injury. Current Medicinal Chemistry 2012; 9: 639–662.
DOI: https://doi.org/10.2174/0929867023370725

46. Choi EK, Jung H, Kwak KH, Yeo J, Yi SJ, Park CY, et al. Effects of Allopurinol and Apocynin on Renal Ischemia-Reperfusion Injury in Rats. Transplantation Proceedings 2015; 47: 1633–1638.
DOI: https://doi.org/10.1016/j.transproceed.2015.06.007

47. Hagar HH, El Medany A, El Eter E, and Arafa M. Ameliorative effect of pyrrolidinedithiocarbamate on acetic acid-induced colitis in rats. European Journal of Pharmacology 2007; 554: 69–77.
DOI: https://doi.org/10.1016/j.ejphar.2006.09.066

48. Baker JG, Hall IP, and Hill SJ. Pharmacology and direct visualisation of BODIPY-TMR-CGP: A long-acting fluorescent β 2-adrenoceptor agonist. British Journal of Pharmacology 2003; 139: 232–242.
DOI: https://doi.org/10.1038/sj.bjp.0705287

49. Lu X, Wang Y, and Zhang Z. Radioprotective activity of betalains from red beets in mice exposed to gamma irradiation. European Journal of Pharmacology 2009; 615: 223–227.
DOI: https://doi.org/10.1016/j.ejphar.2009.04.064

50. Stahl W and Sies H. Antioxidant activity of carotenoids. Molecular Aspects of Medicine 2003; 24: 345–351.
DOI: https://doi.org/10.1016/S0098-2997(03)00030-X

51. Zhang Y, Lu C, and Zhang J. Lactoferrin and its detection methods: A review. Nutrients 2021; 13.
DOI: https://doi.org/10.3390/nu13082492

52. Ohradanova-Repic A, Praženicová R, Gebetsberger L, Moskalets T, Skrabana R, Cehlar O, et al. Time to Kill and Time to Heal: The Multifaceted Role of Lactoferrin and Lactoferricin in Host Defense. Pharmaceutics 2023; 15.
DOI: https://doi.org/10.3390/pharmaceutics15041056

53. González-Chávez SA, Arévalo-Gallegos S, and Rascón-Cruz Q. Lactoferrin: structure, function and applications. International Journal of Antimicrobial Agents 2009; 33: 301.e1-301.e8.
DOI: https://doi.org/10.1016/j.ijantimicag.2008.07.020

54. Li YQ and Guo C. A review on lactoferrin and central nervous system diseases. Cells 2021; 10.
DOI: https://doi.org/10.3390/cells10071810

55. Zhang Q, Zhao HJ, Huang LY, Song CL, Li HQ, and Zhao XH. Low-level Cu-fortification of bovine lactoferrin: Focus on its effect on in vitro anti-inflammatory activity in LPS-stimulated macrophages. Current Research in Food Science 2023; 6: 100520.
DOI: https://doi.org/10.1016/j.crfs.2023.100520

56. Feng L, Li J, Qin L, Guo D, Ding H, and Deng D. Radioprotective effect of lactoferrin in mice exposed to sublethal X-ray irradiation. Experimental and Therapeutic Medicine 2018; 16: 3143–3148.
DOI: https://doi.org/10.3892/etm.2018.6570

57. Wei YL, Xu JY, Zhang R, Zhang Z, Zhao L, and Qin LQ. Effects of lactoferrin on X-ray-induced intestinal injury in Balb/C mice. Applied Radiation and Isotopes 2019; 146: 72–77. DOI: https://doi.org/10.1016/j.apradiso.2019.01.014
58. Nishimura Y, Homma-Takeda S, Kim HS, and Kakuta I. Radioprotection of mice by lactoferrin against irradiation with sublethal X-rays. Journal of Radiation Research 2014; 55: 277–282. DOI: https://doi.org/10.1093/jrr/rrt117
59. Sakai M, Matsushita T, Hoshino R, Ono H, and Ikai K. Identification of the protective mechanisms of Lactoferrin in the irradiated salivary gland. Scientific Reports 2017; 1–8. DOI: https://doi.org/10.1038/s41598-017-10351-9
60. Naz A, Butt MS, Sultan MT, Qayyum MMN, and Niaz RS. Review article : Watermelon Lycopene And Allied Health Claims. EXCLI Journal 2014; 13: 650–666.
61. Zahari CNMC, Mohamad NV, Akinsanya MA, and Gengatharan A. The crimson gem: Unveiling the vibrant potential of lycopene as a functional food ingredient. Food Chemistry Advances 2023; 3: 100510. DOI: https://doi.org/10.1016/j.focha.2023.100510
62. Veljović M, Davidović S, Pecić S, Despotović S, Leskošek-Čukalović I, and Vukosavljević P. Lycopene content and antioxidant capacity of tomato jam. CEFood 2012 - Proceedings of 6th Central European Congress on Food 2012; 138–143.
63. Permadi MR, Solikhah D, Iqbal M, and Damayanti RP. The effect of red watermelon juice on the anaerobic muscle fatigue index during physical exercise. Jurnal Gizi dan Dietetik Indonesia (Indonesian Journal of Nutrition and Dietetics) 2023; 11: 47. DOI: https://doi.org/10.21927/ijnd.2023.11(1).47-54
64. Mohammad MKA, Mohamed MI, Zakaria AM, Abdul Razak HR, and Saad WMM. Watermelon (Citrullus lanatus (Thunb.) Matsum. and Nakai) juice modulates oxidative damage induced by low dose x-ray in mice. BioMed Research International 2014. DOI: https://doi.org/10.1155/2014/512834
65. Kunnumakkara AB, Bordoloi D, Padmavathi G, Monisha J, Roy NK, Prasad S, et al. Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases. British Journal of Pharmacology 2017; 174: 1325–1348. DOI: https://doi.org/10.1111/bph.13621
66. Darwadi RP and Mahdi C. Pengaruh terapi kurkumin terhadap kadar malondialdehid (mda) hasil isolasi parotis dan profil protein tikus putih yang terpapar lipopolisakarida (lps). 2013; 1: 133–139.
67. Polasa K, Naidu AN, Ravindranath I, and Krishnaswamy K. Inhibition of B(a)P induced strand breaks in presence of curcumin. Mutation Research - Genetic Toxicology and Environmental Mutagenesis 2004; 557: 203–213. DOI: https://doi.org/10.1016/j.mrgentox.2003.10.016
68. Kim BH, Lee ES, Choi R, Nawaboot J, Lee MY, Lee EY, et al. Protective effects of curcumin on renal oxidative stress and lipid metabolism in a rat model of type 2 diabetic nephropathy. Yonsei Medical Journal 2016; 57: 664–673. DOI: https://doi.org/10.3349/ymj.2016.57.3.664
69. Mu X, Hu K, Shen M, Kong N, Fu C, Yan W, et al. Protection against influenza A virus by vaccination with a recombinant fusion protein linking influenza M2e to human serum albumin (HSA). Journal of Virological Methods 2016; 228: 84–90. DOI: https://doi.org/10.1016/j.jviromet.2015.11.014
70. Ajloo D, Behnam H, Saboury AA, Mohamadi-Zonoz F, Ranjbar B, Moosavi-Movahedi AA, et al. Thermodynamic and structural studies on the human serum albumin in the presence of a polyoxometalate. Bulletin of the Korean Chemical Society 2007; 28: 730–736. DOI: https://doi.org/10.5012/bkcs.2007.28.5.730
71. Jagetia GC and Reddy TK. Modulation of radiation-induced alteration in the antioxidant status of mice by naringin. Life Sciences 2005; 77: 780–794. DOI: https://doi.org/10.1016/j.lfs.2005.01.015
72. Cervelli T, Panetta D, Navarra T, Gadhiri S, Salvadori P, Galli A, et al. A New Natural Antioxidant Mixture Protects against Oxidative and DNA Damage in Endothelial Cell Exposed to Low-Dose Irradiation. Oxidative Medicine and Cellular Longevity 2017 DOI: https://doi.org/10.1155/2017/9085947
73. Pez Jaeschke D, Rocha Teixeira I, Damasceno Ferreira Marczak L, and Domeneghini Mercali G. Phycocyanin from Spirulina: A review of extraction methods and stability. Food Research International 2021; 143. DOI: https://doi.org/10.1016/j.foodres.2021.110314
74. Chen H, Qi H, and Xiong P. Phycobiliproteins—A Family of Algae-Derived Biliproteins: Productions, Characterization and Pharmaceutical Potentials. Marine Drugs 2022; 20: 1–21. DOI: https://doi.org/10.3390/md20070450
75. García AB, Longo E, and Bermejo R. The application of a phycocyanin extract obtained from Arthrospira platensis as a blue natural colorant in beverages. Journal of Applied Phycology 2021; 33: 3059–3070. DOI: https://doi.org/10.1007/s10811-021-02522-z
76. Campos Assumpção de Amarante M, Cavalcante Braga AR, Sala L, and Juliano Kalil S. Colour stability and antioxidant activity of C-phycocyanin-added ice creams after in vitro digestion. Food Research International 2020; 137: 109602. DOI: https://doi.org/10.1016/j.foodres.2020.109602
77. Luzardo-Ocampo I, Ramírez-Jiménez AK, Yañez J, Mojica L, and Luna-Vital DA. Technological applications of natural colorants in food systems: A review. Foods 2021; 10: 1–34. DOI: https://doi.org/10.3390/foods10030634

78. Park WS, Kim HJ, Li M, Lim DH, Kim J, Kwak SS, et al. Two classes of pigments, carotenoids and c-phycocyanin, in spirulina powder and their antioxidant activities. Molecules 2018; 23: 1–11. DOI: https://doi.org/10.3390/molecules23082065
79. Agrawal M, Bansal S, and Chopra K. Evaluation of the in vitro and in vivo antioxidant potentials of food grade Phycocyanin. Journal of Food Science and Technology 2021; 58: 4382–4390. DOI: https://doi.org/10.1007/s13197-020-04922-4
80. Hardeland R. Melatonin in plants – Diversity of levels and multiplicity of functions. Frontiers in Plant Science 2016; 7: 1–14. DOI: https://doi.org/10.3389/fpls.2016.00198
81. Hardeland R. Melatonin in plants and other phototrophs: Advances and gaps concerning the diversity of functions. Journal of Experimental Botany 2015; 66: 627–646. DOI: https://doi.org/10.1093/jxb/eru386
82. Gulcin I, Buyukokuroglu ME, Oktay M, and Kufrevioglu OI. On the in vitro antioxidative properties of melatonin. Journal of Pineal Research 2002; 33: 167–171. DOI: https://doi.org/10.1034/j.1600-079X.2002.20920.x
83. Nasrallah JB, Rundle SJ, and Nasrallah ME. Zyxwvutsrqponm Zyxwvutsrq Zyxwvutsrqp Zyxwvutsr Zy Zyx Zyx. 1994; 5: 373–384.
84. Wang J, Wang, Xiaoxiao, He Y, Jia L, Yang CS, Reiter RJ, et al. Antioxidant and Pro-Oxidant Activities of Melatonin and In Vivo. Cells 2019; 8: 903.
85. Carrillo-Vico A, Guerrero JM, Lardone PJ, and Reiter RJ. A review of the multiple actions of melatonin on the immune system. Endocrine 2005; 27: 189–200. DOI: https://doi.org/10.1385/ENDO:27:2:189
86. Carrillo-Vico A, Lardone PJ, Álvarez-Śnchez N, Rodrĩguez-Rodrĩguez A, and Guerrero JM. Melatonin: Buffering the immune system. International Journal of Molecular Sciences 2013; 14: 8638–8683. DOI: https://doi.org/10.3390/ijms14048638
87. Kim JM, Lee U, Kang JY, Park SK, Shin EJ, Kim HJ, et al. Anti-amnesic effect of walnut via the regulation of bbb function and neuro-inflammation in aβ1-42-induced mice. Antioxidants 2020; 9: 1–24. DOI: https://doi.org/10.3390/antiox9100976
88. Alhilfi AEMDS and HSQ. Protective E ff ect of Melatonin Against Radiotherapy-Induced Small Intestinal Oxidative Stress : Biochemical Evaluation. medicina 2019.
89. Li N, Wang C, Georgiev MI, Bajpai VK, Tundis R, Simal-Gandara J, et al. Advances in dietary polysaccharides as anticancer agents: Structure-activity relationship. Trends in Food Science and Technology 2021; 111: 360–377. DOI: https://doi.org/10.1016/j.tifs.2021.03.008
90. Medlej MK, Batoul C, Olleik H, Li S, Hijazi A, Nasser G, et al. Antioxidant activity and biocompatibility of fructo-polysaccharides extracted from a wild species of ornithogalum from lebanon. Antioxidants 2021; 10: 1–20. DOI: https://doi.org/10.3390/antiox10010068
91. Zhang Y, Xu M, Hu C, Liu A, Chen J, Gu C, et al. Sargassum fusiforme Fucoidan SP2 Extends the Lifespan of Drosophila melanogaster by Upregulating the Nrf2-Mediated Antioxidant Signaling Pathway. Oxidative Medicine and Cellular Longevity 2019 DOI: https://doi.org/10.1155/2019/8918914
92. Bala S, Chugh NA, Bansal SC, Garg ML, and Koul A. Radiomodulatory effects of Aloe vera on hepatic and renal tissues of X-ray irradiated mice. Mutation Research - Fundamental and Molecular Mechanisms of Mutagenesis 2018; 811: 1–15. DOI: https://doi.org/10.1016/j.mrfmmm.2018.07.001
93. Kubo N, Myojin Y, Shimamoto F, Kashimoto N, Kyo E, Kamiya K, et al. Protective effects of a water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi) mycelia and Agaricus blazei murill against X-irradiation in B6C3F1 mice: Increased small intestinal crypt survival and prolongation of average time to animal. International journal of molecular medicine 2005; 15: 401–406. DOI: https://doi.org/10.3892/ijmm.15.3.401
94. Tiwari M and Upadhayay M. The medicinal plant components and applications (Aloe vera). ~ 89 ~ Journal of Medicinal Plants Studies 2018; 6: 89–95.
95. Grace OM, Buerki S, Symonds MRE, Forest F, Van Wyk AE, Smith GF, et al. Evolutionary history and leaf succulence as explanations for medicinal use in aloes and the global popularity of Aloe vera. BMC Evolutionary Biology 2015; 15: 1–12. DOI: https://doi.org/10.1186/s12862-015-0291-7
96. Hęś M, Dziedzic K, Górecka D, Jędrusek-Golińska A, and Gujska E. Aloe vera (L.) Webb.: Natural Sources of Antioxidants – A Review. Plant Foods for Human Nutrition 2019; 74: 255–265. DOI: https://doi.org/10.1007/s11130-019-00747-5
97. Bala S, Chugh NA, Bansal SC, Garg ML, and Koul A. Protective role of Aloe vera against X-ray induced testicular dysfunction. Andrologia 2017; 49: 1–12. DOI: https://doi.org/10.1111/and.12697
98. Bala S, Gupta LK, and Koul A. Aloe vera modulates X-ray induced bone mineral loss and other deleterious effects on various tissues of mice. Indian Journal of Natural Products and Resources 2022; 13: 176–182. DOI: https://doi.org/10.56042/ijnpr.v13i2.43745

99. Action A and Understanding N. Mechanisms of the Anticancer Action of. 2005; 47: 129–135.

100. Szedlay G. Is the widely used medicinal fungus the Ganoderma lucidum (Fr.) Karst. sensu stricto? (a short review). Acta Microbiologica et Immunologica Hungarica 2002; 49: 235–243. DOI: https://doi.org/10.1556/AMicr.49.2002.2-3.9

101. Lu H, Kyo E, Uesaka T, Katoh O, and Watanabe H. Prevention of development of N,N'-dimethylhydrazine-induced colon tumors by a water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi) mycelia in male ICR mice. International journal of molecular medicine 2002; 9: 113–117. DOI: https://doi.org/10.3892/ijmm.9.2.113

102. Olas B and Bald E. the Protective Effects of Resvera. Pharmacology 2004; 467–76.

103. Ahmad MF. Ganoderma lucidum: A rational pharmacological approach to surmount cancer. Journal of Ethnopharmacology 2020; 260: 113047. DOI: https://doi.org/10.1016/j.jep.2020.113047

104. Babenko LM, Smirnov OE, Romanenko KO, Trunova OK, and Kosakivska I V. Phenolic compounds in plants: Biogenesis and functions. Ukrainian Biochemical Journal 2019; 91: 5–18. DOI: https://doi.org/10.15407/ubj91.03.005

105. Akomolafe IR and Chetty N. Radioprotective potential of costus afer against the radiation-induced hematological and histopathological damage in mice. Radiation Oncology Journal 2021; 39: 61–71. DOI: https://doi.org/10.3857/roj.2021.00017

106. Achel DG, Alcaraz-Saura M, Castillo J, Olivares A, and Alcaraz M. Radioprotective and antimutagenic effects of Pycnanthus angolensis warb seed extract against damage induced by x rays. Journal of Clinical Medicine 2020; 9. DOI: https://doi.org/10.3390/jcm9010006

107. Katkar K, Suthar A, and Chauhan V. The chemistry, pharmacologic, and therapeutic applications of Polyalthia longifolia. Pharmacognosy Reviews 2010; 4: 62–68. DOI: https://doi.org/10.4103/0973-7847.65329

108. Doshi G, Zine S, Chaskar P, and Une H. Solicitation of HPLC and HPTLC Techniques for Determination of Rutin from Polyalthia longifolia Thwaites. Pharmacognosy Research 2014; 6: 234–239. DOI: https://doi.org/10.4103/0974-8490.132601

109. Rk S, Mandal S, Gp R, Gupta N, and Dp S. Available online http://www.ijddr.in Covered in Official Product of Elsevier, The Netherlands Antiulcer And Anti-inflammatory Activity Of Fresh Leave Extracts Of Polyalthia Longifolia In Rats. 2011; 3: 351–359. DOI: https://doi.org/10.13140/RG.2.2.21871.10402

110. Jothy SL, Aziz A, Chen Y, and Sasidharan S. Antioxidant activity and hepatoprotective potential of polyalthia longifolia and cassia spectabilis leaves against paracetamol-induced liver injury. Evidence-based Complementary and Alternative Medicine 2012. DOI: https://doi.org/10.1155/2012/561284

111. Chester K, Zahiruddin S, Ahmad A, Khan W, Paliwal S, and Ahmad S. Bioautography-based Identification of Antioxidant Metabolites of Solanum nigrum L. and Exploration Its Hepatoprotective Potential agChester, 'Bioautography-based Identification of Antioxidant Metabolites of Solanum nigrum L. and Explorati. Pharmacognosy Magazine 2017; 13 (Suppl: 179–188. DOI: https://doi.org/10.4103/pm.pm

112. Jothy SL, Saito T, Kanwar JR, Chen Y, Aziz A, Yin-Hui L, et al. Radioprotective activity of Polyalthia longifolia standardized extract against X-ray radiation injury in mice. Physica Medica 2016; 32: 150–161. DOI: https://doi.org/10.1016/j.ejmp.2015.10.090

113. Tonkiri A, Essien ES, and Akaninwor JO. Evaluation of Hepatoprotective and in vivo Antioxidant Activity of the methanolic stem extract of Costus afer (Bush Cane) in alcohol induced liver Cirrhosis in rats. Journal of Biological and Food Science Research 2014; 3: 29–34.

114. Anyasor GN, Olusola Ogunwenmo K, Oyelana OA, and Akpofunure BE. Phytochemical constituents and antioxidant activities of aqueous and methanol stem extracts of Costus afer Ker Gawl. (Costaceae). African Journal of Biotechnology 2010; 9: 4880–4884.

115. Anyanwu BO, Orish CN, Ezejiofor AN, Nwaogazie IL, and Orisakwe OE. Neuroprotective effect of Costus afer on low dose heavy metal mixture (lead, cadmium and mercury) induced neurotoxicity via antioxidant, anti-inflammatory activities. Toxicology Reports 2020; 7: 1032–1038. DOI: https://doi.org/10.1016/j.toxrep.2020.08.008

116. Azhagu Madhavan S, Ganesan S, Sripriya R, and Priyadharshini R. A Literature Review of Anti- Diabetic Medicinal Plant Properties (Costus speices). Journal of Biomedical Research & Environmental Sciences 2021; 2: 305–310. DOI: https://doi.org/10.37871/jbres1231

117. Kamel SEMTEK. Adverse effect of rheumatoid arthritis on male Wistar rat's fertility: protective role of Costus extract. Environmental Science and Pollution Research 2022; 29: 4193–4205. DOI: https://doi.org/10.1007/s11356-021-16001-y

118. Bhattacharyya R, Medhi KK, and Borkataki S. Phytochemical analysis of drymaria cordata (l.) willd. ex schult. (whole plant) used by tea tribes of erstwhile nagaon district of assam, india. international journal of pharmaceutical sciences and research 2019; 10: 4264. DOI: https://doi.org/10.13040/IJPSR.0975-8232.10(9).4264-69

119. Ghanbari, R.; Anwar, F.; Alkharfy, K.M.; Gilani, A.-H.; Saari, N. Valuable nutrients and functional bioactives in different parts of olive (*Olea europaea* L.)-A Review. Int. J. Mol. Sci. 2012, *13*, 3291-3340. DOI: https://doi.org/10.3390/ijms13033291

120. Şahin S and Bilgin M. Olive tree (Olea europaea L.) leaf as a waste by-product of table olive and olive oil industry: a review. Journal of the Science of Food and Agriculture 2018; 98: 1271–9. DOI: https://doi.org/10.1002/jsfa.8619