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Systematic Review: Detoxification Of Free Radicals From Ionizing Radiation With Glutathione Intake

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Abstract:

Introduction: Radiation is the process of introducing energy that has a detrimental effect. If radiation hits the human body, radiation can ionize. If radiation penetrates body tissues, it can cause ionization and generate free radicals. Glutathione is one form of antioxidant-rich intake. **Purpose:** To determine the effect glutathione intake on the detoxification of free radicals from ionizing radiation. **Methods:** The inclusion criteria used are the population of rats, clinical trials, articles published between 2012 and 2022 and English. While the exclusion criteria used are title, abstract, free access and full text. Data sources are from PubMed, Scopus, Science Direct, and Google Scholar. Literature review writing starts from September 2022. **Results:** Based on a literature review conducted on 5 articles, it was found that total data using keywords the effect of free radical detoxification from ionizing radiation (n= 104) data focused on glutathione intake (n=96), searched based on exclusion criteria (n=44), search based on inclusion criteria (n=7), number of articles synthesized and analyzed (5). **Conclusions:** There is a direct effect of glutathione intake on the detoxification of free radicals from ionizing radiation. There is limited evidence so further research is needed on the effect of glutathione intake on free radical detoxification by testing the levels of free radicals and antioxidants in cells.

Key words : Free Radical, Ionizing Radiation, Glutathione

Introduction

Detoxification is the removal of harmful compounds or natural toxins from inside the body. Free radicals are harmful compounds that can arise from the presence of ionizing radiation. Free radical detoxification is a metabolic process of free radicals in the human body so that they can be excreted through organ excretion. Free radical detoxification can be done by consuming intakes rich in antioxidants such as glutathione (Kemenkes, 2022).

Radiation is the process of introducing energy that has a detrimental effect. If radiation hits the human body, radiation can ionize. Ionization is a material that consists of atoms and molecules. When radiation passes through matter, some or all of the radiation energy will be transferred due to scattering and absorption. Thus the radiation energy will be reduced. The process of reducing radiation energy is due to the interaction between radiation and matter. As a result of the interaction process between radiation and matter causes an event called ionizing radiation. If radiation penetrates the tissue, it can cause ionization and produce free radicals, such as hydroxyl free radicals (OH), which consist of oxygen atoms and hydrogen atoms. Chemically, free radicals are highly reactive and can change important molecules in cells. Free radicals can be in the body as a result of the oxidation process and the burning of cells in the presence of ionizing radiation. The presence of free radicals in the body can cause damage to normal cells and damage the composition of DNA so that it can cause degenerative diseases such as cance

There are two ways radiation can cause damage to cells. First, radiation can directly ionize DNA molecules that can change the chemical in DNA. Second, radiation can changes the chemical in DNA indirectly If DNA interacts with hydroxyl free radicals. Dikutip dari Dekant (2018), The occurrence of chemical changes in DNA can cause adverse biological effects such as cancer and genetic disorders. Indirect ionizing radiation exposure to biological systems produces reactive species such as reactive oxygen species (ROS), and reactive nitrogen species (RNS) and also triggers free radicals.

Menurut Dekant (2018), In free radicals, there are unpaired electrons so that free radicals are very reactive and able to change all biological molecules including lipids, DNA, and proteins. Free radicals are triggered by the formation of ROS (Reactive Oxygen Species) species. Reactive oxygen species (ROS) in excessive amounts can deleterious effects on molecular, lipid, RNA, and DNA molecules because they are very small and highly reactive. ROS can attack nucleic acids, amino acid chains in proteins, and double unsaturated fatty acids because •OH is a strong oxidant. ROS attack macromolecules are often called oxidative stress. To prevent or reduce ROS-induced oxidative damage, the human body requires antioxidants in an effort to detoxify free radicals.

Ionizing radiation can trigger oxidative stress through free radicals that cause an imbalance between antioxidants and pro-oxidants in cells. The most important function of glutathione in xenobiotic biotransformation is the detoxification of electrophiles and toxic radicals (Alizadeh, et al. 2022). Glutathione is important in cellular defense against chemically reactive toxic compounds that induce oxidative stress (Shirazi, 2012). Glutathione is also one of the antioxidant-rich intakes. Antioxidants are compounds that have a molecular structure that can donate electrons to free radical molecules and can break the chain reaction of free radicals. The body has the enzyme GPx (Glutathione Peroxidase) as an endogenous antioxidant enzyme that plays an active role in breaking down H2O2 in the body and converting it to convert glutathione (GSH) into oxidized glutathione (GSSG). Reaction with glutathione is the most important detoxification reaction for metabolically formed electrophilic and electrophilic compounds. Many toxic compounds are eliminated as mercapturic acid derivatives with the urine or as glutathione (GSH) conjugates with bile. Glutathione transferase (GST) also catalyzes the

detoxification of reactive oxygen species. In this reaction, glutathione is oxidized to glutathione disulfide.

Research on the detoxification of free radicals from ionizing radiation with glutathione intake is still limited. So it is necessary to conduct a library search through a literature review to obtain a library with sufficient quantity and quality to analyze the detoxification effect of free radicals from ionizing radiation with glutathione intake. The purpose of this paper is to study and determine the detoxification effect of free radicals from ionizing radiation with glutathione intake

Method

A systematic review in this article is to determine the free radical detoxification effect of ionizing radiation with glutathione intake. The intake criteria were clinical trial, English written, and animal population. The exclusion criteria were review article, duplicate article, and irrelevant. Searched articles through PubMed, ScienceDirect, Scopus, and Google Scholar databases. The keywords used are free radical detoxification, ionizing radiation, and glutathione. Reference articles in English with the year published between 2012-2022.

Results

There are 5 articles that match the inclusion and exclusion criteria requirements. Below is shown the prisma flowchart of the results of searching for data with the PICOS method and its explanation.

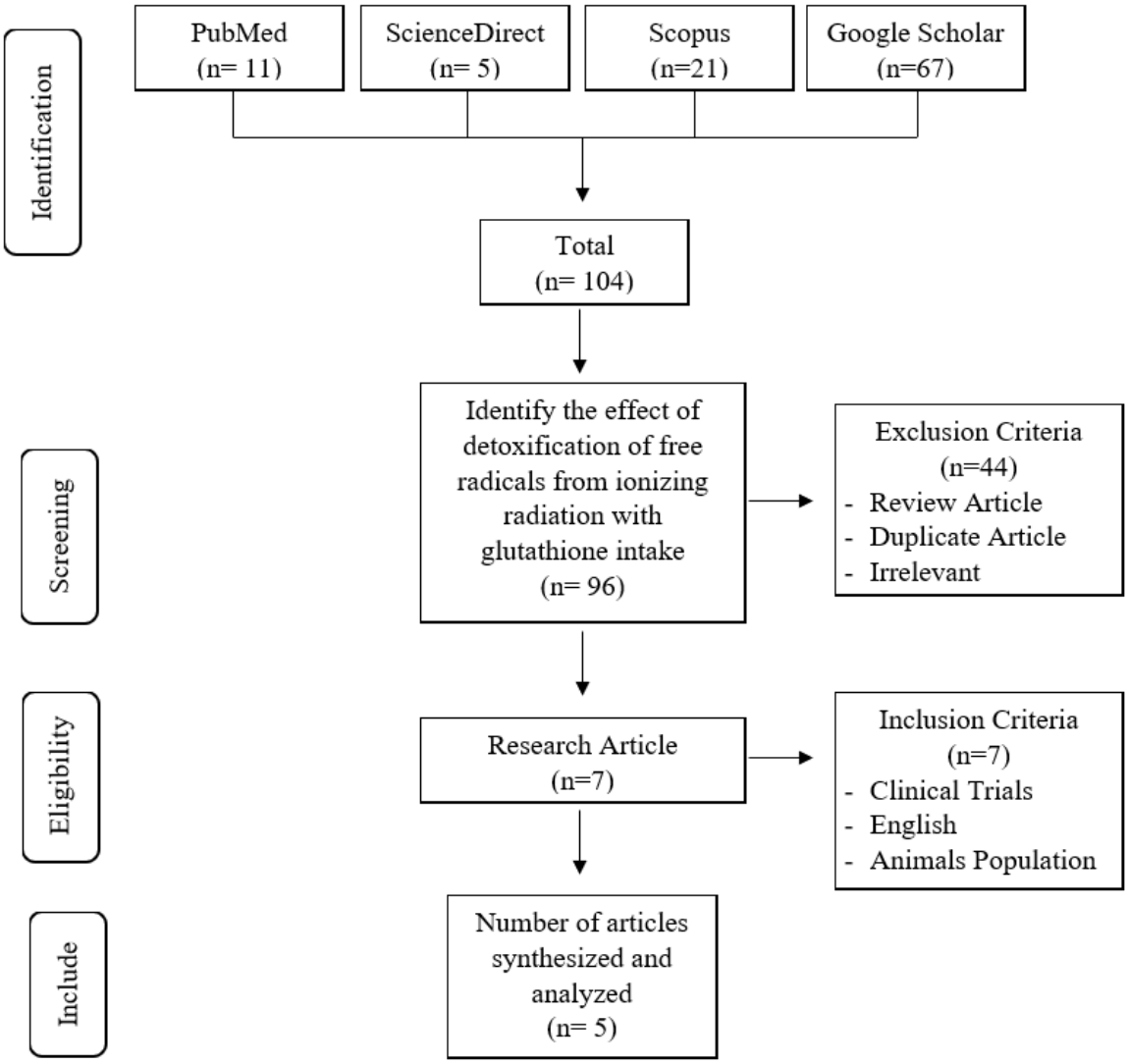

Image 1. Diagram of the process of searching for data the effect detoxification of free radicals from ionizing radiation with glutathione intake

Total search data based on the effect of free radical detoxification from ionizing radiation (n= 104) data focused on glutathione intake (n=96), then searched based on exclusion criteria (n=44) from 44 types of research articles, article selection was analyzed based on PICOS inclusion criteria (Population, Intervention, Comparison, Results, Study Design, and language) as follows:

1) Research Articles
2) Clinical Trials
3) English
4) Animal Population

Each article was studied and analyzed according to the inclusion criteria. Some articles were eliminated because they did not meet the criteria, such as: no search article, not clinically tested, non-English, non-animal population. There are 5 article that match with the criteria. Shown in table 1

Table 1. Detoxification of Free Radicals from Ionizing Radiation with Glutathione Intake

No	Title	Design, Samples, Measurements	Analysis Techniques	Result
1.	Anticlastogenic, radiation antagonistic, and anti-inflammatory activities of Persea americana in albino Wistar rat model	This study used albino Wistar rats against whole body X-ray irradiation. Rats were orally administered with (25, 50, 100, 200, and 400 mg/kg body weight) of P. americana leaf extract for five days. On the fifth day after last administration, animals were exposed to whole body X-rays of 8 Gy.	Data were analysed by one-way analysis of variance (ANOVA) following post hoc test Tukey using IBM SPSS statistics 20. $P < 0.05$ was considered significant.	P. americana leaf extract restored the levels of reduced glutathione, catalase, and reduced the levels of lipid peroxidation, protein carbonyls, and cyclooxygenase-2 levels in liver homogenates of pre-treated group. Decrease in micronucleated polychromatic erythrocytes ($P < 0.05$) was witnessed in P. americana pretreated group when compared to radiation control. Pretreatment also resulted in the increase of animal survival with dose reduction factor of 1.28.
2.	Dose-dependent effects of gamma radiation on the early zebrafish development and gene expression	The present work focuses on changes in developmental traits and gene expression in zebrafish were assessed after continuous external gamma irradiation (0.4, 3.9, 15 and 38 mGy/h) with corresponding controls, starting at 2.5 hours post fertilization (hpf) and lasting through embryogenesis and the early larval stage. The lowest	In this study, using logistic regression reported as odds ratios (OR). If significant, multiple comparisons were conducted using Tukey's or Dunnett's tests (Graphpad Prism 6, La Jolla, USA). Statistical significance was set to $p < 0.05$. For analysis of gene expression, the dataset was TMM normalized first (trimmed mean of M-values, edgeR v3.4.2	- The timing of hatching was significantly affected by irradiation, as a premature onset of hatching in the 0.4 mGy/h group ($p < 0.0001$) and a delayed onset of hatching in the 38 mGy/h group ($p = 0.0072$) - The deformity frequency at 96 hpf increased linearly in response to dose for both the 43.8- and 92-hour exposure (linear regression, $R2 = 0.93$ and $R2 = 0.99$, respectively) and was

		dose rate corresponded to recommended benchmarks at which adverse effects are not expected to occur in aquatic ecosystems (2–10 mGy/day). The survival observed at 96 hours post fertilization (hpf) in the 38 mGy/h group was significantly lower, while other groups showed no significant difference compared to controls. The total hatching was significantly lower from controls in the 15 mGy/h group and a delay in hatching onset in the 0.4 mGy/h group was observed. The deformity frequency was significantly increased by prolonged exposure duration at dose rates 0.4 mGy/h.	Bioconductor, Robinson, McCarthy, and Smyth 2010), followed by data exploration using the statistical package R v3.0.2. Data was explored for descriptive statistics such as: minimum, maximum, 1st quantile, 3rd quantile, median, mean, standard deviation, also the similarity among samples was determined by correlation analysis and hclust (ward method) analysis to determine the distance between samples. The statistical analysis of differentially expressed genes (DEGs) was based on pairwise comparison between treatment and control RNA-seq samples (biological replicates) with a cut off set to ± 0.40 log2 fold change (1.3 FC). The FDR (false discovery rate) was set up to a significance of p 0.05. Venn diagram (Venny v2.1, Oliveros, (2007–2015)) was used to explore overlapping differential expressed genes among radiation treatments.	significantly higher than in controls ($p < 0.05$) in all exposure groups, except from the 43.8-hour exposure to 0.4 mGy/h and 3.9 mGy/h. The lowest dose rate (0.4 mGy/h) caused significant increase in deformities ($p = 0.049$) only in the group exposed for 92 hours. - A total number of ~10000 genes was expressed in all samples, while the number of differentially expressed genes (DEGs) showed a clear dose rate dependency. - In the two higher dose rates, the most significantly affected signaling pathways were eif2 (eukaryotic initiation factor 2) and mTOR (mechanistic target of rapamycin), which were not affected (p-value > 0.05) in the lowest dose rate group. - Two of the selected genes are common between all three exposure groups (pfkfb3 and crabp2b). Three are common between 0.54 and 10.9 mGy/h groups (vox, ppp1r15a and shisa2) and between 5.4 and 10.9 mGy/h (sox2, tfa and eef2b). Only two genes were found to

			For qPCR, obtained mean relative gene expression values (exposed vs. control) were compared to mean relative gene expression values for the same genes from RNA-seq and a Pearson's correlation coefficient was calculated ($p < 0.05$) for all three exposure groups (Graphpad Prism 6, La Jolla, USA).	have an opposite regulation at one of the dose rates; pfkfb3 in the 5.4 mGy/h group was up-regulated, while shisa2 in the 10.9 mGy/h was down-regulated.
3.	Evaluation of radio-protective effect of melatonin on whole body irradiation induced liver tissue damage	In this experimental study, thirty-two rats were divided into four groups. Three days after irradiation, all rats were sacrified and their livers were excised to measure the biochemical parameters malondialdehyde (MDA) and glutathione (GSH). Each data point represents mean ± standard error on the mean (SEM) of at least eight animals per group.	A one-way analysis of variance (ANOVA) was performed to compare different groups, followed by Tukey's multiple comparison tests ($p<0.05$)	- MDA levels in the irradiated only group (3.7180 ± 0.1076, $p <0.05$) were signifiantly higher compared with either the control group (1.5080 ± 0.2676, $p <0.05$) or the melatonin only group (1.6000 ± 0.2267, $p <0.05$). Melatonin pretreatment and treatment signifiantly reduced MDA levels in the livers of rats subjected to whole body irradiation (2.5040 ± 0.1698, $p <0.05$). - The levels of GSH in the liver tissues signifiantly decreased in the irradiated only group (8.194 ± 0.717, $p <0.05$) when compared to either the control group (15.836 ± 0.316, $p <0.05$) or the

				melatonin only group (16.060 ± 0.427, p <0.05). Melatonin pretreatment and treatment signifiantly reversed the GSH levels of rats exposed to whole body irradiation (14.946 ± 0.841, p < 0.05)
4.	Ketogenic Diet with Concurrent Chemoradiation in Head and Neck Squamous Cell Carcinoma: Preclinical and Phase 1 Trial Results	In this study, mice bearing human head and neck cancer xenografts (FaDu) were fed either standard mouse chow or KetoCal KD (90% fat, 8% carbohydrate, 2% protein) and exposed to ionizing radiation. Tumors were harvested from mice to test for glutathione, a biomarker of oxidative stress. In parallel, patients with locally advanced head and neck cancer were enrolled in a phase 1 clinical trial where they consumed KD and received radiation with concurrent platinum-based chemotherapy. Subjects consumed KetoCal KD via percutaneous endoscopic gastrostomy (PEG) tube and were also allowed to orally	Linear mixed effect regression models and The Kaplan-Meier method. All tests were two-sided and carried out at the 5% level of significance using SAS® version 9.4 software (Cary, NC). Statistics were performed by the Biostatistical Core of the Holden Comprehensive Cancer Center	- All mice consuming a KD had a β-hydroxybutyrate >.0.3 mmol/l by the second day of KD initiation (data not shown). Previously shown that nude mice fed the KD achieve blood β-hydroxybutyrate level of 1.4 ± 0.4 mmol/l by day 3 and maintain blood β-hydroxybutyrate from 0.6–1.8 mmol/l (20). Mice treated with original formula KD and radiation demonstrated a significantly increased survival compared to control or radiation treatment alone (P ≤ 0.01 or 0.05). - Mice administered the original formula KD with radiation had significantly slower tumor growth rate compared to control, irradiation alone, or new formulation diet with radiation (P < 0.01). Mice administered the original KD with

		consume water, sugar-free drinks, and foods approved by a dietitian.		radiation had a slight but insignificant improvement in survival over mice that received irradiation on standard mouse chow . - Four participants completed the KD for five weeks as prescribed. Patients started KD two days prior to receiving CRT and entered ketosis on the first day of CRT as evident by their serum β-hydroxybutyrate ≥0.6 mmol/l. The median weight loss was 2.95% for the KD group over the course of their CRT (range: −9.32% to 7.53%). Median weight loss for patients who did not tolerate the diet over the entire course of CRT was 7.92% (range: −5.77% to 11.27%). - Patients consuming a KD showed a trend toward increased protein carbonyl content compared to those receiving standard CRT. Interestingly, patients who consumed a KD had no change in total GSH and significantly lower glutathione disulfide (GSSG) in their red blood cells compared to pre-diet levels and to patients receiving standard CRT.

5.	Radioprotective effect of Date syrup on radiation-induced damage in Rats	In the present study, the radioprotective effect of Date syrup through biochemical, molecular and histopathological analysis. Signifcant elevations were recorded in the activities of serum ALT, AST, ALP and LDH and in the levels of all lipid profles parameters, while the level of HDL-C was reduced. The concentration of liver MDA was elevated with depletion of hepatic glutathione (GSH) and catalase. DNA damage was evidenced by increased DNA strand breakage and DNA-protein crosslinks. Signifcant elevations were observed in the expression of liver TNF-α and serum activity of matrix metalloproteinase (MMP-9). Pretreatment of rats with Date syrup ameliorated the tissue damage induced by radiation as evidenced by the improvement of liver function,	In this study, comparions between different groups were carried out by one-way analysis of variance (ANOVA) followed by Duncan's Multiple Range test for post hoc analysis using SPSS sofware version 15. Te level of signifcance was set at $P \leq 0.05$.	- Activities of serum ALT, AST, ALP and LDH were signifcantly elevated ($p \leq 0.05$) in rats of Irradiated group that exposed to whole body irradiation in comparison with control. Serum total cholesterol, triglycerides, low LDL-C and VLDL-C concentrations were elevated ($p \leq 0.05$) in irradiated animals, while HDL-C showed signifcant reduction. Pretreatment of animals of Group 4 with Date syrup caused considerable improvement of serum enzymes and lipid profile values. - Hepatic MDA and DNA strand breakage confrmed by its crosslinking with protein (DPCs) signifcantly increased ($p \leq 0.05$) in Irradiated group compared to control. Moreover, hepatic GSH concentration and CAT activity were signifcantly reduced ($p \leq 0.05$) in comparison to control. All these parameters were relatively improved and shifted toward the normal values in rats of Group 4 received Date syrup before irradiation. - The activity of MMP-9

		antioxidant status and reduction of DNA damage. Besides, liver TNF-α expression and serum MMP-9 activity were reduced.		was significantly increased ($P < 0.05$) in the Irradiated group compared to the control group, while pretreatment with Date syrup before irradiation caused partial protection. - The relative expression of TNF-α gene signifcantly increased ($P \leq 0.05$) in liver of Irradiated animals and animals pretreated with Date syrup before radiation to 2.3 and 2.1fold, respectively, in comparison to protected group, i.e. received Date syrup alone.

Discussion

Free radical detoxification is a metabolic process of free radicals in the human body so that they can be excreted through the excretion organs. Free radical detoxification can be done by consuming intakes rich in antioxidants such as glutathione. Ionizing radiation interacts with biological systems to induce excessive free radical fluxes attacking various cellular components including DNA, proteins, and membrane lipids that can cause significant damage (Shirazi, 2012). Ionizing radiation is divided into two, direct and indirect. Direct ionizing radiation is electrically charged particles (alpha, beta, etc.) that directly cause the ionization of atoms or molecules in a material. Ionizing radiation such as X-rays or gamma rays induces oxidative stress via free radicals. It can cause no balance between antioxidant and pro-oxidant status in cells.

Glutathione is a low molecular weight antioxidant molecule. Decreased levels of GSH make cells sensitive to radiation injury. Based on the results, dates containing glutathione can repair tissue damage caused by the whole body of mice by proving liver function and lipid profile and lack of pro-inflammatory cascades. Date syrup provides protection against the destructive effects of radiation on DNA as evidenced by the increase in comet test parameters. The body's antioxidant mechanism is indicated by an increase in the concentration of glutathione in the liver and catalase activity

The effects of radiation exposure on living things form the presence of free radicals in living cells. Exposure to lethal doses of X-rays targets specific tissues in animals resulting in death. The main targets are the differentiating cells found in the bone marrow as well as the gastrointestinal tract. Low doses of ionizing radiation cause various changes in sensitive tissues including the lungs, kidneys, digestive tract, bone marrow, skin, and liver.

This is supported research by Herum et al. (2017) on zebrafish irradiated by gamma rays to determine embryo and larva development, survival, hatching rate, and deformity. In this study, the results showed that

there was a decrease in life in all exposed groups. In addition, hatching time also affects and deformity occurs in fish. The most frequently observed deformities are developmental retardation which is manifested as failed hatching and absence of pigmentation, head and eye irregularity formation, and short or even lack of tail. However, the severity depends on the dose-response which is significant.

In free radicals, there are unpaired electrons so free radicals are very reactive and are able to change all biological molecules including lipids, DNA, and proteins. To prevent or reduce oxidative damage the human body requires antioxidants in an effort to detoxify free radicals. Free radical detoxification use antioxidants that are played by radioprotectors because they have the ability to bind radicals resulting from radiolysis from molecular irradiation. Radioprotectors can prevent exposure to active radiation at the molecular, cellular, or tissue levels.

Based on the results of a review, the effect of glutathione intake on free radical detoxification from ionizing radiation shows that existing glutathione intake can be a radioprotector that acts as an antioxidant in eliminating free radicals from the adverse effects of ionizing radiation. This is in accordance with research by Hurem, et al. (2017) which states that glutathione-mediated free radical detoxification is the most effective way.

This is also consistent with the research by Abou-Zeid (2018) on rats exposed to radiation and given date syrup containing glutathione which proves that date syrup is effective as a potential supplement in radiotherapy to protect normal cells from the damaging effects of radiation. Date syrup repaired whole tissue damage caused by irradiation of the mouse body as evidenced by improved liver function, lipid profile, and decreased pro-inflammatory cascade. The body's antioxidant mechanisms are enhanced as demonstrated by an increase in hepatic glutathione concentrations and catalase activity with a reduction in hepatic malondialdehyde levels. In addition, date syrup provides protection against the destructive effects of radiation on DNA as evidenced by increasing the comet test parameters and reducing the percentage of DPC.

In the study of Kumar, et al. (2017), it was mentioned that one of the glutathione-rich intakes is P. americana leaves which have antigenotoxic, anti-inflammatory, and radioprotective properties. This study was conducted on rats exposed to X-rays. The results showed that P. americana has the ability to scavenge free radicals by maintaining antioxidant levels in cells that reduce oxidative stress and inhibit DNA damage.

Conclusion

1. There is a direct effect of glutathione intake on the detoxification of free radicals from ionizing radiation. This is evidenced by high levels of radioprotector as an antioxidant on the cell.
2. There is limited evidence so further research is needed on the effect of glutathione intake on free radical detoxification by testing the levels of free radicals and antioxidants in cells
3. The results of the literature review are expected to be a reference for the government to take measures to control the harmful effects of ionizing radiation on humans

References

Abou-Zeid. (2018). Radioprotective Effect of Date syrup on Radiation- Induced Damage in Rats. Scientific Reports, 1-10.

Alizadeh M & Sevana D. (2022). Functional Foods, Hormesis, and Oxidative Stress. Academic Press, 581-603.

Daniel C. Ma, C. M. (2021). Ketogenic Diet with Concurrent Chemoradiation in Head and Neck Squamous Cell

Carcinoma: Preclinical and Phase 1 Trial Results. PubMed Central, 213-224.

Darlina. (2016). Potensi Vitamin sebagai Radioprotektor. IPTEK Ilmiah Populer, 7-15.

Greim H. & Robert. S. (2018). Toxicology and Risk Assessment: A Comprehensive Introduction. Chennai, India: Wiley.

Health Promotion Team. (2022). Kementrian Kesehatan Direktorat Jenderal Pelayanan Kesehatan: https://yankes.kemkes.go.id

Kumar A, et al. (2017). Anticlastogenic, Radiation Antagonistic, and Anti-Inflammatory Activities of Persea Americana in Albino Wistar Rat Model. Research in Pharmaceutical Sciences, 488-499.

Selma Hurem, L. M.-L. (2017). Dose-dependent Effects of Gamma Radiation on The Early Zebrafish Development and Gene Expression. PLOS ONE, 1-24.

Shirazi. (2012). Evaluation of Radio-Protective Effct of Melatonin on Whole Body Irradiation Induced Liver Tissue Damage. Cell Journal (Yakhteh), 292-297.