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ORIGINAL RESEARCH

Radioprotective Effects of 2-Deoxy-D-Glucose and Medicinal Plant Extracts on Radiation-Induced Oxidative Stress in Mice

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ABSTRACT
This study explores the potential radioprotective effects of 2-deoxy-D-glucose (2-DG) combined with grape seed (Vitis vinifera), green tea (Camellia sinensis), and ginger (Zingiberofficinale) extracts on radiation-induced oxidative stress in mice. Through the assessment of nitric oxide levels, lipid peroxidation, and antioxidant enzyme activities in kidney cells, the research unveils significant protection against radiation-induced damage. These findings emphasize the promise of these combinations as potent radioprotective agents, offering potential avenues for further research and clinical application.

INTRODUCTION
Ionizing radiation exposure poses a significant threat to living organisms, causing detrimental effects on cellular structures and DNA. One of the key mechanisms underlying radiation-induced injuries is the generation of reactive oxygen species (ROS) and subsequent oxidative stress. This oxidative stress can lead to cellular damage and contribute to the development of various health conditions, including cancer, cardiovascular diseases, and organ dysfunction.Efforts to mitigate the harmful effects of radiation-induced oxidative stress have led to extensive research on natural compounds with antioxidant properties. Among these compounds, grape seed (Vitis vinifera), green tea (Camellia sinensis), and ginger (Zingiberofficinale) extracts have shown promise due to their rich content of bioactive compounds such as polyphenols, flavonoids, and gingerols. These compounds possess potent antioxidant and anti-inflammatory properties and have demonstrated beneficial effects in various pathological conditions by scavenging ROS, reducing oxidative damage, and modulating the activities of antioxidant enzymes.This study aimed to evaluate the radioprotective potential of 2-deoxy-D-glucose (2-DG) in combination with grape seed, green tea, and ginger extracts. The focus was on assessing the levels of nitric oxide (NO), lipid peroxidation, and the activities of key antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx), in kidney cells. The kidney was chosen as the target organ due to its susceptibility to radiation-induced damage and its vital role in maintaining overall homeostasis.By investigating the impact of these combinations on oxidative stress markers and antioxidant defense systems in kidney cells, this study aimed to gain insights into their protective mechanisms against radiation-induced damage. Furthermore, elucidating the molecular pathways involved could contribute to the development of novel radioprotective strategies and potentially translate these findings into clinical applications.Understanding the radioprotective effects of 2-DG in combination with grape seed, green tea,

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and ginger extracts on kidney cells' oxidative stress response holds great significance. It not only sheds light on the potential therapeutic applications of these combinations but also provides a foundation for further exploration of radioprotective interventions. By unraveling the intricate mechanisms underlying these protective effects, this research could open new avenues for advancements in the field of radiation biology and contribute to the development of strategies for mitigating radiation-induced oxidative stress.

MATERIALS AND METHODS

Chemicals: All chemicals used in the present study were of Analar grade (AR) and obtained from Merck (Mumbai, India), Ranbaxy (New Delhi, India), and HiMedia (Mumbai, India).

Preparation of Plant Extracts

1. **Grape Seed (Vitis vinifera) Extract:**
- **Source:** Grape seeds were procured from Sula Vineyards, Nashik.
- **Preparation:** Seeds were dried, ground into powder, and extracted using a Soxhlet extractor with 95% ethanol. The extract was concentrated and stored.

2. **Green Tea (Camellia sinensis L.) Extract:**
- **Source:** Long leaf green tea was purchased from a local supermarket.
- **Preparation:** Leaves were powdered and extracted with 95% ethanol. The extract was concentrated and stored.

3. **Ginger (Zingiberofficinale) Extract:**
- **Source:** Fresh rhizomes of ginger were purchased from a local market.
- **Preparation:** Rhizomes were washed, dried, and milled into fine powder. The powder was extracted with 95% ethanol. The extract was concentrated and stored.

Biochemical Estimations

1. **Nitric Oxide (NO) Levels:**
- Measured using a standard assay for NO content in tissue samples.

2. **Lipid Peroxidation (TBARS):**
- Assessed by measuring thiobarbituric acid reactive substances (TBARS).

3. **Antioxidant Enzyme Activities:**
- Superoxide Dismutase (SOD), Catalase, and Glutathione Peroxidase (GPx) activities were measured using specific assays.

Experimental Design

1. **Dietary Treatment (45 Days):**

Mice were divided into ten groups with varying treatments involving radiation, 2-DG, and plant extracts.

Extracts were administered orally according to the specified dosages for 45 days, daily in the morning. Control group received normal saline daily.

Radiation Treatment (15 Days Post Dietary Treatment):

Groups 2 to 10 were irradiated with Linear Accelerator 6 MV teletherapy (5 Gy/fraction).

Mice were kept on their respective diets for another 15 days post-radiation treatment.

Sample Collection and Analysis

- **Blood Samples:** Collected by puncturing the heart after 15 days of radiation treatment.
- **Animal Sacrifice:** Euthanization by cervical dislocation, followed by immediate sample collection.

Statistical Analysis

- One-Way ANOVA and Tukey-Kramer multiple comparisons test were applied to analyze the data.

RESULTS

Table 1: Changes in Body Weight of Mice

Group of Mice	Dietary Treatment	Initial Avg. Body Weight (gm)	Avg. Body Weight (gm) after 45 Days of Dietary Treatment	Avg. Body Weight (gm) after 60 Days of Dietary Treatment and Radiation
Group 1	Normal diet, no radiation	34.9±3.15	43.7±4.6	52.5±5.4
Group 2	Radiation + Normal diet	33.9±3.1	44.3±3.4	38.8±2.9
Group 3	Radiation + Normal diet + 2-DG	33.7±2.5	42.3±2.5	46.7±2.8
Group 4	Radiation + Normal diet + 2-DG + GS	33.9±2.5	43.3±4.4	50.5±5.4
Group 5	Radiation + Normal diet + 2-DG + GT	33.7±2.9	38.0±3.2	46.0±5.3
Group 6	Radiation + Normal diet + 2-DG + Gin	34.7±2.4	43.6±4.2	50.2±4.3
Group 7	Radiation + Normal diet + 2-DG + GS +	34.5±3.1	39.6±2.5	45.5±1.5

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Group 8	Radiation + Normal diet + 2-DG + GS + Gin	34.8±2.4	41.6±3.4	47.2±4.4
Group 9	Radiation + Normal diet + 2-DG + GT + Gin	33.1±2.8	39.3±3.8	50.1±5.3
Group 10	Radiation + Normal diet + 2-DG + GS + GT + Gin	33.6±2.4	41.1±3.3	48.4±3.8

From Table 1, it is observed that all groups of mice showed an increase in body weight after 45 days of dietary treatment. However, after radiation treatment, Group 2 showed a decrease in body weight. The radiation dose was mild and single, with no mortality observed in the present study.

Table 2: Nitric Oxide, Lipid Peroxidation, SOD, Catalase, and GPx in Kidney

Group	Description	NO (units/gm tissue)	TBARS (nmol/mg tissue protein)	SOD (units/mg tissue protein)	Catalase (µmoles of H2O2 utilized/min/mg tissue protein)	GPx (µmoles of GSH consumed/min/mg tissue protein)
Group 1	Control - Normal diet No radiation	1.71±0.49	1.21±0.06	4.67±0.99	48.55±3.12	0.76±0.08
Group 2	Expt. Cont-Radiation + Normal diet	5.82***c±1.1	1.68***c±0.6	3.21***c±0.72	38.90***c±4.0	0.40***c±0.08
Group 3	Radiation + Normal diet + 2-DG	4.54*a±0.66	1.59*a±0.62	4.72*a±0.79	41.65*a±2.74	0.68*a±0.08
Group 4	Radiation + Normal diet + 2-DG + GS	3.79*a±0.93	1.51*a±0.76	4.83*a±0.99	42.57*a±4.39	0.71*a±0.79
Group 5	Radiation + Normal diet + 2-DG + GT	3.62*a±0.68	1.50*a±0.41	4.72*a±0.70	41.79*a±2.73	0.71*a±0.04
Group 6	Radiation + Normal diet + 2-DG + Gin	4.19*a±0.88	1.51*a±0.75	4.34*a±0.64	40.65*a±3.4	0.64*a±0.07
Group 7	Radiation + Normal diet + 2-DG + GS + GT	2.54**b±0.21	1.30**b±0.42	5.40**b±0.66	43.37**b±2.94	0.66**b±0.04
Group 8	Radiation + Normal diet + 2-DG + GS + Gin	2.78**b±0.16	1.33**b±0.29	5.55**b±0.86	42.41**b±2.67	0.69**b±0.05
Group 9	Radiation + Normal diet + 2-DG + GT + Gin	3.17**b±0.92	1.43**b± 0.42	5.67**b±1.13	44.36**b± 1.79	0.71**b±0.07
Group 10	Radiation +Normal diet + 2 DG+GS+GT+Gin	2.33d± 0.81	1.24d± 0.49	5.75d± 0.64	52.54d± 3.55	0.97d± 0.05

The observation of Table 2 reveals significant insights into the levels of nitric oxide (NO), lipid peroxidation, and the activities of superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) in kidney cells. The data from various sources indicates a consistent pattern of alterations in these parameters under different physiological and pathological conditions. Specifically, the findings suggest a notable association between oxidative stress markers, such as NO and lipid peroxidation, and the activities of key antioxidant enzymes, highlighting the intricate interplay between oxidative stress and the cellular antioxidant defense system. These observations underscore the importance of maintaining a balanced redox state for cellular homeostasis and provide valuable insights into the potential implications for various health conditions.

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DISCUSSION

From the results in Table 6.1, it is evident that all groups of mice exhibited an increase in body weight after 45 days of dietary treatment, demonstrating the absence of adverse effects related to the administered compounds. Notably, Group 2, subjected to radiation and normal diet, showed a decrease in body weight after radiation treatment, indicating potential radiation-induced stress impacts on the mice. In Table 6.9, the significant increase in nitric oxide (NO) and lipid peroxidation (TBARS) levels in the kidney cells of Group 2 animals, exposed to radiation and normal diet, compared to the control group, reflects the substantial oxidative stress induced by radiation. This elevation in oxidative stress markers aligns with the suppression of antioxidant enzyme activities observed in Group 2, suggesting a compromised antioxidant defense mechanism due to radiation exposure. The protective role of 2-deoxy-D-glucose (2-DG) against radiation-induced oxidative stress is supported by the findings in Group 3, where a significant reduction in NO and TBARS levels, along with an increase in antioxidant enzyme activities, was observed compared to Group 2. These results indicate that 2-DG effectively mitigates the oxidative damage induced by radiation. Furthermore, groups treated with combinations of 2-DG and different plant extracts (Groups 4-10) exhibited pronounced protective effects, as evidenced by the significant reduction in oxidative stress markers and the enhancement of antioxidant enzyme activities. These findings suggest a synergistic effect of 2-DG and the medicinal plant extracts in mitigating radiation-induced oxidative stress and enhancing cellular antioxidant defenses.The observed radioprotective effects may be attributed to the rich polyphenolic content and antioxidant properties of the plant extracts. Grape seed, green tea, and ginger extracts have been previously documented for their antioxidant activities, which include scavenging free radicals and upregulating antioxidant enzymes.

CONCLUSION

The results of this study demonstrate the significant radioprotective effects of 2-deoxy-D-glucose (2-DG) alone and in combination with grape seed, green tea, and ginger extracts against radiation-induced oxidative stress in mice. These findings suggest that these combinations hold promise as potential radioprotective agents, offering protection against radiation-induced damage to healthy tissues. The synergistic effects observed with the combination of 2-DG and medicinal plant extracts highlight a promising strategy for mitigating oxidative stress and enhancing antioxidant defenses in the context of radiation therapy. The inclusion of these compounds may contribute to the development of adjunctive treatments aimed at reducing the harmful effects of radiation on healthy tissues.

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