Radiation Measurements 197 (2026) 107766

Contents lists available at ScienceDirect

Radiation Measurements

journal homepage: www.elsevier.com/locate/radmeas

A fully plant-based approach to mitigating radiation exposure

Francesco d'Errico [a,b], Francesca Barco [a,*], Tommaso Butini [c], Mariagrazia Quattrocchi [d], Riccardo Ciolini [a], Andrea Malizia [e], Maurizio Marrale [f], Flores Naselli [c], Paola Sofia Cardinale [c], Sara Volpes [c], Fabio Caradonna [c], Susana de Souza Lalic [a,g,h]

[a] School of Engineering, University of Pisa, Italy
[b] School of Public Health, Yale University, and Yale Center for Emergency Preparedness and Disaster Response, New Haven, CT, USA
[c] Department of Biological, Chemical, and Pharmaceutical Sciences and Technologies "STEBICEF", University of Palermo, Italy
[d] Department of Radiology, St. Luca Hospital, Lucca, Italy
[e] Department of Biomedicine and Prevention, University of Roma 2, Tor Vergata, Italy
[f] Department of Physics and Chemistry "Emilio Segrè", University of Palermo, Italy
[g] Department of Physics, Federal University of Sergipe, São Cristóvão, SE, Brazil
[h] Department of Diagnostic Radiology, Federal University of São Paulo, Brazil

ARTICLE INFO

Keywords:
Allium cepa
Ionizing radiation
Micronucleus test
Mitotic index
Radioprotective compounds

ABSTRACT

The development of effective radioprotective agents has long been a critical research focus due to rising radiation risks from expanding nuclear energy and radiological technologies in civilian and military sectors. Nuclear accidents and the threat of nuclear warfare or terrorism pose major public health challenges, emphasizing the need for pharmacological protection and prevention. Although extensive studies have explored potential radioprotectors, an ideal agent remains elusive. Since ionizing radiation primarily induces free radical-mediated cellular damage, radical scavengers are promising candidates. Synthetic thiol compounds like amifostine gained limited FDA approval, yet no new agents exist for acute radiation syndrome (ARS). In this context, our ongoing research explores non-toxic, natural-origin dietary supplements as potential radioprotectors. Departing from traditional animal-based assays, we employ an innovative, plant-based model using *Allium cepa* (onion) root meristems. This system provides a rapid, cost-effective, and ethically sound platform for preliminary screening of potential radioprotective compounds. Nanovesicles derived from *Opuntia ficus-indica* (prickly pear cactus), known for their antioxidant and anti-inflammatory properties, were evaluated for their ability to mitigate cytogenetic damage induced by ionizing radiation. Preliminary findings reveal potential radioprotective effects of *Opuntia ficus-indica*-derived nanovesicles, warranting further investigation. These results contribute to the global effort to develop accessible, effective countermeasures against radiation exposure, enhancing both civilian and military radiological defense capabilities.

1. Introduction

The search for effective radioprotective agents has gained increasing importance due to growing exposure risks associated with medical, industrial, and environmental sources of ionizing radiation (IR). Numerous compounds have demonstrated radioprotective potential (Obrador et al., 2020); however, their classification remains inconsistent. Among the major categories, free radical scavengers have attracted particular attention for their ability to neutralize radiation-induced reactive oxygen species (ROS) and enhance the endogenous antioxidant defense systems of biological tissues (Abou-Hamdan et al., 2016; Kura et al., 2019; Mulinacci and Valletta, 2019). These agents include molecular hydrogen, sulfhydryl compounds, and various plant-derived extracts, each acting through antioxidant and free radical–quenching mechanisms.

Sulfhydryl-based compounds, such as WR2721 and cysteamine, represent early synthetic efforts in radioprotection. Although effective in reducing oxidative damage, their clinical utility has been limited by toxicity and narrow therapeutic indices.

Beyond these conventional synthetic radioprotectors, recent

This article is part of a special issue entitled: SSD21 published in Radiation Measurements.

* Corresponding author.
E-mail address: francesca.barco@phd.unipi.it (F. Barco).

https://doi.org/10.1016/j.radmeas.2026.107766
Received 3 November 2025; Received in revised form 13 June 2026; Accepted 3 July 2026
Available online 3 July 2026
1350-4487/© 2026 Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

research has also explored nanotechnology-based approaches, including fullerene-derived nanostructures and other engineered nanoparticles, due to their antioxidant and radical-scavenging potential (Grebowski et al., 2024; Kazmierska-Grebowska et al., 2025).

Nevertheless, despite their promising radioprotective activity, the clinical translation of several synthetic and nanotechnology-based formulations may still be limited by concerns regarding long-term biocompatibility, accumulation, and context-dependent biological effects (Guo et al., 2023; Kazmierska-Grebowska et al., 2025).

Consequently, research has increasingly focused on natural antioxidants, particularly plant extracts rich in polyphenols, flavonoids, and anthocyanins, as safer alternatives. Naturally derived compounds may offer advantages such as improved biocompatibility, lower systemic toxicity, and multi-target biological activity through the simultaneous modulation of oxidative stress, inflammation, and cellular stress responses (Shivappa and Bernhardt, 2022; Li et al., 2025).

Among naturally derived compounds, polyphenols represent one of the most extensively investigated classes of phytochemicals. Polyphenols are plant-derived organic molecules characterized by the presence of two or more phenolic groups and serve vital roles in plant defense against environmental stressors such as ultraviolet (UV) radiation, temperature extremes, and pathogen attack (Bravo, 1998; Manach et al., 2004; Dai and Mumper, 2010).

Experimental studies suggest that natural polyphenols can provide radioprotection through potent antioxidant and free radical-scavenging activities (Fischer et al., 2018). Compounds such as genistein, resveratrol, naringenin, and green tea catechins have been shown to mitigate oxidative and DNA damage induced by ionizing radiation in various biological models (Landauer et al., 2003; Lee et al., 2008; Koide et al., 2011; Kumar and Tiku, 2016). Despite these promising results, no polyphenolic compound has yet demonstrated consistent or comprehensive radioprotective efficacy (Mun et al., 2018). A major limitation lies in their poor water solubility, rapid metabolism, and low systemic bioavailability (Shoji and Nakashima, 2004; Ozdal et al., 2016; Estrela et al., 2017). Following ingestion, polyphenols undergo extensive conjugation with glucuronide, sulfate, and methyl groups, resulting in low circulating concentrations of active compounds and diminished antioxidant activity compared to their parent molecules (Serreli and Deiana, 2019). Addressing these pharmacokinetic limitations is critical for the development of clinically viable polyphenol-based radioprotectors. Approaches such as structural modification to enhance solubility or formulation into more bioavailable complexes have been proposed as potential strategies.

Topical application of polyphenols has also shown potential, particularly in protecting against chronic UV-induced oxidative damage. For example, pterostilbene, a methoxylated analog of resveratrol, has demonstrated complete protection against UVB-induced carcinogenesis in experimental models by stimulating endogenous skin antioxidant mechanisms (Sirerol et al., 2015). However, other polyphenols, including resveratrol, curcumin, epigallocatechin gallate (EGCG), and genistein, have not exhibited comparable photoprotective effects under similar conditions (Estrela et al., 2013).

Beyond polyphenols, other phytochemicals with distinct chemical structures have been explored for radioprotection (Mun et al., 2018). Caffeine, a methylxanthine derivative, exhibits antioxidant and anti-inflammatory properties and has been linked to reduced radiation-related toxicity in both experimental and clinical contexts (Stelzer et al., 1994; George et al., 1999; Hall et al., 2015). Similarly, sesamol, a phenolic compound from sesame seeds, has shown protective effects on hematopoietic and gastrointestinal systems following radiation exposure (Khan et al., 2015). Another compound, 3,3′-diindolylmethane (DIM), derived from cruciferous vegetables, has displayed significant radioprotective effects in preclinical studies, though its efficacy and safety in humans remain under investigation (Fan et al., 2013).

Collectively, current evidence underscores the potential of naturally derived antioxidants and phytochemicals as low-toxicity candidates for radiation protection. However, the successful translation of these compounds into clinical or environmental radioprotective applications requires further optimization of their stability, bioavailability, and mechanistic effectiveness. In the present study, we report preliminary findings obtained using FicoVes nanovesicles derived from *Opuntia ficus-indica* (Naselli et al., 2024) and an innovative biological test system based on *Allium cepa* (onion) root meristems (Grant, 1978; Bonciu et al., 2018; Bolsunovsky et al., 2019; Xavier et al., 2021). Although the *Allium cepa* model does not reproduce mammalian metabolic activation pathways, systemic pharmacokinetic processes, or carcinogenic mechanisms typical of animal systems, it represents a sensitive and widely used tool for detecting genotoxic damage. Due to its high sensitivity to cytogenetic alterations, low experimental cost, and the possibility of analyzing large numbers of genetically comparable samples under controlled conditions, the model has been extensively employed in environmental toxicology and biodosimetry (Bonciu et al., 2018).

Consequently, it represents a valuable platform for the preliminary evaluation of genotoxic and radioprotective effects prior to validation in more complex biological systems. Previous studies have also reported correlations between *Allium cepa* and mammalian cellular responses to genotoxic agents (Palmieri et al., 2016), supporting its applicability in preliminary radiobiological investigations.

The aim of this study was to investigate whether FicoVes nanovesicles could mitigate radiation-induced cytogenetic damage in *Allium cepa* root meristems exposed to 6 MeV electrons. To this end, biological responses to irradiation were evaluated using micronucleated cell frequency and mitotic index (MI), two of the most widely established cytogenetic endpoints in the *Allium cepa* assay (Leme and Marin-Morales, 2009).

The frequency of micronucleated cells was used as a marker of genotoxic damage, whereas the MI, calculated as the proportion of dividing cells within the analyzed population, provided an indirect measure of cellular stress and proliferative activity. Although not a direct indicator of cytotoxicity, changes in MI reflect alterations in cell cycle progression and, when interpreted alongside micronucleated cell frequency, offer a more comprehensive assessment of the interplay between radiation-induced DNA damage and the consequent impairment of cellular proliferation.

2. Materials and methods

2.1. Treatment and germination of Allium cepa seeds

Meristematic cells, plant stem cells located in root tips, of *Allium cepa* (red onion variety, pesticide-free) were used as a sensitive indicator of chromosomal and DNA alterations. Previous studies performed using the *Allium cepa* model suggest that the observed genetic damage patterns exhibit notable similarities to those reported in established animal models of radiation exposure (d'Errico et al., 2023; Barco et al., 2024; Butini et al., 2024).

As a potential radioprotector, nanovesicles derived from Opuntia ficus-indica at the University of Palermo were evaluated. Previous studies have demonstrated their biocompatibility, antioxidant capacity, and anti-inflammatory properties, including reduced ROS generation, nutrigenomic/epigenetic effects, and promotion of epithelial cell regeneration (Ragusa et al., 2023, 2025; Naselli et al., 2024a, 2024b).

FicoVes were isolated from *Opuntia ficus-indica* fruits collected in Sicily (FicoVes, batch no. 30; stock concentration: 4900 μg/mL). The juice, obtained by manual pressing, was sequentially centrifuged at increasing speeds to remove debris, then sonicated and ultracentrifuged at 120,000×g. The final vesicle pellet was resuspended in PBS, aliquoted, and stored at −80 °C for analysis.

A working suspension with a final concentration of 100 μg/mL was prepared by mixing 26 μL of the FicoVes stock solution with 1274 μL of distilled water, yielding a final volume of 1.3 mL.

Allium cepa seeds were germinated in 6-well plates, each containing

10 seeds and 1.3 mL of the corresponding treatment solution (Fig. 1). Experimental groups included an unirradiated negative control (sterile water), a FicoVes control group (100 μg/mL, non-irradiated), an irradiated control group (sterile water + 2 Gy), and a FicoVes-treated irradiated group (100 μg/mL + 2 Gy). The plates were sealed with Parafilm to minimize evaporation and incubated at (25 ± 1) °C for 4 days, until root length reached approximately 4-5 mm.

2.2. Irradiation with electrons

Electron beam irradiations were performed at the San Luca Hospital (Lucca, Italy) using a medical linear accelerator (LINAC) operating with 6 MeV electrons (Fig. 2). The dose rate was calibrated using a PTW 30013 Farmer-type® ionization chamber and set to 1 Gy/min. All irradiated groups received a dose of 2 Gy, while the negative control and the FicoVes control group were maintained under non-irradiated conditions.

To ensure homogeneous exposure conditions, a custom-designed contoured build-up cover was employed to eliminate air gaps and to guarantee proper electronic equilibrium, as detailed by Butini et al. (2026).

Following exposure, the germinated seeds were returned to the incubator for 24 h at (25 ± 1) °C to allow cell cycle progression and the subsequent manifestation of micronuclei. They were then fixed in Carnoy's solution (3:1 ethanol/acetic acid) for 20-24 h.

Finally, the samples were transferred to 70% ethanol and stored at 4 °C until slide preparation, following the procedure described by Guerra and de Souza (2002).

2.3. Preparation and compression of samples

Sample preparation and mechanical compression were carried out following the protocol described by d'Errico et al. (2023), Barco et al. (2024).

Root tips were hydrolyzed in 1 M HCl at (60 ± 2) °C for 6 min, rinsed in distilled water, and subsequently treated with 45% acetic acid. Samples were then stained with 2% acetic orcein for 15 min, a DNA-specific dye that highlights genetic structures such as nuclei and micronuclei.

After staining, the meristematic region was excised, placed on a microscope slide, covered with a coverslip, and gently compressed using a custom-built mechanical device designed and fabricated at the University of Pisa (Butini et al., 2024). This compression step was essential to obtain single-cell monolayers (Fig. 3) suitable for accurate cytogenetic analysis.

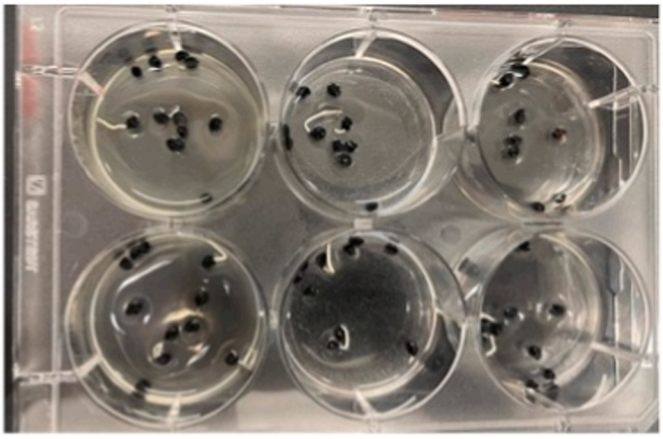

Fig. 1. Germination of *Allium cepa* seeds in a six-well plate with different treatment conditions.

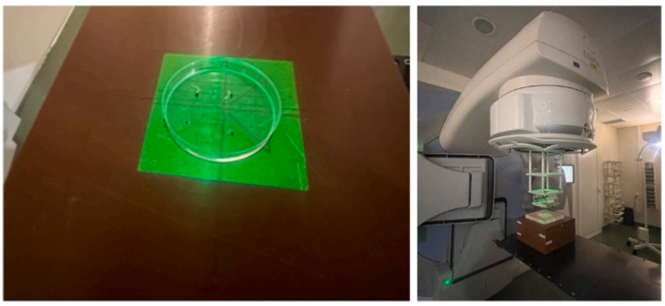

Fig. 2. Electron irradiation setup.

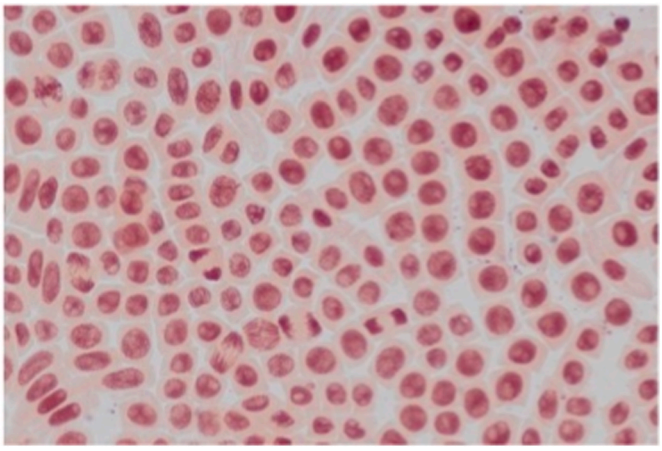

Fig. 3. Example of a monolayer of cells (400X magnification).

2.4. Sample analysis

Microscopic observations were performed using an Olympus Evident BX43 optical microscope at a total magnification of 400×. For each experimental condition, three independent biological replicates were analyzed, and 1000 cells with intact cytoplasmic membranes were evaluated per slide, resulting in a total of 3000 cells scored per group. These cells were simultaneously used for both cytogenetic endpoints considered in the study: micronucleated cell frequency and mitotic index determination.

Micronuclei originate from acentric chromosome fragments or whole chromosomes that fail to be incorporated into daughter nuclei during cell division and are therefore considered reliable biomarkers of chromosomal damage and genomic instability. Micronuclei were identified according to the criteria established by Fenech (1993, 2000).

Genotoxicity was assessed by quantifying the percentage of cells containing one or more micronuclei (Fig. 4), whereas changes in proliferative activity were indirectly evaluated through the mitotic index

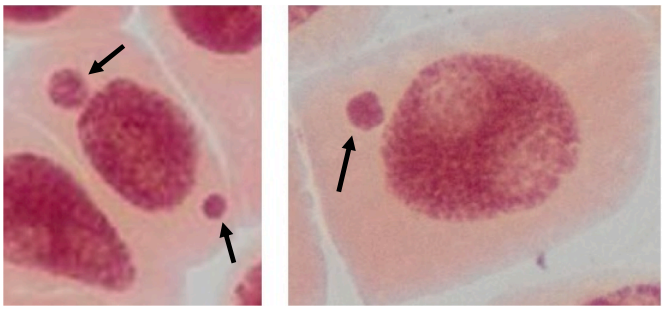

Fig. 4. Examples of cells with micronuclei.

(MI), calculated as the ratio of dividing cells to the total number of analyzed cells.

Although the MI is not a direct measure of cytotoxicity, it provides valuable information on cellular stress and cell cycle progression by reflecting the proportion of actively dividing cells (Leme and Marin-Morales, 2009). Combined with micronucleated cell frequency, a well-established indicator of chromosomal damage, the MI enables a more comprehensive evaluation of the relationship between genotoxic damage accumulation and alterations in proliferative activity.

Together, micronucleated cell frequency and MI constitute two of the most widely used and validated cytogenetic endpoints in the *Allium cepa* assay for assessing genotoxic and cytotoxic responses.

All scoring procedures were conducted under double-blind conditions, as reported by Barco et al. (2024).

The Shapiro-Wilk test was applied to assess the normality of data distributions. Differences among experimental groups were evaluated by one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test. A p-value lower than 0.05 was considered statistically significant. Statistical analyses were performed using PAST software, version 4 (Hammer et al., 2001).

3. Results

The Shapiro-Wilk test confirmed that the data followed a normal distribution, thereby allowing the use of parametric statistical methods. Results were therefore presented in the graphs as mean, with ±2 as standard deviations (SD), which, under the assumption of normality, corresponds approximately to a 95% confidence interval (Hazra and Gogtay, 2016). This representation was applied consistently to both micronucleus frequency data and the mitotic index, enabling uniform comparisons across experimental groups and facilitating the identification of potential outliers or significant variability.

3.1. Micronucleus frequency

We analyzed the FicoVes 100 μg/mL treatment group in comparison with two controls.

- **Group I**: negative control, consisting of seedlings germinated in sterile water and not exposed to irradiation.
- **Group II:** FicoVes control, consisting of seedling germinated in a 100 μg/mL FicoVes solution without irradiation.
- **Group III**: irradiated control, consisting of seedlings germinated in sterile water and exposed to 2 Gy of electrons.
- **Group IV**: FicoVes-treated group, consisting of seedlings germinated in a 100 μg/mL FicoVes solution and then irradiated with 2 Gy of electrons.

Preliminary analysis of micronucleus frequency (Fig. 5) showed a marked increase in the number of micronucleated cells in the irradiated control group (Group III) compared with the negative control (Group I).

The FicoVes control group (Group II) did not show statistically significant differences compared with the negative control, suggesting that the treatment alone did not induce detectable cytogenetic alterations under the adopted experimental conditions.

In the FicoVes-treated irradiated group (Group IV), micronucleus frequency was significantly reduced compared with the irradiated control group (Group III), suggesting a possible attenuation of radiation-induced cytogenetic damage.

3.2. Mitotic index

In addition to the evaluation of genotoxic effects, the mitotic index (MI) was analyzed as an indirect indicator of cellular stress and proliferative activity in response to irradiation and FicoVes treatment.

No statistically significant alterations in mitotic index were observed among the analyzed groups (Fig. 6). In particular, the FicoVes control group (Group II) did not differ significantly from the negative control, suggesting good tolerability of the tested concentration under the adopted experimental conditions.

Similarly, the values observed in the irradiated control group (Group III) and in the FicoVes-treated irradiated group (Group IV) remained comparable to those of the negative control group (Group I), indicating that neither irradiation nor FicoVes treatment substantially affected proliferative activity.

Further analyses on larger sample sets will be necessary to confirm these observations.

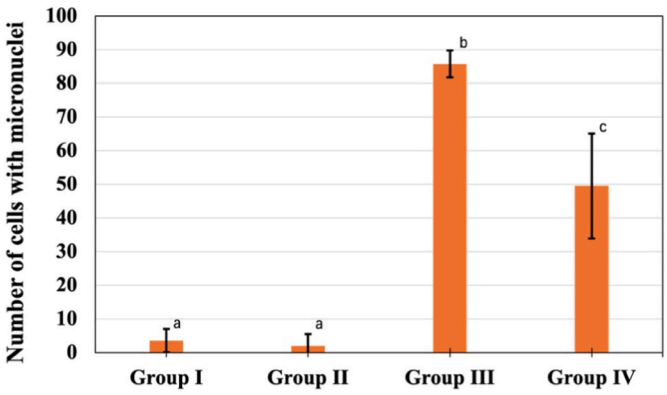

Fig. 5. Frequency of micronucleated cells in *Allium cepa* root meristems from the negative control group (Group I), FicoVes control group (Group II, 100 μg/mL), irradiated control group (Group III, 2 Gy electrons), and FicoVes-treated irradiated group (Group IV, 100 μg/mL + 2 Gy). Values are expressed as mean ± 2 SD. Groups sharing the same letter are not significantly different, whereas groups labeled with different letters are significantly different from one another according to one-way ANOVA followed by Tukey's post-hoc test ($p < 0.05$).

4. Discussion

Ionizing radiation is known to induce biological damage both through direct interactions with DNA and through indirect mechanisms associated with water radiolysis and the subsequent generation of reactive oxygen species (ROS). These processes may lead to chromosomal instability and micronucleus formation, one of the most widely used cytogenetic endpoints for the assessment of radiation-induced

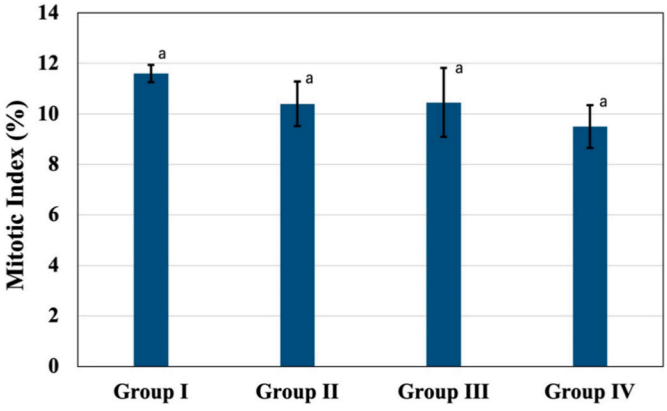

Fig. 6. Mitotic index in *Allium cepa* root meristems from the negative control group (Group I), FicoVes control group (Group II, 100 μg/mL), irradiated control group (Group III, 2 Gy electrons), and FicoVes-treated irradiated group (Group IV, 100 μg/mL + 2 Gy). Values are expressed as mean ± 2 SD. Groups sharing the same letter are not statistically significantly different according to one-way ANOVA followed by Tukey's post-hoc test ($p < 0.05$).

genotoxicity.

The *Allium cepa* model is widely recognized as a sensitive system for detecting cytogenetic damage in radiation biology and environmental genotoxicity studies (Grant, 1978; Leme and Marin-Morales, 2009). In addition, unlike isolated cell cultures, the use of organized meristematic tissue enables the evaluation of radiation-induced effects within a multicellular structure.

Preliminary findings from the present study suggest that treatment with FicoVes was associated with a reduction in the number of micronucleated cells in irradiated *Allium cepa* roots exposed to 2 Gy of 6 MeV electrons. Although the mechanisms underlying this response were not directly investigated in the present study, the observed effect may be related to a partial mitigation of the indirect action of ionizing radiation, possibly through the scavenging of reactive species generated by water radiolysis.

Previous studies on FicoVes nanovesicles derived from Opuntia ficus-indica reported antioxidant, anti-inflammatory, and nutrigenomic activities, including reduced intracellular ROS generation and modulation of inflammatory cytokine expression (Naselli et al., 2024). In this context, the reduction in micronucleus frequency observed after FicoVes treatment appears compatible with these previously described biological properties.

In addition, the absence of significant differences between the FicoVes control group and the negative control suggests that the tested FicoVes concentration did not induce detectable genotoxic effects in the absence of irradiation.

No statistically significant alterations were observed in the mitotic index among the analyzed groups. Since this parameter provides indirect information regarding proliferative activity and cellular stress, the absence of marked variations may suggest good tolerability of the tested FicoVes concentration under the adopted experimental conditions. Moreover, the reduction in micronucleus frequency observed in treated samples did not appear to be associated with major inhibition of cell division.

Although preliminary, the present findings provide a basis for future investigations aimed at further characterizing the biological response induced by FicoVes treatment.

However, although statistically significant, these findings should be regarded as a highly promising preliminary result. The micronucleus assay, while a well-established and accredited test for detecting genotoxic damage, should be complemented by additional biomarkers and independent assays to further consolidate and extend these observations.

Future studies integrating larger sample populations, different irradiation conditions, and complementary molecular or oxidative stress biomarkers could contribute to a more comprehensive understanding of the mechanisms potentially involved in the observed effects.

5. Conclusions

The present study provides preliminary evidence of a potential radioprotective effect exerted by FicoVes nanovesicles derived from Opuntia ficus-indica in *Allium cepa* root meristems exposed to 2 Gy of 6 MeV electrons. The observed reduction in micronucleus frequency, together with the absence of substantial alterations in the mitotic index, supports the potential of these plant-derived nanovesicles as candidate low-toxicity radioprotective compounds.

Overall, these findings contribute to the growing interest in naturally derived radioprotective agents and support further investigation of plant-derived compounds as innovative candidates in radioprotection research.

CRediT authorship contribution statement

Francesco d'Errico: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Francesca Barco:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Tommaso Butini:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Mariagrazia Quattrocchi:** Investigation. **Riccardo Ciolini:** Investigation. **Andrea Malizia:** Investigation. **Maurizio Marrale:** Investigation. **Flores Naselli:** Investigation, Methodology. **Paola Sofia Cardinale:** Investigation, Methodology. **Sara Volpes:** Investigation, Methodology. **Fabio Caradonna:** Data curation, Formal analysis, Investigation, Methodology, Resources, Validation. **Susana de Souza Lalic:** Investigation, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This research was partially supported by institutional funding from the Italian Ministry of University and Research. The work was carried out in preparation for the upcoming MANDRA Project funded by the Italian Ministry of Defense and also involving the Military Institute of Pharmaceutical Chemistry in Florence and University of Florence. SSL acknowledges support from the Brazilian Agency CNPq (grants no. 443464/2023-5 and 307621/2023-5).

Data availability

Data will be made available on request.

References

Abou-Hamdan, M., Gardette, B., Montagnier, O., Lemaire, B., Madelin, G., Verneuil, L., Youssef, J., Billard, P., Taverna, M., Pignatelli, A., Cadet, J., 2016. Molecular hydrogen attenuates radiation-induced nucleobase damage to DNA in aerated aqueous solutions. Int. J. Radiat. Biol. 92 (9), 536–541. https://doi.org/10.1080/09553002.2016.1206234.

Barco, F., Butini, T., Cascone, M.G., Chierici, A., Ciolini, R., Rosellini, E., Torres Novaes, J.A., Xavier, M.N., de Souza Lalic, S., d'Errico, F., 2024. Biodosimetry of UV radiation through the detection of cytogenetic endpoints in *Allium cepa* meristems. Radiat. Meas. 176, 107213. https://doi.org/10.1016/j.radmeas.2024.107213.

Bolsunovsky, A., Dementyev, D., Trofimova, E., Iniatkina, E., Kladko, Y., Petrichenkov, M., 2019. Chromosomal aberrations and micronuclei induced in onion (Allium cepa) by gamma-radiation. J. Environ. Radioact. 207, 1–6. https://doi.org/10.1016/j.jenvrad.2019.05.014.

Bonciu, E., Firbas, P., Fontanetti, C.S., Wusheng, J., Karaismailoğlu, M.C., Liu, D., Menicucci, F., Pesnya, D.S., Popescu, A., Romanovsky, A.V., Schiff, S., Ślusarczyk, J., de Souza, C.P., Srivastava, A., Sutan, A., Papini, A., 2018. An evaluation for the standardization of the Allium cepa test as cytotoxicity and genotoxicity assay. Caryologia 71 (3), 191–209. https://doi.org/10.1080/00087114.2018.1503496.

Bravo, L., 1998. Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. Nutr. Rev. 56, 317–333. https://doi.org/10.1111/j.1753-4887.1998.tb01670.x.

Butini, T., Barco, F., Cascone, M.G., Ciolini, R., Quattrocchi, M., Rosellini, E., Novaes Torres, J.A., Xavier, M.N., Lalic, S.S., d'Errico, F., 2024. Biodosimetry of ionizing radiations at different LET levels through cytogenetic endpoints in Allium cepa meristems. Radiat. Meas. 176, 107223. https://doi.org/10.1016/j.radmeas.2024.107223.

Butini, T., Barco, F., Quattrocchi, M., Ciolini, R., Marrale, M., Cascone, M.G., Rosellini, E., Xavier, M.N., Souza, S.O., d'Errico, F., 2026. Dose-response characterization of Allium cepa meristematic cells exposed to 6 MV X-rays. Radiat. Meas., 107715 https://doi.org/10.1016/j.radmeas.2026.107715.

d'Errico, F., Barco, F., Butini, T., Cascone, M.G., Ciolini, R., Quattrocchi, M., Rosellini, E., Hulber, T., Torres Novaes, J.A., Xavier, M.N., de Souza Lalic, S., 2023. Radiation monitoring with plant-based biotas and an automated micronucleus scoring approach. EPJ Web Conf. 288, 09007. https://doi.org/10.1051/epjconf/202328809007.

Dai, J., Mumper, R.J., 2010. Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. Molecules 15, 7313–7352. https://doi.org/10.3390/molecules15107313.

Estrela, J.M., Mena, S., Obrador, E., Benlloch, M., Castellano, G., Salvador, R., Dellinger, R.W., 2017. Polyphenolic phytochemicals in cancer prevention and

therapy: bioavailability versus bioefficacy. J. Med. Chem. 60, 9413–9436. https://doi.org/10.1021/acs.jmedchem.6b01026.
Estrela, J.M., Ortega, A., Mena, S., Rodriguez, M.L., Asensi, M., 2013. Pterostilbene: Biomedical Applications, 50. Critical Reviews in Clinical Laboratory Sciences, pp. 65–78. https://doi.org/10.3109/10408363.2013.805182.
Fan, S., Meng, Q., Xu, J., Jiao, Y., Zhao, L., Zhang, X., Sarkar, F.H., Brown, M.L., Dritschilo, A., Rosen, E.M., 2013. DIM (3,3′-diindolylmethane) confers protection against ionizing radiation by a unique mechanism. Proceeding of the national academy of sciences. USA 110, 18650–18655. https://doi.org/10.1073/pnas.1308206110.
Fenech, M., 1993. The cytokinesis-block micronucleus technique: a detailed description of the method and its application to genotoxicity studies in human populations. Mutat. Res. Fundam. Mol. Mech. Mutagen. 285 (1), 35–44. https://doi.org/10.1016/0027-5107(93)90049-L.
Fenech, M., 2000. The in vitro micronucleus technique. Mutat. Res. Fundam. Mol. Mech. Mutagen. 455 (1–2), 81–95. https://doi.org/10.1016/S0027-5107(00)00065-8.
Fischer, N., Seo, E.-J., Efferth, T., 2018. Prevention from radiation damage by natural products. Phytomedicine 47, 192–200. https://doi.org/10.1016/j.phymed.2017.11.005.
George, K.C., Hebbar, S.A., Kale, S.P., Kesavan, P.C., 1999. Caffeine protects mice against whole-body lethal dose of gamma-irradiation. J. Radiol. Prot. 19, 171–176. https://doi.org/10.1088/0952-4746/19/2/306.
Grant, W.F., 1978. Chromosome aberrations in plants as a monitoring system. Environ. Health Perspect. 27, 37–43. https://doi.org/10.1289/ehp.782737.
Grebowski, J., Konarska, A., Piotrowski, P., Wolszczak, M., Litwinienko, G., 2024. Kinetics of metallofullerenol reactions with the products of water radiolysis: implications for radiotherapeutics. ACS Appl. Nano Mater. 7 (1), 539–549. https://doi.org/10.1021/acsanm.3c04747.
Guerra, M., de Souza, M.J., 2002. Como Observar Cromossomos: Um Guia De Técnicas Em Citogenética Vegetal, Animal E Humana, 201. Ribeirão Preto: FUNPEC.
Guo, J., Zhao, Z., Shang, Z.F., Tang, Z., Zhu, H., Zhang, K., 2023. Nanodrugs with intrinsic radioprotective exertion: turning the double-edged sword into a single-edged knife. Exploration 3 (2), 20220119. https://doi.org/10.1002/EXP.20220119.
Hall, S., Desbrow, B., Anoopkumar-Dukie, S., Davey, A.K., Arora, D., McDermott, C., Schubert, M.M., Perkins, A.V., Kiefel, M.J., Grant, G.D., 2015. A review of the bioactivity of coffee, caffeine and key coffee constituents on inflammatory responses linked to depression. Food Res. Int. 76, 626–636. https://doi.org/10.1016/j.foodres.2015.07.027.
Hammer, Ø., Harper, D.A.T., Ryan, P.D., 2001. Past: paleontological statistics software package for education and data analysis. Palaeontol. Electron. 4 (1), 1–9. http://palaeo-electronica.org/2001_1/past/issue1_01.htm.
Hazra, A., Gogtay, N., 2016. Biostatistics series module 1: basics of biostatistics. Indian J. Dermatol. 61 (1), 10–20. https://doi.org/10.4103/0019-5154.173988.
Kazmierska-Grebowska, P., Jankowski, M.M., Obrador, E., Kolodziejczyk-Czepas, J., Litwinienko, G., Grebowski, J., 2025. Nanotechnology meets radiobiology: fullerenols and metallofullerenols as nano-shields in radiotherapy. Biomed. Pharmacother. 184, 117915. https://doi.org/10.1016/j.biopha.2025.117915.
Khan, S., Kumar, A., Adhikari, J.S., Rizvi, M.A., Chaudhury, N.K., 2015. Protective effect of sesamol against 60Co γ-ray-induced hematopoietic and gastrointestinal injury in C57BL/6 male mice. Free Radic. Res. 49, 1344–1361. https://doi.org/10.3109/10715762.2015.1071485.
Koide, K., Osman, S., Garner, A.L., Song, F., Dixon, T., Greenberger, J.S., Epperly, M.W., 2011. The use of 3,5,4′-tri-O-acetylresveratrol as a potential prodrug for resveratrol protects mice from γ-irradiation-induced death. ACS Med. Chem. Lett. 2, 270–274. https://doi.org/10.1021/ml100159p.
Kumar, S., Tiku, A.B., 2016. Biochemical and molecular mechanisms of radioprotective effects of naringenin, a phytochemical from citrus fruits. J. Agric. Food Chem. 64, 1676–1685. https://doi.org/10.1021/acs.jafc.5b05067.
Kura, B., Bagchi, A.K., Singal, P.K., Barancik, M., LeBaron, T.W., Buday, J., Slezak, J., 2019. Molecular hydrogen: potential in mitigating oxidative-stress-induced radiation injury. Can. J. Physiol. Pharmacol. 97 (4), 287–292. https://doi.org/10.1139/cjpp-2018-0604.
Landauer, M.R., Srinivasan, V., Seed, T.M., 2003. Genistein treatment protects mice from ionizing radiation injury. J. Appl. Toxicol. 23, 379–385. https://doi.org/10.1002/jat.904.
Lee, H.J., Kim, J.S., Moon, C., Kim, J.C., Lee, Y.S., Jang, J.S., Jo, S.K., Kim, S.H., 2008. Modification of gamma-radiation response in mice by green tea polyphenols. Phytother Res. 22, 1380–1383. https://doi.org/10.1002/ptr.2507.
Leme, D.M., Marin-Morales, M.A., 2009. Allium cepa test in environmental monitoring: a review on its application. Mutation research/reviews in mutation research 682 (1), 71–81. https://doi.org/10.1016/j.mrrev.2009.06.002.
Li, X., Yu, L., Xu, H., Xing, X., Wu, W., Feng, Y., Ma, L., Zhou, Z., Li, B., He, Y., 2025. Research on the mechanisms of natural products in radiation protection. Front. Bioeng. Biotechnol. 13, 1640682. https://doi.org/10.3389/fbioe.2025.1640682.
Manach, C., Scalbert, A., Morand, C., Rémésy, C., Jiménez, L., 2004. Polyphenols: food sources and bioavailability. Am. J. Clin. Nutr. 79, 727–747. https://doi.org/10.1093/ajcn/79.5.727.
Mulinacci, N., Valletta, A., 2019. Effects of ionizing radiation on bio-active plant extracts useful for preventing oxidative damages. Nat. Prod. Res. 33 (8), 1106–1114. https://doi.org/10.1080/14786419.2018.1457663.
Mun, G.-I., Kim, S., Choi, E., Kim, C.S., Lee, Y.-S., 2018. Pharmacology of natural radioprotectors. Arch Pharm. Res. (Seoul) 41, 1033–1050. https://doi.org/10.1007/s12272-018-1083-6.
Naselli, F., Bellavia, D., Costa, V., De Luca, A., Raimondi, L., Giavaresi, G., Caradonna, F., 2024a. Osteoarthritis in the elderly population: preclinical evidence of nutrigenomic activities of flavonoids. Nutrients 16 (1), 112. https://doi.org/10.3390/nu16010112.
Naselli, F., Volpes, S., Cardinale, P.S., Palumbo, F.S., Cancilla, F., Lopresti, F., Villanova, V., Girgenti, A., Nuzzo, D., Caradonna, F., Picone, P., 2024b. New nanovesicles from prickly pear fruit juice: a resource with antioxidant, anti-inflammatory, and nutrigenomic properties. Cells 13 (21), 1756. https://doi.org/10.3390/cells13211756.
Obrador, E., Salvador, R., Villaescusa, J.I., Soriano, J.M., Estrela, J.M., Montoro, A., 2020. Radioprotection and radiomitigation: from the bench to clinical practice. Biomedicines 8 (11), 461. https://doi.org/10.3390/biomedicines8110461.
Ozdal, T., Sela, D.A., Xiao, J., Boyacioglu, D., Chen, F., Capanoglu, E., 2016. The reciprocal interactions between polyphenols and gut microbiota and effects on bioaccessibility. Nutrients 8, 78. https://doi.org/10.3390/nu8020078.
Palmieri, M.J., Andrade-Vieira, L.F., Trento, M.V.C., Eleutério, M.W.F., Luber, J., Davide, L.C., Marcussi, S., 2016. Cytogenotoxic effects of spent pot liner (SPL) and its main components on human leukocytes and meristematic cells of Allium cepa. Water, Air, Soil Pollut. 227 (5), 156. https://doi.org/10.1007/s11270-016-2809-z.
Ragusa, M.A., Gentile, C., Nicosia, A., Costa, S., Volpes, S., Greco, L., Naselli, F., Caradonna, F., 2025. Epigenetic remodeling of regulatory regions by indicaxanthin suggests a shift in cell identity programs in colorectal cancer cells. Int. J. Mol. Sci. 26 (13), 6072. https://doi.org/10.3390/ijms26136072.
Ragusa, M.A., Naselli, F., Cruciata, I., Volpes, S., Schimmenti, C., Serio, G., Mauro, M., Librizzi, M., Luparello, C., Chiarelli, R., La, Rosa C., Lauria, A., Gentile, C., Caradonna, F., 2023. Indicaxanthin induces autophagy in intestinal epithelial cancer cells by epigenetic mechanisms involving DNA methylation. Nutrients 5 (15), 3495. https://doi.org/10.3390/nu15153495.
Serreli, G., Deiana, M., 2019. In vivo formed metabolites of polyphenols and their biological efficacy. Food Funct. 10, 6999–7021. https://doi.org/10.1039/C9FO01733J.
Shivappa, P., Bernhardt, G.V., 2022. Natural radioprotectors on current and future perspectives: a mini-review. J. Pharm. BioAllied Sci. 14 (2), 57–71. https://doi.org/10.4103/jpbs.jpbs_502_21.
Shoji, Y., Nakashima, H., 2004. Nutraceutics and delivery systems. J. Drug Target. 12, 385–391. https://doi.org/10.1080/10611860400003817.
Sirerol, J.A., Feddi, F., Mena, S., Rodriguez, M.L., Sirera, P., Aupí, M., Pérez, S., Asensi, M., Ortega, A., Estrela, J.M., 2015. Topical treatment with pterostilbene, a natural phytoalexin, effectively protects hairless mice against UVB radiation-induced skin damage and carcinogenesis. Free Radic. Biol. Med. 85, 1–11. https://doi.org/10.1016/j.freeradbiomed.2015.03.027.
Stelzer, K.J., Koh, W.J., Kurtz, H., Greer, B.E., Griffin, T.W., 1994. Caffeine consumption is associated with decreased severe late toxicity after radiation to the pelvis. Int. J. Radiat. Oncol. Biol. Phys. 30, 411–417. https://doi.org/10.1016/0360-3016(94)90022-1.
Xavier, M.N., Pantaleao, S.M., Scher, R., Ciolini, R., d'Errico, F., Souza, S.O., 2021. Allium cepa used as a dosimetry system in nuclear and radiological emergencies. European Physical Journal Plus 136 (6). https://doi.org/10.1140/epjp/s13360-021-01674-8.