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PII: S0969-806X(17)30380-8

DOI: <https://doi.org/10.1016/j.radphyschem.2017.12.022>

Reference: RPC7728

To appear in: *Radiation Physics and Chemistry*

Received date: 31 March 2017

Revised date: 22 December 2017

Accepted date: 27 December 2017

Cite this article as: Michiru Toyama, Takashi Mori, Junko Takahashi and Hitoshi Iwahashi, Luteolin as reactive oxygen generator by X-ray and UV irradiation, *Radiation Physics and Chemistry*, <https://doi.org/10.1016/j.radphyschem.2017.12.022>

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## Title

Luteolin as reactive oxygen generator by X-ray and UV irradiation

ACCEPTED MANUSCRIPT

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## Abstract

Non-toxic X-ray-responsive substances can be used in the radiosensitization of cancer, like porphyrin mediated radiotherapy. However, most X-ray-responsive substances are toxic. To find novel non-toxic X-ray-responsive substances, we studied the X-ray and UV reactivity of 40 non-toxic compounds extracted from plants. Dihydroethidium was used as an indicator to detect reactive oxygen species (ROS) generated by the compounds under X-ray or UV irradiation. We found that 13 of the investigated compounds generated ROS under X-ray irradiation and 17 generated ROS under UV irradiation. Only 4 substances generated ROS under both X-ray and UV. In particular, luteolin exhibited the highest activity among the investigated compounds; therefore, the ROS generated by luteolin were thoroughly characterized. To identify the ROS, we employed a combination of ROS detection reagents and their quenchers.  $O_2^{\cdot -}$  generation by luteolin was monitored using dihydroethidium and superoxide dismutase (as an  $O_2^{\cdot -}$  quencher).  $OH^{\cdot}$  and  $^1O_2$  generation was determined using aminophenyl fluorescein with ethanol ( $OH^{\cdot}$  quencher) and Singlet Oxygen Sensor Green<sup>®</sup> with  $NaN_3$  ( $^1O_2$  quencher), respectively. Generation of  $O_2^{\cdot -}$  under X-ray and UV irradiation was observed; however, no  $OH^{\cdot}$  or  $^1O_2$  was detected. The production of ROS from luteolin is surprising, because luteolin is a well-known antioxidant.

## Keywords

X-ray, radiosensitizer, reactive oxygen species (ROS), luteolin

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