Letter

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A comment on: *Research progress in the radioprotective effect of superoxide dismutase*

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I thank and commend the authors Xiaojing Huang *et al.* of the article titled *"Research progress in the radioprotective effect of superoxide dismutase"* for having brought a comprehensive review of the molecular, cellular, tissue, and organ level mechanism of radioprotection by superoxide dismutase (SOD) (*1*). The authors in the article have made the following statements:

- *"Thus, to seek the radiation modifiers with selective protection for normal tissues has been a realm of intense investigation."*

- *"Therefore, the search for other radioprotectors with high potency and low toxicity should be the primary subject of further research."*

Supporting the authors, it is acknowledged that the exposure to radiation would chiefly produce intracellular reactive oxygen species (ROS, *viz.*, superoxide and hydroxyl radicals), causing DNA strand breaks and conformational alterations of biomolecules. This will certainly cause damage to surrounding normal cells. Consequently, certain compounds/formulations could be envisaged to competently scavenge the free radicals and thus protect the adjacent normal cells from radiation induced injury.

It might be proposed that the use of radioprotective compounds, like antioxidants, which selectively safeguard normal tissues against radiation injury, will also permit use of higher doses of radiation to obtain better control of cancers.

Traditionally, the critical findings on the radioprotective capacity of naturally occurring amino-metabolites like cysteine and cysteamine encouraged the quest for other thiolamines which would defend patients from the acute effects of radiation. Thus, amifostine ([S-2-[3-aminopropylamino] ethylphosphorothioic acid) was developed as a prospective radioprotector molecule (*2-4*).

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However, until now no ideal radioprotectors are available because most synthetic compounds, including the Food and Drug Administration (FDA), USA, approved aminothiol, *S*-2-(3-aminopropyl-amino) ethyl phosphorothioic acid, [WR-2721, amifostine, ethiophos (USA), or gammaphos (former USSR)], are toxic at their optimal concentrations. Obviously, there has been limited success using these agents in clinics (*5*).

This drawback might possibly be overcome by the use of herbal drugs or dietary modifications which offer a substitute for the synthetic compounds as they are considered either non-toxic or less toxic than their synthetic counterparts. Plants and their phytochemicals, especially with free radical scavenging, antioxidant properties, and immunostimulatory effects have been evaluated for their radioprotective effects. Preclinical studies in the past two decades have shown that some commonly used medicinal plants and their phytochemicals possess radioprotective effects. Additionally, screening and testing of compounds from natural sources have been carried out over the last few decades in order to find effective radioprotectors capable of inhibiting radiation damage not only during radiotherapy of cancer patients, but also to healthy individuals subjected to occupational and accidental exposure to radiation.

Substantial evidence from pre-clinical studies advocates the usefulness of mint (peppermint) in averting the toxic effects of ionizing radiation at non-toxic concentrations. Similarly, *Ocimum sanctum*, *Panax ginseng*, *Podophyllum hexandrum*, *Emblica officinalis*, *Tinospora cordifoila*, *Syzygium cumini*, *Zingiber officinale*, *Ageratum conyzoides*, *Aegle marmelos*, and *Aphanamixis polystachya* have also demonstrated radioprotective effects (*5*).

Aloe arborescens, *Azadirachta indica*, *Biophytum sensitivum*, *Boerhaavia diffusa*, *Citrus sinensis*, *Grewia asiatica*, *Moringa oleifera*, and *Punica granatum* has been reviewed by Hazra B *et al.* for their prospective role in radioprotection (*6*).

Whereas most studies of plants and their phytochemicals have been with animals, clinical applicability to humans necessitates further exploration. Furthermore, *in vitro* studies with pertinent propagatory cell lines and primary cultures will benefit in

understanding the molecular mode of action responsible for the radioprotection. Additional studies defining the radioprotective activity of plants and their active components should be with tumor-bearing animals of diverse histological and metastatic potentialities, essentially to observe for normal tissue protection. Since most published radioprotective studies have been with γ-radiation and Swiss albino mice, it is vital that analogous experiments are performed with other sources of ionizing radiation, particularly high linear energy transfer (LET) sources and with additional species of experimental animals because only then will the radioprotective spectrum be understood.

Therefore, there is an imperative requisite for investigators to clinically explore such remedies to be used in conjunction with chemo- and radio-therapy of cancer in order to curtail adverse effects, and to augment the overall curative outcome in patients.

Likewise, plants and their components with pharmacological activities that may be pertinent to amelioration of radiation-mediated damage, including antiemetic, antiinflammatory, antioxidant, cell proliferative, wound healing, and hemopoietic stimulatories should also be investigated.

If these medicinal plants/dietary constituents are effective in enhancing the radioprotective effects of low doses or decrease the systemic toxicity and delay cytogenetic damage (polyploidy and chromatid breaks), it will be an immense help in clinics and will also reduce treatment cost.

The eventual objective is to cultivate multi-disciplinary proficiency and therapeutic synergy between conventional and complementary therapies. Owing to its abundance, cost-effectiveness, and safety in consumption, these herbal/dietary radioprotectors have remarkable prospects and numerous opportunities for further investigation. This has the possibility to produce a non-toxic radioprotective agent, however, only when gaps in the prevailing understanding are linked.

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