

## Antioxidant Systems' Interventions (ASIs) for Ionizing-Radiation and Other Oxidative-Insults

Alvah C. Bittner, PhD, CPE<sup>1</sup>

<sup>1</sup>Bittner & Associates  
Kent, WA 98042, USA

Priyadarshini Dasgupta, ScD<sup>2</sup>

<sup>2</sup>Southeastern Louisiana University  
Hammond, LA, 70402, USA

Corresponding author's Email: [drbittner@comcast.net](mailto:drbittner@comcast.net)

**Author Note:** Dr. Bittner is a researcher-practitioner with a long interest in antioxidant systems' contributions to performance and wellbeing. He is an ISOES Past-President and Human Factors & Ergonomics Society Fellow. Dr. Dasgupta – with continuing interests in terrestrial worker and astronaut health – is an Associate Professor in the Department of Industrial and Engineering Technology at Southeastern Louisiana University.

**Abstract** *Nutraceutical and Environmental Antioxidant Interventions (NIs & EIs)* are reviewed regarding their applications for minimizing the adverse impacts of *Ionizing-Radiation and/or other Oxidative Insults* Antioxidant systems (ASIs) – *Nutraceutical- and Environmental- Interventions (NIs & EIs)* -- are a systematic spectrum of means for addressing occupational and other *E-ROS* (Bittner & Sakuragi; 2006; Bittner, Lile et al., 2007; Bittner & Dasgupta, 2023). This review parallels our earlier review of *NI&EIs regarding spinal health maintenance in astronautic and terrestrial workers*. Among adverse *I-RADvOI* impacts is its generation of *Excessive-Reactive Oxidative Species (E-ROS)* in tissues. In addition to apoptotic, genotoxic, and other adverse potentials, *E-ROS* serves to reduced erythrocyte (RBC) flexibilities; and thereby required “foldings” for RBC passage through smaller diameter capillaries. This in turn can block: 1) *Delivery of required O<sub>2</sub>, nutrients, hormones etc.*, 2) *Removal of CO<sub>2</sub> and other waste products (esp. inflammatory substances promoting increases in local, if not general E-ROS)*. Interrupting this inflammatory cascade, *NIs* – e.g., *Vitamin C*, various *Thiols* (e.g., *NAC* and *R-Lipoic Acid*) as well as *ORP-reducing Probiotics* – address *E-ROS*, but typically with dose limitations (e.g., diarrhea for excessive Vit. C). In this review, *NIs* are found to have *individual I-RADvOI* protective and ameliorative effects (with a scatter of similar effects for various *NI-combinations*). *Likewise, EIs* – including *H<sup>+</sup>Water (neg. ORP)*, *H<sub>2</sub> Gas* and *H<sub>2</sub>.Saline* – are shown to have broad individual protective and ameliorate effects for *I-RADvOI*. Interestingly, given its long history as an *EI* addressing *E-ROS*, *Neg. Ion Air* has not been evaluated regarding its *I-RAD* protective and/or ameliorative utilities (and remains a target for future research). More intriguing for future studies, are the relative absence of “*NI-EI Combinations*” that synergically promise enhanced *I-RADvOI* protective and ameliorative effects (the combination of *Probiotics (NI)* and *H<sup>+</sup>Water* offering particular promise).

Two conclusions are drawn from our review: (1) There is near global confirmation of the effects of individual *EI&NI* antioxidant system interventions for addressing *I-RADvOIs*; (2) *EI&NI* combinations – as shown earlier for *spinal health* – hold unique potential for broadly addressing *I-RADvOI* across the afflicted range of terrestrial to astronautic workers.

**Keywords:** Ionizing Radiation (I-RAD), Excessive Reactive Oxidative Species (*E-ROS*), RBC Inflexibility, Impaired Capillary Flow, Environmental, and Nutraceutical Interventions (*NIs & EIs*)

### 1. INTRODUCTION

#### 1.1 Overview

This report reviews two systems of ASIs– *Nutraceutical (NIs)* and *Environmental (EIs)* – and their potential for reducing adverse impacts of *Ionizing-Radiation and/or(v) other Oxidative Insults (I-RADvOI)*. In the following (1.2), we outline: the scope of affected worker populations; and identify *E-ROS* as a common core issue. Subsequently

(2.0), setting the stage f, outlines the core nature of E-ROS damage and disease across affected occupations. This is followed (3.0) with a tabular introduction to ASI Category members and their efficacies addressing *E-ROS* (*OIs* generally). This sets the stage for a tabular review of ASI members specific efficacies addressing *I-RAD* (4.0). Research opportunities and conclusions are offered in the concluding section (5.0)

## 1.2 *I-RAD&OI* Problem Scope

E-ROS associated ionizing-radiation risks are prominent in a range of occupations that span the depths-to-height of human endeavors (Hanafi et al., 2024). Regarding I-RAD, these include Underground hardrock miners; Oil-and-gas flowback fracking operators; Medical, Manufacturing, and Security personnel; Nuclear-plant operators, maintainers, and decommissioning staff; as well Aircrew (Pilots and Attendants) and Astronauts (e.g., Niu, 2011; UNSCEAR, 2008, Vol I 282-323). Likewise, other classical OI risks – e.g., chemical exposures to *cleaning agents, organic solvents, and engine* emissions -- cross both these as well as other groups not occupationally exposed to *I-RAD*. Of note, Stephan-Recaido et al. (2021), have tabulated estimates of the *occupational distributions of chemical, physical, biological, and psychosocial exposures in the USA* (albeit with most immediate interest in sociodemographic groupings). Adverse exposures, however occupational source, have a “core” commonality in potential for engendering *E-ROS*, with result of remarkably parallel, if not identical disease patterns (Hanafi et al., 2024; Pooja et al., 2025). This common core of *I-RAD* and other *OI* resultant damage is delineated in the following (2.0).

## 2. COMMON CORE OF *I-RAD* AND OTHER *OI* DAMAGE

Oxidative Stress and Inflammation increasingly have been identified as at the core of both *I-RAD* and other *OI* diseases (e.g., Bittner & Sakuragi, 2006; Bittner & Dasgupta, 2023; Hanafi et al., 2024; Pooja et al., 2025). *I-RAD* and other *OIs* -- much as *E-ROS* produced in unbalanced physical stress processes (e.g., Bittner & Dasgupta, 2023) – can cause severe oxidative harm to lipids, proteins, metabolites, and essential cellular functions, as well as DNA (Einor et al. 2016; Mohanty et al., 2014; Obrador et al, 2022). Regarding *I-RAD* (Obrador et al, 2022), “[t]he primary event for the formation of a free radical in the radiolysis of water is the release of an electron in the interaction of low linear energy transfer (LET) ionizing radiation with the water molecule.... While the physicochemical events are a quick result of radiation exposure, the damage propagates the reaction by producing repeating waves of ROS, reactive nitrogen species (RNS), cytokines, chemokines, and other factors with related incendiary penetration. Moreover, the inflammatory response generates recurring waves of ROS, cytokines, chemokines, and growth factors with associated inflammatory infiltrates.... This represents a vicious circle where both oxidative stress and inflammation induce each other” This “viscous circle”, it is noteworthy, parallels that previously showing that E-ROS both serves to: (1) Reduce RBC flexibility and consequently (2) Impair, if not block, blood flow through capillary bores smaller than RBC breadths (Bittner & Sakuragi, 2006; Bittner, Croffut et al., 2007; Bittner & Dasgupta, 2023; Hanafi et al., 2024). These, as they pointed out, would impact serviced-tissue with disruptions to: 1) Deliveries of required  $O_2$ , nutrients, hormones etc., 2) removal of  $CO_2$  and other waste products (including inflammatory substances that promote high-levels of local, if not general ROS). These longer-term disruptions not-unexpectedly lead to a wide spectrum of pathological conditions associated with both I-RAD and other OIs (Bittner & Dasgupta, 2023; Hanafi et al., 2024; Talapko et al., 2024; Pooja et al., 2025).

These parallel I-RAD and IO considerations altogether reinforce the historic use of “antioxidants” as a profound means to address the E-ROS-inflammatory effects of I-RAD and IOs (e.g., Obrador et al., 2022; Bittner & Dasgupta, 2023; Hanafi et al., 2024; Pooja et al., 2025). We introduce – in the next section (3.0) – our antioxidant systems approach.

## 3. ANTIOXIDANT SYSTEM INTERVENTIONS (ASIs)

Antioxidant systems (ASIs) – *Nutraceutical- and Environmental- Interventions (NIs & EIs)* -- are a wide-spectrum of means for prospectively addressing occupational and other *E-ROS* (Bittner & Sakuragi; 2006; Bittner, Lile et al., 2006; Bittner & Dasgupta, 2023). Table 1 overviews *NI*, *EI*, and *Mixed ASI* categories with emphasis on proven antioxidant

members identified both: 1) Earlier in our review addressing spinal health (Bittner & Dasgupta, 2023); and 2) More recent literature explorations regarding *I-RADvOI* (Addressed later in Table 2).

CATEGORY	SUB CATEGOR Y	MEMBERS	REFERENCES:
NUTRACEUTICAL ANTIOXIDANT INTERVENTIONS (NIs)	Nutritional Supplements	<ul style="list-style-type: none"> <li>• <b>Vitamins:</b> C, E, A, &amp;)</li> <li>• <b>Thiols:</b> <i>NAC</i></li> <li>• <b>Phytochemicals</b> <i>Curcumin, Melatonin etc.</i></li> <li>• <b>Other:</b> e.g., <i>Omega 3 Fat, Acid</i></li> </ul>	<b>Bittner &amp; Dasgupta, 2023:</b> Review with spinal health primary focus. <b>Cao et al., 2022; Kang et al., 2022 &amp; Zhang et al., 2025:</b> Medical efficacies including <i>disc degeneration</i>
	Probiotic & Other Microbiome Augments	<ul style="list-style-type: none"> <li>• <b>Probiotics</b></li> <li>• <b>Prebiotics</b></li> <li>• <b>Microbiome Transplant</b></li> </ul>	<b>Schneider et al, 2023 &amp; Ma et al 2025:</b> <i>Probiotic enhances cognition &amp; brain functions in depressed patients.</i> <b>Bittner &amp; Dasgupta, 2023:</b> Review across this sub-category's members with spinal health focus
ENVIRONMENTAL INTERVENTIONS (EIs)	Negative-Ion Air (NIA)	<ul style="list-style-type: none"> <li>• <b>Non-Water-Shear</b></li> <li>• <b>Water-Shear</b></li> <li>• <b>Water Shear &amp; Grounding</b></li> </ul>	<b>Xiao et al., 2023:</b> review and research showing NIA is <i>antioxidative, anti-inflammatory, and antiapoptotic.</i> <b>Bittner &amp; Dasgupta, 2023:</b> Review across members generally with spinal health focus.
	Molecular Hydrogen (MH2)	<ul style="list-style-type: none"> <li>• <b>H<sub>2</sub> Gas</b></li> <li>• <b>H<sup>+</sup> Water</b></li> <li>• <b>H<sub>2</sub> Saline</b></li> </ul>	<b>Yanagihara et al., 2005:</b> <i>Chemical Oxidants.</i> <b>Ohsawa et al., 2007:</b> <i>Cytotoxic oxygen radicals.</i> <b>Nicolson, et al. 2016:</b> <i>Diseases: Organ, Metabolic, &amp; Induced Inflammatory as well as Exercise Recovery</i> <b>Bittner &amp; Dasgupta, 2023:</b> Review – across with spinal health focus.
MIXED INTERVENTION (NIs+EIs)	Within Sub-Categories	<b>Mixed Interventions Within NIs or Within EIs (Not NI-EI Crossed)</b>	<b>Bittner &amp; Dasgupta, 2023:</b> Review generally across this sub-category's members with spinal health focus. <b>Bittner and colleagues 2005; 2007:</b> Outline broad frame for combinations.
	Across Sib-Categories	<b>Mixed Interventions Across NI &amp; EI</b>	<b>Belyi et al., 2003:</b> <i>Fermented milk probiotic with vitamin cocktail to reduce oxidation effects in orbiting Cosmonauts.</i> <b>Vorobjeva, 2005:</b> <i>Electroized (H<sup>+</sup>) water stimulates anaerobic microflora.</i> <b>Ostojic, 2021:</b> <i>H<sup>+</sup> water as a positive modulator of gut microbiota.</i> <b>Million &amp; Raoult, 2018:</b> <i>Vitamins and other “nutritional” can stimulate the {microbiome} “commensals” and thereby antioxidant capabilities).</i> <b>Bittner and colleagues 2005; 2007:</b> Outline broad frame for combinations.

TABLE 1. ASI NI, EI & MIXED CATEGORY MEMBERS WITH PROVEN *E-ROS* QUENCHING EFFICACIES

Examining this table, *ASI category members* clearly have efficacies over an exceptional-range of *E-ROS* associated conditions. These include *Chemical Oxidants; Cytotoxic Oxygen Radicals; Organ & Metabolic Diseases and Induced Inflammatory Conditions*. The “*antioxidative, anti-inflammatory, and antiapoptotic*” commonalities – across these broad *OI* conditions – motivated our current review of *I-RAD efficacies* (Summarized in following Sec .4.0).

#### 4. REVIEW ASI MEMBER *I-RAD* EFFICACIES

Antioxidant Systems Intervention (NIs & EIs) members were individually and collectively reviewed regarding their respective *I-RAD Efficacies*. Table 2 selectively – focused on capturing trends – summarizes the results of both early research and recent reviews (following the layout of our earlier Table 1).

**TABLE 2. ASI NI, EI & MIXED CATEGORY MEMBERS WITH PROVEN *I-RAD* EFFICACIES**

CATEGORY	SUB-CATEGORY	MEMBERS	REFERENCE: <i>I-RAD</i> APPLICATION
NUTRACEUTICAL ANTIOXIDANT INTERVENTIONS (NIs)	Nutritional Supplements	<ul style="list-style-type: none"> <li>• <b>Vitamins:</b> C, E &amp; A.)</li> <li>• <b>Thyos:</b> NAC</li> <li>• Phytochemicals Curcumin, Melatonin etc.</li> <li>• <b>Other:</b> e.g., Omega 3</li> </ul>	<b>Obrador et al, 2022:</b> Vitamins C and E, & flavonoids <b>Dobney et al., 2023:</b> Vitamins, Thyos & Polyphenols <b>Lledó et al, 2023:</b> Vitamins A,C, E, & D as well Thyos, & Phytos
	Probiotic And Other Microbiome) Supplements	<ul style="list-style-type: none"> <li>• Probiotics</li> <li>• Prebiotics</li> <li>• Microbiome Transplants</li> </ul>	<b>Ren et al. 2023:</b> Probiotics and fecal transplants as treatment of radiation enteritis. <b>Wang et al., 2023:</b> Probiotic and Fecal transplant as well as products of probiotics developed outside body.
ENVIRONMENTAL INTERVENTIONS (EIs)	Negative-Ion Air (NIA)	<ul style="list-style-type: none"> <li>• Non-Water- Shear</li> <li>• Water-Shear</li> <li>• Water Shear &amp; Grounding</li> </ul>	N/A
	Molecular Hydrogen (MH2)	<ul style="list-style-type: none"> <li>• H<sub>2</sub> Gas</li> <li>• H<sup>+</sup> Water</li> <li>• H<sub>2</sub> Saline</li> </ul>	<b>Hirano et al. 2021:</b> broadly reviews MH2 members and efficacies across organ systems as well as whole-body. <b>Nicolson, et al., 2016:</b> All H <sub>2</sub> Members, but mixed cellular and others with some specific members in human studies <b>Obrador et al. 2022:</b> All H <sub>2</sub> Members in human studies
MIXED INTERVENTION (NIs+EIs)	Within Sub- Category	Within NIs or Within EIs (Not Crossed)	<b>Dobney et al, 2023:</b> Substances, i.e., Drugs, Nutri, etc. <b>Lledó et al, 2023:</b> Vitamin combinations alone and with others in NS Sub-category
	Across Categories	Across NIs+EIs (Crossed)	N/A

Examining this table, it is evident that – except Negative Ion Air (NIA) – the other singular *ASI category members* have all demonstrated E-ROS efficacies. This exception, we note, is quite surprising given Xiao et al.’s (2023) broad review finding that NIA is broadly *antioxidative, anti-inflammatory, and anti-apoptotic*. Also evident is the void in the Mixed-Across NI and EI Category. Here we note the possibilities of future *I-RAD* explorations in this mixed category, given mixed NI-EI efficacies in other *OIs* shown in Table 1 (esp., Million & Raoult, 2018; Ostojic, 2021; Bittner & Dasgupta, 2023).

## 5. RESEARCH OPPORTUNITIES AND CONCLUSIONS

*Nutraceutical (NIs) and Environmental (EIs) individual members* were all shown herein to have: (i) *E-ROS* quenching capabilities with general *OI* efficacy (Table 1); and (ii) Broad *I-RAD* efficacy, expecting unexplored NIA (Table 2). In contrast, “mixed” intervention studies were – excepting Within-NS (i.e., Vitamins, Phytochemicals etc.) – relatively sparse. Further, there was a dearth of “mixed” Across-Category studies, especially with regard *I-RAD*, with none found in our review (See Table 2). Interestingly, these patterns parallel those found in our kindred study of *ASI* potential for enhancing “spinal

health” (Bittner & Dasgupta, 2023). Together, they point toward research opportunities toward: Initial selections of *NI-EI* member mixes to optimally address any-cause *E-ROS*, and Secondary selection, within these, toward addressing any specific *Ionizing-Radiation and/or(v) other Oxidative Insult (I-RADvOI)*.

**Two conclusions can be drawn from our review: (1) There is near global confirmation of the effects of individual EI&NI antioxidant system interventions for addressing I-RADvOIs; (2) EI&NI combinations – as shown earlier for spinal health– hold unique potential for broadly addressing I-RADvOI across the afflicted range of terrestrial to astronautic workers.**

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