JOURNEY OF FREE RADICALS AND ANTIOXIDANT RESEARCH IN BARC

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Abstract
This book chapter describes the contributions of the Bhabha Atomic Research Centre (BARC) towards understanding the role of free radicals and antioxidants in biological systems. Free radicals, which highly reactive molecules, not only play crucial roles in multiple cellular processes such as signalling and immune responses but also contribute to oxidative stress, which can lead to diseases. This chapter highlights the pioneering research carried out in BARC in the field of free radical biology, focusing on their impact on radiation-induced damage, which is particularly relevant to the Atomic Energy Program of DAE. Additionally, extensive research has been carried out using antioxidants which were shown protect against oxidative damage to vital biomolecules, ensuring cellular function and reducing radiation induced damage. The modern facilities at BARC enabled the study of free radical lifetimes and the development of effective antioxidant strategies, crucial for development of radiation countermeasures. The chapter also explores the development of radioprotective molecules, such as AKTOCYTE and Sanjeevani rice, designed to boost immunity and improve the outcome of cancer therapy. Looking ahead, the Free Radical Biology Program at the Department of Atomic Energy (DAE) is set to further

advance the understanding of oxidative stress and biological effects of radiation for possible therapeutic applications.

1. Introduction

The study of free radicals and antioxidants has been a cornerstone of research at the Bhabha Atomic Research Centre (BARC). This book chapter explores the profound journey and contributions of BARC in free radical and antioxidant research. Free radicals, with their high reactivity, play crucial roles in various biological systems, influencing processes ranging from cellular signaling to disease pathogenesis. A better understanding of oxidative stress and developing effective antioxidants is paramount, especially within the context of atomic energy programs where radiation-induced oxidative damage can have significant implications. The journey of free radical research in BARC has been marked by pioneering approaches and innovative discoveries. BARC has modern facilities and infrastructure for studying free radicals and measuring their lifetimes. Antioxidants, essential for maintaining redox balance, have been a focal point of this research. This work has far-reaching applications, impacting the safety and efficiency of Nuclear Energy Programs. Looking ahead, the Free Radical Biology Program at the Department of Atomic Energy (DAE) is poised to explore deeper into this vital area, aiming to enhance our understanding and application of these critical biological entities.

2. Role of free radicals in biological systems

Free radicals are highly reactive molecules containing unpaired electrons which makes them unstable and prone to participate in chemical reactions. While they are often associated with damage and disease, free radicals also play essential roles in biological systems related to various biological process and function such as cellular signaling, metabolism, homeostasis, immune system function, antioxidant defense system regulation, adaptation to environmental stressors, development and aging etc. Reactive oxygen species (ROS) such as hydrogen peroxide (H_2O_2) and superoxide (O2•-) serve as signaling molecules in cellular pathways. They regulate several biological processes such as cell division, differentiation, apoptosis, and immune responses. Low levels of ROS can induce hormetic responses, where cells activate defense mechanisms and adapt to stressors, leading to improved resilience and longevity. Phagocytes (neutrophils and macrophages) produce ROS to destroy invading pathogens, including bacteria, viruses, and fungi, through a process known as the respiratory burst. ROS are natural by-products of mitochondrial respiration. They participate in metabolic signaling, regulating processes such as energy production, nutrient sensing, and thermogenesis. Nitric oxide (NO•), a reactive nitrogen species (RNS), acts as a signaling molecule in blood flow regulation and neurotransmission.

ROS play a role in apoptosis and act as signaling molecules that trigger programmed cell death in response to stress or damage, and as executioners of apoptosis by damaging cellular components. ROS regulate transitions between cell cycle phases by altering the activity of cyclins and cyclin-dependent kinases (CDKs). Cells activate antioxidant defense mechanisms in response to oxidative stress induced by environmental factors viz radiation, pollutants, and toxins. Free radicals are generated during exposure to ionizing radiation, leading to DNA damage and cellular stress. Cells activate repair mechanisms and antioxidant defenses to mitigate radiation-induced damage. ROS are also involved in embryonic development, tissue remodeling, and organogenesis by regulating cell proliferation, differentiation, and morphogenesis. The accumulation of oxidative damage over time contributes to aging and associated disorders. However, moderate levels of oxidative stress can activate stress response pathways that promote longevity and health span.

3. Importance of studies on oxidative stress and antioxidants in Atomic Energy Program

The inception of free radical research can be traced back to efforts to comprehend the indirect effects of radiation exposure, particularly following the atomic bomb explosions in Hiroshima and Nagasaki in 1945. The catastrophic impact of these events prompted scientific inquiry into the biological consequences of radiation. Radiation has long been a mystery to the general public, often met with a sense of uncertainty and skepticism. Today, ionizing radiation finds wide application beyond nuclear power generation, extending into numerous therapeutic, industrial, and other fields. It also plays a key role in developing high-yielding crop varieties and extending the shelf life of food products. Radiotherapy has emerged as a key mode of cancer therapy wherein radiation specifically destroys cancerous cells with minimal harm to healthy tissues surrounding the tumor. However, normal tissue toxicity is still a liming factor in radiotherapy and hence a better understanding of the mechanisms of radiation toxicity is important to identify compounds that can act as radioprotectors. One key area of research in this regard is the study of role of free radicals in radiation-induced damage. In this context research on free radicals and antioxidants are relevant to the Atomic Energy Program. This research aims to develop strategies to protect individuals who are at risk of radiation exposure, whether in medical, industrial, or research settings. By advancing our understanding of how free radicals contribute to radiation damage and how antioxidants can counteract this damage, scientists can improve safety protocols and develop novel treatments to prevent or alleviate radiation-induced injuries.

4. Genesis and journey of research on free radical reactions

In recent years, there is increasing awareness about one’s health. In this respect, the possible role of free radicals in human health and its prevention is of immense interest. Free radicals as well as the agents that keep them in check, namely antioxidants have attracted lot of attention from both health professionals as well as basic scientists involved in biomedical research. Free radical biology has many potential applications both in disease prevention and therapy, apart from radioprotection. In this section we will explore the genesis and journey of free radical reaction studies carried out at BARC during different time periods.

4.1. Studies before 1995

Although free radical research was initiated as early as 1945, the progress of research in this area in our country was quite slow. The initial studies at BARC centered around spin trapping using electron spin resonance and pulse radiolysis in the 1970s.. Biochemical studies started much later. In 1980s assays for free radical damage in the form of lipid peroxidation were developed and publications using different rat tissues during some physiological states were published in standard biochemical journals such as BBA, BBRC and FEBS Letters. Pioneering studies carried by different scientists became the foundation to initiate research programs for deeper understanding of the role of free radicals in radioresistance of cancer cells, discovery of redox active agents, development of radioprotectors and radiosensitizers in BARC.

4.2. Studies between 1995 to 2003

Later on assays and methods were developed for evaluating DNA, lipid and protein damage and combined with pulse radiolysis and other techniques. Further, collaborations within Biomedical Group and with scientists from Chemistry Group, Radiochemistry Group besides other Institutes from both India and abroad, led to several publications. These studies also involved natural products for possible prevention of damage in relation to human diseases such as cancer, diabetes, and radiation damage. The collaborations with other institutes include Indian Institute of Technology, Mumbai; Amala Cancer Centre, Thrissur; University of Pune; ACTREC, Navi Mumbai and many other institutes of repute. The Institutes from abroad include, Kyoto Prefectural University of Medicine, National University of Singapore and Palm oil research Institute of Malaysia. These collaborative studies also lead to publication of good reviews on free radicals, antioxidants, radioprotection, natural products for prevention of human disease and these received many citations. In 2001, scientists from BARC who were working in this formed the Society for Free Radical Research, India (SFRR-India). Annual meetings of this society, involving many scientists working in the same field were conducted. This also promoted interaction between many groups working on free radicals in our country and abroad. During this period several research projects were initiated which are described below;

4.2.1. Research on radioprotection and radiosensitization

Cancer, a major cause of illness and death, is often treated with radiotherapy, a highly effective approach. However, it is crucial to protect healthy cells from radiation damage during such treatments. Hence there is a need to understand the mechanisms of radiation damage and its possible prevention by compounds such as antioxidants that can act as radioprotectors.

The currently used radioprotectors have numerous downsides such as high cost and toxicity etc. Novel approaches are being worked upon to identify newer radioprotectors. In this aspect, natural products have many advantages such as being non-toxic and have proven therapeutic effects. There are several studies at BARC in this aspect that have examined the radioprotective properties of natural compounds like caffeine, curcumin, chlorophyllin, vanillin, Troxerutin, tocotrienol besides extracts from mushrooms, *Asparagus racemosus* and *Phyllanthus amarus.*

BARC has contributed significantly to the field of the radiosensitization for better tumor control. A radiosensitizer is a compound that enhances the cytotoxic efficacy of radiation, thereby improving the outcome of radiotherapy. Radiosensitization is traditionally achieved through (i) suppression of intrinsic radioprotective elements, (ii) transformation of the radiosensitizer into a cytotoxic agent via radiolysis, (iii) blocking of DNA repair mechanisms, (iv) use of thymine analogs, and (v) mimicking oxygen. Inhibition of the thioredoxin system can augment ionizing radiation-induced oxidative stress and potentiate cytotoxic effects. Scientists from BARC extensively worked on Sanazole (AK-2123), a hypoxia sensitizer, and showed that it enhances gamma-radiation-induced apoptosis in murine fibrosarcoma and anaerobic yeast. Sanazole is currently in advanced stages of clinical trials. In recent research, scientist from BARC demonstrated that thioredoxin (Trx) and thioredoxin reductase (TrxR) play a critical role in reducing oxidized cysteine thiols across various proteins, thereby influencing cellular redox balance, survival, proliferation, DNA synthesis, transcription factor activity, and apoptosis. TrxR is particularly vital for sustaining a redox environment conducive to tumor growth, survival, and therapy resistance. Additionally, researchers from BARC have shown that dimethoxycurcumin (DIMC), a structural analog of curcumin, can significantly enhance the effectiveness of radiation therapy in killing cancer cells by specifically targeting the thioredoxin system. In our recent study, we utilized current research strategies and identified that the clobetasol propionate (FDA-approved anti-psoriatic drug) can be repurposed as a promising radiosensitizer for Keap-1 mutant lung cancers. At present, several research activities are ongoing towards the radiosensitization of cancer cells using small molecules or natural compounds.

4.2.2. Advances in instrumentation and methodology and free radical research (upto 2003)

There are various methods for estimating free radical damage to biomolecules and determination of the antioxidant properties. There is great advancement of methodologies in recent years that has helped in the progress of research on free radicals. Measurement of damage to lipids include estimation of thiobarbituric acid reactive substances (TBARS) by spectrophotometry and spectrofluorometry; spectrophotometric assays for lipid hydroperoxides and conjugated dienes; HPLC analysis for 4-hydroxynonenal; HPLC and ELISA assay for isoprostanes; gaschromatography assay for exhaled gases and fluorescence assay for lipid-DNA adducts. For measurement of endogenous antioxidants such as glutathione, protein thiols, superoxide dismutase, glutathione peroxidase and catalases spectrophotometric assays were developed. For measurement of DNA damage gel electrophoresis, comet assay, HPLC and GC-MS assays were also developed. Physico-chemical and radical scavenging methods involve studies using pulse radiolysis, cyclic voltammetry, singlet oxygen detection by germanium diode, stopped flow spectrophotometry, different spectrophotometric scavenging assays, electron spin resonance (ESR) etc.

4.3. Studies after 2003

The journey of research on free radicals and antioxidants, initiated and propelled by our esteemed seniors and colleagues, has evolved significantly since 2003 within the Bio-Science group at BARC. This evolution marks a profound advancement in our understanding of these critical biological entities. Initially focused on fundamental mechanisms, the research has now permeated almost every division of the Bio-Science group and extended to various other groups, demonstrating the interdisciplinary nature and wide-reaching implications of this work. One key area of exploration involves elucidating the molecular mechanisms by which anticancer drugs exert their effects. Free radicals play a dual role in this context: they can induce cancerous mutations, but they also participate in the mechanism of action of certain chemotherapeutic agents. By understanding how free radicals generated by an anticancer drug, researchers can design more effective treatments with reduced side effects, potentially enhancing patient outcomes.

Radiation-induced mutation breeding is another significant area where free radical research is pivotal. The role of free radicals in DNA damage and repair mechanisms is crucial for developing improved strategies for inducing beneficial mutations in crops, thus contributing to agricultural advancements and food security. In the field of food science, investigating the antioxidant capacity of irradiated foods is vital. Irradiation, used for food preservation, can lead to the formation of free radicals. Understanding how antioxidants in food can neutralize these radicals ensures the safety and nutritional quality of irradiated food products. Furthermore, the modulation of immune responses by antioxidants is a growing research focus. Free radicals are involved in immune signaling pathways, and antioxidants can influence these processes. By deciphering these interactions, there is a potential to develop novel therapeutic approaches for immune-related disorders.

4.3.1. Advances in instrumentations and methodologies and free radical research (2003 onward)

After 2003, the Bioscience group made significant progresses in the study of free radicals and antioxidants research by acquiring advanced instruments and establishing state-of-the-art facilities. Notable acquisitions include flow cytometer, multi-mode plate reader, confocal microscope, high-throughput cell analyzer, live cell imaging, and a hypoxia facility. These tools enabled sophisticated analyses and experiments that were previously unattainable, facilitating groundbreaking research in this field. The availability of free radical-specific probes, coupled with the advanced instrumentation at their disposal, empowered the Bioscience group to conduct high-precision and high-throughput studies. This led to a surge in high-quality research output, with numerous articles published in prestigious, high-impact journals. The integration of these advanced tools allowed researchers to observe deeper into the mechanisms of oxidative stress, explore the role of antioxidants in various biological processes, and develop new therapeutic strategies to combat oxidative damage. In this way, Bioscience group's research extended beyond the country and establishes a robust global presence. Our findings contributed significantly to the scientific community's understanding of free radicals and antioxidants, influencing research agendas both in India and internationally. This period marked a transformative phase for the Bioscience group, positioning it at the forefront of antioxidant and free radical research, and cementing its reputation as leaders in the field.

5. Facilities and Infrastructure to study Free Radical Generation and Lifetime Measurements

Free radical reactions can be studied by a variety of techniques that can be used to detect, quantify, and characterize these highly reactive short-lived species. Most widely used techniques include electron paramagnetic resonance (EPR) spectroscopy, which measures the magnetic moments of unpaired electrons to identify and quantify radicals and study their environments; pulsed laser photolysis, which generates excited states and radicals with a pulsed laser to investigate reaction kinetics and lifetimes, pulse radiolysis technique which utilizes high-energy radiation to generate and monitor radicals, offering insights into reaction kinetics and mechanisms (**Fig. 1**).

Fig. 1: EPR spectrometer facility at FIPLY

Chemiluminescence is another technique that utilizes detection of light emitted from radical-involved reactions, particularly in biological and environmental systems. To decipher the mechanism of a free radical reaction, it is also equally important to quantify the end product of such reaction. Here chromatographic technique like HPLC coupled to mass spectrometry (MS) plays an important role in identifying and quantifying the reactions induced by free radicals. Additionally, computational methods, like density functional theory (DFT) and molecular dynamics (MD), often complement the experimental results to predict and analyze radical properties. The stopped-flow spectrometer is an important indispensable tool in the study of persistent free radicals, providing rapid mixing, high temporal resolution, and versatile detection capabilities. It enables detailed kinetic analysis and mechanistic insights, contributing significantly to our understanding of free radical chemistry with various biologically important molecules like proteins, DNA and low molecular weight compounds that exhibits antioxidant/radioprotection properties. Each technique offers unique advantages, often requiring a combination of methods to fully understand the nature, behavior, and reactivity of these important chemical species.

5.1. Advancement in the instrumentation and basic understanding of free radical research

There has been substantial progress in the understanding of reactions of biologically relevant free radicals, by utilizing both biochemical studies and monitoring their free radical scavenging abilities. Biochemical techniques help to evaluate the efficacy of a molecule. However, in the development of new antioxidants and radioprotectors, it is important to have a deeper insight into the probable reactions taking place in the cellular milieu, which can be deduced from the kinetic parameters and lifetime of the intermediates. In this context, rapid kinetic methods such as pulse radiolysis have proven highly effective for directly investigating the interactions between antioxidants and free radicals with brief lifetimes, ranging from a few microseconds to seconds. Pulse radiolysis technique utilizes radiation chemical protocols where desired free radicals can be generated, quantified and their interactions with potential protective compounds can be monitored by different detection techniques like absorption, conductivity, EPR, Raman, polarographic technique.

The pulse radiolysis facility in Chemistry Group, BARC has a pulse linear electron accelerator (LINAC) of 7 MeV energy coupled to absorption-based detection. The LINAC was procured from Radiation Dynamics, UK in the year 1986 and the optical detection system and the software for kinetic analysis were developed indigenously. The LINAC, which is currently 38 years old, is still the main working instrument driving the radiation chemistry group in BARC. Most of the components, except the waveguide, have been upgraded by the competent team of RPCD and the current machine is capable of generating 7MeV electrons in pulses of 25, 50, 100, 200, 500 ns as well as 2 μs pulse width. The LINAC allows controlled generation of free radicals, which allows monitoring their reactions on different time scales from ns to μs, revealing detailed mechanisms, identifying transient species and monitoring their formation as well as decay kinetics. In the year 2023, to improve its operational efficiency furthermore, an application software using for the 7MeV LINAC accelerator was developed which features a user-friendly GUI for intuitive operation. It incorporates soft interlocks and precise timing optimization using a delay generator. Additionally, the program includes both soft and hardware-based safety interlocks to ensure safe operation. The pulse radiolysis facility has contributed tremendously in collecting the large databases and facilitating structure-activity relationship studies, optimizing the chemical structures of protective compounds for enhanced efficacy. The work on Radiation Chemistry is highly appreciated and acknowledged in the international arena.

Similar experimental support one gets by utilizing stopped flow spectrometer which is utilized to understand the reaction of persistent free radicals and molecular oxidants like hydrogen peroxide, peroxynitrite, hypochlorite, etc. with antioxidants. Using stopped flow spectrometer the reaction kinetics and mechanism of various natural and synthetic antioxidants with peroxynitrite has been evaluated and documented in scientific journals. Similarly, the reaction of curcumin and its derivatives with superoxide radical has been studied.

5.2. Advancement in instrumentation, multidisciplinary approach and collaborations

In the last 25 years, the Radiation Chemistry section of the Chemistry group, BARC has contributed immensely towards antioxidant research. Initially, a number of naturally occurring and synthetic compounds belonging to phenols and non-phenol functional group were studied for their ability to scavenge free radical using pulse radiolysis. These diverse compounds were synthesized in house (Chemistry Group) and some were procured through various national and international collaborations. Our research has explored various natural molecules such as curcumin, folic acid, eugenol, isoeugenol, dehydrogingerone, resveratrol, embelin, sesamol, bergenin, ferulic acid, caffeic acid, cinnamic acid, plumbagin, bakuchiol, ellagic acid, vanillin, chlorophyllin, and capsaicin. These investigations have identified the vulnerable sites for free radical and the factors that enhance the stability of phenoxyl radicals. These studies were published and were well cited in scientific community and one of the natural compound, chlorophyllin is now established as radioprotector. In addition to the pure compounds, plant extracts and herbal formulations enriched with phenols were also evaluated. Extracts of plant products like *Phyllanthus amarus Linn*, *Phyllanthus emblica (amla)*, T*rigonella foenumgraecum*, *Plumbago zeylanica, Momardica charantia Linn, Glycyrrhiza glabra, Acacia catechu, Terminalia chebula*, *Terminalia arjuna*, *Cysalpinea digyna, etc.* have been examined for antioxidant activity. While initial findings in this area are promising, the complexity of formulations and the influence of various components, which depend on processing and environmental conditions, have limited these studies to screening purposes rather than detailed evaluation of reaction mechanisms. In last decade a new program on developing selenium based radioprotector was initiated in Chemistry Group, BARC. The main challenge for developing selenium based radioprotectors is their toxicity in presence of redox active agents. The radiation chemical studies played a pivotal role in exploring the role of structure and substitution on the reactivity of selenium compounds towards free radicals and molecular redox agents. This research led to the design of selenium compounds having moderate reactivity and stability under in vivo redox conditions and identifying the lead compound diselenodipropanoic acid (DSePA). During the investigation, it was observed that certain phenomena take place within picoseconds timescale and hence the current nanosecond facility is not sufficed to venture in the short time window. In view of this a new facility is being developed in RPCD, Chemistry Group in collaboration with RRCAT, Indore to build a picosecond electron accelerator facility where picoseconds electron pulses were initially planned to generate at the photocathode electron gun by using a femtosecond laser.

6. Critical role of antioxidants in maintaining the redox balance

Antioxidants are molecules that are key to maintaining the redox balance in biological systems. Redox balance refers to the equilibrium between oxidants (such as free radicals) and antioxidants in the body. This balance is essential for proper cellular function and overall health. Various critical role of antioxidants in maintaining redox balance includes; neutralizing ROS, protecting biomolecules from oxidative damage, regenerating other antioxidants, modulating cellular signaling pathways etc. ROS, including O2•-, •OH, and H2O2, are natural by-products of cellular metabolism. However, excessive ROS production, due to factors like environmental stressors or metabolic dysfunction, can lead to oxidative damage. Antioxidants act as scavengers, neutralizing ROS and preventing their harmful effects. Enzymatic antioxidants (Superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx)) and non-enzymatic antioxidants (vitamin C, vitamin E, glutathione (GSH), flavonoids) play key roles in ROS detoxification. ROS can damage lipids, leading to lipid peroxidation, a chain reaction that produces harmful lipid hydroperoxides and aldehydes. This process damages cell membranes and can lead to cell dysfunction or death. ROS can also oxidize proteins, altering their structure and function. This can disrupt enzymatic activity, impair signaling pathways, and contribute towards age-related diseases such as neurodegenerative disorders. ROS-induced damage to DNA, such as base modifications and DNA strand breaks, can lead to mutations, genomic instability, and increased risk of cancer. Some antioxidants can regenerate other antioxidants, for example, vitamin C can regenerate oxidized vitamin E, while glutathione can recycle vitamin C and repair oxidized proteins. Enzymatic antioxidants such as glutathione reductase and thioredoxin reductase play key roles in maintaining the reduced state of antioxidants like GSH and thioredoxin, ensuring their availability for ROS scavenging. Antioxidants help in regulating redox signaling by modulating ROS levels and protecting against excessive oxidative stress. Moderate ROS levels can activate cellular defense mechanisms, such as the upregulation of antioxidant enzymes and heat shock proteins, leading to cellular adaptation and improved stress resistance. Redox imbalance, characterized by excessive ROS production or antioxidant deficiency, results in oxidative stress. Oxidative stress contributes to the pathogenesis of numerous diseases, including cardiovascular diseases, neurodegenerative disorders, cancer, and metabolic disorders. Oxidative damage to biomolecules impairs cellular function and can lead to cell death or senescence. Chronic oxidative stress accelerates aging by promoting cellular senescence, telomere shortening, and the accumulation of damaged macromolecules. Oxidative damage is linked to various age-related conditions, including Alzheimer's disease and age-related macular degeneration.

7. Application and impact of antioxidant research in Nuclear Energy Program

Antioxidant research has significant applications in various fields, including radioprotection within the nuclear energy program. The impact of antioxidants in this context is multifaceted, encompassing protection against ionizing radiation, mitigation of radiation-induced damage, and enhancement of cellular repair mechanisms. One of the major application and impact of antioxidant research in nuclear energy program is development of radioprotector. Antioxidants can mitigate the harmful effects of ionizing radiation by scavenging free radicals generated during irradiation. This includes ROS such as •OH, and O2•-, which are produced by the radiolysis of water molecules. Antioxidants protect biomolecules, including DNA, proteins, and lipids, from oxidative damage caused by these harmful radicals. By preventing oxidation and maintaining the integrity of cellular components, antioxidants help in preserving cellular function and reduces the risk of radiation-induced mutations and cell death. Antioxidants can be used to protect radiation workers in nuclear reactors and facilities from the harmful effects of chronic low-dose radiation exposure. Supplementation with antioxidants may help reduce the risk of radiation-induced health problems, such as oxidative stress-related diseases and cancer. In the event of a radiation emergency, such as a nuclear accident or radiation spill, antioxidants can be given to affected individuals to mitigate acute radiation injury and support recovery. By reducing oxidative stress and DNA damage, antioxidant supplementation can improve the health and well-being of workers in the nuclear energy sector, thereby enhancing occupational safety. Antioxidant-based radioprotection strategies have the potential to safeguard public health in the aftermath of nuclear accidents by minimizing the health risks associated with radiation exposure. Thus, antioxidant research is needed to identify and develop novel antioxidants with enhanced radioprotective properties, as well as formulations optimized for specific applications in nuclear energy programs. Determining the optimal dosage and delivery methods for antioxidant supplementation in radiation protection contexts is essential for maximizing efficacy while minimizing potential side effects.

8. Free Radical and Antioxidant Research for Society

Free radical and antioxidant research at the BARC has led to the development of products such as AKTOCYTE and the medicinal rice variety Sanjeevani. These innovations serve as adjuvants and immunity-boosting products with potential applications in cancer treatment and overall health enhancement. AKTOCYTE is a Chlorophyllin-based formulation designed to offer radioprotection to normal cells while sensitizing cancer cells. It also aids in the regeneration and repair of damaged tissues following radiotherapy. This dual action makes it a promising candidate for enhancing the effectiveness of cancer treatments and improving patient outcomes. AKTOCYTE has received approval from the Food Safety and Standards Authority of India (FSSAI) for marketing as a nutraceutical. Additionally, it is currently at an advanced stage of clinical trials for use in cancer patients, further underscoring its potential therapeutic benefits. Sanjeevani rice is a medicinal variety of rice developed for its immunity-boosting properties. The research has resulted in the creation of three products derived from this rice: Sanjeevani Kalk, Sanjeevani Bar, and Sanjeevani Instant product. These products are designed to enhance immune function, contributing to overall health and wellness. The development of Sanjeevani rice and its related products highlights the innovative use of traditional crops in modern health applications. Thus, AKTOCYTE and Sanjeevani rice, represent significant contributions to both cancer therapy and general health promotion.

9. Future directions of free radical biology program in the department of atomic energy

The Department of Atomic Energy (DAE) plays a pivotal role in various domains, including nuclear energy, agriculture, food security, nuclear medicine, and basic radiation research. Incorporating a Free Radical Biology Program within the DAE holds immense potential for advancing our understanding of oxidative stress, radiation biology, and radioprotection. Some of the future directions for the Free Radical Biology Program within the DAE may be, integration of free radical biology with radiation research, to investigate the molecular mechanisms underlying radiation-induced oxidative stress, application of free radical biology in nuclear medicine. Other than this discovery and validate biomarkers of radiation exposure and oxidative stress for use in bio-dosimetry and radiation emergency preparedness. We can also utilize state-of-the-art spectroscopic, imaging, and omics technologies to investigate free radical biology and oxidative stress in nuclear settings. Foster collaborations with other research institutions, universities, and industry partners to leverage expertise in free radical biology, radiation biology, and nuclear science for mutual benefit.

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