Journal of Ayurveda and Integrative Medicine 7 (2016) 62–68

Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: http://elsevier.com/locate/jaim

Review article

Prospects in the development of natural radioprotective therapeutics with anti-cancer properties from the plants of Uttarakhand region of India

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ARTICLE INFO

Article history:
Received 30 May 2015
Received in revised form
24 July 2015
Accepted 25 September 2015
Available online 28 May 2016

Keywords:
Anti-cancer
Herbal radioprotective agents
Uttarakhand

ABSTRACT

Radioprotective agents are substances those reduce the effects of radiation in healthy tissues while maintaining the sensitivity to radiation damage in tumor cells. Due to increased awareness about radioactive substances and their fatal effects on human health, radioprotective agents are now the topic of vivid research. Scavenging of free radicals is the most common mechanism in oncogenesis that plays an important role in protecting tissues from lethal effect of radiation exposure therefore radioprotectors are also good anti-cancer agents. There are numerous studies indicating plant-based therapeutics against cancer and radioprotection. Such plants could be further explored for developing them as promising natural radioprotectors with anti-cancer properties. This review systematically presents information on plants having radioprotective and anti-cancer properties.

1. Introduction

1.1. Ionizing radiations

The harmful effects of radiation are familiar in today's world. The level of radiation is increasing day by day due to rapid technological advancement; therefore there is a need to protect human, animals, and even plants against such harmful effects of ionizing radiation. Radiations are present in our environment from the genesis of the Universe. Actually, radiation is the energy released in the form of particle or electromagnetic waves from radioactive isotopes. It can be terrestrial and cosmic (from outer space) ionizing radiations. Basically, ionizing radiations are of three types:

1. Alpha (α) radiation is emitted from radioactive isotopes and consists of alpha particles
2. Beta (β) radiation is emitted from radioactive nuclei and carries a high energy electron with a negative charge. It has high penetrating power in respect to alpha radiations
3. Gamma (γ) radiation is an electromagnetic radiation like visible light, radio waves, and ultraviolet (UV) light.

Alpha and beta radiations have got the capabilities to ionize the atom in ions. Radiation exposure can be accidental/unwanted or aimed. Radiations may be natural or man-made. The escalating consequence of undesirable radiation (radiography, nuclear, space flights, etc.) lays a demand of an effective radioprotector. Exposure to ionizing radiation causes threatening consequences to different organs such as lungs, reproductive system, gut, skin, and eyes, which can result in pathophysiological disorders [Fig. 1].

Devastating effects of radiation poses a need for radioprotectors for safeguarding different organs of our body and to avoid the lethality associated with these radiations.

1.2. Mechanisms of radiation damage

Ionizing radiations damage cells, tissues and organs through a cascade of molecular events that are triggered by free radical known as reactive oxygen species (ROS). As shown in Fig. 2, radiation exposure lead to DNA damage in terms of single- or double-strand breaks (DSBs), base damage and DNA–DNA or protein cross-links and is ultimately responsible for altered genomic expression, protein modification, cell death, senescence and

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Peer review under responsibility of Transdisciplinary University, Bangalore.

http://dx.doi.org/10.1016/j.jaim.2015.09.001
0975-9476/

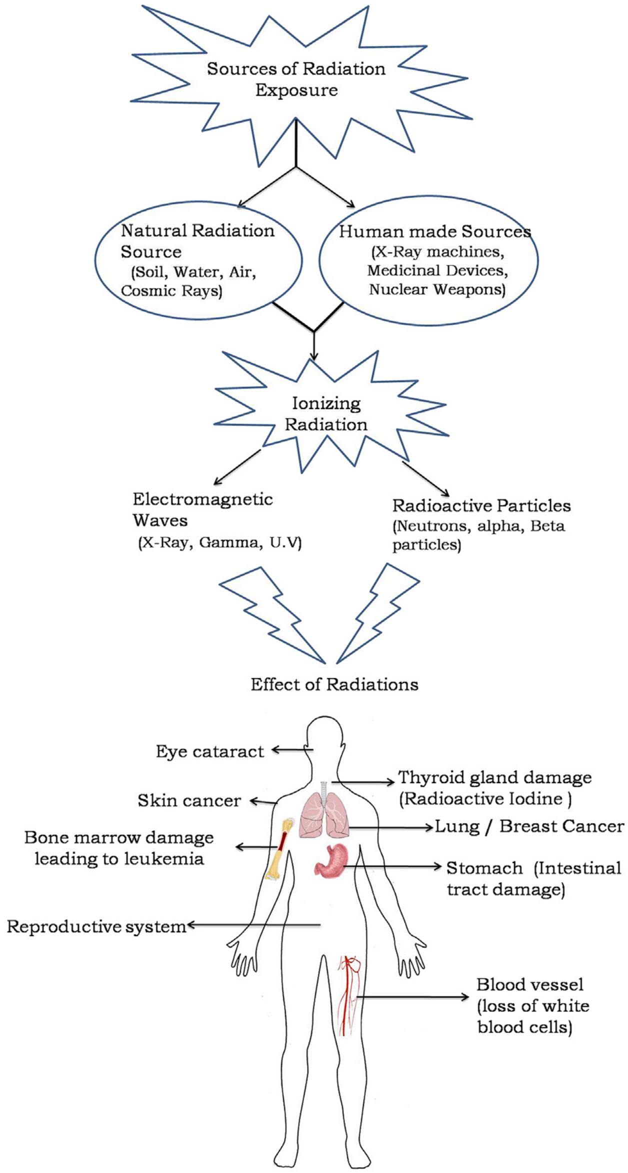

Fig. 1. Effects of radiation exposure on human body.

genomic instability. Genomic instability may also lead to mutations, cancer and birth defects. Among them, DSBs are considered to be an extremely lethal consequence of ionizing radiation.

Radiation affects the integrity and functionality of the cell through the following mechanisms:

1. Direct action: It involves absorption of radiation energy by macromolecules, like DNA or RNA, leading to molecular damage
2. Indirect action: If the molecule is not in reaction path, it can still become chemically altered indirectly via reactions with free radicals and ROS produced primarily from the radiolysis of water.

The rate at which energy is transferred from ionizing radiation to biological system/soft tissues is expressed in terms of linear energy transfer (LET) in kiloelectron volts per micrometer (keV/μm) of track length of soft tissue. Low LET radiation is less effective, whereas high LET radiation is highly efficient and much more effective in producing biological damage than low LET radiations [1].

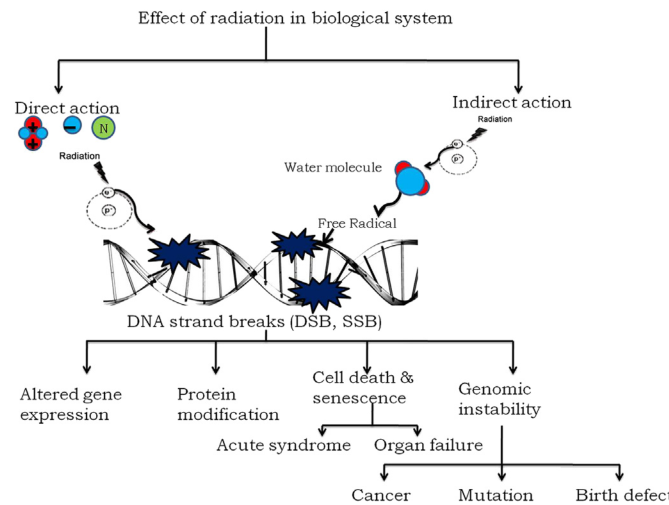

Fig. 2. Effect and mechanism of cellular damage by radiation.

According to the United States Nuclear Regulatory Commission fact sheet, biological effects of radiation on living cells may result in three outcomes: Injured or damaged cells, cell death and incorrect cell repair, resulting in biophysical alterations. The inappropriately repaired DNA breaks are the principal lesions in the induction of mutation, chromosome abnormality, and cancer.

1.3. Radiation and cancer

Radiation exposure is mundane to the people like professionals, handling radioactive materials or to the patients undergoing radiodiagnosis or radiotherapy [2]. According to a report, 22 million people in the world are cancer patients and 6 million die of the disease [3]. Though, indirectly, but radiations may trigger mutation in healthy cells, which further induces molecular alternation within the normal cells. In healthy cells, ionizing radiations generate free radicals from cytoplasmic water and ultimately induce lesions to the DNA content of nucleus. These DNA lesions may lead to cause cancer in normal and healthy cells. Thus, radiations are closely related to cancer.

1.4. Need for radioprotector

Radioprotector is a group of measures, designed to ensure man and his environment protection against the harmful effect of ionizing radiations. They are effective to save our body from wanted or unwanted radiations such as β, γ, UV, or by radio nucleotides (e.g., americium-241, cesium-137. radium, radon, strontium-90, iodine-129 and 131, plutonium, tritium, thorium, and uranium). Hazardous radiations cause consequential injuries to biological systems; therefore, it is a necessity to formulate such pharmacologically dynamic radioprotector that can render protection to human against destructive and damaging outcome of ionizing radiation.

Cellular adaptations and mechanisms to counteract the lethal consequences of damage by radiation are depicted in Fig. 3. Similarly, radioprotectors ensure the elevation of nonprotein sulfhydryl groups, reduction in lipid peroxidation, upregulation of free radicals scavenging activity through transcription upregulation of antioxidant enzymes like glutathione transferase, catalase, superoxide dismutase, glutathione peroxidase. Radiation caused damage can also be neutralized by the upregulation of DNA repair activity.