

Decorporating agents: An insight

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Abstract

Release of radioactive substances into the environment can take place due to certain accidents or increase in usage of radioactive material as nuclear weapons by terrorist to harm the society. These radioactive substances can damage skin (external contamination) or can enter into the systemic circulation of exposed person and can induce various health hazards. Exposed person can suffer from various acute and chronic diseases such as acute radiation syndrome, cancer of lung, thyroid and bone. The release of these radioactive substances has rosined in past few years due to increase in terrorist attack globally and increase in usage of these agents in medical diagnostic imaging. Decorporation therapy is used to treat the contamination induced by these toxic radioactive substances. In decorporation therapy various medicinal agents such as adsorbents, laxatives, mobilizing agents, chelating agents are used. But still there is no single method present which can be used in all conditions of radiological exposure, distance from the exposure site. Research is going on for the development of stable, highly efficacious decorporating agents which are effective in treatment of all type of radiological contaminants. This review article discuss about the currently available decorporating agents and future prospective of developing new highly efficacious decorporating agents.

Introduction

Actinides plutonium (Pu), americium (Am), curium (Cm), uranium (U) and neptunium (Np) are all known as radioactive substances as they release harmful radiations in the form of alpha, beta or gamma rays. Accidental release of these radioactive substances into environment can take place due to nuclear accident or terrorist attack. Human body gets exposed to these substances due to their release into the environment and these can cause the major health consequences even in low quantities [1].

Various such nuclear accidents happened in the last few years which result in the various deleterious effects. On March 2011, Natural disasters in Japan caused a severe accident at the Fukushima Daiichi nuclear power plant. As a result of this nuclear disaster, there is economic loss of billion dollars; hundreds of people have to leave their homes. Due to such disastrous effects, this nuclear accident is considered one of the world's most worst nuclear disaster. [2]. One of the another worst nuclear accident occur 30 years back on 26 April, 1986. Complete destruction in Unit 4 of the reactor system take place at Chernobyl Nuclear power plant due to immediate surge of power which results the destructive explosion and fire. As a result of this explosion and fire, thousands of people got died and hundreds of people have to leave their homes [3].

Frequency of occurring nuclear accident is one to two for every 10 to 20 years according to the study conducted by the scientist. Use of toxic radioactive substances by terrorist as weapons for mass destruction also results in the exposure of the people to these toxic substances .Terrorist can use radiological dispersion device or called dirty bomb as weapon for attacking the society. Various discrete locations have been attacked by terrorist by using nuclear weapons. [4]. Exposure to these toxic radioactive substances could result in the internal contamination of a significant number of people. Internal contamination with these toxic radioactive substances induce major health risks such as cancers of lung, liver, thyroid, stomach, bone and fibrotic changes in tissues such as lungs [5]. Health risks induced by radioactive substances can be reduced by using the decorporating agents. Decorporating agents are those agents which lead to the elimination of these toxic radioactive substances from the body.

The basic purpose of using the decorporating agents is to decrease the concentration of internalized radionuclides in the body by stimulating their excretion and inhibiting their deposition in various tissues [5-6]. Most preferred decorporating agents used for the decontamination purpose are chelating agents. These agents work by forming the water soluble complexes with these substances and stimulate their excretion from the body. This review article discuss about the currently available decorporating agents and future prospective of developing new highly efficacious decorporating agents. [7-8]

Decorporation

Decorporation process is defined as elimination of the toxic radioactive material such as actinides from the body [9]. Elimination of these hazardous actinides is very much essential to save the life of exposed person as these can bind with the vital cells and tissues of body and can cause the acute radiation syndrome and other severe health consequences [10]. Decorporation process is done with two specific aims: one is to make the contaminated area free from contamination and to decrease the level of exposure. Toxic contaminated radioactive material can be adsorbed from the skin and can enter into the systemic circulation. To prevent the systemic circulation, the process of decorporation should start very quickly within the hours of exposure. The choice of decorporating agents depend upon the radioactive material with which person get exposed because not all the radioactive material are hazardous for the human being. Tritium, Plutonium and Uranium are some of the examples of toxic radioactive material [11].

Mechanism of Decorporation

Various treatment approaches can be used for decorporation of toxic radioactive substances and to reduce the toxic effects induced by them. Laxatives are the drugs of choice if the radioactive substance is present in the gastrointestinal track. These drugs work by fastening the elimination of these drugs so as to prevent their systemic circulation. Another approach is the usage of various chelating agents which form the highly stable water soluble complexes. [12]. These complexes do not get adsorbed from the gastrointestinal track and get fastly excreted out from the body. If there is delay in providing the treatment to exposed patient or the radioactive material very fastly get adsorbed by the gastrointestinal track and enter into the systemic circulation, then non-radioactive iodine is used to prevent the interaction of these toxic substances with the thyroid hormone [13].

External Decontamination

Decontamination of contaminants from the skin is done with objective to eliminate the contaminants from the skin which got attached with skin of the body and can act as a pathway for the entry of radionuclide into the systemic circulation. Skin act as protective barrier for the entry of radionuclides into the body. But various contaminated wounds and burns on skin may act as a path for the passage of radionuclides. Various techniques can be used to remove contaminants from the skin. Most common method used is the cleaning of skin with hot water and soap. [15]. Not only the hot water and soap, various decontaminating

solution, washing pastes and shampoos can also be used for the purpose of external decontamination. Saline solution (0.9%) can be used to flush the skin or nose if the radioactive material got entered into the eye or nose. Various toxic radioactive materials also get entered into the various deeper layers of skin and can induce toxic health effects. Thermoplastic hydrophilic gel base skin decontaminating agents augmented with EDTA and triethanolamine can be used as efficacious decorporating agent [15]. Various medicinal agents such as emetics, purgatives, laxatives, ion exchanger can also be used as decorporating agent. These all agents work by inhibiting the adsorption of radioactive contaminants and prevent their entry into the systemic circulation [16]. Gastric pumping procedure can also be used to eliminate the contaminants out of body if person is exposed to high radiations dose. Various emetics such as ipecac and apomorphine and various laxatives such as aluminium hydroxide can be used as decorporating agents. These emetics, purgatives and gastric pumping procedure cannot be used in patients with poor health status. Retention time of these containments in gut can also be reduced by using various non absorbable binding resins such as Prussian blue [17].

Blocking Agents

Various blocking and diluting agents such as potassium iodide are used as decorporating agent as a treatment for various radioactive contaminants. Various hazardous radioactive substances which are present in systemic circulation can be taken up various body tissues. Blocking agents work by inhibiting this uptake of these toxic radioactive substances. For example potassium iodide can be used as decorporating agents to treat contamination induced by radioactive iodine substance. Potassium iodide works by inhibiting uptake of radioactive iodine by thyroid glands

Mobilizing agents

Various mobilizing agents such as diuretics, expectorant, ammonium chloride, parathyroid extract and corticosteroid are also used as decorporating agents. These agents stimulate or mobilize the elimination of radioactive contaminant from the various body tissues by modifying the natural turnover processes. Effectiveness of these depends upon how immediately they are administered to patients after exposure.

Chelating agents

Various chelating agents can also be used as decorporating agents. These form water soluble complex with the toxic radioactive materials. Toxic radioactive material such as plutonium, americium do not get excreted out from kidneys and get accumulated in body tissues and compartments and induce toxic effects.

These chelating agents work by fastening the excretion of these substances from kidneys by forming water soluble complexes with them. Examples of approved chelating decorporating agents are calcium and zinc salt of DTPA agent. Both these agents are approved by FDA. Calcium DTPA is preferred than Zn DTPA for early treatment of radioactive contamination. But it causes inhibition of mitotic cellular mechanism and its use as decorporating agent is contraindicated in pregnant women, person suffering from bone marrow depression. Due to such side effects and contraindications, Zn DTPA is preferred than calcium DTPA [17].

Oral Decorporating agents

Calcium – Various commercial oral calcium supplements are available in the market. A variety of oral calcium supplements are available. Calcium is an alkaline earth, can interfere with absorption of the other alkaline earths, and compete with their deposition in bone. In the event of internal contamination with Sr-90 or Ra-226, generous doses of oral calcium preparations are beneficial. It is used as decorporating drug, it interfere with the absorption of different radioactive materials such as strontium, radium and barium. Calcium can compete with radioactive materials in bone deposition [18].

Recent trends in Radiological Agents Decontamination

Limitation with the available formulations of decorporating agents is the lesser efficacy. So research is done by various lab and industries for the designing of new efficacious formulations of decorporating agents. Modifying the retention time of DTPA in the lung fluid by using inhalable Chitosan Tripolyphosphate Nanoparticles is one of the promising area. Diethylenetriaminepentaacetic acid (DTPA) is approved decorporating agent for toxic actinides such as plutonium and americium due to its strong chelating property [19].

Calcium and zinc salts of DTPA are used as decorporating agents against various radioactive substances such as americium, curium, and plutonium. Out of these calcium and

zinc salts of DTPA, zinc salts are more effective. But the major drawback associated with these salts is their low bioavailability. Within 24 hours of administration of DTPA, 90% of drug gets eliminated out of body [20].

Chelating agents are the currently available options to treat health hazards induced by the radioactive substances. Effectiveness of a particular chelating agent depends upon stability of complex formed by it with the heavy metals and its tendency to bind with the actinides ions. Currently available approved chelating agents to reduce the actinides contamination are trisodium salts of calcium- and zinc-diethylenetriaminepentaacetate. But again the major drawback associated with DTPA is that its bioavailability is very low when it is administered orally. It is also very less effective against the actinides such as Am^{3+} . Two multidentate Hydroxypyridonate ligands named 3,4,3-LI(1,2-HOPO) and 5-LIO(Me-3,2-HOPO) have been developed by using the biomimetic approach. Effectiveness of both these ligands is higher than the already approved pentacetate salt of DTPA [21].

Other advantage associated with these ligands is that they are very selective towards different isotopes of plutonium, americium, uranium and neptunium is also very high. In vitro testing of these developed ligands has also been carried out in which cells are isolated from the three different human sources and then ligands are administered at a concentration of 1Mm. Animal testing of these compounds also carried out in which they are orally administered to rats continuously for 28 days at high doses ($> 100 \mu\text{mol kg}^{-1} \text{day}^{-1}$) [22]. Animal and human testing gives evidence that these both ligands are safe and their oral bioavailability is very high. Both these developed ligands are on advanced stage for their use in clinical practice [23].

Oral Decorporation agents

Various oral formulations have been designed by DRDO as decorporating agents. These oral formulations work by fastening the elimination of the radioactive contaminants. [19]. Traditional injectable agents are replaced by these oral formulations. The mechanism of working of these formulations as decorporating agents is to form the complexes with the various radioactive containments. The main advantages associated with these formulations are that they are cheaper and less painful as comparison to the injectable [24].

RS Decon lotion

RS decon lotion is the another decontamination formulation developed by the Healthcare Protective Products division of Bracco Diagnostics Inc. This formulation is very effective as decontaminating agent. It has the potential to eliminate the various toxic radioactive contaminants from the skin. The one of the advantage associated with this lotion is it can be taken by patient as emergency without the supervision of doctor [25].

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