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REVIEW

Prussian blue as an antidote for radioactive thallium and cesium poisoning

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Background: Following the attacks on the US on September 11, 2001, potentially millions of people might experience contamination from radioactive metals. However, before the specter of such accidents arose, Prussian blue was known only as an investigational agent for accidental thallium and cesium poisoning. The purpose of this review is to update the state of the art concerning use of Prussian blue as an effective and safe drug against possible bioterrorism attacks and to disseminate medical information in order to contribute to the production of Prussian blue as a biodefense drug.

Methods: We compiled articles from a systematic review conducted from January 1, 1960 to March 30, 2011. The electronic databases consulted were Medline, PubMed, the Cochrane Library, and Scopus.

Results: Prussian blue is effective and safe for use against radioactive intoxications involving cesium-137 and thallium. The US Food and Drug Administration has approved Prussian blue as a drug, but there is only one manufacturer providing Prussian blue to the US. Based on the evidence, Prussian blue is effective for use against radioactive intoxications involving cesium-137 and thallium, but additional clinical research on and production of Prussian blue are needed.

Keywords: Prussian blue, radioactive cesium, thallium, intoxication, biodefense drug

Introduction

After the attacks on the US on September 11, 2001 and up to 2003, there were no approved treatments for human internal contamination with radioactive or nonradioactive thallium or radioactive cesium (cesium-137).[1] Prussian blue as a nonapproved antidote for thallium poisoning has experienced a dramatic increase in health care-related uses. Due to potentially harmful levels of thallium or cesium-137, the US Food and Drug Administration (FDA) approved the first new drug application for treatment of people exposed to radiation contamination in October 2003. In 2008, they approved a label for Radiogardase® (Heyltex Corporation, Katy, TX), ie, insoluble Prussian blue capsules, as a medicinal agent.[1–3]

The events of September 11, 2001 reinforced the need to enhance the security of the US. Since then, to prepare the nation better for such threats, the US congress passed several laws that also had an effect on the Food and Drug Administration (FDA). The FDA plays a critical, multidimensional role in the security of the US. On June 12, 2002, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Act) was passed into law.[1] In 2004, section 564 of the Federal Food, Drug, and Cosmetic Act (21 USC 360bbb-3) was amended by the Project Bioshield Act of 2004 (Public law 108-276). The FDA is responsible for carrying out certain provisions of the Bioterrorism Act, particularly Title III,

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Subtitle A (Protection of Food Supply) and Subtitle B (Protection of Drug Supply).[4]

The Project Bioshield Act 2004 permits the FDA Commissioner to authorize the use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency involving a heightened risk of attack on the public or US military forces, or one that has a significant potential to affect national security.[4]

The FDA reviewed the published medical literature on the use of Prussian blue as an investigational drug against cesium-137 and thallium poisoning and determined that 500 mg of insoluble Prussian blue capsules, when manufactured under the conditions of an approved new drug application, are safe and effective for the treatment of patients with known or suspected internal contamination with radioactive thallium, nonradioactive thallium, or radioactive cesium.[5]

Some of the published investigations were performed in developing and developed countries in the 1970s and 1980s; an incident in Brazil in 1987 occurred when a rotating assembly of the shielding head of a teletherapy unit was removed and the capsule containing 50.9 TBq (1375 Ci) of cesium-137 was dismantled and 250 people were contaminated with cesium-137, while in Ukraine, the Chernobyl nuclear reactor accident in 1986 led to widespread contamination with both cesium-137 and cesium-134 in many regions in Europe.[6–9] These investigations renewed interest in Prussian blue compounds in many Europeans countries affected by the incident.[10–12] In addition, the International Atomic Energy Agency and the United Nations have reported the use of Prussian blue to reduce radioactive cesium contamination of milk and meat produced in territories affected by the Chernobyl accident.[13,14]

Worldwide, thallium intoxication is considered the second most frequent cause of deliberate or accidental human poisoning.[15] Until the late 1990s, Mexico was one of the countries where thallium salts were widely used as rodenticides, and thallium poisoning occurred frequently in humans due to accidental or intentional ingestion. Deliberate and/or accidental human poisoning continues to occur sporadically in Mexico, and is treated with medicinal Prussian blue synthesized in our laboratory, but no pharmaceutical laboratory manufactures medicinal Prussian blue.[15]

Further, the relationship between the physicochemical properties of Prussian blue and its efficacy as an antidote to thallium poisoning has been investigated.[15] Synthesized Prussian blue protected 100% of animals against the median lethal dose (LD_{50}) of thallium, and experimental data have suggested that the size and structure of the Prussian blue particle are of great importance for the antidotal efficacy of the compound. Synthetic procedures must be optimized to produce a substance with adequate properties for the exchange and adsorption of thallium ions, which has also been suggested by other authors.[15]

The FDA wants doctors to know that Prussian blue can be used to treat contamination that may occur from accidental poisoning, as well as to treat contamination associated with a terrorist event.[16] The FDA also continues to strive to ensure that Prussian blue consistently meets high standards of quality and that proper instructions for product use are available. The agency continues to encourage the industry to file marketing applications.[16]

The objectives of the present work are to update the state of the art concerning use of Prussian blue as an effective and safe agent for use against possible bioterrorism attacks and to disseminate medical information in order to contribute to the production of Prussian blue as a biodefense drug for the US and countries worldwide. The importance of such information cannot be underestimated, given that radioactive contamination might also occur due to a natural disaster, such as the earthquake and tsunami tragedy in Japan in 2011.

Materials and methods

Search strategy

A literature search was performed using Medline, PubMed, the Cochrane Library, and Scopus from January 1, 1960 to March 30, 2011. Key search terms used were "Prussian blue", "Prussian blue AND drug", "thallium", "radioactive thallium", "cesium", "radioactive cesium", "Prussian blue AND side effects", "bioterrorism", "dirty bomb", "drug–drug interactions", and "thallium intoxication". These terms were combined with specific medical and radioactive disorders and conditions. The bibliographies of selected articles were reviewed manually to supplement the results of the online search. We selected articles published in the last 10 years in peer-reviewed journals, but also included other journals, websites, and relevant older publications. We also searched the reference lists of articles identified by this search strategy and selected additional publications that we considered relevant.

Results

Literature review

Cesium-137 and thallium-201 are radioactive isotopes of cesium and thallium, respectively. Cesium-137 was discovered in 1941 by Seaborg and Melhase, and is produced by nuclear fission for use in medical devices and gauges.[5] Cesium-137 is also one of the byproducts of nuclear fission processes in nuclear reactors and nuclear weapons tests. It has a half-life of 30.17 years. Small quantities of cesium-137 can be detected

in the environment due to nuclear weapons tests that were conducted in the 1950s and 1960s and from nuclear reactor accidents. Cesium-137 bonds with chloride and usually occurs as a crystalline powder rather than in a pure liquid form.[5,17]

Contamination with cesium isotopes can cause serious illness or death, depending on the dose, and has been associated with development of cancer long after exposure. Cesium-137 has been mentioned as a potential component of a radiological device commonly known as a "dirty bomb" containing radioactive material.[18–20]

Internal exposure to cesium-137 through ingestion or inhalation allows the radioactive material to be distributed in the soft tissues, especially muscle tissue, exposing these tissues to beta particles and gamma radiation, and increasing the risk of cancer.[21] Energy released by radioactive cesium isotopes can result in significant damage to living cells. Signs and symptoms of acute toxicity from external and internal exposure to high levels of radiation from both cesium-137 and Cs-134 isotopes are typical of those observed in cases of high exposure to ionizing radiation in general.[22]

On the other hand, thallium occurs naturally in several minerals and ores.[23] William Crookes and Claude Auguste Lamy discovered it independently in the early 1860s.[5] Thallium is considered one of the most toxic metals in the world. Thallium salts are rapidly absorbed by human tissue, where it may remain for about four months after intake. Therefore, the use of antidotal treatment against acute thallium intoxication is vital because of the severity of the symptoms and the high lethality of the poison.[15] Thallium-201 has a half-life of 72.912 hours. Acute exposure to a high dose of radioactive or nonradioactive thallium is generally characterized by severe gastrointestinal symptoms followed by neurological symptoms, which may lead to death. Thallium-201 has also been mentioned as a potential component of a dirty bomb.[5]

Thallium-201 is widely used in very small doses as an approved radioimaging drug.[5] In spite of that, there were no clinical cases of thallium poisoning due to thallium-201 in a form of a medical drug, or articles describing medical concerns about the widespread use of radiation technology. In particular, a paper by Berrington de Gonzalez et al reported that the expansion of imaging technology and interest in early disease detection has led to an estimated 9.1 million tests being performed annually in the US, which is approximately double the number performed in 1996. The radiation exposure from a myocardial perfusion scan is comparable with or higher than that of many computed tomography scans. The combination of high frequency of use and relatively high radiation doses means that perfusion scans are now estimated to contribute 20% of the annual collective radiation dose received from diagnostic procedures in the US population. Also, as reported in the paper by Berrington de Gonzalez et al, from a clinical perspective, positron emission tomography and dual-isotope scans have the lowest and highest exposures, respectively. Cancer risks are low, ranging from two cancers per 10,000 scans (95% confidence interval [CI] 1–5) for ammonia-13 cardiac positron emission tomography to 25 cancers per 10,000 scans (95% CI 9–58) for dual-isotope studies. However, because of widespread use of nuclear myocardial perfusion studies (9.1 million scans per year in the US), it is possible that 7400 additional future cancers could be related to these scans.[24]

We found other publications related to use of radiopharmaceuticals. Thallium-201 has been recommended for routine follow-up of thyroid cancer patients and even as a replacement for Iodine-131 scanning. Thallium-201 single-photon emission computed tomography appears to have an important role in the staging of thyroid cancer. Nevertheless, although the majority of infiltrated radiodiagnostic agents have shown an insignificant skin radiation burden, it appears that thallium-201 has the potential to produce significant radiation burdens when it is infiltrated in highly specific activity.[25–27]

FDA-approved insoluble Prussian blue capsules

Prussian blue was first synthesized in 1704 by a Berlin colormaker named Diesbach and has been used as an industrial and artist's pigment ever since (not for human ingestion).[28,29] Prussian blue is a crystal lattice of potassium ferric (III)-cyanoferrate (II).[29] Insoluble Prussian blue capsules contain insoluble ferric hexacyanoferrate (II), with an empirical formula of $Fe_4^{III}[Fe^{II}(CN)_6]_3$ and have a molecular weight of 859.3 Da. It is available as a blue powder in 0.5 g gelatin capsules without other drug excipients.[28]

Ferric hexacyanoferrate ($Fe_4^{III}[Fe^{II}(CN)_6]_3$) or insoluble Prussian blue is the active pharmaceutical ingredient of the drug product, Radiogardase. Radiogardase 500 mg capsules are the first FDA-approved medical countermeasure for the treatment of internal contamination from radioactive cesium or thallium.[30] Although it decreases radiation exposure, it does not treat its complications.[31]

Biological mechanism

Prussian blue is able to bind metal ions such as cesium and thallium. The therapeutic mechanism of action of cesium and thallium binding by insoluble Prussian blue is not yet known in full detail. When administered orally, insoluble Prussian blue is able to enhance the excretion of radioactive

isotopes of cesium and thallium ions into the feces during the enterohepatic cycle, preventing reabsorption and thereby reducing the radioactive burden to the body.[30] The effectiveness of soluble and insoluble Prussian blue for radioactive cesium and thallium poisoning has been studied. Initially there was more published evidence of the effectiveness of soluble Prussian blue for thallium poisoning than for insoluble Prussian blue, but the effectiveness of insoluble Prussian blue has now been relatively well documented for radioactive cesium poisoning.[32] Chemical ion exchange, physical adsorption, and ion trapping may all be involved. The primary metal binding mechanism for Prussian blue is believed to be monovalent cesium ion exchange with hydrogen ions or from hydronium ions in the Prussian blue crystal lattice. The absorption of ions onto the crystal lattice or their entrapment within the cavities of the crystal lattice may also take place.[30] When administered orally, Prussian blue absorbs the fraction of cesium or thallium secreted into the gut and binds them into the lumen.[33]

Adverse effects

Constipation, hypokalemia, and gastrointestinal upsets have been reported to be the most frequent adverse events after ingestion of Prussian blue.[31] Potassium levels should be monitored because potassium is exchanged for cesium or thallium at the surface of the crystal lattice. However, constipation in patients receiving Prussian blue orally can be disastrous; persistently high blood levels of thallium have been reported in some cases of thallium poisoning, despite Prussian blue therapy in patients who developed constipation.[33]

Some studies have shown that pH and exposure time play major roles in the release of cyanide from Prussian blue.[34] The minimal lethal dose of cyanide is approximately 50 mg; nevertheless, Yang et al demonstrated that the maximal amount of cyanide released (1.6 mg) from Prussian blue does not present a safety concern under physiological conditions. Because the amount of cyanide released under physiologically relevant conditions is approximately one order of magnitude below the minimal toxic dose at most, toxicity resulting from cyanide exposure is not expected following administration of Prussian blue at an appropriate oral dose or even up to 4×5 g/day in adults, as indicated in the package insert for Radiogardase.[34]

Formulation approaches

Some published studies have demonstrated a relationship between the physicochemical properties of Prussian blue and its efficacy as an antidote against cesium and thallium.[15,30] The size and structure of the Prussian blue particle are of great importance for the antidotal efficacy of the compound, suggesting that procedures for synthesis must be optimized to produce a substance with adequate properties of exchange and adsorption of cesium and thallium ions.[15,30] The particle size of Prussian blue is a physical property that is typically the result of crystallization and post-synthetic processing. The ion (cesium or thallium) binding capacity is inversely related to particle size. This suggests that the particle size of Prussian blue should be controlled to ensure its efficient in vivo binding.[15,30]

On the other hand, it is likely that cesium or thallium binding is pH-dependent. The highest ion binding occurs at pH 7.5. The low gastric pH (1–2) can have a negative effect on ion binding to Prussian blue due to greater availability of hydronium ions, which compete with cesium or thallium ions in an effort to bind cyanide in the Prussian blue lattice. This reduction in Prussian blue binding capacity in gastric pH may be controlled through formulation approaches, such as pH-specific controlled release that minimizes exposure during the gastric transit time.[30]

The state of Prussian blue hydration has a significant effect on cesium or thallium binding. This phenomenon is related to the moisture content of the Prussian blue molecule. Drying or storage at elevated temperatures significantly reduces cesium or thallium binding to Prussian blue. Therefore, the long-term stability of Prussian blue in suboptimal storage conditions or manufacturing processes may reduce the moisture in the Prussian blue molecule, thus causing a significant negative effect on the binding capacity of Prussian blue.[30]

Clinical cases

A number of clinical studies around the world have evaluated the use of Prussian blue as an investigational decorporation agent to enhance the excretion of cesium and thallium ions. Fifty cases of thallium intoxication dating from 1978 to 1986 were retrospectively studied in Mexico. Twenty-six patients were treated with Prussian blue 3 g/day for 10–14 days and the rest with sodium iodide and forced diuresis. In general, the thallium source was rodenticide products. The causes of intoxication were accidental in most of the cases; other cases involved suicidal and homicidal intent. It was found that recovery took place faster with Prussian blue than with other treatments, but it is difficult to obtain the antidote in Mexico.[35]

In September 1987, a radiological accident involving a medical source of cesium chloride occurred in Goiânia, Brazil, resulting in numerous children and adults

becoming contaminated. Individuals were exposed to external irradiation and skin and internal contamination. This was a radiation disaster second in magnitude only to the Chernobyl nuclear reactor incident. However, it provided an opportunity to collect data on the efficacy of Prussian blue in treating radioactive cesium poisoning in humans in a systematic way. Several studies were conducted during this emergency with different purposes, and some interesting aspects of Prussian blue were identified. Prussian blue was an effective antidote for cesium-137 deposited in the body and was generally well tolerated when administered orally. Minimal side effects were reported (ie, constipation), and administration of Prussian blue resulted in a significant increase in fecal excretion, which was the prevalent pathway of cesium-137. Elimination of cesium-137 from humans follows a first-order kinetic pattern in individuals with and without Prussian blue treatment; the biological half-life of cesium-137 elimination is 50–150 days, and of the possible biological parameters, weight had the greatest influence on half-life.[7–9,36]

Measurements were made in 15 Chinese subjects internally contaminated with radionuclides released from the Chernobyl accident, while staying at Sofia and Profdef in Bulgaria. Estimation of the initial intake was 170–900 Bq of cesium-134 and 95–1200 Bq of cesium-137. The biological half-life of radiocesium (cesium-134 and cesium-137) in three cases was in the range of 42–71 days. Prussian blue was given successfully to enhance elimination of radiocesium from the body during the period of 114–141 days after contamination.[37]

In Belgium, a 38-year-old woman was admitted to an emergency department 2 hours after drinking 250 mL of a suspension containing 35 g/L of thallium sulfate (Ratten Trnkgift TL, Hannover, Germany).[38] In spite of very high serum thallium (5240 μg/L), her symptomatology was minor and recovery was complete. Prussian blue was administered, diuresis was enhanced by intravenous fluids and a prolonged hemodialysis was started early. This was a successfully treated case of severe thallium intoxication, and aggressive treatment is recommended to prevent well known complications.[38]

The case of a 67-year-old Chinese woman diagnosed with thallotoxicosis and treated with oral Prussian blue (potassium ferric hexacyanoferrate 4 g/8 hours) was reported in 2000. Treatment with Prussian blue was successful, with urinary levels of thallium decreasing into an acceptable range and her condition improving noticeably, although residual weakness remained.[39]

On January 22, 2008, 10 members in two families in Baghdad, Iraq, developed gastrointestinal symptoms due to thallium poisoning. Thallium was detected in a cake that all 10 patients had eaten. Two patients died before treatment with Prussian blue could be administered. Treatment with Prussian blue was initiated in the eight surviving patients 11 days after they had eaten the contaminated cake. However, two of the eight patients were already comatose with severe cerebral edema and subsequently died. Over the next 30 days, all six survivors experienced hair loss, and five developed muscle weakness and spasticity of varying severity in the lower limbs.[40]

In the Czech Republic, a mother and daughter who were repeatedly exposed to thallium poisoning were followed up for two years. They experienced hair loss, polyneuropathy, and visual impairment. Thallium poisoning was confirmed by toxicological analysis of blood and/or urine and feces from both patients and microscopic analysis of the daughter's hair. Both patients were treated with Prussian blue which increased elimination of thallium in their urine and feces. Their hair loss was fully reversible. During two years of follow-up after the poisoning, polyneuropathy in the lower extremities improved substantially, but residual impairment in both motor and sensory function, nerve conduction studies, visual evoked potentials, and changes in brainstem auditory evoked potentials remained. Further, severe asymmetrical visual impairment persisted in both women, with central scotomata and impaired color discrimination in both eyes. Substantial improvement of their visual function is unlikely.[41]

Others drugs limiting absorption of radioactive cesium or toxic thallium

Apple-pectin preparations are administered as a complement to standard radioprotective measures to reduce cesium-137 uptake in children, especially in the Ukraine. Pectin is a polysaccharide found in various fruits. Purified pectin is also prescribed as an oral adsorbent for heavy metal (eg, lead and mercury) intoxication. Nesterenko et al conducted a placebo-controlled study in Ukrainian children to verify if pectin remained active in children when radiologically clean food was provided, because the mode of action of this adsorbent involves binding of heavy metals in the intestinal lumen, with the complex then being eliminated via the feces. This study demonstrated that apple-pectin is effective in the reduction of cesium-137 levels.[42] In contrast, Le Gall et al conducted a placebo-controlled study comparing the efficacy of Prussian blue and apple-pectin in cesium-137 decorporation in rats, and did not find significant differences between untreated rats

and rats treated with apple-pectin, while the fecal excretion of cesium increased fivefold with Prussian blue treatment, and there was an associated reduction in radionuclide retention in the main organs.[43]

Novel decorporation agents are being developed to protect against radiological terrorist attacks. These sorbents, known as the self-assembled monolayers on mesoporous supports (SAMMS™), are hybrid materials in which differing organic moieties are grafted onto mesoporous silica. Copper (II) ferrocyanide on mesoporous silica (FC-Cu-EDA-SAMMS™) was compared in vitro and in vivo against Prussian blue for capturing radioactive cesium. In vitro results demonstrated that a low pH could have a negative effect on cesium binding by Prussian blue; meanwhile, in contrast, pH has little impact on the maximum binding capacity of SAMSS, suggesting that the FC-Cu-SAMMS is not protonated to the degree that Prussian blue is at low pH. However, in vivo results suggested that the performance of FC-Cu-EDA-SAMMS is approximately equivalent to that of Prussian blue. On the other hand, in vitro studies have also demonstrated positive results on binding of thallium to FC-Cu-EDA-SAMMS.[44,45]

The clinical use of metal chelators such as sodium diethyldithiocarbamate, dimercaptoprol (British Anti-Lewisite), 2,3-dimercapto-1-propanesulfonic acid, and D-penicillamine remains controversial because experimental studies in rats have demonstrated redistribution of thallium from inactive depots to the central nervous system.[46–49] Recently, DL-penicillamine was used in rats in combination with Prussian blue, survival of intoxicated rats was increased significantly compared with the control group which received DL-penicillamine alone; when Prussian blue is given in combination with DL-penicillamine, it had an additive effect in the treatment of acute thallotoxicosis.[50] Moreover, the chelator 2,3-dimercaptosucininc acid (DMSA) has been reported to be beneficial in treating other forms of heavy metal poisoning. However, DMSA failed to demonstrate improved survival in a rat model of acute thallium poisoning, and did not decrease whole brain thallium concentrations. These data suggest that DMSA is unlikely to be of benefit in thallotoxicosis.[51] On the other hand, L-methionine and L-cysteine did not demonstrate efficacy against acute thallium toxicity when administered either alone or in combination with Prussian blue in rats.[52]

Other relevant facts concerning Prussian blue

The accident at the Chernobyl nuclear power plant in 1986 resulted in contamination of large tracts of agricultural land and forests in northern Europe, and particularly in Belarus, the Russian Federation, and Ukraine. Of particular radiological significance was that up to 1997, cesium-137 and strontium-90, which migrate through the soil-plant-animal food chain and accumulate in milk and meat, were consumed by the human population inhabiting these contaminated regions.[14] It was thought possible that the radioactive cesium content of milk and meat could be reduced by simple administration of material like Prussian blue to livestock to bind radioactive cesium in the gastrointestinal tract and thereby decrease its absorption and increase its excretion in feces. Investigations were conducted between 1990 and 1995 to evaluate the use of Prussian blue compounds (in the form of boli, salt licks, or direct addition to the diet) in cattle for reducing the radioactive cesium content of milk and meat, and the subsequent effect of dung from treated animals on the transfer of radioactive cesium from soil to plants. Prussian blue has been demonstrated to be cost-effective and to reduce radioactive cesium levels significantly in the meat and milk of cattle grazing on contaminated land.[14,53]

Discussion

Based on the information and clinical cases presented here, the current recommended treatment for thallium and radioactive cesium poisoning is Prussian blue, but limitations as to its availability make it difficult to obtain Prussian blue in a timely fashion. Some researchers have looked into other drugs and drug combinations as potential alternative treatments.

Call for action and study limitations

The present review has not only updated previous reviews, but has also analyzed Prussian blue as an approved drug following the attacks on the US on September 11, 2001. Because Mexico shares 3200 kilometers of frontier border with the US, it is in the national interest of both countries to share bioterrorism countermeasures as well. Before the attacks, many researchers investigated Prussian blue to treat accidental thallium and cesium-137 poisoning in a relatively small population in each country, but Prussian blue is now to be manufactured in vast amounts for potentially millions of users, given that bioterrorism has become an important public health problem. Pharmaceutical laboratories in Japan, Mexico, and the US, as well as in other countries, should carry out further clinical investigations, because little is known about the side effects, drug–drug interactions, doses, and regimes of Prussian blue in special populations such as children and pregnant women.

Recently, the US government has designed and implemented a policy to develop Prussian blue for the

pediatric population aged 0–2 years. The FDA has an incentive policy of contracts awarded by the Biomedical Advanced Research and Development Authority to develop Prussian blue for pediatric use. Contract supports have advanced development of Prussian blue for infants aged newborn to 2 years.[54] On February 24, 2011, the US government awarded a sole source contract under FAR Part 6.302-1 to the Heyltex Corporation (contract award $3,023,094) for research and development of a satisfactory method of administering Radiogardase to pediatric subjects (age 0–2 years) and acquiring FDA approval for language in the Radiogardase package insert that provides for safe and effective use of the current formulation administered to the pediatric population for reducing or eliminating internalized radioactive cesium due to ingestion, inhalation, or other routes of exposure.[55] Nevertheless, the FDA is open to potential suppliers who believe they may be capable of offering the services requested, and those who would like to be considered as an alternative source are requested to contact the contracting specialist by the published response time.[55] The Prussian blue manufacturing process should also be optimized in order to ensure higher efficacy, safety, and access.

The recent unfortunate tragedy in Japan should serve as an opportunity to test the properties of Prussian blue monotherapy further as well as its combinations, and to improve manufacturing procedures. The development of other potential drugs to treat radioactive metal contamination should also be encouraged.

Conclusion

Prussian blue is effective and safe for use against radioactive intoxication involving cesium-137 and thallium. The FDA has approved Prussian blue as a drug, but there is only one manufacturer at present providing Prussian blue to the US. Thus, additional clinical research and production of Prussian blue is needed. In addition, very few physicians and health professionals are informed concerning the effectiveness and safety of Prussian blue. Pharmacists can help their physician colleagues who may not know about Prussian blue as a drug to treat patients, and the present work might be another example of collaboration among health professionals for the benefit of patients. From a public health perspective, accidental threats that involve internal radioactive contamination in humans present a challenge for all parties. However, more investigation is needed to establish the efficacy and safety of Prussian blue, and large-scale production of Prussian blue needed worldwide.

Disclosure

The authors report no conflicts of interest in this work.

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