Comparison of Absorbents and Drugs for Internal Decoeration of Radiocesium: Advances of Polyvinyl Alcohol Hydrogel Microsphere Preparations Containing Magnetite and Prussian Blue

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Radiocesium nuclides, used as a gamma ray source in various types of industrial equipments and found in nuclear waste, are strictly controlled to avoid their leakage into the environment. When large amounts of radiocesium are accidentally incorporated into the human body, decoeration therapy should be considered. Although standard decoeration methods have been studied since the 1960s and were established in the 1970s with the drug Radiogardase® (a Prussian blue preparation), application of recent advances in pharmacokinetics and ethical standards could improve these methods. Here we designed a modern dosage form of hydrogel containing cesium-absorbents to alleviate intestinal mucosa irritation due to the cesium-binding capacity of the absorbents. The effectiveness of the dosage form on fecal excretion was confirmed by quantitative mouse experiments. The total cesium excretion rate of the crystal form (1.37±0.09) was improved by the hydrogel form (1.52±0.10) at the same dose of Prussian blue, with a longer gastrointestinal tract transit time. Using a mouse model, we compared the effects of several drugs on fecal and urinary excretion of internal cesium, without the use of absorbents. Only phenylephrine hydrochloride significantly enhanced cesium excretion (excretion rate of 1.17±0.08) via the urinary pathway, whereas none of the diuretic drugs tested had this effect. These findings indicate that modifying the dosage form of cesium absorbents is important for the decoeration of internal radiocesium contamination.

Key words radiocesium; prussian blue; zeolite; diuretic; phenylephrine

Internal contamination with radiocesium generated by nuclear fission may occur after nuclear weapon testing and serious nuclear plant accidents.1) In addition, concentrated radiocesium is frequently used industrially as a source of gamma rays. Accidental incorporation of radiocesium may also occur due to mishandling, inadequate security, terrorism or complex disasters.2) Studies of contamination countermeasures have been performed, but few studies have examined methods of internal contamination.

Cesium is an alkaline metal and the biokinetics of cesium have been studied in detail.3) Briefly, ingested cesium rapidly disperses throughout the whole-body in ion form without sedimentation. Cesium in body fluids is incorporated into several cell types by ionic pumps, and then leaked back to the fluid via potassium channels in the plasma membrane. Cesium particularly accumulates in skeletal muscle, because of its large influx/efflux rate, where it is retained for several months in human. Cesium in the body fluid is mainly excreted in urine. Although large amounts of cesium are released to the gastrointestinal (GI) tract, most of it is reabsorbed by the intestine and returned to the body fluid. Thus, the final rate of excretion of cesium from the body through feces, urine and sweat is estimated to be 13, 85 and 2%, respectively, in human.3)

Medical treatment for radiocesium decoeration is recommended when the committed dose is predicted to be 30 to 300 mSv.4) The effectiveness of oral administration of Prussian blue [Fe^{III}Fe^{III}(CN)_{6}] microcrystal preparations less than 1 µm in diameter of Prussian blue [Fe^{III}Fe^{III}(CN)_{6}·KCl·nH_{2}O], K_{2}Ni^{II}Fe^{III}(CN)_{6} and K_{2}Co^{II}Fe^{III}(CN)_{6}. The preparations were made by mixing 0.25 mol/L solutions of Fe^{III}Cl_{3}, CoCl_{2}, NiCl_{2}, or K_{2}[Fe^{III}(CN)_{6}] (Wako Pure Chemical Industries, Ltd., Osaka, Japan). Dialysis was performed to purify the preparations or to substitute the alkali metals. Insoluble Prussian blue

MATERIALS AND METHODS

Cesium-Absorbents and Reagents The ferrocyanides used as cesium absorbents in the present study comprised water-soluble colloidal preparations of Prussian blue [KFe^{III}Fe^{III}(CN)_{6}], microcrystal preparations less than 1 µm in diameter of Prussian blue [Fe^{III}Fe^{III}(CN)_{6}·KCl·nH_{2}O], K_{2}Ni^{II}Fe^{III}(CN)_{6} and K_{2}Co^{II}Fe^{III}(CN)_{6}. The preparations were made by mixing 0.25 mol/L solutions of Fe^{III}Cl_{3}, CoCl_{2}, NiCl_{2}, or K_{2}[Fe^{III}(CN)_{6}] (Wako Pure Chemical Industries, Ltd., Osaka, Japan). Dialysis was performed to purify the preparations or to substitute the alkali metals. Insoluble Prussian blue

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with 14 to 16 water molecules corresponding to Radiogardase® was prepared by freeze-drying or dehydrating the microcrystals at 80°C. The sizes of the microcrystals and colloid were measured using the dynamic and static light-scattering method with a DelsaMax (Beckman-Coulter Inc., U.S.A.), supported by Beckman Coulter K.K., Japan. Synthetic zeolite with a mean particle size of 2 to 4 µm (Wako Pure Chemical Industries, Ltd.), and apple pectin (Wako) were also used.

**Drugs for Mouse Experiments** The following drugs were used in this study: Radiogardase® (HEYL Chemisch-Pharmazeutische Fabrik GmbH und Co., KG, Germany), phenylephrine hydrochloride (Neo-Synesin Kowa, Kowa Pharmaceutical Co., Ltd., Japan), adrenaline (Bosmin® injection, Yakuhin, Ltd., Japan), and hydralazine hydrochloride (Apresoline®, Novartis Pharma K.K., Japan), nisoldipine (Baymycard®, Bayer Yakuhin, Ltd., Japan), and hydralazine hydrochloride (Apresoline®, Novartis Pharma). As a cathartic, d-sorbitol (Wako) and magnesium succinate (Magcorol®, Horii Pharmaceutical Ind., Ltd., Japan) were used. As diuretics, acetazolamide sodium (Diamox®, Sanwa Kagaku Kenkyusho Co., Ltd., Japan), furosemide (Lasix®, Nichi-Iko Pharmaceutical Co., Ltd., Japan), trichlormethiazide (Flutran®, Shionogi & Co., Ltd., Japan), indapamide (Natrix®, Kyoto Pharmaceutical Ind., Ltd., Japan), potassium canrenoate (Soldactone®, Pfizer Japan Inc., Japan), and eplerenone (Selara®, Pfizer Japan Inc.) and isosorbide (Iso-bide®, Kowa Pharmaceutical Co., Ltd., Japan). Their administration doses (per kg-body weight) in mice corresponded to the upper limit dose in humans.

**Preparation of Polyvinyl Alcohol (PVA) Hydrogel** A mixture of 5% PVA (polymerization degree ca. 500, Wako) in 0.25 mol/L HCl containing magnetite silica particles (final conc.=20 mg/mL of isicartar-R-M plain, diameter of 350 nm, Micromod Partikeltechnologie GmbH, Germany) and Prussian blue or metal–ferrocyanide microcrystals of K₂NiFe(CN)₆, K₂CoFe(CN)₆ or zeolite which bound to cesium decreased below 500 Bq/mouse. The examinations were continued until the mice were 28 weeks old. The effects of each drug on the excretion rate of radiocesium were calculated as previously reported.9–11) As breeding mice in metabolic cages can induce stress, we habituated young C3H/He inbred mice with a mild nature in metabolic cages. Thus, C3H/He inbred mice 4 weeks of age obtained from Japan SLC Co. were acclimatized to the metabolic cages for 4 weeks with one mouse per metabolic cage in animal room maintained at 23°C with 55% humidity, and lights (10 to 50 lx) on from 07:00 to 19:00. To avoid generating high frequency sounds that are a source of stress for mice, we used the metabolic cages made of methacrylate and polyethylene for housing and collection of excreta, with stainless-steel mesh as the base-plate and cover, and glass tubes to supply food and water (Natsume Seisakusho Co., Ltd., Japan).

**Experiments to Measure GI Tract Passage of the Absorbents** To measure the levels of resorption in GI-tract of radiocesium from cesium absorbents, 5 mg of Prussian blue, K₉NiFe(CN)₆, K₉CoFe(CN)₆ or zeolite which bound to with 11 pmol of ¹³⁷Cs at 37°C overnight were orally administrated. After 24 h, each feces were collected and radioactivity were measured.

The passing rate of the absorbents in the GI tract and intestinal absorption of radiocesium released from the absorbents in the mice were measured. Absorbents were labeled with ¹³⁷Cs at 37°C overnight, then washed with saline. The absorbents were then orally administrated to 4 mice per group at a.m. 10:00. The dose per mouse was 1.20 kBq (2.72 pmol) of ¹³⁷Cs in ferrocyanides [corresponding to 1.0 μmol of Fe⁶⁺(CN)₆] or 1.25 mg of zeolite. The ¹³⁷Cs levels in the feces and urine collected at regular intervals were measured as described above. The amounts of the absorbents retained in the GI tract were determined by subtracting the sum of radioactivity in the feces and urine from the administered dose.

**Experiments to Measure for Internal Decorporation of Radiocesium in Mice** When the mice were 8 weeks old, we measured radiocesium decorporation rates in individual mice to exclude abnormal individuals. After subcutaneous injection of 5.0 kBq ¹³⁷CsCl into the interscapular space at a.m. 10:00, the radioactivity of all the excreted feces and urine was measured daily. Twelve apparently healthy mice were divided into three groups (two test groups and one control group) and used for the following experiments. In each experiment, 5.0 kBq ¹³⁷Cs was injected at Day 0. Test drugs and vehicle (water) were administered for 3 times at 6-h intervals on Day 2. Urine and feces excreted on Day 2 to Day 3 were collected separately, and the radioactivity was measured for each of them as described above. Mean radioactivity in the Day 3 excreta (sum of urine plus feces) from 4 control mice was set at 1.00 as the standard. Relative rates of radioactivity in the urine and feces from the test mice were determined. The mice were reused for the next series of experiments after the internal radiocesium decreased below 500 Bq/mouse. The examinations were continued until the mice were 28 weeks old. The effects of each drug on the excretion rate of radiocesium were calculated using data obtained from two different batches of mice. The significances of the drug effects on the relative excretion rates was determined based on Dunnett’s test following one-way
Doses per kilogram body-weight for the examined drugs were determined based on the upper limit of the daily dose for humans. Orally administered drugs were administered through a stomach tube at the following daily doses per kilogram body-weight: 150 mg Radiogardase®6, 7.2 or 36 µmol of ferrocyanide in Prussian blue, K₂Ni²⁺Fe^{III}(CN)₆, and K₂Co²⁺Fe^{III}(CN)₆, 150 mg zeolite, 50 mg trichlormethiazide, 40.0 mg indapamide, 10 mg eplerenone, 3.0 or 6.0 g isosorbide, 6.0 mg nilsidipine, 1 mmol NaCl, 7.0 g magnesium succinate, or 6.5 g d-sorbitol. The volume was less than 20 mL/kg body-weight and the same volume of water was used as a negative control. Daily doses per kilogram body-weight of drugs for subcutaneous injection were 500 mg acetazolamide sodium, 100 mg furosemide, 160 mg potassium canrenoate, 3.0 g isosorbide, 1.0 mg or 2.0 mg phenylephrine hydrochloride, 0.1 mg adrenaline, 0.6 mg clonidine hydrochloride, 0.5 mg phenolamine mesilate, and 4.0 mg hydralazine hydrochloride.

RESULTS AND DISCUSSION

The present study aimed to improve the drugs currently used for decorporation of internally contaminating radiocesium. First, Prussian blue and related coordination complex were selected as cesium-absorbers, based on in vitro evaluation of the cesium binding capacities of various candidates (Section 1). The absorbents were then modified to hydrogel preparation form for introduction to GI tract (Section 2), and the advantages of the hydrogel preparation form were compared based on in vivo experiments in mice (Section 3). The effects of commercial drugs on cesium excretion were also compared by the in vivo experiments (Section 4).

1. Examination of Cesium-Absorbents Studies of radioce-desium absorbents performed since the 1960s have established the efficacy of porous minerals, such as zeolite, which is also used to bind radioactive cesium. First, Prussian blue and related coordination crystals of ferrocyanides with transition metals were selected as cesium-absorbers, based on in vitro evaluation of the cesium binding capacities of various candidates (Section 1). The absorbents were then modified to hydrogel preparation form for introduction to GI tract (Section 2), and the advantages of the hydrogel preparation form were compared based on in vivo experiments in mice (Section 3). The effects of commercial drugs on cesium excretion were also compared by the in vivo experiments (Section 4).

Prussian blue is a coordination complex of Fe^{III} and Fe^{II}(CN)₆, with water crystals, alkaline metal, and anions. The binding affinity of alkaline metal is Cs > Rb > K > Na. An equimolar complex of Fe^{III} and Fe^{II}(CN)₆ is soluble (Fig. 1a) and a 4:3 complex of Fe^{III} and Fe^{II}(CN)₆ with excess water forms microcrystals (Fig. 1b). Removal of the water crystals by drying under 100°C leads to the formation of stable water-insoluble crystals of Fe^{III}[Fe^{II}(CN)₆]₄·(14—16)H₂O with irregular shapes and sizes (Fig. 1c). Excess dehydration and heating at more than 550°C generates degradative products of iron oxides by the removal of cyanogen. For safe use as a drug, release of cyanogen in the GI tract should be avoided, even though the Fe^{II}(CN)₆ ion is chemically stable. Ultimately, an aqueous complex with 14 to 16 water molecules was determined to be the safest form of Prussian blue and the capsule formulation is used as the medical deco-poration drug called Radiogardase®. Although the surface area of the 14 to 16 water crystals is extraordinarily smaller than that of microcrystals or the colloidal form, large differences in the binding velocity of radioce-sium were not observed (Fig. 2a), indicating that the coordination structure of the water-insoluble crystals is not rigid and alkaline metal ions readily move though the lattice.

A certain type of coordination complex of ferricyanide and non-iron divalent period-4 transition metals, such as Co^{II}[Fe^{III}(CN)₆]₄⁺, also binds cesium similar to Prussian blue. This type of crystal, however, cannot be used as a drug as it easily releases the transition metal ion, which is toxic to humans, due to the instability of the lattice created by non-stoichiometric coordination. Another type of coordination complex of ferrocyanide and divalent period-4 transition metals having a more stable coordination has been used as a conventional cesium absorbent. Examples of such compounds, K₂Ni²⁺Fe^{III}(CN)₆ and K₂Co²⁺Fe^{III}(CN)₆, are shown in Figs. 1d and e. Their maximal absorption capacities of cesium in physiologic saline in vitro are 0.9 and 1.3 mol Cs per mole of Fe^{III}(CN)₆, respectively, and greater than that of Prussian blue [0.7 mol per mole Fe^{II}(CN)₆] (Figs. 2b, c). The 24-h cesium binding capacity of Radiogardase® (water-insoluble crystal of Prussian blue) is maximal at pH 7.5 and 85 to 90% of maximum at pH 9.0. The microcrystal form of Prussian blue, however, exhibits maximal absorption capacity only at pH 7 (Fig. 2b) as like previous report. The microcrystal forms of K₂Ni²⁺Fe^{III}(CN)₆ and K₂Co²⁺Fe^{III}(CN)₆ maintain their capacity among a wide range of pH levels, between 1.0 to 9.0 in saline (Fig. 2b). After binding with the carrier to prevent dissolution of the constituent in the GI tract, they maintained their binding capacity in physiological saline. Currently, ferrocyanide is applied for the removal of radioce-sium from animals and the environment by binding with insoluble carriers. Unfortunately, the recent trends of emphasizing the adverse effects or allergic effects of the transition metals have hampered their medical application.

Ore, such as zeolite, which is also used to bind radioce-sium, and its application for decorporation in livestock have been examined since the 1950s. Zeolite has some cesium-binding capacity of ca. 0.4 µmol/mg at pH 1.0 and pH 7.0 (Fig. 2c, lanes 10, 11). Orally administered zeolite that held radioce-sium (2.2 pmol/mg) loses the bound cesium during passage through the GI tract, while ferrocyanides hold on to the bound cesium in vivo (Fig. 3a). This indicates that cesium would be released from zeolite in the GI tract with its complicated chemical environment and resorbed by the mice body. On the other hand, zeolite is useful for environmental decon-tamination of radionuclides due to its thermal- and chemical-stability, compared with ferrocyanides, which are degraded at temperatures higher than 550°C, at an alkaline pH >12, or with chelates. Incineration at 800°C of zeolite with excreta containing ferrocyanides with radioce-sium created a form of waste suitable for long-term storage and reduced the volume (Figs. 3i, 3c).

Few organic substances that capture radioce-sium, like pe-cin, are known. We tested the effect of apple pectin on cesium incorporation. Dialysis at 37°C of 2.5% pectin in saline solution placed in 133-fold volume of 0.015 or 0.15 mmol/L cesium in saline solution increased the concentration of cesium in the pectin solution to 0.85 mmol/L (57-fold of the original concentra-tion) after 24 h (the data not shown). Reducing the pectin solution to 0.25% pectin reduced the concentration rate to 30-fold with either 0.015 or 0.15 mmol/L cesium solution. These
findings indicate that the ability of pectin to capture cesium was in equilibrium and could be changed by the environment. Even if some dosage form of pectin that maintained a concentration of 2.5% was orally administered to humans or animals, the effect on the fecal cesium excretion would not be obvious because of large individual variations. This is consistent with a previous report that the effect of pectin is not significant for decorporation in animals. Thus, Prussian blue is a much better base material for the preparation of cesium absorbents for medical use.

2. Hydrogel Formulation of Cesium Absorbents

Currently, only one absorbent for radiocesium decorporation is available on the market, Radiogardase®, which is a capsule preparation of Prussian blue 14–16H₂O (e), K₂[NiFe(CN)₆] (d) and K₂[CoFe(CN)₆] (e) used in this study are shown. Mean diameters are indicated at the bottom. The dosage form of the PVA hydrogels containing magnetite and Prussian blue (f), K₂[NiFe(CN)₆] (g), and K₂[CoFe(CN)₆] (h), before (left) and after (right) dehydration plus rehydration are shown. Bars indicate 10 µm. As an example of the disposal process, radiocesium-bound PVA–Prussian blue was magnetically collected from feces (i-left, magnetic field is the upper), then the waste was covered with zeolite (i-middle), and incinerated (i-right).

Fig. 1. Preparations of Cesium Absorbents

Prussian blue in the colloidal form (a), microcrystals of Prussian blue >100 H₂O (b), crystals of Prussian blue(14–16)H₂O (c), K₂[NiFe(CN)₆] (d) and K₂[CoFe(CN)₆] (e) used in this study are shown. Mean diameters are indicated at the bottom. The dosage form of the PVA hydrogels containing magnetite and Prussian blue (f), K₂[NiFe(CN)₆] (g), and K₂[CoFe(CN)₆] (h), before (left) and after (right) dehydration plus rehydration are shown. Bars indicate 10 µm. As an example of the disposal process, radiocesium-bound PVA–Prussian blue was magnetically collected from feces (i-left, magnetic field is the upper), then the waste was covered with zeolite (i-middle), and incinerated (i-right).

of such crystals through the digestive tract is associated with the risk of physical damage. In fact, it has been reported that a maximal daily dose of 10 g leads to dysphoria in the digestive tract. Additionally, it is difficult to control the transit time of Prussian blue with radiocesium in the digestive tract. A longer retention time leads to an increase in the effect/dose rate, which allows for minimization of the dose. Thus, there is room for improvement of radiocesium absorbents as decorporating molecules.

We describe here how Prussian blue preparations for radiocesium decorporation are improved by the use of hydrogel. Hydrated microcrystals less than 1 µm in size of Prussian blue, K₂NiFe(CN)₆ or K₂CoFe(CN)₆ (Figs. 1b, d, e) were suspended with siliconized magnetite in PVA gel. They were solidified into spherical shapes with diameters of 10 to 50 µm (microspheres, Figs. 1f–h). The ferrocyanide crystals were dehydrated by lyophilization of the hydrogel to prevent decomposition of the crystal. The lyophilized preparations could be stored and rehydrated before use. The absorption capacity of radiocesium per mole of Fe(CN)₆ was not changed in the hydrogel dosage form (Fig. 2c).
Hydrogel preparations of drugs cause mucoadhesiveness with minimal physical and chemical stress to the GI mucosa in mammals. The retention time of the hydrogel form in the murine GI tract tended to be longer than that of the Prussian blue 14–16 hydrous crystals (Fig. 3b). Since elongation of the retention time of Prussian blue binding radiocesium increases exposure time in the GI-tract, Radiogardase minimizes the effective dose in the intestine. Large crystals of...
Radiogardase® with a spicular shape, however, physically irritate the digestive tract mucosa and restrict upper limit of dose, as described above. When using the hydrogel dosage form of cesium-absorbents, the required dose is expected to increase because of the mild effect on mucosa, similar to a microsphere preparation for the GI-tract.

3. Excretion of Radiocesium by Hydrogel Preparations of Cesium Absorents in Mice Some factors that cause physiologic and psychologic variations among individuals reduce reproducibility in animal experiments. For example, handling-induced stress increases blood glucocorticoid level,38) which drastically affect the transition and excretion of body.
fluids. Although housing a mouse in a metabolic cage sometimes leads to agitated behaviour, suggesting psychological stress, calm behavior was observed in most of the C3H/He inbred mice that were acclimatized to metabolic cages beginning at 4 weeks of age. When the body-burden of 12 mice injected with radiocesium was measured, similar decreases with small variations among 12 mice were observed from Day 1 to Day 5 (Fig. 3e upper panel). Comparison of the daily decrease rate (Fig. 3e) indicated that individual differences were lower on Days 2, 3 and 5. A similar excretion rate profile was observed in different batches of 12 mice (data not shown). Thus, we administered drugs on Day 2 and measured the daily excretion on Day 3 to compare the effects of the drugs on the daily excretion rate.

The urinary and fecal excretion rate was 0.65±0.03 (95% confidence intervals) and 0.35±0.05, respectively, in C3H/He inbred mice (Fig. 3d, lane 1). To reveal the drug effects on these different excretion pathways, we measured urinary and fecal excretion separately in mice.

The effects of dosage forms of cesium absorbents on decorporation were examined. Oral administration of the standard dose of Prussian blue (Radiogardase) increased the total excretion rate to 1.37±0.09 (Fig. 3d, lane 2), although the urinary excretion rate was reduced to 0.53±0.10 from 0.65±0.03. A similar excretion rate was observed following administration of a 20% dose of the microcrystal form (Fig. 1b) of Prussian blue with a longer retention time in the GI tract (Figs. 3b, d, lane 4). At the standard dose, further increase of the total excretion rate to 1.58±0.09 was observed (Fig. 3d, lane 3). The dose–effect relationship was maintained when the PVA gel containing K$_2$NiIFeII(CN)$_6$ (nickel ferrocyanide) or K$_2$CoIFeII(CN)$_6$ (cobalt ferrocyanide) had a similar excretion rate as Prussian blue (Fig. 3d, lanes 7 or 8), even though they had the cesium binding capacity in vitro of 1.8-fold or 1.2-fold, respectively (Fig. 2c). In all dosage forms, the fecal excretion rate increased 2 to 3 times and the urinary excretion rate was 0.8 to 1.0 times lower than that of the control (Fig. 3d). The results indicated that dosage forms that control transit time in the GI tract are more important for decorporation of radiocesium than the cesium-absorbance capacity of the base substance. The hydrogel dosage form of the cesium-absorbent reported in this paper is also expected to facilitate waste-disposal procedures. Radiocesium with Prussian blue in a hydrogel can be collected from feces using a magnet, and stably stored for a long time by transferring to a stable carrier, such as zeolite, by co-incineration (Fig. 1i).

4. Confirmation of the Drug Effects on Radiocesium Excretion in the Mouse Model

The effects of drugs on decorporation of radiocesium without absorbents have been studied since the 1960s. For example, acetazolamide sodium, a diuretic drug that inhibits carbonate dehydratase enhances cesium excretion. On the other hand, the diuretic drug thiazide, which affects reabsorption of alkaline metals and hydrogen ions in the kidney tubules, has no significant effect on the cesium excretion rate. We examined the effects on urinary and fecal excretion of internal radiocesium using typical and common diuretic drugs. As shown in Fig. 3e (lanes 1 to 8), none of the diuretic drugs significantly enhanced the total excretion rates of radiocesium. Although the urinary excretion rates tended to be enhanced with furosemide, indapamide, and isosorbide, the increase was not significant (Fig. 3e, lanes 3, 5, 8). In contrast, acetazolamide sodium, furosemide, and trichlormethiazide significantly decreased fecal excretion rates (Fig. 3e, lanes 2–4). In particular, trichlormethiazide significantly reduced the total excretion rate (Fig. 3e, lane 4). These findings suggest that forced urination by drugs acting on the kidney may actually decrease the fecal and total excretion rate of internal radiocesium.

Of the drugs examined, only phenylephrine hydrochloride, an α-adrenergic agonist, significantly increased both the urinary and total excretion rates (Fig. 3e, lane 9). The absence of a significant increase in the total or urinary excretion rate with other adrenergic agonists, such as adrenaline and clonidine hydrochloride (Fig. 3e, lanes 11, 12); an antagonist, such as phentolamine mesylate (Fig. 3e, lane 13); or vasodilators, such as nisoldipine and hydralazine hydrochloride (Fig. 3e, lanes 14, 15), suggests that changes in regional blood flow do not markedly affect cesium excretion. Because phenylephrine is used to induce frequent urination in experimental animals, the urinary excretion of cesium is probably enhanced by a decrease in the bladder volume. A significant increase in the urinary excretion rate was observed following NaCl administration (Fig. 3e, lane 16), which stimulates water intake in animals. The fecal excretion rate was significantly increased by the administration of cathartics, magnesium succinate and D-sorbitol (Fig. 3e, lanes 17, 18). No significant increase in the total excretion rate, however, was observed with theses drugs. Therefore, there is no rationale for using diuretic drugs in addition to cesium absorbents for decorporation.

5. Conclusion Regarding Decorporation of Radiocesium

Oral administration of Prussian blue is the standard treatment method for the decorporation of radiocesium in the body. Modification of the dosage form, such as the use of a hydrogel, improves the safety and efficacy by controlling the transit time in the GI tract, and is a more effective approach compared to changing the base absorbent.

Conflict of Interest The authors declare no conflict of interest.

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