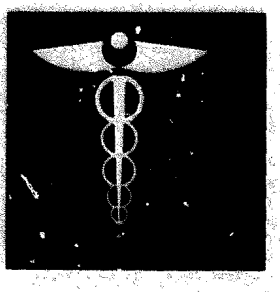
TR-74

ACUTE TOXICITY STUDIES OF CESIUM

AND

RUBIDIUM COMPOUNDS



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16. Abstract (Limit: 200 words)

Recent and projected industrial applications have markedly increased the usage of the hydroxides and iodides of cesium and rubidium. However, the acute toxicologic properties of cesium and rubidium have been investigated only on a very limited scale. It was deemed desirable, therefore, to assess the acute toxicity of these compounds. The single dose oral LD_{50}, primary skin irritation index, degree of eye irritation, and skin allergic sensitization potential procedures were used.

The following hydroxides and halides of cesium and rubidium were studied: cesium hydroxide (CsOH), 50% cesium hydroxide (CsOH) and 50% potassium hydroxide (KOH) mixture, potassium hydroxide (KOH), cesium iodide (CsI), rubidium hydroxide (RbOH), and rubidium iodide (RbI). All compounds except the KOH were identified as "high purity"; and all solutions were prepared on the basis of 100% purity. For purposes of compound administration by the various routes, all test materials were dissolved or suspended in deionized and distilled water. The concentrations used for the eye and primary skin irritation studies were the same as those used in industry. The concentrations used for the skin sensitization studies represented levels for obtaining potential allergic reactions without causing skin irritation.

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b. Identifiers/Open-Ended Terms

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ACUTE TOXICITY STUDIES OF CESIUM AND RUBIDIUM COMPOUNDS

I. INTRODUCTION.

Recent and projected industrial applications have markedly increased the usage of the hydroxides and iodides of cesium and rubidium. However, the acute toxicologic properties of cesium and rubidium have been investigated only on a very limited scale. It was deemed desirable, therefore, to assess the acute toxicity of these compounds. The single dose oral LD_{50}, primary skin irritation index, degree of eye irritation, and skin allergic sensitization potential procedures were used.

The following hydroxides and halides of cesium and rubidium were studied: cesium hydroxide (CsOH), 50% cesium hydroxide (CsOH) and 50% potassium hydroxide (KOH) mixture, potassium hydroxide (KOH), cesium iodide (CsI), rubidium hydroxide (RbOH), and rubidium iodide (RbI). All compounds except the KOH were identified as "high purity"; and all solutions were prepared on the basis of 100% purity. The KOH was labeled "85% pure"; and all KOH solutions were adjusted to 100% purity. For purposes of compound administration by the various routes, all test materials were dissolved or suspended in deionized and distilled water. The concentrations used for the eye and primary skin irritation studies were the same as those used in industry. The concentrations used for the skin sensitization studies represented levels for obtaining potential allergic reactions without causing skin irritation.

II. SUMMARY OF DATA AND CONCLUSION.

The following is a summary of the results from the studies on the acute toxicity of the cesium and rubidium compounds:

A. LD_{50} Studies -- Rats (Oral)

	Compound	Estimated LD_{50} (mg/kg)	95% Confidence Limits for LD_{50}	Estimated Slope (b)
1.	CsOH	1026	929 to 1133	14.8
2.	CsOH + KOH	559	510 to 613	18.7
3.	KOH	365	310 to 429	10.7
4.	CsI	2386	2310 to 2467	17.7
5.	RbOH	586	522 to 655	11.6
6.	RbI	4708	4413 to 5026	18.2

B. Primary Skin Irritation Study -- Rabbits

	Compound	Intact skin	Abraded skin
1.	CsOH (5%)	Non-irritant--safe for human skin contact on intact skin	Mild cellular toxicant Safe for abraded skin provided skin is appropriately protected during contact
2.	CsOH (5%) and KOH (5%)	Irritant--avoid all direct skin contact	Cellular toxicants--avoid all direct skin contact on abraded skin
3.	KOH (5%)	Mild irritant-- safe for human skin contact on intact skin	Cellular toxicants--avoid all direct skin contact on abraded skin
4.	CsI (5%)	Non-irritant--safe for human skin contact on intact skin	Non-toxic--safe for human skin contact on abraded skin
5.	RbOH (5%)	Non-irritant--safe for human skin contact on intact skin	Mild cellular toxicants Safe for abraded skin provided skin is appropriately covered during contact
6.	RbI (5%)	Non-irritant--safe for human skin contact on intact skin	Non-toxic--safe for human skin contact on abraded skin

C. Eye Irritation Studies--Rabbits

		Ocular Reaction	
		Group 1	Group 2
	Compound	5-Minute Exposure	24-Hour Exposure
1.	CsOH (5%)	Extremely irritant and corrosive	Extremely irritant and corrosive
	CsOH (0.5%)	No animals exposed	Negative
	CsOH (0.1%)	No animals exposed	Negative

C. Eye Irritation Studies--Rabbits (Continued)

	Compound	Ocular Reaction Group 1 5-Minute Exposure	Ocular Reaction Group 2 24-Hour Exposure
2.	CsOH (5%) + KOH (5%)	Extremely irritant and corrosive	No animals exposed
	CsOH (1%) + KOH (1%)	Extremely irritant and corrosive	Strongly irritant
	CsOH (0.5%) + KOH (0.5%)	No animals exposed	Marginal
	CsOH (0.1%) + KOH (0.1%)	No animals exposed	Negative
3.	KOH (5%)	Extremely irritant and corrosive	No animals exposed
	KOH (1%)	Irritant	Irritant
	KOH (0.5%)	No animals exposed	Marginal
	KOH (0.1%)	Negative	Negative
4.	CsI (5%)	Negative	Negative
5.	RbOH (5%)	Extremely irritant and corrosive	No animals exposed
	RbOH (1%)	Marginal	Negative
6.	RbI (5%)	Negative	Negative

D. Skin Sensitization Studies--Guinea Pigs

All six compounds are non-sensitizers.

III. CONCLUSION.

The data indicate that the hydroxides of cesium and rubidium are more toxic than the iodides. Cesium hydroxide, potassium hydroxide, and rubidium hydroxide are stong alkalis and contact with the eyes or skin should be avoided.

IV. METHODOLOGY.

A. Range Finding Studies--Rats (Oral)

1. Objective

This procedure provides for a rapid preliminary screening of compounds when no previous toxicologic information is available. It permits a rough estimate of the toxic response and establishment of dosage levels for more precise LD_{50} determinations.

2. Methods

The test materials were administered as a single dose, orally by stomach tube, to caesarean-derived rats weighing between 175 and 250 grams. Eight test groups of three animals per group (24 total) were used for each of the six test materials. The animals were fasted from food for approximately 16 hours prior to dosing. The test materials were dissolved in deionized and distilled water. Observations for morbidity and mortality were recorded at 1 and 4 hours following administration and daily thereafter for the 7-day period. Gross necropsy observations were made on all animals which died or were sacrificed at the end of the 7-day observation period.

3. Results See Table I.

B. LD_{50} Studies

1. Objective

This procedure provides an appraisal of the acute toxicity of a test material and determines the magnitude of the oral dose which kills fifty percent of the animals.

2. Methods

The test materials were administered as a single dose, orally by stomach tube, to cesarean-derived rats weighing between 175 and 250 grams. The animals were fasted from food for approximately 16 hours prior to dosing. The test materials were dissolved or suspended in deionized and distilled water. The number of treatment groups and number of animals per group used for each test material was based on the slope of the dose response curve obtained from the results of the oral range-finding studies. Observations for mortality and gross toxicologic signs were recorded at 1 and 4 hours following administration and daily thereafter for the 14-day period. Gross necropsies were performed on all animals which died or were sacrificed at the

end of the 14-day observation period. The LD_{50} and its 95% confidence limits were calculated by the exact probit analysis method of Finney(1); i.e., by maximum liklihood estimation of parameters of an integrated logarithmic-normal dose-response curve. Whenever the data were nonlinear on log-probit graph paper, the moving average of Thompson(2) was used.

3. Results See Table II.

C. Primary Skin Irritation Study

1. Objective

This procedure is designed to determine the primary skin irritancy of the test compounds following a single application and to compare the irritancy with that of a negative control material, distilled water, producing a rating of 0, and a positive control material, 50% hydrochloric acid, producing a rating of 2 or higher, under identical test conditions.

2. Methods

The six experimental compounds and the negative and positive controls were simultaneously tested on three groups of six albino rabbits, each group receiving two of the six compounds plus the negative and positive controls. For each test and control material, there were two test sites, one abraded and one intact. The backs of the animals were clipped free of hair. The skin on the right side of the backs was abraded at each of the test sites, while the skin on the left side remained intact. The sites were abraded by using a cross-hatch design (#), deep enough to penetrate the epidermis without bleeding. (Abrasions were made using two No. 11 Bard-Parker scalpel blades inserted in a cork stopper approximately 2 mm apart.) The materials, 0.1 ml of each, were applied at each of the test sites. Each site was covered with a gauze patch measuring 20 mm by 20 mm. Each animal was provided with a leather harness for the initial 24-hour exposure.

3. Observations

After 24 hours of exposure, the patches were removed and the skin reactions evaluated. A second evaluation was made after 48 hours of exposure. The reactions were evaluated on the basis of the designated values in the following tables:

Reaction	Intact Skin	Abraded Skin
No irritation	0 (non-irritant)	0 (non-toxic)
Erythema (regardless of degree)	1 (mild irritant)	1 (mild cellular toxicant)
Erythema and edema confined to test area	2 (irritant)	2 (cellular toxicant)

Reaction	Intact Skin	Abraded Skin
Erythema and edema extending beyond test area	3 (strong irritant)	3 (strong cellular toxicant)
Escher	4 (corrosive)	4 (corrosive)

The rating assigned to the test materials is the average response of the six animals rated separately for intact and abraded skin. The rating system is interpreted as follows:

a. Intact skin

A material receiving a rating of less than 1 (0-0.9) is considered a non-irritant and is recommended as safe for intact human skin contact.

A rating from 1-1.9 is considered a mild irritant and may be safe for intact human skin contact; however, it is recommended that appropriate skin protective equipment be utilized during contact.

A rating of 2 or higher indicates that the material is too irritant for human skin contact, and it is recommended that such contact be avoided.

b. Abraded skin

A material receiving a rating of less than 1 (0-0.9) is considered non-toxic to the cellular components of abraded skin and is recommended as safe for human skin contact.

A rating of 1-1.9 is considered a mild cellular toxicant and may be safe for abraded human skin contact provided the precautions stated above are maintained.

A rating of 2 or higher indicates that the material is a cellular toxicant and is too irritant for abraded human skin contact, and it is recommended that such contact be avoided.

c. Mixed reactions

A material may be a non-irritant or a mild irritant on intact skin and a severe irritant on abraded skin. The following table summarizes these possibilities:

Animal Skin Rating		Interpretation
Intact skin	Abraded skin	
0 - 0.9	0 - 0.9	Safe for human skin contact
0 - 0.9	1 - 1.9	Safe for intact human skin; safe for abraded skin when protection is maintained.
0 -0.9	2 - 4	Safe for intact human skin; abraded skin contact should be avoided.
1 - 1.9	1 - 1.9	Safe for both intact and abraded human skin when protection is maintained.
1 - 1.9	2 - 4	Safe for intact human skin when protection is maintained; abraded skin contact to be avoided.
2 - 4	2 - 4	Unsafe and human skin contact should be avoided.

4. Results See Table III.

D. Eye Irritation Studies

1. Objective

This study is designed to evaluate the potential degree of eye irritancy to the cornea, iris and conjunctivae of the eye as produced by the six test materials.

2. Methods

Eight albino rabbits weighing between 2.0 and 3.0 kg were used for each test substance. Prior to application, the eyes were examined for corneal damage by using one drop of fluorescein sodium ophthalmic solution instilled directly onto the cornea. After a few seconds the excess stain was flushed out with distilled water and the eyes examined under ultraviolet light. Only animals without eye defects were used. The test materials were placed in one eye of each animal by gently pulling the lower lid away from the eyeball to form a cup into which the test substances were instilled. The lids were gently held together for one second and the animal released. The other eye remained untreated and served as a control. Doses of 0.1 milliliter by volume of the test materials were instilled into each test eye. The animals were divided into two groups. Group 1 animals (5) were exposed to the test material for five minutes and Group 2 animals (3) were exposed to the test material for 24 hours and then examined before washing. Eyes were washed with a gentle, continuous stream of distilled water until a volume of approximately 250 milliliters was used. The eyes were examined at 1, 24, 48, and 72 hours at 7 days. If any injury persisted, the animals were re-examined at 14 and/or 21 days.

Grades were assigned for presence and/or degree of ulceration or opacity of the cornea and iris for redness (erythema), chemosis and ulceration or necrosis of the conjunctival mucosa according to the method of Draize described in the following table:

Grades for Ocular Reaction

Cornea	
No ulceration or opacity	0
Scattered or diffuse areas of opacity, details of iris visible	1(*)
Easily discernible translucent areas of opacity, details of iris obscured	2(*) (**)
Nacreous area of opacity, no details of iris visible, size of pupil barely discernible	3(*) (**)
Complete corneal opacity, iris not discernible	4(*) (**)
Ulceration, absence of a gross patch of corneal epithelium	4(**)
Iris	
Normal	0
Markedly deepened folds, congestion, swelling, moderate circumcorneal injection (any of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive)	1(*)
No reaction to light, hemorrhage, gross destruction (any or all of these)	2(*)
Conjunctivae	
Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
Vessels normal	0
Some vessels definitely injected	1
Diffuse, crimson red, individual vessels not easily discernible	2(*)
Diffuse beety red	3(*)

Chemosis

No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of lids	2(*)
Swelling with lids about half closed	3(*)
Swelling with lids more than half closed	4(*)
Ulceration or necrosis of palpebral and bulbar conjunctivae or nictitating membrane	4(**)

(*) Grades considered positive for irritation

(**) Grades considered positive for corrosiveness. (In addition, grade 1 opacity evident for any six or more days will be considered as corrosive.)

The method used for assessment of eye irritancy was based on that described in the Federal Register, Vol. 37, No. 83, April 28, 1972, p. 8534.

Classification

Compound	Concentration	Group No.	Rating or Classification
CsOH	5%	1	Extremely irritant and corrosive
1		2	Extremely irritant and corrosive
CsOH +	5%	(1)	Extremely irritant and Corrosive
KOH	1%	1	Extremely irritant and corrosive
2		2	Strongly irritant
	0.5%	(3)	Marginal
	0.1%	(3)	Negative
KOH	5%		Extremely irritant and corrosive
3	1%	1	Irritant
		2	Irritant
	0.5%	(1)	Marginal
	0.1%	(2)	Negative
RbOH	5%	(1)	Extremely irritant and corrosive
4	1%	1	Marginal
		2	Negative
RbI	5%	1	Negative
5		2	Negative
CsI	5%	1	Negative
6		2	Negative

3. Results See Table V.

E. Skin Sensitization Studies

1. Objective

The purpose of this study is to evaluate the potential of the test substances to produce skin sensitization.

2. Methods

Fifteen young adult male albino guinea pigs weighing between 300 and 400 grams were used for each of the six compounds tested. Five animals served as a control group and 10 animals were assigned to the test group. The backs of the animals were clipped free of hair and the clipping repeated at various intervals during the study. The test materials, 0.1 ml, were injected intradermally to separate skin sites of the animals three times weekly for a total of nine treatments. The five control animals were treated in a manner identical to the test group but using the solvent, distilled water, as a control material. Twenty-four hours following each injection the reaction was measured for size. The animals in both the test and control groups were rested for a two-week period following the ninth injection. At the end of the two-week rest period a challenge dose of 0.1 ml was administered to both the test and control animals in the same manner as before. Test sites were examined and reactions recorded at 24, 48, and 72 hours.

3. Results

If the response to the challenge injection is greater in terms of intensity or local inflammatory response than to the sensitizing doses, or the number of animals responding is substantially greater, then the material is considered to be a skin sensitizer. On the basis of these guinea pig studies, the results listed in Table VI indicate that all of the six compounds are non-sensitizers.

Table I. Range Finding Studies

Compounds	Levels (mg/kg)	Deaths	Principal Behavioral Effects	Necropsy Observation
1. CsOH	129	0/3	None	None
	215	0/3	None	None
	359	0/3	None	None
	599	0/3	Weakness & listlessness from 1 hr. post-dose until sacrifice	Erythema of pyloric region of stomach; adhesions of abdominal region organs (stomach, spleen, pancreas, liver, small intestine)
	1000	2/3	Weakness, listlessness, & gasping from 1 hr. post-dose until death or sacrifice	Stomach and intestinal hemorrhage; adhesions of abdominal region organs (stomach, spleen, pancreas, liver, small intestine)
	1670	3/3	Ditto	Ditto
	2788	3/3	Ditto	Ditto
	4656	3/3	Ditto	Ditto
Estimated LD_{50}: 1000 mg/kg				
2. CsOH (50%) & KOH (50%)	148	0/3	None	None
	237	0/3	None	None
	395	1/3	Weakness & listlessness from 1 hr. post-dose until death or sacrifice	Erythema of pyloric region of stomach; adhesions of abdominal region organs (stomach, spleen, pancreas, liver and small intestine)
	659	0/3	Ditto	Ditto
	1100	3/3	Ditto	Ditto
	1837	3/3	Ditto	Ditto
	3068	3/3	Ditto	Ditto
	5124	3/3	Ditto	Ditto
Estimated LD_{50}: 650 mg/kg				
3. KOH	153	0/3	None	None
	256	0/3	None	None
	427	0/3	None	None
	713	2/3	Weakness & listlessness from 1 hr. post-dose until death or sacrifice	Stomach and intestinal hemorrhage; bloody fluid exudate in abdominal cavity
	1200	3/3	Ditto	Ditto
	2004	3/3	Ditto	Ditto
	3347	3/3	Ditto	Ditto
	5589	3/3	Ditto	Ditto
Estimated LD_{50}: 601 mg/kg				

Table I. (Cont'd)

Compound	Levels (mg/kg)	Deaths	Principal Behavioral Effects	Necropsy Observation
4. CsI	180	0/3	None	None
	301	0/3	None	None
	502	0/3	None	None
	838	0/3	None	None
	1400	0/3	None	None
	2338	2/3	Weakness & listlessness from 1 hr. post-dose until death or sacrifice	Stomach distended with fluid; apparent blockage at pyloric sphincter
	3904	3/3	Death immediately following dosing	Ditto
	6520	3/3	Ditto	Ditto
Estimated LD_{50}: 1970 mg/kg				
5. RbOH	390	0/3	Weakness & sedation	None
	507	0/3	Ditto	Stomach & liver adhered together in one animal with large pocket of gas in stomach
	659	1/3	Ditto	Ditto for all animals
	857	3/3	Ditto	Intestinal hemorrhage
	1116	3/3	Ditto	Ditto
	1451	3/3	Ditto	Ditto
	1886	3/3	Ditto	Ditto
	2452	3/3	Ditto	Ditto
Estimated LD_{50}: 694 mg/kg				
6. RbI	1563	0/3	None	None
	1954	0/3	None	None
	2463	0/3	None	None
	3079	0/3	None	None
	3464	0/3	None	None
	3849	2/3	Weakness & listlessness	Spleens appeared active
	4330	1/3	Ditto	Ditto
	4871	3/3	Ditto	Ditto
Estimated LD_{50}: 4034 mg/kg				

Table II. LD_{50} STUDIES

Compounds	Levels (mg/kg)	Deaths	Principal Behavioral Effects	Necropsy Observation
1. CsOH	500	0/10	None	None
	625	0/10	Listlessness at 1- and 4-hour post-dose until sacrifice	Adhesions of abdominal organs (stomach, spleen pancreas, liver and small intestine)
	781	0/10	Ditto	Ditto
	976	5/10	Listlessness at 1- and 4-hour post-dose. Survivors at sacrifice weak & thin	Stomach and intestinal hemorrhage; adhesions of abdominal organs (stomach, spleen, pancreas, liver, small intestine); large amt. of bloody fluid exudate in peritoneal cavity
	1220	8/10	Ditto	Ditto
	1525	10/10	Ditto	Ditto
Estimated LD_{50}: 1026 mg/kg 95% confidence limits: 929 to 1133 mg/kg Slope: 14.8				
2. CsOH 50% + KOH 50%	400	0/10	None	None
	500	1/10	Listlessness at 1- and 4-hour post-dose. All survivors were weak, thin, bloated at sacrifice.	Stomach and intestinal hemorrhage; adhesions, abdominal organs (stomach, spleen, pancreas, liver, small intestine)
	625	8/10	Ditto	Ditto
	781	10/10	Ditto	Ditto
	976	10/10	Ditto	Ditto
	1220	10/10	Ditto	Ditto
Estimated LD_{50}: 559 mg/kg 95% confidence limits: 510 to 613 mg/kg Slope: 18.7				

Compounds	Levels (mg/kg)	Deaths	Principal Behavioral Effects	Necropsy Observation
3. KOH	250	0/9	None	None
	355	5/9	Listlessness, weakness and thin throughout study. Survivors bloated at sacrifice	Stomach and intestinal hemorrhage for dead animals; adhesions of abdominal organs (stomach, spleen, pancreas, liver, and small intestine)
	504	8/9	Ditto	Ditto
	716	9/9	Ditto	Ditto
	1020	9/9	Ditto	Ditto
	1450	9/9	Ditto	Ditto
Estimated LD_{50}: 601 mg/kg 95% confidence limits: 310 to 429 mg/kg Slope: 10.7				
4. CsI	820	0/9	None	None
	1170	0/9	None	None
	1660	0/9	None	None
	2350	3/9	Weakness & listlessness at 1- & 4-hour post-dose. Survivors were weak & thin & some exhibited bloody nasal exudate & eye discharge at sacrifice	Stomach distended with fluid
	3340	9/9	Ditto	Ditto
	4750	9/9	Ditto	Ditto
	1890	0/9	None	None
	2120	0/9	None	None
	2515	3/9	Ditto	Ditto
	2680	9/9	Listlessness & weakness from immediately post-dose until death	Stomach and cecum distended & filled with fluid; apparent blockage at the pyloric sphincter
	3010	9/9	Ditto	Ditto
Estimated LD_{50}: 2386 mg/kg 95% confidence limits: 2310 to 2467 mg/kg Slope 17.7				

Table II. (Cont'd)

Compounds	Levels (mg/kg)	Deaths	Principal Behavioral Effects	Necropsy Observation
5. RbOH	410	0/9	None	None
	506	2/9	All survivors appeared weak & listless throughout study	Stomach & intestinal hemorrhage
	625	3/9	Ditto	Ditto
	771	9/9	Weakness & sedation immediately post-dose & bloody exudate around mouth & nostrils	Massive stomach & intestinal hemorrhage; bloody fluid in the abdominal cavity
	951	9/9	Ditto	Ditto
	1174	9/9	Ditto	Ditto

Estimated LD_{50}: 586 mg/kg
95% confidence limits: 522 to 655 mg/kg
Slope: 11.6

6. RbI	3066	0/9	None	None
	3441	0/9	None	None
	3861	1/9	None	None
	4332	1/9	Weakness & listlessness until death or sacrifice. Labored breathing for the first 3 to 4 days post-dose	None
	4862	7/9	Ditto	None
	5457	7/9	Ditto	None
	6057	9/9	Ditto	Stomachs distended with fluid

Estimated LD_{50}: 4708 mg/kg
95% confidence limits: 4413 to 5026 mg/kg
Slope: 18.2

Table III. Skin Reactions

Rabbit No.	Intact Skin Reactions 24 hr.	48 hr.	Total Rating	Average Rating	Abraded Skin Reactions 24 hr.	48 hr.	Total Rating	Average Rating
Test 1				**5% CsOH**				
1	0	0	0	0	2	2	4	2
2	0	0	0	0	2	1	3	1.5
3	0	0	0	0	2	1	3	1.5
4	0	0	0	0	1	1	2	1
5	0	0	0	0	2	1	3	1.5
6	0	0	0	0	2	2	4	2
Totals	0	0	0	0	11	8	19	9.5
				5% CsOH + 5% KOH				
1	2	2	4	2	2	2	4	2
2	1	2	3	1.5	2	4	6	3
3	1	2	3	1.5	2	4	6	3
4	2	2	4	2	2	3	5	2.5
5	1	3	4	2	2	4	6	3
6	2	4	6	3	2	4	6	3
Totals	9	15	24	12	12	21	33	16.5
				Distilled H_2O				
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
Totals	0	0	0	0	0	0	0	0

Table III. (Cont'd)

50% HCl

Rabbit No.	Intact Skin Reactions 24 hr.	48 hr.	Total Rating	Average Rating	Abraded Skin Reactions 24 hr.	48 hr.	Total Rating	Average Rating
1	1	0	1	0.5	2	1	3	1.5
2	0	0	0	0	2	1	3	1.5
3	0	0	0	0	1	1	2	1
4	0	0	0	0	1	1	2	1
5	0	0	0	0	2	1	3	1.5
6	1	0	1	0.5	2	2	4	2
Totals	2	0	2	1.0	10	7	17	8.5
TEST 2				**5% KOH**				
1	2	1	3	1.5	2	2	4	2.0
2	1	2	3	1.5	3	4	7	3.5
3	1	1	2	1.0	2	3	5	2.5
4	1	1	2	1.0	3	3	6	3.0
5	1	1	2	1.0	3	3	6	3.0
6	1	1	2	1.0	2	3	5	2.5
Totals	7	7	14	7.0	15	18	33	16.5
				5% CsI				
1	0	0	0	0	1	0	1	0.5
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	1	0	1	0.5
5	0	0	0	0	1	0	1	0.5
6	0	0	0	0	1	0	1	0.5
Totals	0	0	0	0	4	0	4	2.0
				Distilled H_2O				
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
Totals	0	0	0	0	0	0	0	0
				50% HCl				
1	0	0	0	0	1	1	2	1.0
2	0	0	0	0	1	1	2	1.0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	1	2	3	1.5
5	0	0	0	0	2	2	4	2.0
6	0	0	0	0	1	2	3	1.5
Totals	0	0	0	0	6	8	14	7.0

TEST 3

Rabbit No.	Intact Skin Reactions 24 hr.	48 hr.	Total Rating	Average Rating	Abraded Skin Reactions 24 hr.	48 hr.	Total Rating	Average Rating
5% RbOH								
1	1	1	2	1	2	2	4	2
2	0	0	0	0	2	2	4	2
3	0	0	0	0	2	2	4	2
4	1	0	1	0.5	1	1	2	1
5	1	1	2	1	2	1	3	1.5
6	0	1	1	0.5	1	2	3	1.5
Totals	3	3	6	3	10	10	20	10.0
5% RbI								
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
Totals	0	0	0	0	0	0	0	0
Distilled H_2O								
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
Totals	0	0	0	0	0	0	0	0
50% HCl								
1	0	0	0	0	1	1	2	1
2	0	0	0	0	2	1	3	1.5
3	0	0	0	0	1	1	2	1
4	0	0	0	0	1	0	1	0.5
5	0	1	1	0.5	1	2	3	1.5
6	0	0	0	0	1	0	1	0.5
Totals	0	1	1	0.5	7	5	12	6.0

Table IV. Primary Skin Indices

Test 1

5% CsOH

Intact Skin Rating = 0 = Non-Irritant; safe for human skin contact on intact skin

Abraded Skin Rating = 1.6 = Mild cellular toxicant; safe for abraded skin provided skin is appropriately protected during contact

5% CsOH and 5% KOH	Intact Skin Rating	= 2 =	Irritant; avoid all direct skin contact
	Abraded Skin Rating	= 2.8 =	Cellular toxicant; avoid all direct skin contact
Distilled H_2O	Intact Skin Rating	= 0 =	Non-irritant; safe for human skin contact
	Abraded Skin Rating	= 0 =	Non-toxic; safe for human skin contact
50% HCl	Intact Skin Rating	= 0.2 =	Non-irritant; safe for human skin contact
	Abraded Skin Rating	= 1.4 =	Mild cellular toxicant; safe for abraded skin provided skin is appropriately protected during contact

Test 2

5% KOH	Intact Skin Rating	= 1.2 =	Mild irritant; safe for human skin contact when skin is appropriately protected during contact
	Abraded Skin Rating	= 2.8 =	Cellular toxicant; irritant for abraded skin contact and such is to be avoided
5% CsI	Intact Skin Rating	= 0 =	Non-irritant; safe for human skin contact on intact skin
	Abraded Skin Rating	= 0.3 =	Non-toxic; safe for human skin contact on abraded skin
Distilled H_2O	Intact Skin Rating	= 0 =	Non-irritant; safe for human skin contact on intact skin
	Abraded Skin Rating	= 0 =	Non-toxic; safe for human skin contact on abraded skin
50% HCl	Intact Skin Rating	= 0 =	Non-irritant; safe for human skin contact on intact skin
	Abraded Skin Rating	= 1.2 =	Mild cellular toxicant; safe for abraded skin contact when skin is appropriately protected during contact

Test 3

5% RbOH	Intact Skin Rating	= 0.5 =	Non-irritant; safe for human skin contact on intact skin
	Abraded Skin Rating	= 1.7 =	Mild cellular toxicant; safe for abraded human skin provided skin is appropriately protected during contact

5% RbI	Intact Skin Rating	= 0 = Non-irritant; safe for human skin contact on intact skin
	Abraded Skin Rating	= 0 = Non-toxic; safe for human skin contact on broken skin
Distilled H_2O	Intact Skin Rating	= 0 = Non-irritant, safe for human skin contact on intact skin
	Abraded Skin Rating	= 0 = Non-toxic; safe for human skin contact
50% HCl	Intact Skin Rating	= 0.1 =Non-irritant; safe for human skin contact on intact skin
	Abraded Skin Rating	= 1.0 =Mild cellular toxicant; safe for abraded human skin provided skin is appropriately protected during contact

Table V. Eye Irritation Studies

CsOH

INTERVAL AND REACTION

Group No.	Animal No.	1 Hour I	1 Hour C	24 Hour I	24 Hour C	48 Hour I	48 Hour C	72 Hour I	72 Hour C	7 Day I	7 Day C	14 Day I	14 Day C	21 Day I	21 Day C
1	1	+	0	+	0	+	0	+	0	0	0	0	0	0	0
	2	+	0	+	0	+	0	+	0	+	0	+	0	+	0
5 minute	3	+	0	+	0	+	0	+	0	+	0	+	0	+	0
exposure	4	0	0	+	0	+	0	0	0	0	0	0	0	0	0
to	5	+	0	Died											
5% CsOH															
2	6	+	0	+	0	+	0	+	0	+	0	+	0	+	0
24 Hour	7	+	0	+	0	+	0	+	0	+	0	+	0	+	0
exposure	8	+	0	+	0	+	0	+	0	+	0	+	0	0	0
to															
5% CsOH															

Classification 5% CsOH Group 1 Extremely irritant and corrosive
Group 2 Extremely irritant and corrosive

CsOH + KOH

1	1	+	0	+	0	0	0	0	0	0	0	0	0	0	0
5 minute	2	+	0	+	0	0	0	0	0	0	0	0	0	0	0
exposure	3	+	+	+	+	+	+	+	+	+	+	+	+	+	+
to	4	+	0	+	0	+	0	+	0	0	0	0	0	0	0
1% CsOH	5	+	0	+	0	+	0	0	0	0	0	0	0	0	0
and															
1% KOH															
2															
24 Hour															
exposure	6	+	0	+	0	0	0	0	0	0	0	0	0	0	0
to	7	+	0	+	0	+	0	+	0	0	0	0	0	0	0
1% CsOH	8	+	0	+	0	+	0	+	0	0	0	0	0	0	0
and															
1% KOH															
3															
5 minute															
exposure	1	0	0	0	0	0	0	0	0	0	0				
to	2	0	0	0	0	0	0	0	0	0	0				
0.1% CsOH	3	0	0	0	0	0	0	0	0	0	0				
and															
0.1% KOH															

Table V. (Cont'd)

Group No.	Animal No.	1 Hour I	1 Hour C	24 Hour I	24 Hour C	48 Hour I	48 Hour C	72 Hour I	72 Hour C	7 Day I	7 Day C	14 Day I	14 Day C	21 Day I	21 Day C
4															
5 minute exposure	1	0	0	0	0	0	0	0	0	0	0				
to	2	0	0	0	0	0	0	0	0	0	0				
0.5% CsOH	3	0	0	0	0	0	0	0	0	0	0				
&															
0.5% KOH															

Classification 1% CsOH + 1% KOH Group 1 Extremely irritant and corrosive
Group 2 Strongly irritant
0.5% CsOH+0.5% KOH - Marginal
0.1% CsOH+0.1% KOH - Negative

Note: Upon instillation of 0.1 ml of 5% CsOH + 5% KOH into the eye of the first rabbit, it was immediately apparent that the substance was an extremely severe and corrosive one

KOH

1	1	+	0	+	0	+	0	+	0	+	0	+	0	0	0
5 minute	2	+	0	+	0	+	0	+	0	+	0	+	0	0	0
exposure	3	+	0	+	0	0	0	0	0	0	0	0	0	0	0
to	4	+	0	+	0	0	0	0	0	0	0	0	0	0	0
1% KOH	5	+	0	0	0	0	0	0	0	0	0	0	0	0	0
24 Hour	6	+	0	+	0	+	0	0	0	0	0	0	0	0	0
exposure	7	+	0	+	0	0	0	0	0	0	0	0	0	0	0
to 1% KOH	8	+	0	+	0	0	0	0	0	0	0	0	0	0	0
24 hour	1	+	0	0	0	0	0	0	0	0	0				
exposure															
0.5% KOH															
24 hour															
exposure	1	0	0	0	0	0	0	0	0	0	0				
0.1% KOH	2	0	0	0	0	0	0	0	0	0	0				

Classification 5% KOH Extremely irritant and corrosive
1% KOH Group 1 Irritant
Group 2 Irritant
0.5% KOH Marginal
0.1% KOH Negative

Table V. (Cont'd)

Group No.	Animal No.	1 Hour I	1 Hour C	24 Hour I	24 Hour C	48 Hour I	48 Hour C	72 Hour I	72 Hour C	7 Day I	7 Day C	24 Day I	24 Day C	21 Day I	21 Day C
							CsI								
1 5 minute exposure 5% CsI	1	0	0	0	0	0	0	0	0	0	0				
	2	0	0	0	0	0	0	0	0	0	0				
	3	0	0	0	0	0	0	0	0	0	0				
	4	0	0	0	0	0	0	0	0	0	0				
	5	0	0	0	0	0	0	0	0	0	0				
2 24 Hour exposure 5% CsI	6	0	0	0	0	0	0	0	0	0	0				
	7	0	0	0	0	0	0	0	0	0	0				
	8	0	0	0	0	0	0	0	0	0	0				

Classification 5% CsI Group 1 Negative
Group 2 Negative

							RbOH								
5 minute exposure 5% RbOH	1	+	+	+	0	+	0	+	0	+	0	+	0	+	0
1 5 minute exposure 1% RbOH	1	0	0	0	0	0	0	0	0	0	0				
	2	0	0	0	0	0	0	0	0	0	0				
	3	0	0	0	0	0	0	0	0	0	0				
	4	0	0	0	0	0	0	0	0	0	0				
	5	0	0	0	0	0	0	0	0	0	0				
2 24 hour exposure 1% RbOH	6	0	0	0	0	0	0	0	0	0	0				
	7	0	0	0	0	0	0	0	0	0	0				
	8	0	0	0	0	0	0	0	0	0	0				

Classification 5% RbOH Extremely irritant and corrosive
1% RbOH Group 1 Marginal
Group 2 Negative

Table VI. Skin Sensitization Studies

Material	Animal No.	Average of Sensitizing Doses Area (mm)	72-Hour Challenge Dose Area (mm)
CsOH (Control 0.1% Group)	1	1.0 x 1.0	0.0 x 0.0
	2	1.0 x 1.0	0.0 x 0.0
	3	2.0 x 2.0	0.0 x 0.0
	4	1.0 x 1.0	2.0 x 2.0
	5	2.0 x 2.0	0.0 x 0.0

Table VI. (Cont'd)

Material	Animal No.	Average of Sensitizing Doses Area (mm)	72-Hour Challenge Dose Area (mm)
CsOH (Test 0.1% Group)	1	3.0 x 3.0	0.0 x 0.0
	2	5.0 x 5.0	2.0 x 2.0
	3	5.0 x 5.0	3.0 x 3.0
	4	5.0 x 5.0	2.0 x 2.0
	5	4.0 x 4.0	2.0 x 2.0
	6	5.0 x 5.0	3.0 x 3.0
	7	4.0 x 4.0	2.0 x 2.0
	8	6.0 x 6.0	2.0 x 2.0
	9	5.0 x 5.0	3.0 x 3.0
	10	5.0 x 5.0	4.0 x 4.0
CsOH 0.1% and KOH 0.1% (Control Group)	1	2.0 x 2.0	2.0 x 2.0
	2	2.0 x 2.0	0.0 x 0.0
	3	2.0 x 2.0	2.0 x 2.0
	4	1.0 x 1.0	2.0 x 2.0
	5	3.0 x 3.0	2.0 x 2.0
0.1% CsOH and 0.1% KOH (Test Group)	1	5.0 x 5.0	2.0 x 2.0
	2	6.0 x 6.0	2.0 x 2.0
	3	5.0 x 5.0	2.0 x 2.0
	4	5.0 x 5.0	3.0 x 3.0
	5	4.0 x 4.0	2.0 x 2.0
	6	5.0 x 5.0	4.0 x 4.0
	7	5.0 x 5.0	3.0 x 3.0
	8	4.0 x 4.0	2.0 x 2.0
	9	5.0 x 5.0	3.0 x 3.0
	10	5.0 x 5.0	2.0 x 2.0
0.1% KOH (Control Group)	1	3.0 x 3.0	3.0 x 3.0
	2	3.0 x 3.0	3.0 x 3.0
	3	3.0 x 3.0	3.0 x 3.0
	4	3.0 x 3.0	3.0 x 3.0
	5	4.0 x 4.0	3.0 x 3.0
0.1% KOH (Test Group)	1	5.0 x 5.0	2.0 x 2.0
	2	5.0 x 5.0	4.0 x 4.0
	3	6.0 x 6.0	3.0 x 3.0
	4	5.0 x 5.0	3.0 x 3.0
	5	5.0 x 5.0	3.0 x 3.0
	6	5.0 x 5.0	3.0 x 3.0
	7	5.0 x 5.0	5.0 x 5.0
	8	5.0 x 5.0	3.0 x 3.0
	9	5.0 x 5.0	3.0 x 3.0
	10	5.0 x 5.0	3.0 x 3.0

Table VI. (Cont'd)

Material	Animal No.	Average of Sensitizing Doses Area (mm)	72-Hour Challenge Dose Area (mm)
0.1% CsI (Control Group)	1	3.0 x 3.0	4.0 x 4.0
	2	3.0 x 3.0	3.0 x 3.0
	3	4.0 x 4.0	2.0 x 2.0
	4	3.0 x 3.0	0.0 x 0.0
	5	5.0 x 5.0	4.0 x 4.0
0.1% CsI (Test group)	1	4.0 x 4.0	3.0 x 3.0
	2	3.0 x 3.0	0.0 x 0.0
	3	5.0 x 5.0	3.0 x 3.0
	4	5.0 x 5.0	0.0 x 0.0
	5	5.0 x 5.0	2.0 x 2.0
	6	5.0 x 5.0	2.0 x 2.0
	7	4.0 x 4.0	(Died)
	8	6.0 x 6.0	3.0 x 3.0
	9	6.0 x 6.0	3.0 x 3.0
	10	6.0 x 6.0	3.0 x 3.0
0.1% RbOH (Control group)	1	3.0 x 3.0	3.0 x 3.0
	2	5.0 x 5.0	3.0 x 3.0
	3	3.0 x 3.0	3.0 x 3.0
	4	5.0 x 5.0	3.0 x 3.0
	5	3.0 x 3.0	(Died)
0.1% RbOH (Test group)	1	3.0 x 3.0	3.0 x 3.0
	2	5.0 x 5.0	3.0 x 3.0
	3	4.0 x 4.0	3.0 x 3.0
	4	4.0 x 4.0	3.0 x 3.0
	5	5.0 x 5.0	5.0 x 5.0
	6	6.0 x 6.0	5.0 x 5.0
	7	5.0 x 5.0	5.0 x 5.0
	8	4.0 x 4.0	3.0 x 3.0
	9	6.0 x 6.0	3.0 x 3.0
	10	4.0 x 4.0	3.0 x 3.0
0.1% RbI (Control group)	1	4.0 x 4.0	3.0 x 3.0
	2	4.0 x 4.0	3.0 x 3.0
	3	5.0 x 5.0	3.0 x 3.0
	4	3.0 x 3.0	3.0 x 3.0
	5	6.0 x 6.0	3.0 x 3.0
0.1% RbI (Test group)	1	4.0 x 4.0	3.0 x 3.0
	2	3.0 x 3.0	3.0 x 3.0
	3	5.0 x 5.0	3.0 x 3.0
	4	(Died)	--
	5	4.0 x 4.0	0.0 x 0.0
	6	(Died)	--
	7	3.0 x 3.0	0.0 x 0.0
	8	3.0 x 3.0	3.0 x 3.0
	9	3.0 x 3.0	3.0 x 3.0
	10	4.0 x 4.0	3.0 x 3.0

Cs and Rb Studies

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