Compatibility of cisatracurium besylate with selected drugs during simulated Y-site administration

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Abstract: The compatibility of cisatracurium besylate with 91 other drugs during simulated Y-site injection was studied.

Five milliliters of cisatracurium 0.1, 2, and 5 mg/mL (as besylate) in 5% dextrose injection was combined with 5 mL of each of 91 drugs in 5% dextrose injection or 0.9% sodium chloride injection. All combinations were prepared in duplicate and stored at ~23 °C. Samples were visually examined under normal laboratory fluorescent light and, if there was no obvious visual incompatibility, under high-intensity monodirectional light. Turbidity was measured as well. Particle sizing and counting was performed for selected combinations. All evaluations were performed at intervals up to four hours.

Cisatracurium besylate at all three concentrations was compatible with most of the drugs tested. However, one drug (cefoperazone) was incompatible with cisatracurium besylate at all three concentrations, 14 (including many cephalosporins) were incompatible with cisatracurium besylate 2 and 5 mg/mL, and 12 were incompatible with cisatracurium 5 mg/mL.

During simulated Y-site administration, cisatracurium 0.1, 2, and 5 mg/mL (as besylate) in 5% dextrose injection was compatible with 64 of 91 drugs for four hours at ~23 °C. Twenty-seven drugs were incompatible with cisatracurium besylate at one or more concentrations.

Index terms: Additives; Anti-infective agents; Cefoperazone sodium; Cephalosporins; Cisatracurium besylate; Concentration; Dextrose; Incompatibilities; Injections; Skeletal muscle relaxants; Sodium chloride; Stability; Storage

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Cisatracurium besylate (Nimbex, Glaxo Wellcome) is a new neuromuscular blocking agent with intermediate onset and duration of action. This agent is indicated for use as an adjunct to general anesthesia and as a skeletal muscle relaxant during surgery.[1]

In addition to cisatracurium besylate, patients may be receiving many other drugs via a Y injection site, including antiemetics, anti-infectives, corticosteroids, and analgesics, as well as other preoperative and operative agents. There is potential for physical incompatibilities to develop during the Y-site administration of

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cisatracurium besylate with these other agents.

The purpose of this study was to evaluate the physical compatibility of cisatracurium besylate with 91 other drugs during simulated Y-site injection.

Methods

Cisatracurium besylate injection[a] was supplied in 20-mL single-use vials, each containing 10 mg/mL of cisatracurium. Cisatracurium in concentrations of 0.1, 2, and 5 mg/mL in 5% dextrose injection[b] was used for this study.

The 91 additives are listed in Table 1. The additives were prepared in 5% dextrose injection[b] unless this posed a known stability problem,[2] in which case 0.9% sodium chloride injection[c] was used as the diluent; the exceptions are noted in Table 1.

Allen et al.[3] reported that the mixing of a fluid in an i.v. administration set with a second fluid from a Y injection site occurs in a 1:1 ratio. Therefore, 5 mL of each cisatracurium dilution was combined with 5 mL of each of the other drug preparations individually in colorless 15-mL borosilicate glass screw-cap culture tubes[d] with polypropylene caps[d] as described elsewhere.[4] Each of the drug preparations (except amphotericin B and lorazepam) was passed through a 0.22-µm filter[e] as it was introduced into the tube. Each

Table 1.
Drugs Tested for Compatibility with Cisatracurium 0.1, 2, and 5 mg/mL (as Besylate) in 5% Dextrose Injection

Drug	Manufacturer	Lot	Concentration (mg/mL)[a]
Supportive Care Drugs			
Alfentanil hydrochloride	Janssen	55D215	0.125
Aminophylline	Abbott	01-211-DK	2.5
Amrinone lactate	Sanofi Winthrop	B825NF	2.5[b]
Bretylium tosylate	Astra	602048	4.0
Bumetanide	Ben Venue	JE816	0.04
Buprenorphine hydrochloride	Reckitt-Colman	3517	0.04
Butorphanol tartrate	Apothecon	G6J130A	0.04
Calcium gluconate	Abbott	02-532-DK	40
Chlorpromazine hydrochloride	Schein	95D880	2
Cimetidine hydrochloride	SmithKline Beecham	F414 ST22	12
Dexamethasone sodium succinate	Fujisawa	160230	2
Diazepam	Elkins-Sinn	026005	0.25, 5[c]
Digoxin	Elkins-Sinn	036094	0.25
Diphenhydramine hydrochloride	Schein	96F860	2
Dobutamine hydrochloride	Eli Lilly	9MM07P	4
Dopamine hydrochloride	Abbott	01-110-DK	3.2
Droperidol	Abbott	89-183-DK	2.5[c]
Enalaprilat	Merck	0290D	0.1
Epinephrine hydrochloride	American Regent	4147	0.05
Esmolol hydrochloride	Ohmeda	6DV203-1	10
Famotidine	Merck	0682D	2
Fentanyl citrate	Abbott	11-109-DK	0.0125
Furosemide	Abbott	16-564-DK	3
Haloperidol lactate	McNeil	UA 1110	0.2
Heparin sodium	Abbott	03-245-DK	100[c,d]
Hydrocortisone sodium succinate	Abbott	02 748Z7	1
Hydromorphone hydrochloride	Elkins-Sinn	085152	0.5
Hydroxyzine hydrochloride	Elkins-Sinn	115030	2
Isoproterenol hydrochloride	Abbott	01-013-DK	0.02
Ketorolac tromethamine	Hoffmann-La Roche	1139	15
Lidocaine hydrochloride	Astra	601065	8
Lorazepam	Wyeth	4950216	0.5
Magnesium sulfate	Abbott	01-100-DK	100
Mannitol	Baxter	C307249	15%[c]
Meperidine hydrochloride	Astra	503802	4
Methylprednisolone sodium succinate	Abbott	03 841Z7	5
Metoclopramide hydrochloride	Abbott	02-628-DK	5
Midazolam hydrochloride	Hoffmann-La Roche	7673	1
Morphine sulfate	Astra	306140	1
Nalbuphine hydrochloride	Astra	511004	10[c]
Nitroglycerin	Dupont	3CV105	0.4
Norepinephrine bitartrate	Sanofi Winthrop	M180NL	0.12
Ondansetron hydrochloride	Cerenex	6ZP0244	1
Phenylephrine hydrochloride	Gensia	P6D023	1
Potassium chloride	Abbott	02-653-DK	0.1[e]
Procainamide hydrochloride	Elkins-Sinn	036016	10
Prochlorperazine edisylate	SoloPak	960638	0.5

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Table 1 (*continued*)

Drug	Manufacturer	Lot	Concentration (mg/mL)[a]
Promethazine hydrochloride	Elkins-Sinn	046035	2
Ranitidine hydrochloride	Glaxo	5ZPS114	2
Sodium bicarbonate	Abbott	04-472-DK	1[c,e]
Sodium nitroprusside	Abbott	96-932-Z7	2
Sufentanil citrate	Elkins-Sinn	066056	0.0125
Theophylline	Abbott	09217-JT	3.2[c]
Thiopental sodium	Abbott	15-173-R1	25
Anti-infectives			
Acyclovir sodium	Burroughs Wellcome	6P1491	7
Amikacin sulfate	Abbott	03-092-DK	5
Amphotericin B	Pharmacia	ALA034	0.6
Ampicillin sodium	SmithKline Beecham	95 510 DA	20[b]
Ampicillin sodium–sulbactam sodium	Roerig	T006A	20/10[b]
Aztreonam	Squibb	6D96437	40
Cefazolin sodium	SmithKline Beecham	01 001 DA	20
Cefoperazone sodium	Pfizer	W055A	40
Cefotaxime sodium	Hoechst-Roussel	1-0190056	20
Cefotetan disodium	Stuart	5210M	20
Cefoxitin sodium	Merck	6081D	20
Ceftazidime (sodium carbonate)	SmithKline Beecham	95 012 DA	40
Ceftazidime (arginine)	Glaxo	6ZP0210	40
Ceftizoxime sodium	Fujisawa	515C17	20
Ceftriaxone sodium	Hoffmann-La Roche	3748	20
Cefuroxime sodium	Lilly	8NL37M	30
Ciprofloxacin	Bayer	6D1E	1
Clindamycin phosphate	Astra	505100	10
Doxycycline hyclate	Fujisawa	160309	1
Fluconazole	Roerig	PS045633	2[c]
Ganciclovir sodium	Syntex	06046A	20
Gentamicin sulfate	Elkins-Sinn	014033	5
Imipenem–cilastatin sodium	Merck	6181D	10[b]
Metronidazole	Abbott	19-944-JT	5[c]
Mezlocillin disodium	Miles	51JA	40
Miconazole	Janssen	64B734	3.5
Minocycline hydrochloride	Lederle	405-815	0.2
Netilmicin sulfate	Schering	4UWH1	5
Ofloxacin	McNeil	15276FJ	4
Piperacillin sodium	Lederle	393-704	40
Piperacillin sodium–tazobactam sodium	Cyanamid	P91-0117	40/5
Ticarcillin disodium	SmithKline Beecham	95-519-DA	30
Ticarcillin disodium–clavulanate potassium	SmithKline Beecham	DR5408	30
Tobramycin sulfate	Abbott	01-150-DK	5
Trimethoprim–sulfamethoxazole	Elkins-Sinn	085087	0.8/4
Vancomycin hydrochloride	Abbott	01 70027	10
Zidovudine	Burroughs Wellcome	3T2249	4

[a]Tested in 5% dextrose injection unless noted otherwise.
[b]Tested in 0.9% sodium chloride injection.
[c]This concentration was tested as the undiluted solution.
[d]Units per milliliter.
[e]Milliequivalents per milliliter.

combination was prepared in duplicate, with the order of addition being reversed between the two samples.

All samples were examined with the unaided eye in normal laboratory fluorescent light. Combinations with no obvious visual incompatibility were examined further with a Tyndall beam (high-intensity monodirectional light source)[f] as described elsewhere.[4] Samples were inspected during the first 15 minutes after preparation and at one and four hours. The samples were stored at room temperature (~23 °C) under constant fluorescent light.

Cisatracurium (as besylate) 0.1, 2, and 5 mg/mL in 5% dextrose injection, and the additives, served as control solutions. Incompatibility was defined as any visible particulate matter, haze or turbidity exceeding that in the control solutions, color change, or gas evolution.

The samples were also assessed immediately after preparation and at one and four hours with a formazin-standardized turbidimeter[g] calibrated as previously described.[5,6] An incompatibility was defined as a turbidity increase of 0.5 nephelometric turbidity unit (NTU) or more that did not occur upon simple dilution of either drug alone.[4-6] For drugs that are normally hazy, a substantial decrease in the expected haze may also constitute an incompatibility.[5,6]

Table 2.
Turbidity of Cisatracurium 0.1, 2, and 5 mg/mL (as Besylate) in 5% Dextrose Injection and with Other Drugs That Exhibited Incompatibilities

Drug and Sample[a]	Mean ± S.D. Nephelometric Turbidity Unit(s) (n = 3) 0 hr	1 hr	4 hr	Observed Result[b]
Cisatracurium 0.1 mg/mL	0.093 ± 0.004	0.092 ± 0.003	0.091 ± 0.001	Clear and colorless
Cisatracurium 2 mg/mL	0.109 ± 0.001	0.107 ± 0.001	0.108 ± 0.001	Clear and colorless
Cisatracurium 5 mg/mL	0.083 ± 0.001	0.083 ± 0.002	0.080 ± 0.001	Clear and colorless
Acyclovir sodium	0.386 ± 0.001	0.583 ± 0.004	0.383 ± 0.001	
With cisatracurium 5 mg/mL				
A	18.8 ± 0.2	19.2 ± 0.2	6.45 ± 0.03	White cloudiness formed
B	23.0 ± 1.1	18.3 ± 0.0	7.08 ± 0.01	immediately
Aminophylline	0.149 ± 0.002	0.155 ± 0.000	0.160 ± 0.001	
With cisatracurium 5 mg/mL				
A	0.244 ± 0.002	0.249 ± 0.001	0.444 ± 0.010	Gray haze[c] formed in 1 hr
B	0.278 ± 0.002	0.718 ± 0.011	1.12 ± 0.03	
Amphotericin B	6.00 ± 0.01	7.61 ± 0.01	13.4 ± 0.00	
With cisatracurium 2 mg/mL				
A	29.7 ± 0.4	29.8 ± 0.3	30.2 → 35.1[c]	Cloudiness formed immediately;
B	27.9 ± 0.1	28.7 ± 0.3	29.1 ± 0.1	gel-like precipitate formed in 1
With cisatracurium 5 mg/mL				hr
A	41.8 ± 0.2	42.3 ± 0.3	42.3 ± 0.3	
B	40.9 ± 0.9	42.8 ± 0.7	44.5 ± 1.0	Turbidity formed immediately
Ampicillin sodium	0.184 ± 0.000	0.194 ± 0.002	0.204 ± 0.003	
With cisatracurium 5 mg/mL				
A	1.32 ± 0.02	3.13 ± 0.06	2.38 ± 0.02	
B	1.04 ± 0.03	2.80 ± 0.00	2.10 ± 0.00	Gray haze[c] formed in 1 hr
Ampicillin sodium–sulbactam sodium	0.198 ± 0.001	0.205 ± 0.001	0.205 ± 0.000	
With cisatracurium 5 mg/mL				
A	3.06 ± 0.01	4.86 ± 0.01	4.03 ± 0.04	
B	1.72 ± 0.01	2.96 ± 0.01	2.67 ± 0.01	Haze[c] developed in 15 min
Cefazolin sodium	0.519 ± 0.001	0.569 ± 0.002	0.820 ± 0.016	
With cisatracurium 2 mg/mL				
A	4.30 ± 0.04	4.67 ± 0.01	5.18 ± 0.03	
B	4.55 ± 0.01	4.97 ± 0.01	5.33 ± 0.05	Gray haze[c] formed immediately
With cisatracurium 5 mg/mL				
A	10.2 ± 0.2	8.02 ± 0.07	9.04 ± 0.06	
B	10.9 ± 0.0	8.70 ± 0.02	9.20 ± 0.08	Gray haze formed immediately
Cefoperazone sodium	0.131 ± 0.002	0.136 ± 0.002	0.138 ± 0.003	
With cisatracurium 0.1 mg/mL				
A	88.7 ± 0.4	135 ± 1	186 ± 3	
B	4.73 ± 0.15	15.1 ± 0.7	201 ± 1	White cloudiness formed
With cisatracurium 2 mg/mL				immediately
A	>2000	>2000	>2000	
B	>2000	>2000	>2000	White cloudiness formed
With cisatracurium 5 mg/mL				immediately
A	>2000	>2000	>2000	
B	>2000	>2000	>2000	White cloudiness formed
Cefotaxime sodium	0.092 ± 0.000	0.092 ± 0.001	0.086 ± 0.001	immediately
With cisatracurium 2 mg/mL				
A	0.176 ± 0.002	0.549 ± 0.008	1.06 ± 0.01	
B	0.155 ± 0.001	0.510 ± 0.002	1.09 ± 0.01	Light haze[c] formed in 4 hr
With cisatracurium 5 mg/mL				
A	0.405 ± 0.002	1.23 ± 0.01	2.39 ± 0.05	
B	0.481 ± 0.001	1.34 ± 0.01	2.61 ± 0.01	Light haze[c] formed immediately
Cefotetan disodium	0.132 ± 0.003	0.138 ± 0.001	0.138 ± 0.002	
With cisatracurium 5 mg/mL				
A	141 ± 1	193 ± 3	222 ± 3	
B	420 ± 2	379 ± 7	325 ± 1	Dense turbidity formed
Cefoxitin sodium	0.108 ± 0.001	0.108 ± 0.002	0.115 ± 0.002	immediately
With cisatracurium 2 mg/mL				
A	1.05 ± 0.01	1.71 ± 0.01	2.25 ± 0.01	
B	1.27 ± 0.01	1.93 ± 0.01	2.50 ± 0.01	Light haze[c] formed immediately
With cisatracurium 5 mg/mL				
A	3.72 ± 0.01	5.63 ± 0.02	7.55 ± 0.01	
B	3.94 ± 0.02	5.72 ± 0.01	7.61 ± 0.05	Haze[c] formed immediately
Ceftazidime (sodium carbonate)	0.194 ± 0.001	0.196 ± 0.001	0.207 ± 0.001	
With cisatracurium 5 mg/mL				
A	1.32 ± 0.00	1.43 ± 0.01	1.35 ± 0.03	
B	1.23 ± 0.03	1.32 ± 0.01	1.26 ± 0.00	Light haze[c] formed immediately

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Table 2 (*continued*)

Drug and Sample[a]	Mean ± S.D. Nephelometric Turbidity Unit(s) (n = 3) 0 hr	1 hr	4 hr	Observed Result[b]
Ceftazidime (arginine)[d]	0.226 ± 0.001	0.223 ± 0.001	0.229 ± 0.001	
With cisatracurium 5 mg/mL				
A	0.162 ± 0.001	0.171 ± 0.001	0.155 ± 0.001	Clear and colorless
B	0.160 ± 0.001	0.165 ± 0.002	0.159 ± 0.001	
Ceftizoxime sodium	0.095 ± 0.002	0.097 ± 0.001	0.095 ± 0.002	
With cisatracurium 5 mg/mL				
A	0.135 ± 0.007	0.467 ± 0.003	0.741 ± 0.002	Haze[c] formed in 1 hr
B	0.156 ± 0.002	0.594 ± 0.003	0.869 ± 0.024	
Cefuroxime sodium	0.317 ± 0.002	0.268 ± 0.001	0.292 ± 0.002	
With cisatracurium 2 mg/mL				
A	28.6 ± 0.1	33.6 ± 0.2	23.4 → 27.8[e]	White cloudiness formed
B	32.2 ± 1.0	38.3 ± 0.1	34.4 ± 0.2	immediately
With cisatracurium 5 mg/mL				
A	28.4 ± 0.5	33.7 ± 0.1	25.3 → 29.2[e]	Turbidity formed immediately
B	33.3 ± 0.1	37.0 ± 0.1	29.6 ± 0.9	
Furosemide	0.079 ± 0.001	0.075 ± 0.001	0.075 ± 0.000	
With cisatracurium 2 mg/mL				
A	>2000	>2000	11.4 ± 0.5	White cloudiness formed
B	>2000	>2000	34.4 ± 0.2	immediately
With cisatracurium 5 mg/mL				
A	>2000	>2000	32.4 ± 0.9	White cloudiness formed
B	>2000	>2000	44.2 ± 0.4	immediately
Ganciclovir sodium	0.340 ± 0.001	0.419 ± 0.000	0.148 ± 0.001	
With cisatracurium 5 mg/mL				
A	21.9 ± 0.1	15.0 ± 0.3	3.22 ± 0.01	White cloudiness formed
B	18.3 ± 0.1	1 3.2 ± 0.1	2.83 ± 0.01	immediately
Heparin sodium	0.066 ± 0.001	0.066 ± 0.001	0.069 ± 0.000	
With cisatracurium 5 mg/mL				
A	575 ± 2	>2000	>2000	White cloudiness formed
B	1002 ± 2	>2000	>2000	immediately
Methylprednisolone sodium succinate	0.676 ± 0.001	0.702 ± 0.000	0.750 ± 0.002	
With cisatracurium 2 mg/mL				
A	1.03 ± 0.01	1.24 ± 0.00	1.60 ± 0.01	Light haze[c] formed immediately
B	1.21 ± 0.01	1.37 ± 0.02	1.65 ± 0.01	
With cisatracurium 5 mg/mL				
A	16.1 ± 0.2	10.2 ± 0.0	8.03 ± 0.02	Haze formed immediately
B	18.6 ± 0.3	11.2 ± 0.0	9.11 ± 0.01	
Mezlocillin disodium	0.132 ± 0.001	0.131 ± 0.001	0.132 ± 0.001	
With cisatracurium 2 mg/mL				
A	1.39 ± 0.02	2.23 ± 0.03	9.10 ± 0.09	Light haze[c] formed immediately;
B	3.03 ± 0.04	4.38 ± 0.10	14.60 ± 0.00	became turbid[b] in 4 hr
With cisatracurium 5 mg/mL				
A	1383 → ≥2000[e]	1120 ± 3	202 ± 5	White cloudiness formed
B	506 ± 3	513 ± 1	380 ± 2	immediately
Miconazole	2.71 ± 0.01	2.71 ± 0.02	2.71 ± 0.01	
With cisatracurium 2 mg/mL				
A	5.56 ± 0.05	5.59 ± 0.00	5.62 ± 0.00	Turbidity[c] increased immediately
B	5.59 ± 0.00	5.60 ± 0.01	5.62 ± 0.00	
With cisatracurium 5 mg/mL				
A	5.44 ± 0.01	5.39 ± 0.01	5.52 ± 0.00	Haze[c] formed immediately
B	5.43 ± 0.00	5.44 ± 0.00	5.63 ± 0.01	
Piperacillin sodium	0.150 ± 0.000	0.147 ± 0.001	0.145 ± 0.001	
With cisatracurium 2 mg/mL				
A	2.46 ± 0.02	3.23 ± 0.02	6.11 ± 0.19	Light haze[c] formed immediately
B	2.25 ± 0.00	3.08 ± 0.02	6.59 ± 0.25	
With cisatracurium 5 mg/mL				
A	8.13 ± 0.00	9.86 ± 0.02	14.7 ± 0.1	Haze formed immediately
B	9.28 ± 0.02	11.0 ± 0.2	16.9 ± 0.2	
Piperacillin sodium–tazobactam sodium	0.157 ± 0.001	0.151 ± 0.001	0.153 ± 0.001	
With cisatracurium 5 mg/mL				
A	0.917 ± 0.002	1.10 ± 0.01	1.55 ± 0.06	Tiny particles with light haze[c]
B	0.856 ± 0.024	1.00 ± 0.01	1.37 ± 0.00	formed within 4 hr
Sodium bicarbonate	0.047 ± 0.006	0.052 ± 0.001	0.054 ± 0.001	
With cisatracurium 2 mg/mL				
A	0.169 ± 0.001	1.13 ± 0.01	1.55 ± 0.01	Light brown color[c] formed and
B	0.172 ± 0.006	1.08 ± 0.01	1.45 ± 0.05	turbidity[c] increased in 1 hr

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Table 2 (*continued*)

Drug and Sample[a]	Mean ± S.D. Nephelometric Turbidity Unit(s) (n = 3) 0 hr	1 hr	4 hr	Observed Result[b]
With cisatracurium 5 mg/mL				
A	0.487 ± 0.009	6.27 ± 0.07	8.40 ± 0.03	Haze[c] formed immediately; light brown color[c] and turbidity[b] increase occurred within 4 hr
B	0.473 ± 0.002	5.83 ± 0.06	7.79 ± 0.03	
Sodium nitroprusside	0.118 ± 0.001	0.127 ± 0.001	0.110 ± 0.001	
With cisatracurium 2 mg/mL				
A	>2000	>2000	72.2 ± 0.1	White cloudiness formed immediately
B	>2000	>2000	67.8 ± 0.1	
With cisatracurium 5 mg/mL				
A	>2000	>2000	87.3 ± 0.2	White cloudiness formed immediately
B	>2000	>2000	84.2 ± 0.6	
Thiopental sodium	0.086 ± 0.001	0.085 ± 0.001	0.074 ± 0.003	
With cisatracurium 2 mg/mL				
A	1.85 ± 0.04	1.92 ± 0.01	3.25 ± 0.05	White turbidity formed immediately but dissipated after 1 min; light haze[c] remained
B	2.14 ± 0.00	2.35 ± 0.00	2.57 ± 0.02	
With cisatracurium 5 mg/mL				
A	>2000	>2000	>2000	White cloudiness formed immediately
B	>2000	>2000	>2000	
Ticarcillin disodium–clavulanate potassium	0.133 ± 0.004	0.134 ± 0.001	0.155 ± 0.001	
With cisatracurium 5 mg/mL				
A	0.441 ± 0.003	0.548 ± 0.003	0.690 ± 0.003	Light haze[c] formed immediately
B	0.443 ± 0.000	0.565 ± 0.017	0.728 ± 0.001	
Trimethoprim–sulfamethoxazole	0.088 ± 0.000	0.097 ± 0.001	0.110 ± 0.001	
With cisatracurium 2 mg/mL				
A	0.681 ± 0.001	0.940 ± 0.002	0.907 ± 0.004	Light haze[c] formed in 1 hr
B	0.779 ± 0.001	1.06 ± 0.01	1.10 ± 0.00	
With cisatracurium 5 mg/mL				
A	3.28 ± 0.02	4.32 ± 0.02	3.96 ± 0.06	Light haze[c] formed immediately
B	3.23 ± 0.03	4.20 ± 0.04	4.04 ± 0.05	

[a]Sample A = test drug solution added to cisatracurium besylate solution; sample B = cisatracurium besylate solution added to test drug solution.
[b]Observed in normal room light with the unaided eye unless specified otherwise. The comments are for samples A and B.
[c]Observed with a Tyndall beam.
[d]Compatible combination.
[e]Measurements fluctuated within the range noted.

Combinations that exhibited small amounts of tiny particles when observed under high-intensity light or that had changes in the observed or measured haze level were further evaluated with a particle sizer–counter.[h] These samples were prepared as described above except that 7.5-mL portions of each solution were added to the test tubes. Three milliliters of each of these samples was tested immediately after preparation and at one and four hours for content of particles in the size range of 1.04–112 µm, the detection limits of the particle sizer–counter.

Results

Cisatracurium besylate 0.1, 2, and 5 mg/mL in 5% dextrose injection, when viewed either in normal room light or with a Tyndall beam, appeared as clear, colorless solutions throughout the study period. After filtration, the solutions were without haze and had measured turbidities of about 0.1 NTU and very low background particle counts.

Except as noted, the test combinations were visually clear and exhibited no color change. Most of these compatible combinations were essentially without haze, having turbidities of less than 0.15 NTU. A total of 27 drugs exhibited incompatibilities with cisatracurium besylate in one or more concentrations (Table 2).

Cefoperazone 40 mg/mL (as the sodium salt) mixed with any of the three concentrations of cisatracurium besylate immediately resulted in a white cloudy mixture and a substantial increase in measured turbidity. Cefoperazone sodium was the only drug incompatible with the lowest concentration of cisatracurium besylate tested. Fourteen of the test drugs, including many cephalosporins, were incompatible with cisatracurium 2 and 5 mg/mL. Twelve of the drugs were incompatible with cisatracurium besylate only at the highest concentration.

Cisatracurium besylate at all three concentrations combined with diazepam 5 mg/mL immediately formed a heavy white turbid precipitate. The final diazepam concentration in these combinations was 2.5 mg/mL, well above diazepam's solubility in aqueous solutions. Diazepam at a lower concentration (0.25 mg/mL, a concentration at which the drug is soluble in water[2]), when mixed with cisatracurium in all three concentrations, resulted in clear, colorless mixtures without turbidity or changes in particulate content within four hours. Thus, the precipitation that occurred

at the higher diazepam concentration was the result of diluting diazepam in an aqueous vehicle, not of an incompatibility with cisatracurium besylate.

Thiopental sodium formed a transient precipitate when combined with cisatracurium 2 mg/mL. White turbidity formed immediately when the drugs were mixed but dissipated within one minute. However, the initial measured turbidity was about 20 times higher than the turbidity level in either drug before mixing. Therefore, this combination was considered to be incompatible because of subvisual haze formation. Thiopental sodium was also incompatible with cisatracurium 5 mg/mL; the combination immediately formed a white turbid precipitate that persisted and did not dissipate.

Ceftazidime (sodium carbonate-containing formulation) was incompatible with cisatracurium besylate only at the highest concentration. An increase in haze occurred immediately. However, ceftazidime (arginine formulation) was compatible with cisatracurium besylate at all three concentrations throughout the four-hour study. No increase in haze or particulates was observed or measured.

Conclusion

During simulated Y-site administration, cisatracurium 0.1, 2, and 5 mg/mL (as besylate) in 5% dextrose injection was compatible with most of the drugs in this study for four hours at ~23 °C. However, 27 drugs were incompatible with cisatracurium besylate at one or more concentrations.

[a]Nimbex, Glaxo Wellcome Inc., Research Triangle Park, NC 27709, lot 602454.
[b]Abbott Laboratories, North Chicago, IL 60064, lot 02-214-JT.
[c]Abbott Laboratories, lot 06-613-JT.
[d]Kimble, Division of Owens-Illinois, Toledo, OH 43666.
[e]Millex-GS, Millipore Products Division, Bedford, MA 01730.
[f]Dolan-Jenner Industries, Woburn, MA 01801.
[g]Ratio X/R, Hach Company, Loveland, CO 80539.
[h]Model 8003, Hiac-Royco, Division of Pacific Scientific Company, Silver Spring, MD 20904.

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