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STABILITY STUDIES OF CEFPIROME SULPHATE I.V WITH METRONIDAZOLE I.V ADMIXTURE

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ABSTRACT

The physical and chemical stability of Cefpirome, a fourth generation and Cefotaxime, a third generation cephalosporin was determined when stored at three different temperatures namely 5°C (refrigeration), 25°C (room temperature) and 45° C (which is seen in temperate countries like India). The drug was quantified by a microbiological method using *Staphylococcus aureus* – NCIM 2079 as test organism in addition to an instrumental method (colorimetric method). The clarity and pH were monitored to assess the physical stability of Cefotaxime sodium I.V and Cefpirome sulphate I.V. The clarity was monitored against a black and white background respectively. The pH was monitored using digital pH meter. The compatibility of cefotaxime and Cefpirome when admixed with ranitidine and metronidazole respectively was evaluated by monitoring cefotaxime and Cefpirome concentration by two methods (microbiological assay method and spectrophotometric method) and also ranitidine and metronidazole by UV spectrophotometric method. Decrease in concentration of cefotaxime and Cefpirome I.V by more than 10%, from initial concentration (0 time) was considered unstable. Change in pH by more than 1 was considered unstable.

Keywords: Cefpirome sulphate, Metronidazole, Stability studies,

1. INTRODUCTION

Drug stability and compatibility are critical elements in the accurate and appropriate delivery of the drug therapy to patients. Both the therapeutic adequacy of the treatment and safety of the therapy can be adversely affected by drug instability or incompatibility. This is especially important in case of parenteral dosage form particularly antibacterial agents given by I.V.route. Newer life saving techniques such as cardio-pulmonary resuscitation and parenteral nutrition, along with life saving parenteral antibiotics has led to increased importance of parenteral therapy. The increased use of parenteral drugs is revealed in surveys that shows that, in the average hospital, 40% of the total dosage forms dispensed to inpatients are in the form of injections. In the rational design and evaluation of dosage forms for drugs, the stability of the active components must be the major criteria in determining their suitability. Several forms of instability can lead to rejection of a drug product. First, there may be chemical degradation of the active drug leading to substantial lowering of the quantity of the therapeutic agent in the dosage form. Although chemical degradation of the active drug may not be extensive, a toxic product may be formed in the decomposition process. There may be instability of a drug product that can lead to a decrease in its bioavailability, rather than the loss of drug or to the formation of toxic degradation products. Substantial changes may occur in the physical appearance of the dosage form also. Therefore, a drug product must satisfy stability criteria chemically, toxicologically, therapeutically, and physically. Basic principle in pharmaceutical kinetics can often be applied to anticipate and quantify the undesirable changes so that they can be circumvented by stabilization techniques. Antibacterial agents, especially third and fourth generation cephalosporins like cefotaxime and cefpriome respectively are so commonly used parenterally especially by I.V route alone and in combination therapy for treating severe infections in hospitalized patients. Stability at room temperature (25° C) and refrigeration (5°C) have been reported in most monographs of cefotaxime sodium IV. But not much data are available on stability at temperature greater than 25°. Hence in our work we wanted to check the physical and chemical stability of cefotaxime I.V when stored at 45°C temperature commonly reached in temperate countries like India. The chances of combination therapy involving cefotaxime and ranitidine I.V is possible in ICU patients with severe lower respiratory infection and for mixed aerobic-anaerobic coverage of severe infections. In such conditions, physicians generally administer two or more drugs through the same I.V line, in order to reduce total infusion volume and avoid discomfort to the patients. Hence our work involved the

compatibility and stability study of cefotaxime I.V when admixed with ranitidine I.V respectively at three different temperatures. Cefpirome is a fourth generation cephalosporin antibiotic. Cephalosporins are derivatives of 7- aminocephalosporic acid and are closely related to penicillins in structure. Cephalosporins have a six membered sulphur containing ring adjoining a β-lactam ring. Cefpirome is effective in a large variety of bacterial infections such as respiratory tract, ear, skin, septicaemia, infections in immunocompromised patients and urinary tract infections. Metronidazole has an extremely broad spectrum of anti-protozoal and antimicrobial activity which is used clinically in several infections. It is having antibacterial activity against all anaerobic cocci and both anaerobic and aerobic gram negative bacilli and anaerobic spore. Metronidazole can be considered as a prodrug in the sense that it requires metabolic activity by sensitive organism. But not much data are available on stability at temperature greater than 25°. Hence in our work we wanted to check the physical and chemical stability of Cefpirome I.V when stored at 45°C temperature commonly reached in temperate countries like India. The chances of combination therapy involving Cefpirome and metronidazole I.V is possible in ICU patients with severe lower respiratory infection and for mixed aerobic-anaerobic coverage of severe infections. In such conditions, physicians generally administer two or more drugs through the same I.V line, in order to reduce total infusion volume and avoid discomfort to the patients. Hence our work involved the compatibility and stability study of Cefpirome I.V when admixed with and metronidazole I.V respectively at three different temperatures.

2. MATERIALS AND METHODS

2.1 Materials: Cefpirome sodium pure sample, Cefpirome sulphate pure sample, Cefpirome sulphate vial (1gm), Cefotaxime sodium vial (1gm), Ranitidine hydrochloride(2ml), Metronidazole infusion (100 ml), Sodium nitrite, Citric Acid, Water for injection.

2.2 Methodology

2.2.1 Calibration graph of Cefpirome sulphate using colorimetric method: To 3ml of the aqueous (deionised water) solution of Cefpirome sulphate contains 50, 100 150,200,250,300 and 350µg/ml. 0.2ml of 1% citric acid and also 0.2ml of 0.5% sodium nitrite solutions were added and kept at room temperature. The color started to develop within few minutes and full after development after 1 hour, after which the absorbance at 500nm was measured by using a spectrophotometer.

2.2.2 Preparation of Coloring Reagent: 1. 1% citric acid: 1g of pure citric acid was dissolved in 100mL of deionized water. 2. 0.5% sodium nitrite: 50mg of pure sodium nitrite was dissolved in 100mL of deionized water.

2.2.3 Preparation of Stock Solution: 100 mg of cefotaxime was dissolved in 100mL of pure deionized water to produce 1mg/mL. From this 0.5, 1, 1.5, 2, 2.5, 3, 3.5mL was pipetted and made up to 10mL with deionized water. The concentrations were 50, 100, 150, 200, 250, 300 and 350 µg/mL respectively. Cefpirome sulphate is sensitive to light. Hence throughout the study necessary precaution was taken.

2.2.4 **Calibration graph of Cefpirome sulphate by microbiological test assay (K.B method) using *staphylococcus aureus* using ncim 2079 as a test organism:** 10mg of Cefpirome sulphate was weighed, transferred to 10 ml volumetric flask and made up to the mark with sterile water for injection to give a concentration of 1mg/ml. From these aliquots of 5, 2, 1, 0.5, 0.25, 0.125 and 0.0625 ml were made upto 10ml volumetric flask with sterile water for injection to get a concentration of 500, 200, 100, 50, 25, 12.5 and 6.25 µg/ml respectively. From this solution 10µl was added to sterile disc to get a concentration of 5, 2, 1, 0.5, 0.25, 0.125, and 0.0625µg/disc respectively. The sterile discs were placed on Mueller Hinton Agar plates which was previously swabbed by using *Staphylococcus aureus* as test organism. The plates were incubated for 24 hours at 37^0C and zone of inhibition was observed.

2.3. Protocol for stability testing of Cefpirome sulphate I.V at different temperatures (Quantification by colorimetric method): This study was carried out to determine the stability of Cefpirome sulphate I.V. at different temperature conditions of storage i.e. room temperature (≈ 25^0C) refrigeration (≈5^0C) and 45^0C. The parameters evaluated were changes in physical stability and chemical stability of Cefpirome sulphate.Three 1g vials of Cefpirome sulphate I.V. (kept in duplicate) were reconstituted with 5ml of water for injection. These vials were marked (as room temperature [25^0C], 45^0C and refrigeration [5^0C]) for identification and were kept at different storage conditions. From the above reconstituted solution, 0.1mL solution was withdrawn and made up to 10mL, and again diluted 10 times to get concentration of 200µg/mL.

To 3mL of this solutions 0.2mL of 1% citric acid, 0.5 % $NaNO_2$ were added and kept for 1 hour. Absorbance was noted at 500nm using UV- Spectrophotometer. pH and clarity tests were also monitored. The above procedure was repeated for 4 days with samples with drawn from vials kept at 5^0C, 25^0C and 45^0C at various time intervals of 0 min, 15min, 30 min, 1hr, 2hr, 4hr, 6hr and 24^{th} hour. The pH and clarity were noted. The results obtained were observed and recorded.

2.4 Protocol for stability study of Cefpirome sulphate injection by microbiological assay (K.B.method) using *staphylococcus aureus*-ncim 2079 as test organism: Three 1g vials of Cefpirome sulphate were reconstituted with 5ml of sterile water for injection. These vials were marked as room temperature [25^0C], 45^0C and refrigeration [5^0C], for identification and were kept at different storage conditions. From the above reconstituted solutions (i.e. stock solution), 0.1ml (100µL) was pipetted and made up to 1ml, so as to get a concentration of 20mg/mL. From the above solution 0.025mL (25µL) was pipetted and diluted with 1ml of sterile water for injection, so as to get a concentration of 0.5mg/mL From these solutions 10µL was pipetted out so as to contain 5µg of Cefpirome sulphate and was added to the sterile disc kept on Muller Hinton agar plates, already swabbed using *Staphylococcus aureus* as test organism. Plates were incubated at 37^0C for 24 hours and observed for zone of inhibition. The above procedure was repeated for various temperatures with sampling at different time intervals for 72 hours (0 min, 30 min, 1hr, 2hr, 4hr, 6hr).

2.5. **Calibration graph of Cefpirome sulphate admixed with metronidazole by spectrophotometeric method:**

2.5.1. Preparation of stock solution for Cefpirome sulphate: 100 mg of Cefpirome sulphate dissolved in 100 ml of water for injection to get a concentration of 1 mg/ml.

Preparation of various drug concentrations for Cefpirome sulphate: From the above stock solution aliquots for 0.3, 0.4, 0.5 and 0.6ml were taken and made up to 10ml with water for injection to give a concentration of 30, 40, 50 and 60 µg/ml respectively.

Preparation of stock solution for metronidazole: 2 ml was taken from 5mg/ml metronidazole injection and made upto 10ml to give a concentration of 1mg/ml from this solution 0.1ml was taken and made upto 10ml to give a concentration of 10µg/ml and used for calibration graph.

Preparation of various drug concentrations from metronidazole: From the above stock solution 0.75, 1,1.25 and 1.5 ml of solution were taken and made upto 10ml with water for injection to give a concentration 0.75, 1,1.25 and 1.5µg/ml. The ratio of 40:1(cefpriome sulphate and metronidazole) was used because the same ratio was used during the admixture of the two drugs 4 different admixtures of same ratio were prepared(0.75:30, 40:1, 50:1.25, and 60: 1.5) and used for the calibration graph. The absorbance of the solution were noted using UV spectrophotometer at λmax of 265nm for Cefpirome sulphate and λmax 317nm for metronidazole and calibration graph was plotted

2.6. Protocol for stability testing of Cefpirome sulphate I.V With metronidazole I.V. at three different temperature conditions (by spectrophotometeric method-simultaneous determination: The study was to determine the stability of Cefpirome sulphate I.V. when admixed with metronidazole I.V. in different temperature condition such as room temperature (25^0C), refrigeration (5^0C) and 45^0C. The parameters evaluated were changes in pH, clarity and concentration of Cefpirome sulphate and metronidazole respectively.

2.6.1. Preparation of stock solution: 2g of Cefpirome sulphate from the vial was mixed with 50mg equivalent of metronidazole I.V. (10ml of 5mg/ml) and volume made upto 10ml. The final concentration (Cefpirome sulphate: metronidazole) ratio of 40:1 is commonly used in clinical practice. The three admixtures prepared in duplicate were maintained at three different temperatures (25^0C, 45^0C, and 5^0C) and samples were withdrawn at intervals of 0min, 10min, 20min, 30min, 45min and 1hr. 0.1 mL of admixture was withdrawn and made up to 1mL with water for injection to give a concentration of 20mg/mL of Cefpirome sulphate and 500µg/mL of metronidazole. From this sample 0.1ml was withdrawn and made upto 1ml with water for injection to give a concentration of 2mg/ml of Cefpirome sulphate and 50µg/ml of metronidazole. From the above solution 0.2ml was withdrawn and made up to 10ml to give a concentration of 40µg/ml and 1µg/ml of Cefpirome sulphate and metronidazole respectively. The absorbance of above solution was noted at 265nm for Cefpirome sulphate and 317nm for metronidazole respectively (UV spectrophotometeric), pH and clarity tests were also performed.

2.7. **Protocol for stability study of Cefpirome sulphate I.V.With metronidazole i.v. Hydrochloride I.V. by microbial assay (K.B. Method) using *staphylococcus aureus* – NCIM 2079 as test organism:** 2g of Cefpirome sulphate from the vials was mixed with 50mg equivalent of metronidazole I.V. (10ml of 5mg/ml) and volume made upto 10ml. The final concentration (Cefpirome sulphate: metronidazole) ratio of 40:1 is commonly used in clinical practice. The three admixtures prepared in duplicate were maintained at three different temperatures (25^0C, 45^0C, and 5^0C) and samples were withdrawn at intervals of 0min, 5min, 10min, 15min, 20min, 25min, 30min, 45min, 1 hour. From the above samples 100 µL was withdrawn made upto 1ml with water for injection to give a concentration of 20mg/ml. From the above solution, 25µL was pipetted and made upto 1ml with water for injection to give a concentration of 0.5mg/ml. From this solution, 10µL was pipetted out, so as to contain 5µg of Cefpirome sulphate required for one sterile disc placed on the surface of Muller Hinton agar media, which was already swabbed with *Staphylococcus aureus* as test organism. Plates were incubated at 37^0C upto 24 hours were observed for the zone of inhibition. Any interference in the results due to metronidazole was checked by using a control without Cefpirome sulphate and checked for absence of zone of inhibition.

3. RESULTS AND DISCUSSIONS

Table no1 Chemical stability of cefpirome sulphate I.V. at different temperature using *Staphylococcus aureus* as test organism (Expected concentration: 200 µg/ml)

Temp	Time Interval	0 min	15 min	30 min	60 min	120 min	240 min	360min	1st day
Refrigeration 5 ˚C	Absorbance and concentration (µg/ml)	0.4590 (196.33)	0.4587 (196.24)	0.4580 (196.03)	0.4565 (195.57)	0.4530 (194.50)	0.4501 (193.61)	0.4474 (193.03)	0.4211 (184.02)
Room temp. 25 ˚C	Absorbance and concentration (µg/ml)	0.4594 (196.45)	0.4560 (195.41)	0.4521 (194.22)	0.4502 (193.64)	0.4486 (193.15)	0.4319 (188.05)	0.4101 (181.38)	0.3512 (179.19)
45 ˚C	Absorbance and concentration (µg/ml)	0.4589 (196.30)	0.4498 (193.52)	0.4260 (186.24)	0.4105 (181.50)	0.3902 (175.30)	0.3739 (172.21)	0.3521 (170.31)	0.2513 (141.10)

Table no 2 Percentage deviation of Cepirome sulphate I V at different temperature conditions by colorimetric method

Sampling time	Refrigeration (5˚C)	Room temperature (25˚C)	At 45 ˚C
15 min	0.04	0.52	1.41
30 min	0.15	1.13	5.12
60 min	0.38	1.43	7.53
120 min	0.91	1.67	10.70
240 min	1.40	4.27	13.23
360 min	1.68	7.67	16.63
24 hours	6.27	8.78	28.12

Table no 3 End of first day

Temperature	Expected concentration (µg/ml)	Average value (µg/ml)
Refrigeration (5˚C)	196.33	184.02
Room temperature (25˚C)	196.40	179.19
45 ˚C	196.30	141.10

The stability study of cefpirome sulphate I.V. stored at refrigeration temperature proved to be more stable even after 24 hrs (% deviation = 6.27) than the other solutions stored at room temperature (% deviation=8.78) and 45˚C (% deviation = 28.12). At 45˚C, the percentage deviation was > 10% (considered

unstable) after nearly 2 hours of storage (value indicates between 1-2 hours). As per this method cefpirome sulphate was found stable at 5°C for 6 hours at 25°C for 4 hours at 45°C for upto slightly less than for 1 hour.

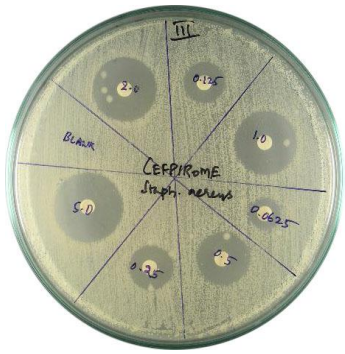

Figure no 1 Zone of inhibition of Cefpirome sulphate I V by microbiological assay at various concentrations using *Staphylococcus aureus* as test organism

Table no 4 Chemical stability (with percentage deviation) of cefpirome sulphate IV at different temperatures by microbiological assay method (kb method) using *Staphylococcus aureus* – ncim 2079 as test organism

	Sampling time in min	Zone of inhibition and concentration (mm)			Percentage deviation		
		5°C	25°C	45°C	5°C	25°C	45°C
Expected Concentration = 5 µg/disc	0	23.00 (5.00)	23.00 (5.00)	23.00 (5.00)	0	0	0
	30	23.00 (5.00)	23.00 (5.00)	23.00 (5.00)	0	0	0
	60	23.00 (5.00)	23.00 (5.00)	20.00 (4.5)	0	0	10
	120	23.00 (5.00)	23.00 (5.00)	20.00 (4.5)	0	0	10
	240	23.00 (5.00)	21.00 (4.5)	20.00 (4.5)	0	0	10
	360	23.00 (5.00)	21.00 (4.5)	16.00 (4.00)	0	10	20

Table no 5 Physical stability of Cefpirome sulphate I.V at three different temperatures

Temperature		0 min	15 min	30 min	1 hour	2 hour	4 hour	6 hour	24 hour
5°C	pH	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.6
	Clarity	clear	clear	clear	clear	clear	clear	clear	Clear
	Color	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow
25°C	pH	6.5	6.5	6.5	6.5	6.5	6.5	6.6	6.7
	Clarity	Clarity	clear	clear	clear	clear	clear	clear	clear
	Color	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Dark yellow	Reddish yellow
45°C	pH	6.5	6.5	6.5	6.5	6.6	6.7	-	-
	Clarity	clear	clear	clear	clear	clear	clear	-	-
	Color	Pale yellow	Pale yellow	Pale yellow	Dark yellow	Reddish yellow	Reddish yellow	Reddish yellow	-

The study was done in duplicate and the average value has been tabulated. The expected concentration of cefpirome sodium =40 (µg/ml) metronidazole hydrochloride = 1.00 (µg/ml) The increase in pH was slightly more at 45˚C than 25˚C and 5°C but was not significant. The solutions remained clear throughout the study. It was found out that the admixture of cefpirome sulphate and METRONIDAZOLE

stored at refrigeration (5˚C), (25˚C) proved to be more stable even after almost 1 hour. Then the other solutions stored at 45˚C. The stability of the cefpirome sulphate IV admixture with metronidazole IV by microbial method of assay. As per this method cefpirome sulphate was found to be stable. 5°C 25°C and 45°C for 60 min.

Table no 6 Calibration graph of cefpirome sulphate admixed with metronidazole by U.V. spectrophotometric method (simultaneous determination)

Sl. No.	Concentration (µg/ml)		Absorbance	
	Cefpirome sulphate (µg/ml)	Metronidazole (µg/ml)	Cefpirome sulphate at 265nm	Metronidazole at 317nm
1	30	0.6963	0.75	0.1400
2	40	0.9314	1.0	0.2029
3	50	1.1503	1.25	0.2510
4	60	1.3753	1.5	0.3118

Table no 7 Physical and chemical stability study of Cefpirome I.V. admixed with metronidazole i.v. at three different temperatures (by simultaneous determination using uv spectrophotometric method)

Time of Sampling (min)	Absorbance and concentration at 5˚C		Absorbance and concentration at 25˚C		Absorbance and concentration at 45˚C	
	Cefpirome (µg/ml)	Metronidazole (µg/ml)	Cefpirome (µg/ml)	Metronidazole (µg/ml)	Cefpirome (µg/ml)	Metronidazole (µG/Ml)
0	0.9309(39.80)	0.2021(0.996)	0.9311(39.83)	0.2024(0.997)	0.9304(39.77)	0.2020(0.995)
5	0.9302(39.75)	0.2018(0.994)	0.9287(39.81)	0.2016(0.990)	0.9243(39.62)	0.2016(0.990)
10	0.9289(39.63)	0.2002(0.990)	0.9250(39.60)	0.2007(0.986)	0.9218(39.55)	0.1987(0.981)
15	0.9276(39.56)	0.1990(0.982)	0.9227(39.42)	0.1982(0.983)	0.9163(39.43)	0.1963(0.963)
20	0.9263(39.49)	0.1976(0.975)	0.9192(39.21)	0.1970(0.980)	0.9101(39.26)	0.1903(0.9500)
30	0.9201(39.42)	0.1958(0.961)	0.9118(38.93)	0.1933(0.9720)	0.9016(38.70)	0.1860(0.942)
45	0.9185(39.31)	0.1919(0.950)	0.9007(38.75)	0.1901(0.9600)	0.8913(38.20)	0.1740(0.940)
60	0.9157(39.15)	0.1886.(0.946)	0.8926(38.46)	0.1867(0.953)	0.8737(37.70)	0.1701(0.921)

Table no 8 Percentage deviation of Cefpirome sodium I V admixed with metronidazole hydrochloride I V at different temperature conditions (by simultaneous determination using UV spectrophotometric method)

Sampling time(min)	Refrigeration (5˚C)		Room temperature (25˚C)		45˚C	
	Cefpirome	Metronidazole	Cefpirome	Metronidazole	Cefpirome	Metronidazole
5	0.12	0.30	0.05	0.60	0.37	0.50
10	0.42	0.70	0.57	1.004	0.55	1.40
15	0.60	0.50	1.02	1.30	0.85	3.21
20	0.77	2.20	1.55	1.70	1.30	4.51
30	0.95	3.61	2.25	2.40	2.69	5.32
45	1.23	4.71	2.71	3.61	3.94	5.32
60	1.63	4.71	3.43	5.11	5.20	7.53

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Table no 9 Chemical stability (with percentage deviation) of cefpirome sulphate i.v. Admixed with metronidazole at different emperatures by microbiological assay method (kb method) using staphlococcus aureus – ncim 2079 as test organism

	Sampling time in min	Zone of inhibition and concentration (mm)			Percentage deviation		
		5°C	25°C	45°C	5°C	25°C	45°C
Expected Concentration = 20 µg/disc	0	23(5)	23(5)	23(5)	0	0	0
	10	23(5)	23(5)	23(5)	0	0	0
	20	23(5)	23(5)	23(5)	0	0	0
	30	23(5)	23(5)	23(5)	0	0	0
	45	23(5)	23(5)	23(5)	0	0	0
	60	23(5)	23(5)	23(5)	0	0	0

Table no 10 Summary of results stability of Cepirome sulphate when admixed with metronidazole IV at three different temperatures

Formulation and its admixture	Stability details	Refrigeration 5 °C	Room temperature 25 °C	45 °C
Cefpirome sulphate	Stability of cefpirome sulphate as per colorimetric method	Stable for 24 hrs	Stable for 24 hrs	Stable for 2 hrs
	Stability of cefpirome sulphate as per microbiological assay.	Stable for 6 hrs	Stable for 4 hrs	Stable for 1 hr
Cefpirome sulphate admixture with metronidazole	Stability of Cefpirome sulphate as per UV spectrophotometric method	Stable for more than 1 hr	Stable for more than 1 hr	Stable for more than 1 hr
	Stability of Cefpirome sulphate as per microbiological assay.	Stable for more than 1 hr	Stable for more than 1 hr	Stable for more than 1 hr
	Stability of metronidazole as per UV spectrophotometric assay.	Stable for more than 1 hr	Stable for more than 1 hr	Stable for more than 1 hr

CONCLUSION

Metronidazole is widely used as a drug of choice in anaerobic infections and most often used in combination with other antimicrobial agents for treatment of mixed aerobic- anaerobic infections. A recent study by Kelly A. Sprandel *et.al* 2005 has suggested metronidazole I.V to be stable when admixed along with levofloxacin I.V at 23°C for upto three hours. It could be of advantage to combine metronidazole with cefpirome, which being a fourth generation cephalosporin, is widely used in several infections. From our study it is clear that both drugs, cefpirome I.V and metronidazole I.V when admixed were stable for one hour even at 45°C. This indicates that the two drugs could be given as an admixture with the advantage of reduced total infusion volume and a possibility of once daily regimen. The combinations selected in our study could be used in clinical practice after a detailed study with larger sample size to get more valuable data.

REFERENCES

Ahmed ST, Parkinson.R. Stability of drugs in pre-filled syringes; flucloxaciclin, ampicillin, cefuroxime, ceftazidime; Hosp Pharm Pract; 1992 April; Vol 2: P.285-289.

Alfeso R. Gennaro; Remington; The Science and practice of Pharmacy; 20th Edition; PP 984 -92.

Alfred Martin: Physical Pharmacy; 4th edition; PP 313-16.

Allen LV Jr, Stiles ML. Prince SJ, Sylvestiri, MF, Stability of Cefpirome sulfate in the presence of commonly used intensive care drugs during simulated Y-site injection. Am J Health system Pharm 1995 Nov; Vol. 52: p.2427-33.

Barnest A.R.and Nasht S. Stability of ceftazidime in a viscous eye drop formulation. Journal of Clinical Pharmacy and Therapeutics., 1999; Vol.24: p.299-302.

Belliveau PP, Nightingale CH; Quintilliani R. Stability of cefotaxime sodium and metronidazole in 0.9% sodium chloride injection or in ready-to-use metronidazole bags, Am. J. Hosp. Pharm, 1995 Jul; Vol 52: P. 1561-1563.

Berge SM, Henderson NL, Frank MJ. Kinetics and mechanism of degradation of cefotaxime sodium in aqueous solution.J Pharm Sci., 1983 Jan; Vol:72 (1):59-63.

Carter S. J., Cooper and Gun's Dispensing for Pharmaceutical Students; 12th Edition; PP 253- 264.

Christopher M. Paap and Milap C.Nahata. Stability of cefotaxime in two peritoneal dialysis solutions. Am J Hosp Pharm., 1990 Jan; Vol.47:p.147-50.

Das Gupta .V. Stability of cefotaxime sodium as determined by high performance liquid chromatography. J.Pharm sci ; 1984; Vol 73: P.565-567.

Das Gupta .V., Stewart .K.R., Gunter .J.M. Stability of cefotaxime sodium and moxalactam sodium in 5% dextrase and 0.9% sodium chloride injections. Am.J. TV. Ther chin Nutr; 183 Jan; Vol.10:P.27-29.

Das Gupta V, Charlie Bethea and Manuel dela Torre. Chemical stabilities of Ceforperazone sodium and ceftazidime in 5% dextrose and 0-9% sodium chloride injections. Journal of Clinical Pharmacy and Therapeutics., 1998; Vol.13:p. 199-205.

Drug facts and comparisons 1998 edition, P 2257-2260.

Eric Viaene, Hugues Chanteux, Helene Servais, marie-Paule Mingeot-Leclercq and Paul M.Tulkens. Comparative stability studies of Antipseudomonal β-Lactama for Potential administration through portable elastomeric pumps(Home therapy for cystic fibrosis patients) and Motor-Operated syringes (Intensive Care Units). Antimicrobial agents and chemotherapy., 2002 Aug; Vol. 46: p. 2327-2332.

Foley .P.T., Bosso.J.A., Bair .J.N., Hownsed.R.J. Stability and compatibility of clindamycin phosphate plus either cefotaxime sodium or netilmicin sulfate in small-volume intraneous admixtures. Am.J.Hosp. Pharm, 1985 April; Vol 42 : P.834-843.

Galanti L.M, Hecq J.D, Vanbeckbergen D. and Jamart J. Long-term stability of cefuroxime and cefazolin sodium in intravenous infusions. Journal of Clinical Pharmacy and Therapeutics., 1996; Vol.21;185-189.

Girishkumar K, Chowdary K.P.R. and Devala Rao G. Spectrophotometric determination of cefatoxime sodium in Pharmacological dosage forms. The Eastern Pharmacist., 1999 Oct:p. 125-126.

Helene Servais and Paul M.Tulkens. Stability and compatibility of Ceftazidime Adminstered by Continuous Infusion to Intensive Care Patients, Antimicrobial agents and Chemotherapy., 2001 Sep; Vol. 45: p.2643-2647.

Houff J.E., Lifshin .L.S., FOXJL, Soldins. Stability of cefuroxime and cefotaxime sodium diluted in 5% for syringe pump administration. ASHP midyear clinical meeting; 1992 Dec; Vol 27 : P. 511E.

Inagaki, Gill.M.A., Okamoto.M.P. Stability of cefmetazolesodium and ranitidine hydrochloride during simulated Y-site administration. J.Parenter Sci Technol 1993 Feb; Vol 47: P.35-39.

Inagaki. K., Gill .M.A. Okamoto. M.P.. Stability of ranitidine hydrochloride with ciftazidime or piperacillin sodium during simulated Y-site administration. Am.J.Hosp. Pharm; 1992 Nov; Vol 49 : P.2769-2772.

James T, Steward, Flynn W, Warren, Susan M. Johnson L.Fox and June Mullaney. Stability of ceftazidime in plastic syringes and glass vials under various storage conditions. Am. J. Hosp. Pharm., 1992 Nov; Vol.49:p: 2765-8.

Jamis T, Stewart, Flynn W. Warren, and Susan M.Johnson. Satbility of cefuroxime sodium and aminophylline or theorphylline. Am. J. Hosp. Pharm., 1994 Mar; Vol. 51: p. 809-811.