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# STABILITY STUDIES OF CEFOTAXIME SODIUM I.V WITH RANITIDINE HYDROCHLORIDE ADMIXTURE

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## ABSTRACT

The physical and chemical stability of 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. The clarity was monitored against a black and white background respectively. The pH was monitored using digital pH meter. The compatibility of Cefotaxime when admixed with ranitidine was evaluated by monitoring Cefotaxime concentration by two methods (microbiological assay method and spectrophotometeric method) and also ranitidine by UV spectrophotometeric method. Decrease in concentration of cefotaxime I.V by more than 10%, from initial concentration (0 time) was considered unstable. Change in pH by more than 1 was considered unstable.

**KEY WORDS:** Ranitidine, Cefpotaxime sodium, Stability, *Staphylococcus aureus.*

## 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. Cefotaxime sodium is a semisynthetic, broad spectrum cephalosporin antibiotic for parenteral administration. Solutions of cefotaxime sodium range from very pale yellow to light amber depending on the concentration and the diluent used. Cefotaxime is given as sodium salt by deep intramuscular injection or intravenously by slow injection over 3.5 minutes or by infusion over 20 to 60 minutes. Doses of Cefotaxime should be reduced in severe renal impairment, after initial loading dose of 1gm while maintaining the usual frequency of dosing suggested. It has sometimes been used with other β- lactam antibiotics to broaden the spectrum of activity. Cefotaxime has also been used in association with metronidazole in the treatment of mixed aerobic – anaerobic infections. Ranitidine injection is clear colorless to yellow, non-pyrogenic liquid. The yellow color of the liquid tends to intensify without adversely affecting potency. Ranitidine injection tends to exhibit a yellow color that may intensify overtime without adversely affecting potency. Ranitidine injection is stable for 48 hrs at room temperature when added or diluted with most commonly used IV solutions given intramuscularly at a dose of 50mg (2ml) every 6- 8 hrs were no dilution necessary. 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.

**2. Materials and methods**

**2.1 Materials:** Cefotaxime sodium pure sample and Cefotaxime sodium vial (1gm) was obtained as a gift sample from Orchid pharma, Chennai, Ranitidine hydrochloride (2ml) was obtained as gift sample from Zydus Alidac, Sodium nitrite, Citric Acid was obtained as a gift sample from S.D Finechem, and Water for injection was obtained from core health care, *Staphylococcus aureus*- NCIM 2079 was obtained from Microbiology dept, Nagarjuna University.

**2.2 Methodology**

**2.2.1 Calibration graph of cefotaxime sodium by microbiological assay (K.B.method) using *staphylococcus aureus* – NCIM 2079 as test organism:** Weigh 100 mg of cefotaxime sodium was weighed, transferred to 10ml volumetric flask and made upto 10 ml with sterile water for injection to give a concentration of 10mg/ml. From these aliquots of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 and 0.7 ml were taken and made up to 10ml in a volumetric flask with sterile water for injection to get a concentration of 1, 2, 3, 4, 5, 6, 7 mg/ml. From each of these solutions, 10µl was added to sterile disc to get concentration of 10, 20, 30, 40, 50, 60, 70 µg/disc respectively. The sterile discs were placed on Muller Hinton a agar plate, which was previously swabbed by using *staphylococcus aureus* as test organism. The plates were incubated for 24hours at 37ºC and observed for zone of inhibition.

**2.3 Protocol for stability testing of Cefotaxime I.V. at different temperatures (quantification by colorimetric method):** This study was carried out to determine the stability of cefotaxime I.V. at different temperature conditions of storage i.e. room temperature ($\approx 25^0$C) refrigeration ($\approx 5^0$C) and $45^0$C. The parameters evaluated were changes in physical stability and chemical stability of cefotaxime. Three 1g vials of Cefotaxime I.V. (kept in duplicate) were reconstituted with 10ml of water for injection. These vials were marked (as room temperature [$25^0$C], $45^0$C and refrigeration [$5^0$C]) for identification and were kept at different storage conditions. From the above reconstituted solution, 0.2mL solution was withdrawn and made up to 10mL, and again diluted 10 times to get concentration of 200µg/mL. To 3mL of this solution 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 performed. The above procedure was repeated for 4 days with samples with drawn from vials kept at $5^0$C, $25^0$C, $45^0$C at various time intervals of 0 min, 30 min,1hr,2hr,3hr,4hr, 6hr, and 24hr,$2^{nd}$ day and $4^{th}$ day. The pH and clarity were noted. The results obtained were observed and recorded.

**2.3 Protocol for stability study of cefotaxime injection by microbiological assay (K.B.method) using *staphylococcus aureus*-NCIM 2079 as test organism:** Three 1g vials of cefotaxime were reconstituted with 10ml of sterile water for injection. These vials were marked as room temperature [$25^0$C], $45^0$C and refrigeration [$5^0$C], for identification and were kept at different storage conditions. From the above reconstituted solutions (i.e. stock solution), 0.25ML (250µL) was pipetted and made up to 10ml in a standard flask, so as to get a concentration of 2.5mg/mL . Similarly from the stock solution 0.5mL (500µL) was pipetted and diluted with 1ml of sterile water for injection, so as to get a concentration of 50mg/mL. From these solutions 10µL was pipeted out to contain 25µg of cefotaxime 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 $37^0$C 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, 30 minutes, $2^{nd}$ hour, $6^{th}$ hour, $24^{th}$ hour and 72 hours).

**2.4 Calibration graph of cefotaxime sodium admixed with Rantidine hydrochloride by UV spectrophotometeric method simultaneous of both drugs**

**2.4.1 Preparation of stock solution for cefotaxime sodium:** 10mg of cefotaxime sodium dissolved in 10mL of water for injection to get a concentration of 1 mg/mL from this solution 0.1mL was taken and made up to 10mL with water for injection to give a concentration of 8,16,24,32, and 40 µg/mL respectively.

**2.4.2 Preparation of stock solution of Ranitidine:** 0.4mL was taken from 25mg/mL of ranitidine hydrochloride injection and made upto 10mL to give a concentration of 1 mg/mL, from this solution 0.1 mL was taken and made upto 10mL to give a concentration of 10 µg/mL was taken and made upto 10mL, to give a concentration of 1 µg/ml.

**2.4.3 Preparation of various drug concentrations for rantidine hydrochloride:** From the above stock solution, aliquots of 2, 4, 6 and 8 mL was taken and made up to 10 mL to give a concentration of 0.2, 0.4, 0.6, and 0.8 µg/mL respectively. 8 ml from 1 µg/mL fo cefotaxime sodium and 2 mL from 1 µg/mL of ranidine hydrochloride were mixed to gather and made up to 10 mL to get a concentration of 8 µg/mL of cefotaxime sodium and 0.2 µg/m of ranitidine hydrochloride respectively. The ratio of 40:1 (cefotaxime sodium; ranitidine hydrochloride) was used, because the same ratio was used during admixture of two drugs. 5 different mixtures of same ratio were prepared (8:0.2, 16:0.4, and 32.0.8, 40.1) and used for calibration graph. The absorbance of the above solution were noted using UV spectrophotometer at λ max of 236nm for cefotaxime and 316 for ranitidine and calibration graph was plotted.

**2.5 Protocol for stability testing of cefotaxime iv with ranitidine hydrochloride in three different temperature conditions (by UV spectrophotometry-simultaneous determination):** The study was top determine the stability of cefotaxime sodium I.V. when admixed with ranitidine I.V.in different condition such as room temperature (25 ° C), refrigeration (5 °C) and 45 °C. The parameters evaluated were changes in pH, clarity and concentration of cefotaxime sodium and ranitidine respectively.

**2.5.1 Preparation of stock solution:** 20 mg of cefotaxime sodium from the vial (1g) was mixed with 0.5 mg of ranitidine hydrochloride and volume was made up to 10 mL with sterile water. The final concentration of cefotaxime sodium was 2 mg/mL and 0.05 mg/mL of ranitidine hydrochloride. The ration of 40:1 (cefotaxime sodium : ranitidine hydrochloride) is commonly used in clinical practice. The three admixtures prepared in duplicate were maintained at three different temperatures (25°C, 45°C and 5°C) and samples were withdrawn at intervals of 0, 15,30min, 1,2,3 and 4 hours. 0.1mL of admixture was withdrawn and made up to 10 mL with water for injection to give a concentration of 20 µg/ml of cefotaxime and 0.5 µg/mL of ranitidine hydrochloride. The absorbance of above solution was noted at 236nm for cefotaxime sodium and 316nm for rantidine hydrochloride respectively UV spectrophotometry.

**2.6 Protocol for stability study of cefotaxime sodium i.v. with ranitidine hydrochloride i.v. By microbial assay (k.b. Method) using *staphylococcus aureus*- NCIM 2079 as test organism:** Weigh 20mg of cefotaxime sodium from the vial (1g) was mixed with 0.5 mg of ranitidine hydrochloride and volume is made up to 10 mL with sterile water. The final concentration of cefotaxime sodium was 2mg/ml and 0.05 mg/mL of ranitidine hydrochloride. The ratio of (cefotaxime sodium: ranitidine hydrochloride) is commonly used in clinical practice. The three admixtures prepared in duplicate were maintained at three different temperatures (25°C, 45°C and 5°C) and samples were withdrawn at intervals of 0,15,30 min, 1,2,3,4 hours. From the above sample, 10 µL was pippeted out, so as to contain 20 µg of Cetfotaxime sodium required for one sterile disc placed on the surface of Muller Hinton agar media, which was already swabbed with *Staphylococcus aureus* test organism. Plates were incubated at 37° C upto 24 hours were observed for the zone of inhibition. Any interference in the results due to ranitidine hydrochloride was checked by using a control without cefotaxime sodium and checked for absence of zone of inhibition. It involves the various steps such as Calibration graph of Cefotaxime sodium pure drug using Colorimetric method, Calibration of Cefotaxime sodium using Microbiological assay method (using Staphylococcus aureus), Stability Testing Protocol of I.V preparation of Cefotaxime sodium at different temperatures by Colorimetry and Microbilogical assay method, Calibration graph of Admixture of Cefotaxime sodium admixed with Rantidine hydrochloride by U.V-Spectrophotmetric method simultaneously.

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## 3. RESULTS AND DISCUSSIONS

**Table.1 Calibration of Cefotaxime sodium by colorimetric method**

| Concentration of the pure drug | Volume of the drug solution | 1 % citric acid | 0.5% $NaNO_2$ | Absorbance of cefotaxime at 500nm |
|---|---|---|---|---|
| 50µg/ml | 3 ml | 0.2 ml | 0.2 ml | 0.2895 |
| 100µg/ml | 3 ml | 0.2 ml | 0.2 ml | 0.5623 |
| 150µg/ml | 3 ml | 0.2 ml | 0.2 ml | 0.8231 |
| 200µg/ml | 3 ml | 0.2 ml | 0.2 ml | 1.0689 |
| 250µg/ml | 3 ml | 0.2 ml | 0.2 ml | 1.3564 |
| 300µg/ml | 3 ml | 0.2 ml | 0.2 ml | 1.6023 |
| 350µg/ml | 3 ml | 0.2 ml | 0.2 ml | 1.9046 |

**Table.2 Calibration using Microbiological assay**

| Concentration ( µg/disc) | Log Concentration | Zone of inhibition (in mm) | | Average Zone of inhibition (in mm) |
|---|---|---|---|---|
| | | I | II | |
| 10 | 1.0000 | 29 | 29 | 29 |
| 20 | 1.3010 | 30 | 32 | 31 |
| 30 | 1.4771 | 32 | 33 | 32.5 |
| 40 | 1.6020 | 34 | 34 | 34 |
| 50 | 1.6989 | 35 | 37 | 36 |
| 60 | 1.7781 | 37 | 38 | 37.5 |
| 70 | 1.8450 | 39 | 39 | 39 |

**Table.3 Chemical stability of cefotaxime sodium I.V. at different temperature by Colorimetry: Expected concentration: 200 µg/ml**

| Temp | Time Interval | 0 min | 30 min | 60 min | 120 min | 180 min | 240 min | 360min | 1st day | 2nd day | 3rd day | 4th day |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Refrigeration 5 ˚C | Con (µg/ml) | 190.71 | 190.66 | 190.42 | 190.14 | 189.72 | 189.49 | 189.16 | 187.57 | 187.34 | 186.91 | 186.61 |
| Room temp. 25 ˚C | Con (µg/ml) | 190.92 | 190.50 | 190.30 | 190.11 | 190.72 | 189.46 | 186.13 | 179.14 | 177.45 | 177.35 | 172.15 |
| Acc. Condt 45 ˚C | Con (µg/ml) | 190.73 | 190.25 | 189.45 | 188.5 | 187.8 | 184.9 | 179.0 | 177.7 | 155.0 | 140.20 | 122.10 |

**Table.4 Percentage deviation of cefotaxime sodium I.V. at different temperature conditions by colorimetric method**

| Sampling time | Refrigeration (5˚C) | Room temp (25˚C) | 45 ˚C |
|---|---|---|---|
| 30 min | 0.02 | 0.21 | 0.25 |
| 60 min | 0.15 | 0.32 | 0.67 |
| 120 min | 0.29 | 0.42 | 1.12 |
| 180 min | 0.51 | 0.60 | 1.50 |
| 240 min | 0.63 | 0.76 | 3.03 |
| 360 min | 0.80 | 2.51 | 6.15 |
| 24 hours | 1.64 | 6.17 | 6.80 |
| 2nd day | 1.76 | 7.00 | 18.70 |
| 3rd day | 1.99 | 7.10 | 26.49 |
| 4th day | 2.4 | 9.30 | 35.98 |

**Table.5 End of four days**

| Temperature | Expected concentration (µg/ml) | Average value (µg/ml) |
|---|---|---|
| Refrigeration (5˚C) | 190.71 | 186.10 |
| Room temperature(25˚C) | 190.92 | 173.15 |
| 45 ˚C | 190.73 | 122.10 |

**Table.6 Physical Stability of Cefotaxime Sodium I.V. at Three Different Temperatures**

| Temperature | | 0 hour | 1 hour | 2 hour | 4 Hour | 7 Hour | 24 hour | 72 hour | 120 hour |
|---|---|---|---|---|---|---|---|---|---|
| 5ºC | pH | 5.9 | 5.9 | 5.9 | 5.9 | 5.9 | 5.8 | 5.8 | 5.4 |
| | Clarity | clear | clear | clear | clear | Clear | clear | clear | Clear |
| | Color | colorless | colorless | colorless | colorless | Colorless | colorless | colorless | colorless |
| 25ºC | pH | 5.9 | 5.9 | 5.9 | 5.9 | 5.7 | 5.4 | 5.4 | 5.2 |
| | Clarity | Clarity | clear | clear | clear | Clear | clear | clear | clear |
| | Color | Color | colorless | colorless | colorless | Colorless | Dark yellow | Dark yellow | Reddish yellow |
| 45ºC | pH | 5.9 | 5.9 | 5.8 | 5.8 | 5.6 | 5.2 | - | - |
| | Clarity | clear | clear | clear | clear | Clear | clear | - | - |
| | Color | colorless | colorless | Pale yellow | Pale yellow | Dark yellow | Reddish yellow | - | - |

The stability study of cefotaxime sodium I.V. stored at refrigeration temperature proved to be more stable even after 24 hrs (% deviation = 1.64) than the other solutions stored at room temperature (% deviation=6.17) and 45˚C (% deviation = 6.80). At 45˚C, the percentage deviation was > 10% (considered unstable) after nearly 24 hours of storage (value indicates between 4-6 hours). At 25˚C > 10% degradation was seen between 6 hrs and 24 hrs. The result obtained for pH and clarity test showed no change even after 4 days at three different temperatures.

**Table.7 Microbiological assay method: Zone of inhibition and concentrations (with percentage deviation) of cefotaxime sodium by microbial assay using *Staphylococcus aureus* NCIM 2079 as test organism**

| Time of sampling | Expected concentration | Refrigeration (5ºC) | RoomTemp (25ºC) | (45ºC) | Percentage deviation | | |
|---|---|---|---|---|---|---|---|
| | | | | | 5ºC | 25ºC | 45ºC |
| 0 | 20µg/10µl | 31 (20) | 31 (20) | 31 (20) | 0 | 0 | 0 |
| 30 min | 20µg/10µl | 31 (20) | 31 (20) | 31 (20) | 0 | 0 | 0 |
| 2 hr | 20µg/10µl | 31 (20) | 31 (20) | 31 (20) | 0 | 0 | 0 |
| 6 hr | 20µg/10µl | 31 (20) | 31 (20) | 29 (10) | 0 | 0 | 50 |
| 24 hr | 20µg/10µl | 31 (20) | 31 (20) | 29 (10) | 0 | 0 | 50 |
| 72 hr | 20µg/10µl | 31 (20) | 29 (10) | 21 (5) | 0 | 50 | 75 |

Values recorded are the zone of inhibition values and the values given within brackets are the concentration of Cefotaxime sodium I.V. in mcg/spot. Cefotaxime sodium was more stable at refrigeration temperature when compared with room temperature and 45ºC as per microbiological method of assay. As per this method cefotaxime was stable at 5ºC for 72 hours, at 25ºC for 24hours and at 45ºC only for 4 hours.

**Table.8 Calibration graph of cefotaxime sodium admixed with ranitidine hydrochloride by spectrophotometric method (Simultaneous determination)**

| Sl. No. | Concentration (µg/ml) | | Absorbance | |
|---|---|---|---|---|
| | Cefotaxime sodium (µg/ml) | Ranitidine hydrochloride (µg/ml) | Cefotaxime sodium at 236nm | Ranitidine hydrochloride at 316nm |
| 1 | 8 | 0.2 | 0.3400 | 0.0748 |
| 2 | 16 | 0.4 | 0.7023 | 0.1546 |
| 3 | 24 | 0.6 | 1.0450 | 0.2313 |
| 4 | 32 | 0.8 | 1.3980 | 0.3050 |
| 5 | 40 | 1 | 1.7327 | 0.3800 |

**Table.9 Physical and chemical stability study of cefotaxime I.V., when admixed with ranitidine hydrochloride I.V. at three different temperatures by simultaneous determination using UV spectrophotometric method**

| Time of Sampling (mins) | Absorbance and concentration at 5˚C | | Absorbance and concentration at 25˚C | | Absorbance and concentration at 45˚C | |
|---|---|---|---|---|---|---|
| | Cefotaxime (µg/ml) | Ranitidine (µg/ml) | Cefotaxime (µg/ml) | Ranitidine (µg/ml) | Cefotaxime (µg/ml) | Ranitidine (µg/ml) |
| 0 | 0.8483(19.51) | 0.1869(0.49) | 0.8481(19.51) | 0.1863(0.49) | 0.8480(19.50) | 0.1865(0.49) |
| 15 | 0.8480(19.50) | 0.1861(0.49) | 0.8430(19.39) | 0.1859(0.49) | 0.8201(18.86) | 0.1843(0.48) |
| 30 | 0.8461(19.46) | 0.1853(0.48) | 0.8370(19.25) | 0.1852(0.48) | 0.8001(18.40) | 0.1822(0.48) |
| 60 | 0.8449(19.43) | 0.1840(0.48) | 0.8320(19.14) | 0.1839(0.48) | 0.7820(17.99) | 0.1793(0.47) |
| 120 | 0.8420(19.37) | 0.1833(0.48) | 0.8269(19.02) | 0.1831(0.48) | 0.7629(17.55) | 0.1765(0.46) |
| 180 | 0.8410(19.32) | 0.1815(0.47) | 0.8157(18.76) | 0.1810(0.47) | 0.7318(16.83) | 0.1739(0.45) |
| 240 | 0.8400(19.31) | 0.1802(0.47) | 0.8110(18.63) | 0.1792(0.47) | 0.7176(16.51) | 0.1711(0.45) |

The study was done in duplicate and the average value has been tabulated. The expected concentration of cefotaxime sodium =20 (µg/ml) Ranitidine hydrochloride = 0.5(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.

**Table.10 Percentage deviation of cefotaxime sodium I.V when admixed with ranitidine hydrochloride I.V at different temperature conditions (by simultaneous determination using UV spectrophotometric method)**

| Sampling time (minutes) | Percentage deviation when admixture was stored at refrigeration (5˚C) | | Percentage deviation when admixture was stored at room temperature (25˚C) | | Percentage deviation when admixture was stored at 45 ˚C | |
|---|---|---|---|---|---|---|
| | cefotaxime | ranitidine | cefotaxime | ranitidine | cefotaxime | ranitidine |
| 15 | 0.05 | 2.04 | 0.61 | 2.04 | 3.28 | 2.04 |
| 30 | 0.25 | 2.04 | 1.33 | 2.04 | 5.64 | 2.04 |
| 60 | 0.41 | 2.04 | 1.89 | 2.04 | 7.74 | 4.8 |
| 120 | 0.71 | 4.08 | 2.51 | 4.08 | 10 | 6.12 |
| 180 | 0.97 | 4.08 | 4.81 | 4.08 | 13.69 | 8.6 |
| 240 | 1.02 | 4.08 | 4.51 | 4.08 | 15.33 | 8.6 |

It was found out that the admixture of cefotaxime sodium and ranitidine hydrochloride stored at refrigeration (5˚C) & (25˚C) proved to be more stable even after almost 4 hours than the other solutions stored at 45˚C.

**Table 11: Chemical stability (with percentage deviation) of cefotaxime sodium i.v. admixed with ranitidine at different temperatures by microbiological assay method (Kirby Bauer method) using *Staphylococcus aureus* – NCIM 2079 as test organism**

| Sampling time in mins | Zone of inhibition and concentration (mm) | | | Percentage deviation | | |
|---|---|---|---|---|---|---|
| | 5°C | 25°C | 45°C | 5°C | 25°C | 45°C |
| 0 | 31(20) | 31(20) | 31(20) | 0 | 0 | 0 |
| 15 | 31(20) | 31(20) | 31(20) | 0 | 0 | 0 |
| 30 | 31(20) | 31(20) | 30(15) | 0 | 0 | 25 |
| 60 | 31(20) | 31(20) | 30(15) | 0 | 0 | 25 |
| 120 | 31(20) | 31(20) | 29(10) | 0 | 0 | 50 |
| 240 | 31(20) | 30(15) | 28(9.5) | 0 | 25 | 55 |
| 480 | 31(20) | 30(15) | 28(9.5) | 0 | 25 | 55 |

The stability studies of the cefotaxime sodium IV admixture with ranitidine IV by microbial method of assay. As per this method cefotaxime sodium was found to be stable at 5°C, 25°C for 1 hour at 45°C for 15 min.

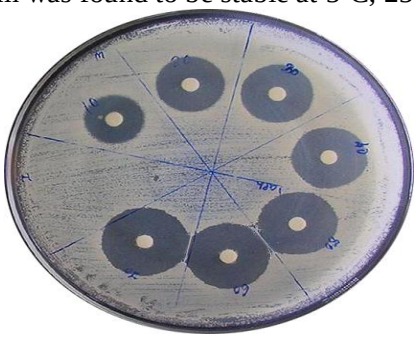

**Figure.1 Zone of inhibition of cefotaxime sodium by microbiological assay at various concentrations using Staphylococcus aureus – NCIM 2079 as test organism**

**Table.12 Summary of results**

| Formulation and its admixture | Stability details | Refrigeration 5 °C | Room temperature 25 °C | 45 °C |
|---|---|---|---|---|
| Cefotaxime sodium | Stability of cefotaxime sodium as per colorimetric method | Stable for more than 4 days | Stable for 4 days | Stable for 2 days |
| | Stability of cefotaxime sodium as per microbiological assay. | Stable for more than 4 days | Stable for 1 day | Stable for 4 hrs |
| Cefotaxime sodium admixture with ranitidine | Stability of cefotaxime sodium as per UV spectrophotometeric method | Stable for more than 4 hrs | Stable for more than 4 hrs | Stable for 30 minutes |
| | Stability of cefotaxime sodium as per microbiological assay. | Stable for 4 hrs | Stable for 2 hrs | Stable for 15 minutes |
| | Stability of ranitidine as per UV spectrophotometeric assay. | Stable for more than 4 hrs | Stable for more than 4 hrs | Stable for 2 hrs |

Stability of cefotaxime sodium when admixed with ranitidine hydrochloride and metronidazole I.V. respectively at three different temperatures has been shown in the table 12.

**4. CONCLUSION**

Ranitidine I.V is extensively used as $H_2$ receptor antagonist in ICU patients on parentral antimicrobial therapy. Hence our study involving the stability and compatibility study on cefotaxime –

ranitidine admixture, which indicates that both drugs remain stable for upto one hour even at 45°C, could be useful in clinical therapy. Combining these two drugs through the same I.V line could help in improved patient compliance, which could be saved of one extra I.V line. The combination selected in our study could be used in clinical practice after a detailed study with larger sample size to get more valuable data.

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