INTERACTIONS OF CEFTIOFUR SODIUM WITH H₂-RECEPTOR ANTAGONIST

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ABSTRACT

The purpose of this study is to study the possible drug-drug interactions between ceftiofur sodium and ranitidine on co-administration. These studies have been carried out at normal as well as the elevated temperature at pH corresponds to full gut (pH = 7.4). The spectrophotometric method has been used to study the bioavailability studies of each drug individually and in the presence of the other drug. Change in the bioavailability of ceftiofur sodium in the presence of ranitidine as compared to the bioavailability in the absence of ranitidine supported the possible interactions between the two drugs.

Keywords: Cephalosporins, Ranitidine, Absorbance, H₂-Receptor Antagonists, Bioavailability

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INTRODUCTION

Ceftiofur sodium is a third-generation cephalosporin having strong antibiotic activity which can kill bacteria and some anaerobe. It possesses broad-spectrum activity against both types of bacteria i.e. gram-positive as well as gram-negative.¹ In a similar fashion to that of other cephalosporins, its antibiotic activity results from the inhibition of mucopeptide synthesis in the cell wall. It has worldwide approval for respiratory disease ruminants, horses and swine. IUPAC name of ceftiofur sodium is (6R,7R)-7-[[[(2Z)-2-(2-Amino-1,3-thiazol-4-yl)-2-methoxyiminoacetyl]amino]-3-(furan-2-carbonyl sulfanylmethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid. It's stabilized molecular structure which cannot be destroyed by β -lactamase (Fig.-1). It is reported to form metal complexes which act as better antibacterial agents.²

Fig.-1: Structure of Ceftiofur

The use of cephalosporins is associated with the risk of gastrointestinal complications. Therefore co-administration of the acid suppressant drugs like H₂-receptor antagonist is usually prescribed along with the cephalosporins.³ But it is well established in literature that the simultaneous administration of one drug in the presence of the other may lead to drug-drug interactions which may affect the pharmacokinetic properties of the interacting drugs. Numbers of reports are available in literature where

cephalosporins are known to interact with probenecids⁴⁻⁵, alcohols⁶⁻⁹, cholestyramines¹⁰, theophyllines¹¹, aminoglycosidic antibiotics¹² and anticoagulants¹³. The cephalosporins like cephalixin¹⁴, Cefetamet pivoxil¹⁵, Cefixime¹⁶ and cefpodoxime proxetil¹⁷ are also known to interact with H₂-receptor antagonists. H₂-receptor antagonists have been assayed by various methods in literature.¹⁸⁻¹⁹ In the present study, an attempt has been made to study the effect of simultaneous administration of ranitidine and ceftiofur sodium on the bioavailability of each drug at 7.4 pH (which corresponds to full gut pH) at normal as well as elevated temperature by using spectrophotometer.

EXPERIMENTAL

Analytical grade chemicals were used for the proposed study and were purchased from Merck. Reference standard tablet formulation rantidine.HCl (150mg, Zantac, Glaxo SmithKline) and ceftiofur sodium (250mg, Naxcel, Pfizer, Inc.) were purchased from the local pharmacy. Reference standards of ceftiofur sodium and cimetidine were obtained from Mcleods pharmaceuticals, Mumbai, as a gift. All the solutions were prepared by using double distilled water. An absorbance study was done by using Shimadzu UV-1800ENG240V1 spectrophotometer.

Preparation of Phosphate Buffer of pH=7.4

Disodium hydrogen phosphate (17.90 gm) was dissolved in double-distilled water and the total volume was made to 500 ml in volumetric flask. In another volumetric flask, potassium dihydrogen phosphate (6.80 gm) was dissolved in double-distilled water and the total volume was made to 100ml. For the preparation of 1 liter of the required buffer solution, disodium hydrogen phosphate (31.4 ml) and potassium dihydrogen phosphate (5.7 ml) solutions were dissolved in 1 liter of double distilled water in 1-liter volumetric flask. Few drops of disodium hydrogen phosphate were used to achieve required pH of 7.4.

Preparation of Solution of Ceftiofur Sodium and Ranitidine

Preparation of Stock Solutions

To prepare 1 mmol/L of stock solution, 0.035 gm of the reference standard of ranitidine and 0.055gm of reference standard of ceftiofur sodium were dissolved in 100 ml of phosphate buffer solution in 100 ml volumetric flasks separately.

Preparation of Working Standard Solutions

1 to 20 ml of the stock solutions were taken in the 100 ml volumetric flasks separately and the total volume was made to 100 ml by using phosphate buffer solution in each case to obtain the working standard solutions from 0.01 mmol to 0.2 mmol.

Calculation of $\lambda_{\max}$ for Ceftiofur Sodium and Ranitidine

The $\lambda_{\max}$ of each reference standard was measured at 0.001mmol of concentration which was prepared by dilution of 1ml of stock solution to 100 ml by the use of phosphate buffer solution.

Calibration Curve for Ceftiofur Sodium and Ranitidine

To establish the working concentration range for the proposed study, the validation of the Beer-Lambert law was done. For this, the absorption maxima of the working standard solutions of each drug were measured in the UV region against region blank. Further, the samples of ceftiofur sodium were scanned at the wavelength of its absorption maxima and at the absorption maxima of the ranitidine. In the same way, the samples of ranitidine were scanned at the wavelength of its absorption maxima and at the absorption maxima of ceftiofur sodium. The graphs (FigS.-2 to 5) of concentration Vs absorption maxima were plotted which gave rise to straight-line confirming the linearity of Beer-Lambert law. Further, molar absorptivity (ϵ) values were obtained by using equation-1

$$\epsilon = A/b.c \quad (1)$$

Where,

A = Absorbance of given sample at a specific wavelength

ϵ = molar absorptivity

b = path length of cell

c = specific concentration of the sample

Studies of Bioavailability of Ceftiofur Sodium and Ranitidine

A known amount of tablet formulation of each drug was poured into 1 liter of buffer solution maintained at specific temperature (37°C and 60 °C). The aliquots were drawn after every 15 minutes till 240 minutes and were analyzed for the drug content by using equation-2. The total volume of the solution was kept constant by addition of same volume of buffer solution maintained at the same temperature as the aliquots were withdrawn.

$$\% \text{age of drug dissolved} = (c/x) \times 100 \quad (2)$$

Where

c = concentration obtained from equation-1

x = amount of the drug dissolved

Interaction of Ceftiofur Sodium with Ranitidine

The interaction studies between ceftiofur sodium and ranitidine were done at 37°C and 60°C. For this, the tablet formulation of ceftiofur sodium was added into 1 liter of buffer solution at zero time and tablet formulation of ranitidine was added to the dissolution medium after 15 minutes. Aliquots were withdrawn after every 15 minutes till 240 minutes and were assayed for the concentration of each drug by using equations 3-4.

$$C_a = \epsilon_{b'} \cdot A_{293} - \epsilon_b \cdot A_{232} / \epsilon_a \cdot \epsilon_{b'} - \epsilon_{a'} \cdot \epsilon_b \quad (3)$$

and

$$C_b = \epsilon_{a'} \cdot A_{293} - \epsilon_a \cdot A_{232} / \epsilon_{a'} \cdot \epsilon_b - \epsilon_a \cdot \epsilon_{b'} \quad (4)$$

Where,

C_a is the concentration of a sample of ceftiofur sodium C_b is the concentration of ranitidine

ϵ_a and ϵ_b correspond to the molar absorptivities values of ceftiofur sodium and ranitidine at 293nm

$\epsilon_{a'}$ and $\epsilon_{b'}$ correspond to the molar absorptivities of ceftiofur sodium and ranitidine at 232nm

RESULTS AND DISCUSSION

$\lambda_{\max}$ of Ceftiofur Sodium and Ranitidine

To calculate the $\lambda_{\max}$ ranitidine hydrochloride and ceftiofur sodium, 0.001 mmol solutions of each drug were scanned from 150-400 nm. A strong absorption maxima was obtained at 232 nm for ranitidine and at 293 nm for ceftiofur sodium.

The linearity of Beer-Lambert Law

To obtain the working concentration range for each drug to determine the drug-drug interaction, the linearity of the Beer-Lambert law was established. For this purpose, the working standard solutions of each drug were subjected to spectrophotometric analysis at their respective absorption maxima as well as at the absorption maxima of the other drug. Table-1 presents the results obtained for Ceftiofur sodium whereas Table-2 presents the results obtained for Ranitidine hydrochloride.

Table-1: UV Absorption Studies for Ceftiofur Sodium

S. No.	Stock (ml)	Buffer ^a (ml)	Conc. ^b (mmol)	Absorbance at $\lambda_{\max}$	
				293nm ^c	232nm ^d
1	1	99	0.01	0.230	0.190
2	2	98	0.02	0.481	0.420
3	3	97	0.03	0.803	0.654
4	4	96	0.04	1.012	0.820
5	5	95	0.05	1.441	1.000
6	6	94	0.06	1.460	1.107
7	7	93	0.07	1.660	1.242

8	8	92	0.08	1.844	1.380
9	9	91	0.09	1.681	1.432
10	10	90	0.10	1.955	1.580
11	11	89	0.11	2.391	1.844
12	12	88	0.12	2.631	2.000
13	13	87	0.13	2.840	2.170
14	14	86	0.14	3.267	2.521
15	15	85	0.15	3.462	2.720
16	16	84	0.16	3.701	2.840
17	17	83	0.17	3.622	2.890
18	18	82	0.18	3.819	3.266
19	19	81	0.19	4.051	3.409
20	20	80	0.20	4.150	3.466

^a pH = 7.4; ^b conc in mmol/L; ^c $\lambda_{\max}$ for ceftiofur sodium; ^d $\lambda_{\max}$ for ranitidine hydrochloride

Table-2: UV Absorption Studies for Ranitidine.HCl

S.No.	Stock (ml)	Buffer ^a (ml)	Conc. ^b (mmol)	Absorbance at $\lambda_{\max}$	
				293nm ^c	232nm ^d
1	1	99	0.01	0.142	0.121
2	2	98	0.02	0.251	0.342
3	3	97	0.03	0.410	0.590
4	4	96	0.04	0.530	0.701
5	5	95	0.05	0.521	0.712
6	6	94	0.06	0.641	0.871
7	7	93	0.07	0.830	1.102
8	8	92	0.08	0.781	1.060
9	9	91	0.09	0.830	1.182
10	10	90	0.10	1.051	1.473
11	11	89	0.11	1.060	1.501
12	12	88	0.12	1.173	1.641
13	13	87	0.13	1.311	1.800
14	14	86	0.14	1.430	1.201
15	15	85	0.15	1.601	2.141
16	16	84	0.16	1.751	2.311
17	17	83	0.17	0.890	2.360
18	18	82	0.18	1.930	2.570
19	19	81	0.19	2.141	2.921
20	20	80	0.20	2.040	2.840

^a pH = 7.4; ^b conc in mmol/L; ^c $\lambda_{\max}$ for ceftiofur sodium; ^d $\lambda_{\max}$ for ranitidine hydrochloride;

Molar Absorptivity (ϵ) Studies for Ceftiofur Sodium and Ranitidine Hydrochloride

The results obtained from Beer-Lambert law were further used to calculate the ϵ values of Ranitidine hydrochloride and Ceftiofur sodium which are presented in Table-3 and Table- respectively.

Table-3: ϵ Value of Ranitidine.HCl

S. No.	Conc. (M)	Absorbance at $\lambda_{\max}$		ϵ	
		293nm	232nm	ϵ_{293}	ϵ_{232}
1	0.00001	0.142	0.121	14200.00	12100.00
2	0.00002	0.251	0.342	12550.00	17100.00
3	0.00003	0.410	0.590	13666.67	19666.67
4	0.00004	0.530	0.701	13250.00	17525.00
5	0.00005	0.521	0.712	10420.00	14240.00

6	0.00006	0.641	0.871	10683.33	14516.67
7	0.00007	0.830	1.102	11857.14	15742.86
8	0.00008	0.781	1.060	9762.50	13250.00
9	0.00009	0.830	1.182	9222.22	13133.33
10	0.00010	1.051	1.473	10510.00	14730.00
11	0.00011	1.060	1.501	9636.364	13645.45
12	0.00012	1.173	1.641	9775.00	13675.00
13	0.00013	1.311	1.800	10084.62	13846.15
14	0.00014	1.430	1.201	10214.29	8578.57
15	0.00015	1.601	2.141	10673.33	14273.33
16	0.00016	1.751	2.311	10943.75	14443.75
17	0.00017	0.890	2.360	5235.294	13882.35
18	0.00018	1.930	2.570	10722.22	14277.78
19	0.00019	2.141	2.921	11268.42	15373.68
20	0.00020	2.040	2.840	10200.00	14200.00
			Summation	214875.20	288200.60
			Mean	10743.76	14410.03

Table-4: ϵ Value of Ceftiofur Sodium

S.No.	Conc. (M)	Absorbance at $\lambda_{\max}$		ϵ	
		293nm	232nm	232nm	293nm
1	1×10^{-5}	0.230	0.190	19000	23000
2	2×10^{-5}	0.481	0.420	21000	24050
3	3×10^{-5}	0.803	0.654	21800	26766
4	4×10^{-5}	1.012	0.820	20500	25300
5	5×10^{-5}	1.441	1.000	20000	28820
6	6×10^{-5}	1.460	1.107	18450	24333
7	7×10^{-5}	1.660	1.242	17742	23714
8	8×10^{-5}	1.844	1.380	17250	23050
9	9×10^{-5}	1.681	1.432	15911	18677
10	10×10^{-5}	1.955	1.580	15800	19550
11	11×10^{-5}	2.391	1.844	16763	21736
12	12×10^{-5}	2.631	2.000	16666	21925
13	13×10^{-5}	2.840	2.170	16692	21846
14	14×10^{-5}	3.267	2.521	18007	23335
15	15×10^{-5}	3.462	2.720	18133	23080
16	16×10^{-5}	3.701	2.840	17750	23131
17	17×10^{-5}	3.622	2.890	17000	21305
18	18×10^{-5}	3.819	3.266	18144	21216
19	19×10^{-5}	4.051	3.409	17942	21321
20	20×10^{-5}	4.150	3.466	17330	20750

			Summation	361883	456910
			Mean	18094	22845

Bioavailability Studies

The ϵ values calculated in Table-3 and Table-4 were used further for the bioavailability studies of each drug at 7.4 pH at 37°C and 60°C which the results of which are produced in Table-5 and Table-6 for Ceftiofur sodium and Rantidine hydrochloride respectively.

Table-5: Bioavailability Studies of Ceftiofur Sodium at λ_{293}

S.No.	Time (min.)	Absorbance	Conc. (M)	% of Drug Dissolved
At 37 °C				
1	15	0.9511	4.1632×10^{-5}	90.90
2	30	0.9671	4.2333×10^{-5}	92.43
3	45	0.9678	4.2365×10^{-5}	92.5
4	60	0.9649	4.2237×10^{-5}	92.22
5	75	0.9590	4.1980×10^{-5}	91.66
6	90	0.9540	4.1760×10^{-5}	91.18
7	105	0.9380	4.1060×10^{-5}	89.65
8	120	0.9321	4.0803×10^{-5}	89.09
9	135	0.9053	3.9626×10^{-5}	86.52
10	150	0.9038	3.9562×10^{-5}	86.38
11	165	0.8966	3.9246×10^{-5}	85.69
12	180	0.8813	3.8577×10^{-5}	84.23
13	195	0.8763	3.8358×10^{-5}	83.75
14	210	0.8668	3.7941×10^{-5}	82.84
15	225	0.8588	3.7593×10^{-5}	82.08
16	240	0.8551	3.7432×10^{-5}	81.73
At 60 °C				
1	15	0.9880	4.3249×10^{-5}	94.43
2	30	0.9837	4.3061×10^{-5}	94.02
3	45	0.9707	4.2489×10^{-5}	92.77
4	60	0.9511	4.1632×10^{-5}	90.90
5	75	0.9104	3.9851×10^{-5}	87.01
6	90	0.8690	3.8037×10^{-5}	83.05
7	105	0.8675	3.7973×10^{-5}	82.91
8	120	0.8617	3.7721×10^{-5}	82.36
9	135	0.8603	3.7657×10^{-5}	82.22
10	150	0.8595	3.7625×10^{-5}	82.15
11	165	0.8588	3.7593×10^{-5}	82.08
12	180	0.8581	3.7561×10^{-5}	82.01
13	195	0.8443	3.6956×10^{-5}	80.69
14	210	0.8348	3.6544×10^{-5}	79.79
15	225	0.8304	3.6351×10^{-5}	79.37
16	240	0.8283	3.6255×10^{-5}	79.16

Table-6: Bioavailability Studies of Rantidine.HCl at λ_{232}

S.No.	Time (min.)	Absorbance	Conc. (M)	% of Drug Dissolved
At 37°C				
1	15	0.5940	4.1218×10^{-5}	86.23
2	30	0.6092	4.2279×10^{-5}	88.45
3	45	0.6452	4.4774×10^{-5}	93.67
4	60	0.6528	4.5305×10^{-5}	94.78

5	75	0.6705	4.6529×10^{-5}	97.34
6	90	0.6751	4.6849×10^{-5}	98.01
7	105	0.6758	4.6901×10^{-5}	98.12
8	120	0.6812	4.7269×10^{-5}	98.89
9	135	0.6829	4.7389×10^{-5}	99.14
10	150	0.6841	4.7475×10^{-5}	99.32
11	165	0.6858	4.7594×10^{-5}	99.57
12	180	0.6879	4.7738×10^{-5}	99.87
13	195	0.6887	4.7795×10^{-5}	99.99
14	210	0.6891	4.7824×10^{-5}	100.05
15	225	0.6955	4.8268×10^{-5}	100.98
16	240	0.6955	4.8268×10^{-5}	100.98
At 60°C				
1	15	0.6573	4.5616×10^{-5}	95.43
2	30	0.6623	4.5960×10^{-5}	96.15
3	45	0.6720	4.6634×10^{-5}	97.56
4	60	0.6766	4.6954×10^{-5}	98.23
5	75	0.6803	4.7207×10^{-5}	98.76
6	90	0.6812	4.7269×10^{-5}	98.89
7	105	0.6824	4.7355×10^{-5}	99.07
8	120	0.6829	4.7394×10^{-5}	99.15
9	135	0.6843	4.7485×10^{-5}	99.34
10	150	0.6879	4.7738×10^{-5}	99.87
11	165	0.6887	4.7795×10^{-5}	99.99
12	180	0.6887	4.7795×10^{-5}	99.99
13	195	0.6889	4.7805×10^{-5}	100.01
14	210	0.6894	4.7843×10^{-5}	100.09
15	225	0.6967	4.8350×10^{-5}	101.15
16	240	0.6988	4.8493×10^{-5}	101.45

Interaction Studies Ceftiofur Sodium and Ranitidine Hydrochloride

The results of interaction studies of Ceftiofur sodium and Ranitidine hydrochloride are summarized in Table-7 and Table-8 at 37°C and 60°C respectively.

Table-7: Interaction Studies of Ceftiofur Sodium and Ranitidine.HCl at 37 °C

S.No.	Time (min)	A ₂₉₃	A ₂₃₂	C _a ^a	C _b ^b	% age of Ceftiofur Sodium	%age of Ranitidine.HCl
1	0	1.0894	0.9058	4.4263×10^{-5}	7.2779×10^{-5}	96.56	15.2
2	15	1.1446	0.9932	4.3195×10^{-5}	1.4685×10^{-5}	94.23	30.67
3	30	1.2461	1.1320	4.2989×10^{-5}	2.4577×10^{-5}	93.78	51.33
4	45	1.2469	1.1426	4.2228×10^{-5}	2.6268×10^{-5}	92.12	54.86
5	60	1.2786	1.1953	4.1412×10^{-5}	3.0950×10^{-5}	90.34	64.64
6	75	1.3380	1.2745	4.1462×10^{-5}	3.6380×10^{-5}	90.45	75.98
7	90	1.3292	1.2793	4.0133×10^{-5}	3.8386×10^{-5}	87.55	80.17
8	105	1.3291	1.2863	3.9565×10^{-5}	3.9583×10^{-5}	86.31	82.67
9	120	1.3379	1.2982	3.9551×10^{-5}	4.0431×10^{-5}	86.28	84.44
10	135	1.3311	1.3020	3.8529×10^{-5}	4.1972×10^{-5}	84.05	87.66
11	150	1.3063	1.2797	3.7644×10^{-5}	4.1542×10^{-5}	82.12	86.76
12	165	1.2957	1.2759	3.6823×10^{-5}	4.2303×10^{-5}	80.33	88.35
13	180	1.2928	1.2798	3.6204×10^{-5}	4.3351×10^{-5}	78.98	90.54
14	195	1.2715	1.2722	3.4527×10^{-5}	4.4932×10^{-5}	75.32	93.84
15	210	1.2446	1.2624	3.2436×10^{-5}	4.6875×10^{-5}	70.76	97.9
16	225	1.2647	1.2841	3.2854×10^{-5}	4.7857×10^{-5}	71.67	99.95

17	240	1.2135	1.2446	3.0529×10^{-5}	4.8039×10^{-5}	66.60	100.33
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^aC_a = conc. of ceftiofur sodium; ^bC_b = conc. of ranitidine.HCl

Table-8: Interaction Studies of Ceftiofur Sodium and Ranitidine.HCl at 60 °C

S.No.	Time (min)	A ₂₉₃	A ₂₃₂	C _a ^a	C _b ^b	%age of ceftiofur sodium	%age of ranitidine.HCl
1	0	1.0802	0.8839	4.5019×10^{-5}	4.8120×10^{-6}	98.21	10.05
2	15	1.4432	1.3712	4.4987×10^{-5}	3.8669×10^{-5}	98.14	80.76
3	30	1.4887	1.4434	4.4098×10^{-5}	4.4797×10^{-5}	96.2	93.56
4	45	1.4881	1.4452	4.3896×10^{-5}	4.5171×10^{-5}	95.76	94.34
5	60	1.4252	1.3976	4.0967×10^{-5}	4.5549×10^{-5}	89.37	95.13
6	75	1.4084	1.3849	4.0183×10^{-5}	4.5650×10^{-5}	87.66	95.34
7	90	1.3970	1.3774	3.9565×10^{-5}	4.5908×10^{-5}	86.31	95.88
8	105	1.3760	1.3620	3.8538×10^{-5}	4.6129×10^{-5}	84.07	96.34
9	120	1.3714	1.3576	3.8400×10^{-5}	4.5994×10^{-5}	83.77	96.06
10	135	1.3462	1.3428	3.6892×10^{-5}	4.6861×10^{-5}	80.48	97.87
11	150	1.3551	1.3548	3.6878×10^{-5}	4.7713×10^{-5}	80.45	99.65
12	165	1.3232	1.3325	3.5256×10^{-5}	4.8202×10^{-5}	76.91	100.67
13	180	1.3311	1.3519	3.4550×10^{-5}	5.0438×10^{-5}	75.37	105.34
14	195	1.3003	1.3354	3.2569×10^{-5}	5.1774×10^{-5}	71.05	108.13
15	210	1.2893	1.3345	3.1474×10^{-5}	5.3086×10^{-5}	68.66	110.87
16	225	1.2415	1.2941	2.9581×10^{-5}	5.2664×10^{-5}	64.53	109.99
17	240	1.1895	1.2554	2.7096×10^{-5}	5.3100×10^{-5}	59.11	110.9

^aC_a = conc. of ceftiofur sodium; ^bC_b = conc. of ranitidine.HCl

Establishment of Beer-Lambert Law

The graphical representations of the results obtained in Table-1 and Table-2 for Ceftiofur sodium and Ranitidine hydrochloride are presented in Figs.-2 & 3 and Figs. 4 & 5 respectively. It is well clear from the graphs that both, Ceftiofur sodium and Ranitidine hydrochloride obey Beer-Lambert law within the working concentration range of 0.01-0.02 mmol.

Fig.-2: Establishment of Beer-Lambert Law at 293 nm for Ceftiofur Sodium

Bioavailability Study of Ceftiofur Sodium

The bioavailability studies of Ceftiofur sodium at 37°C and 60°C is presented in Figure-6 at 293 nm. It is clear from the studies that at 37°C, 91% of the bioavailability was obtained after 15 minutes and attains 93% as the maximum value after 45 minutes. The decrease in bioavailability was observed post 15 minutes where minimum of 82% bioavailability was observed after 240 minutes. This decrease in the bioavailability of Ceftiofur sodium with increase in time may be attributed to the degradation of the drug

in buffer solution of pH= 7.4 [20]. On the other hand at 60°C, the bioavailability 94% was observed after 15 minutes which then decreases with time and attained a minimum bioavailability of 79% after 240 minutes. The studies show that the increase in the temperature results in quick release of Cefotiofur sodium but it also assist the degradation of the drug with time to a greater extent as compared to degradation at lower temperature.

Fig.-3: Establishment of Beer-Lambert Law at 232 nm for Cefotiofur Sodium

Fig.-4: Establishment of Beer-Lambert Law at 293 nm for Ranitidine Hydrochloride

Fig.-5: Establishment of Beer-Lambert Law at 232 nm for Ranitidine Hydrochloride

Bioavailability Study of Ranitidine.HCl

The graphical representation of bioavailability studies of Ranitidine hydrochloride is presented in Figure-7. At 37°C, the drug achieves bioavailability of 86% after 15 minutes and attains maximum value of 99% after 135 minutes. Post 135 minutes, the bioavailability remains almost same and reaches 100% after 2409 minutes. Further, increase in temperature results in quick release of the drug with 95% bioavailability after 15 minutes. The same bioavailability was achieved at both the temperatures after 120 minutes after which the increase in temperature does not affect the release of the drug and same bioavailability was achieved.

Fig.-6: Bioavailability Study of Ceftiofur Sodium

Fig.-7: Bioavailability of Ranitidine Hydrochloride at 232 nm

Ceftiofur Sodium-Ranitidine Hydrochloride Interactions

Figure-8 depicts the bioavailability study of Ceftiofur sodium in the absence and presence of Ranitidine hydrochloride at 37°C. It can be inferred from the figure that till 30 minutes, the presence of Ranitidine hydrochloride assists the release of Ceftiofur sodium. Post 30 minutes, ceftiofur sodium is less available in the presence of Ranitidine hydrochloride attaining a minimum value of approximately 70% after 240 minutes as compared to approximately 90% of bioavailability of ceftiofur alone. On the other hand at 60°C (Figure-9), ceftiofur sodium shows maximum bioavailability at the start of the experiment after 15 minutes. Further, the presence of Ranitidine hydrochloride assists the quick release of ceftiofur sodium attaining value of 98% as compared to 94% of release in the case of ceftiofur sodium alone. Further, ceftiofur sodium shows better availability in the presence of Ranitidine hydrochloride till 120 minutes after which the bioavailability starts decreasing as compared to ceftiofur sodium alone reaching to minimum value of 59% in the presence of Ranitidine hydrochloride after 240 minutes as compared to the 79% bioavailability in the case of ceftiofur sodium alone.

Fig.-8: Ceftiofur Sodium-Ranitidine.HCl interactions Sodium at 37°C

Fig.-9: Ceftiofur Sodium-Ranitidine.HCl interactions Sodium at 60°C

Figure-10 shows the comparison of bioavailability studies of ceftiofur sodium in the presence of ranitidine at 37°C and 60°C. It is observed that at both temperatures, the availability of the drug decreases with time.

Fig.-10: Ceftiofur Sodium-Ranitidine.HCl interactions at 37°C and 60°C

Till 45 minutes, the drug shows more availability at elevated temperatures than normal temperature. The trend reverses after 45 minutes, with drug being lesser available at higher temperatures than at lower temperatures. After 240 minutes it is observed that 59% of ceftiofur sodium is available at 60°C in comparison to 67% at 37°C. The results found are in accordance with those reported for cephradine-

ranitidine interactions²¹ where the availability of cephradine was found to increase at the beginning of the experiment and then decrease as compared to the availability of the drug in the absence of ranitidine.

CONCLUSION

It is well established from the results that the presence of Ranitidine hydrochloride does affect the bioavailability of Ceftiofur sodium at moderate and elevated temperatures. Further, the presence of Ranitidine hydrochloride assists the quick release of Ceftiofur sodium at the start of the experiment at both temperature but after some time interval the bioavailability of Ceftiofur sodium was found to decrease in the presence of Ranitidine hydrochloride. This may be attributed to the possible formation of new intermediate due to drug-drug interactions which absorb at different wavelength eventually leading to change in the bioavailability of ceftiofur sodium in the presence of Ranitidine hydrochloride.

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