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IN VITRO MONITORING OF CIPROFLOXACIN ANTACIDS INTERACTIONS BY UV & HPLC

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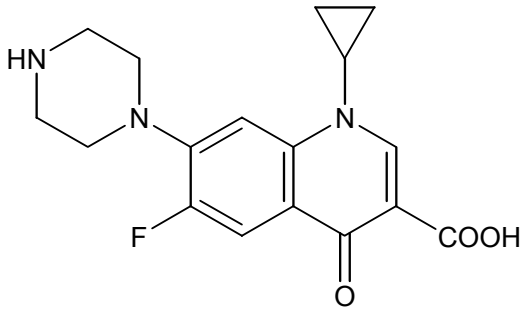
Ciprofloxacin or 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl]-3-quinoline carboxylic acid is a fluorinated quinolone antibacterial agent extensively used worldwide. There are number of drug interactions reported for this antibacterial agent. In present studies, *in vitro* release of ciprofloxacin hydrochloride in presence of various antacids like sodium bicarbonate, calcium hydroxide, calcium carbonate, aluminum hydroxide, magnesium hydroxide, magnesium carbonate, magnesium trisilicate and magaldrate has been studied on BP 2002 dissolution test apparatus. Drug in each case was analyzed either by measuring the absorbance of aliquots at 278 and 316nm on a UV/VIS spectrophotometer, or by reversed-phase high-performance liquid chromatographic (RP-HPLC) method These studies were carried out in simulated gastric and intestinal juices for three hours at 37^{o}C. The availability of ciprofloxacin was found to be markedly retarded in presence of all the antacids studied.

Keywords: Ciprofloxacin, antacid, *in vitro*, drug interaction.

INTRODUCTION

Ciprofloxacin is a synthetic broad spectrum antimicrobial agents for oral administration. It is 1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid (Structure 1) with a faintly yellowish to light yellow crystalline appearance. It is a synthetic congener of nalidixic acid having broad spectrum of activity (Fass 1983; Barry *et al.,* 1986; Hoogkamp-Korstanje 1984 and Naber *et al.,* 1986), *in vitro* against Gram-positive and Gram-negative aerobic organisms and has little activity against anaerobes (Physicians' Desk Reference 1989; Abraham, 2003). Significant interactions with ciprofloxacin have been described (Janknegt 1990), which reduce intestinal absorption after oral administration and may result in potentially serious problems via inhibition of various metabolic pathways. The availability of ciprofloxacin like other drugs is the proportion of the administered dose that is absorbed into the blood stream; it can be enhanced or reduced by interaction with other drugs. The availability of ciprofloxacin administered in tablet form is reported to be nearly the same as obtained with an aqueous solution (Janknegt 1985; Deppermann & Lode 1993). Bergan *et al*. (1986, 1987) found the bioavailability of ciprofloxacin to be about 85%, but values as low as 70% have been reported (Dursano *et al.,* 1986).

It is well established that antacids containing divalent or trivalent cations such as Ca^{2+}, Mg^{2+}, or Al^{3+} reduce oral absorption of fluoroquinolones by chelation in the gut (Deppermann & Lode 1993 and Teixeira *et al.,* 1995). Coadministration of antacids, notably combinations of aluminum and magnesium hydroxide, 2 hour before to 6 hour after dosing, consistently reduces bioavailability by 30-90% (Polk *et al*., 1989). The mechanisms involved in drug interactions may be either pharmacokinetic or pharmacodynamic. Pharmacokinetic interactions are the leading events and are caused by alterations in absorption, distribution, metabolism, and elimination of one drug by another. The reported interactions of new quinolones are due to a decrease in antimicrobial activity at low pH, a Mg^{++}-dependent reduction in efficacy, and a probenecid-induced decrease in tubular secretion of ciprofloxacin (Lode, 1988).



(Structure 1)

A number of mechanisms have been reported in the literature based on the changes in the pH of gastric fluid leading to degradation or depressed dissolution and absorption of the antibiotic. Current speculation about the mechanism of this interaction has focused on drug-cation chelation, which is also considered to be the mechanism responsible for the decreased absorption of the antibiotic in presence of antacids.

In this work we illustrated the effect of calcium hydroxide, calcium carbonate, magnesium hydroxide, magnesium

carbonate, magnesium trisilicate, aluminum hydroxide, sodium bicarbonate, and a combination of aluminum and magnesium hydroxides and sulphates on the *in vitro* availability of ciprofloxacin hydrochloric acid. The mechanism of interaction between antibiotic and antacids was also studied.

MATERIALS AND METHODS

Materials

Ciprofloxacin base and ciprofloxacin tablets were gift from Ali Gohar Pharmaceutical Laboratories Ltd., Karachi, Pakistan. The antacids were of Pharmaceutical grade. All antacids were used after passage through a 170-mesh screen.

Table 1
Concentration of ciprofloxacin (%) in presence of antacids at different time intervals in stimulated gastric juice at 278 nm

Sample	Time (min)												
	0	15	30	45	60	75	90	105	120	135	150	165	180
Ciprofloxacin	06.86	88.31	90.46	95.07	95.50	95.60	96.47	96.68	97.65	99.79	99.90	100	100
Cipro + Sodium bicarbonate	02.69	80.94	95.51	98.07	94.29	98.20	96.32	98.20	96.18	92.94	98.34	98.47	98.61
Cipro + Calcium hydroxide	13.19	86.81	89.34	89.49	89.60	90.13	95.50	95.61	95.61	95.71	95.71	95.82	95.93
Cipro + Calcium carbonate	12.01	49.89	51.07	51.40	51.50	51.61	51.83	52.47	52.47	52.58	52.58	52.68	52.79
Cipro+Magnesium carbonate	16.05	45.59	46.54	46.94	46.67	47.21	47.62	48.29	48.56	48.02	46.54	48.83	49.37
Cipro+Aluminum hydroxide	02.66	68.57	68.71	85.54	76.57	84.70	85.33	86.49	83.86	84.00	84.56	86.95	87.09
Cipro+Magnesium hydroxide	06.34	52.20	66.10	66.91	66.77	67.04	67.31	67.18	67.58	68.53	68.80	69.07	69.97
Cipro+Magnesium trisilicate	21.18	42.89	43.16	43.57	43.70	44.11	43.84	44.51	44.78	45.05	44.92	45.32	45.46
Cipro+Magaldrate	04.34	80.07	84.56	84.00	90.45	90.59	90.45	90.45	90.59	90.73	90.45	90.59	90.73

Table 2
Concentration of ciprofloxacin (%) in presence of antacids at different time intervals in stimulated gastric juice at 316 nm

Sample	Time (min)												
	0	15	30	45	60	75	90	105	120	135	150	165	180
Ciprofloxacin	14.65	89.38	90.48	90.85	90.85	91.22	91.22	91.22	93.41	95.25	97.08	99.64	100.01
Cipro + Sodium bicarbonate	35.46	79.67	95.79	99.94	95.33	97.63	96.25	98.55	94.87	91.18	98.09	98.55	99.01
Cipro + Calcium hydroxide	18.31	87.92	88.65	89.02	89.02	89.38	90.12	90.48	90.48	91.22	91.54	92.32	92.68
Cipro + Calcium carbonate	15.75	53.85	13.92	56.05	45.41	57.15	58.25	58.61	58.61	58.61	58.60	58.61	58.61
Cipro+Magnesium carbonate	15.19	46.51	48.35	48.35	49.27	50.20	49.74	50.66	51.58	52.96	52.96	53.88	53.88
Cipro + Aluminum hydroxide	03.06	46.96	47.64	48.74	46.62	51.05	53.16	45.48	66.69	67.03	67.37	69.42	69.76
Cipro+Magnesium hydroxide	07.36	56.18	58.95	62.17	65.39	64.47	68.16	68.62	68.62	69.08	69.08	70.00	70.46
Cipro+Magnesium trisilicate	28.09	46.97	47.43	46.51	47.89	47.89	48.35	49.72	48.81	49.74	49.74	50.20	50.20
Cipro + Magaldrate	21.09	62.95	72.48	68.39	78.60	67.71	74.86	76.56	77.24	77.24	77.58	77.58	77.92

Equipment

The dissolution equipment (USP 25, 2002) was manufactured to the B.P. 2002 (British Pharmacopoeia 2002) standards, which included the dissolution motor and variable speed controller with a stainless steel basket assembly. The top of the basket was modified and replaced by a conical head in order to eliminate air entrapment using dissolution, which is not inconsistent with the present apparatus description. The dissolution container was a flat bottomed glass vessel with an internal diameter of 100 mm and with a capacity of 1-liter dissolution fluid. The variable speed motor was modified to reduce unwanted vibrations by incorporation of 1000 230 μF capacitor in the speed control circuit and was maintained within ± 0.5 % of the required speed.

Rotation of the basket assembly was fixed at 100, ± 0.5 rpm throughout the experiment. The dissolution assembly was

Table 3

Concentration of ciprofloxacin (%) in presence of antacids at different time intervals in stimulated gastric juice at 271 nm

Sample	Time (min)												
	0	15	30	45	60	75	90	105	120	135	150	165	180
Ciprofloxacin	12.62	30.43	36.32	40.81	49.22	69.98	73.62	90.45	98.03	99.99	100.21	100.41	100.97
Cipro + Sodium bicarbonate	05.47	37.16	31.97	35.48	51.04	47.12	49.78	70.40	49.64	54.55	54.79	54.83	57.92
Cipro + Calcium hydroxide	17.53	48.52	36.88	36.46	37.30	35.62	37.16	39.68	43.89	45.01	41.09	46.98	47.12
Cipro + Calcium carbonate	08.13	43.19	36.74	41.51	40.95	41.65	41.65	69.18	46.84	53.29	51.18	49.64	62.94
Cipro+Magnesium carbonate	10.58	34.78	30.43	31.41	25.10	43.61	40.67	31.55	39.40	32.67	39.26	36.60	43.89
Cipro + Aluminum hydroxide	17.11	42.91	36.88	38.70	39.54	39.82	37.79	37.16	39.96	46.70	40.53	35.62	40.25
Cipro+Magnesium hydroxide	02.80	34.92	31.55	28.32	25.52	27.62	29.03	30.57	30.57	37.86	32.39	31.41	37.86
Cipro+Magnesium trisilicate	13.60	42.49	42.49	47.96	45.86	48.80	47.68	55.95	44.59	46.28	49.78	48.52	44.59
Cipro+Magaldrate	09.39	38.70	35.34	36.74	38.00	34.64	36.04	40.11	40.25	42.35	42.35	42.63	43.61

Table 4

Concentration of ciprofloxacin (%) in presence of antacids at different time intervals in stimulated gastric juice at 323 nm

Sample	Time (min)												
	0	15	30	45	60	75	90	105	120	135	150	165	180
Ciprofloxacin	12.69	35.39	36.75	41.17	45.60	58.19	64.99	77.24	93.24	97.32	99.02	99.70	100.04
Cipro + Sodium bicarbonate	02.04	30.96	27.90	29.26	43.55	41.17	40.15	42.53	43.21	52.06	47.98	51.38	52.06
Cipro + Calcium hydroxide	17.35	35.05	36.07	35.73	35.73	35.73	38.45	39.13	43.21	43.21	40.83	46.96	47.30
Cipro + Calcium carbonate	26.20	58.87	70.78	73.84	70.44	72.14	71.12	72.82	70.10	67.37	72.48	72.48	73.16
Cipro+Magnesium carbonate	09.86	29.94	27.22	27.22	23.14	43.55	37.09	29.94	35.39	30.96	33.34	34.03	37.43
Cipro+Aluminum hydroxide	17.35	36.75	34.03	35.05	36.75	35.73	38.45	31.30	36.41	43.21	35.05	34.37	38.79
Cipro+Magnesium hydroxide	03.06	27.22	26.20	25.18	22.46	25.52	27.22	27.90	27.22	29.26	29.94	28.58	30.28
Cipro+Magnesium trisilicate	13.95	37.43	41.17	41.85	44.57	44.91	47.64	43.55	43.89	44.23	47.98	48.32	48.32
Cipro+Magaldrate	09.18	30.62	31.64	34.03	36.41	31.98	33.68	38.45	38.79	39.13	38.45	43.89	43.89

Table 5
Various dissolution times and first-order dissolution constants in the presence some of antacids

Sample	Simulated gastric juice			Simulated intestinal juice								
	$T_{50\%}$	$T_{90\%}$	K_{278nm}	$T_{50\%}$	$T_{90\%}$	K_{316nm}	$T_{50\%}$	$T_{90\%}$	K_{271nm}	$T_{50\%}$	$T_{90\%}$	K_{323nm}
Ciprofloxacin	4.96	6.57	0.014	4.92	6.53	0.014	6.15	7.76	0.004	6.19	7.80	0.004
Cipro + Sodium bicarbonate	4.43	6.04	0.023	4.35	5.96	0.025	6.03	7.63	0.004	6.23	7.84	0.003
Cipro + Calcium hydroxide	4.72	6.33	0.017	4.92	6.53	0.014	5.47	7.08	0.008	5.40	7.01	0.009
Cipro + Calcium carbonate	6.17	7.78	0.004	6.01	7.62	0.004	5.89	7.50	0.005	5.61	7.22	0.007
Cipro + Magnesium carbonate	6.18	7.79	0.004	6.90	8.51	0.002	6.43	8.04	0.003	6.64	8.25	0.002
Cipro + Aluminum hydroxide	5.16	6.77	0.011	5.70	7.31	0.006	6.54	8.15	0.002	6.59	8.20	0.002
Cipro + Magnesium hydroxide	5.72	7.33	0.006	5.68	7.29	0.006	6.99	8.60	0.001	7.092	8.70	0.001
Cipro + Magnesium trisilicate	6.38	7.99	0.003	6.24	7.85	0.003	6.41	8.02	0.003	6.30	7.91	0.003
Cipro + Magaldrate	5.64	7.25	0.007	5.91	7.52	0.005	6.44	8.05	0.003	6.43	8.04	0.003

Table 6
Adsorption capacities (%) of antacids towards ciprofloxacin analyzed by reversed-phase HPLC

Sample	Simulated gastric juice		Simulated intestinal juice	
	Peak Area	% Drug absorbed	Peak Area	% Drug absorbed
Cipro + Sodium bicarbonate	191698	22.50	183377	53.48
Cipro + Calcium hydroxide	149786	39.50	219751	44.25
Cipro + Calcium carbonate	46506	81.20	179063	54.57
Cipro + Magnesium carbonate	196566	20.60	194027	50.77
Cipro + Aluminum hydroxide	236644	04.40	23440	94.05
Cipro + Magnesium hydroxide	66587	73.10	184295	53.24
Cipro + Magnesium trisilicate	109616	55.70	7145	98.19
Cipro + Magaldrate	9864	96.10	186437	52.70

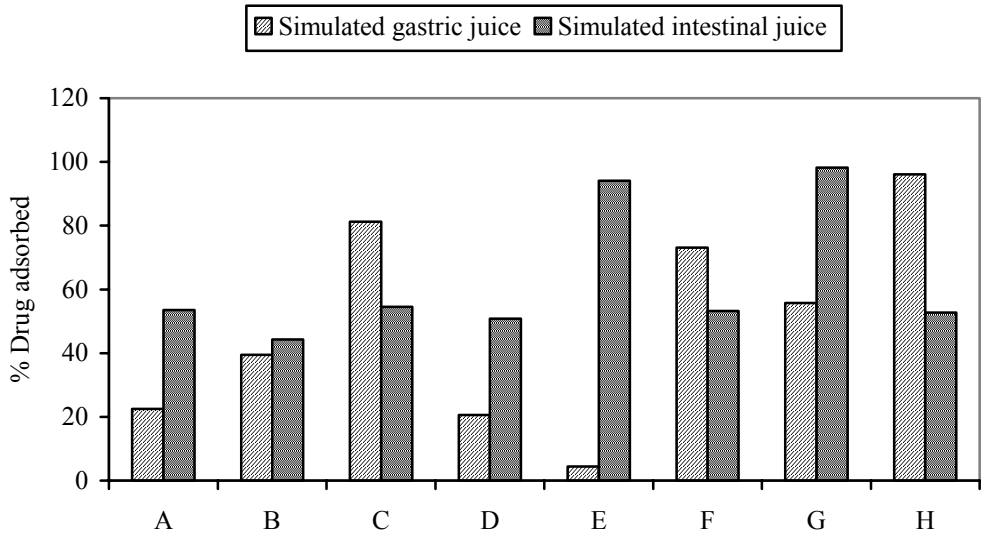
immersed in water bath at 37 ± 0.1°C. Drug in each case was analyzed either by measuring the absorbance of aliquots at 278 and 316nm on a UV/VIS (Shimadzu 1601) spectrophotometer, or by RP-HPLC method. The chromatographic system Shimadzu comprised of LC 10AT VP pump, SPD 10A VP UV/VIS detector and Communication Bus Module integrator (102). Separations were performed on a Shim-pack CLC-ODS 0.4 x 25 cm, 5µm particle size column at 37°C. The samples were introduced through a Rheodyne injector valve with a 20-µL sample loop using the mobile phase acetonitrile-water [13:87 V/V] and pH was adjusted at 3.2 with 85% orthophosphoric acid. Mobile phase filtered through a 0.2µm Millipore filter and degassed in an ultrasonic bath. The flow rate of the mobile phase was 1.5 ml/min and UV detection was performed at 278 nm.

Procedure for dissolution studies

In vitro availability was obtained for ciprofloxacin hydrochloride on the dissolution apparatus as detailed above. The dissolution fluid was 1000 ml of simulated gastric and intestinal juices. Samples were withdrawn periodically with an interval of 15 min for 180 min. The volume of dissolution fluid was maintained by adding an equal amount of dissolution fluid withdrawn, which had previously been maintained at the same temperature in the same bath.

Table 7
Adsorption capacities (%) of antacids towards ciprofloxacin in simulated gastric and intestinal juices

Sample	Adsorption capacity [mg (mmol)/g] for ciprofloxacin			
	Simulated gastric juice		Simulated intestinal juice	
	278 nm	316 nm	271 nm	323 nm
Sodium bicarbonate	599 (0.0146)	125 (0.0104)	520 (0.0132)	212 (0.0130)
Magnesium carbonate	491 (0.0120)	139 (0.0116)	532 (0.0135)	224 (0.0138)
Calcium carbonate	258 (0.0063)	117 (0.0097)	540 (0.0137)	230 (0.0142)
Magnesium hydroxide	581 (0.0142)	122 (0.0101)	490 (0.0124)	194 (0.0119)
Calcium hydroxide	734 (0.0179)	107 (0.0089)	540 (0.0137)	230 (0.0142)
Aluminum hydroxide	284 (0.0069)	123 (0.0102)	555 (0.0141)	229 (0.0141)
Magnesium trisilicate	341 (0.0083)	102 (0.0085)	216 (0.0054)	110 (0.0067)
Magaldrate	141 (0.0098)	118 (0.0098)	614 (0.0156)	260 (0.0160)



A = Cipro+$NaHCO_3$, B = Cipro+$MgCO_3$, C = Cipro+$CaCO_3$, D = Cipro+$Mg(OH)_2$
E = Cipro+$CaCO_3$, F = Cipro+$AI(OH)_3$, G = Cipro+$Mg(SiO_3)_3$, H = Cipro+Magaldrade

Fig. 1: Adsorption of ciprofloxacin by antacids

In testing the effect of antacids on the dissolution behaviour of the antibiotic 2g of antacid was added to the dissolution medium with appropriate concentration of ciprofloxacin at the start of the experiment and aliquots were drawn similarly. The concentration of the antibiotic in solution was determined by the standard method. Data is shown in tables 1-4 and the results were satisfactorily reproducible.

Adsorption studies

The desired quantities of antacid powders were weighed accurately in 25 ml Erlenmeyer flasks. Aqueous solution of ciprofloxacin (10 ml of appropriate concentration) was added to each flask. The flasks were shaken in a constant temperature bath at 37°C for 2 hours. It had been established previously that equilibrium was attained within this period. At the end of this time aliquots were filtered through a Millipore filter (0.2 μm) and analyzed for the residual antibiotic content. The quantities of ciprofloxacin adsorbed were calculated by subtracting the equilibrium concentration from the initial concentration. No difference in concentration was found in samples to which antacid has not been added.

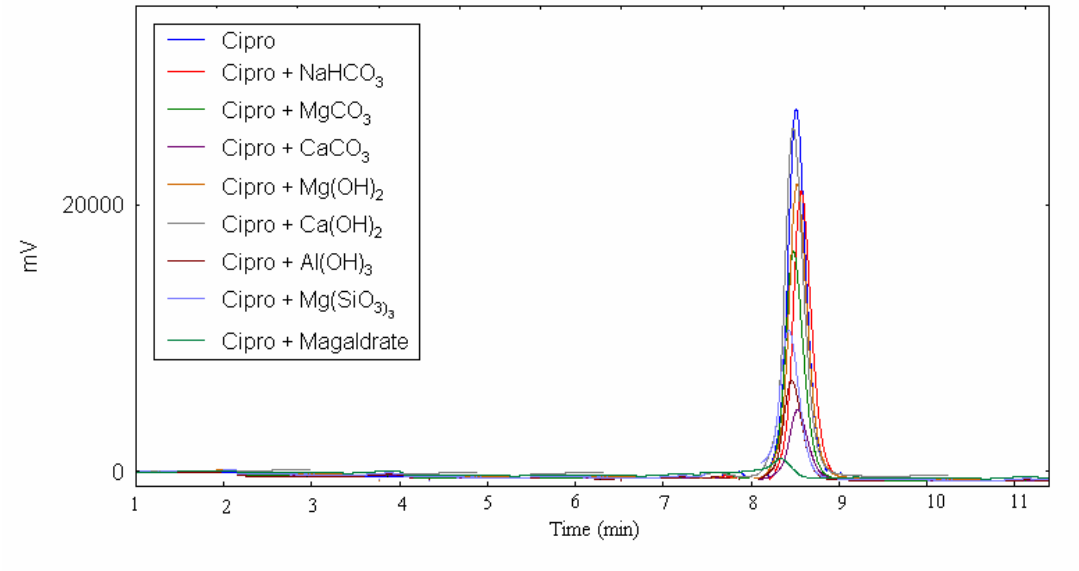


Fig. 2

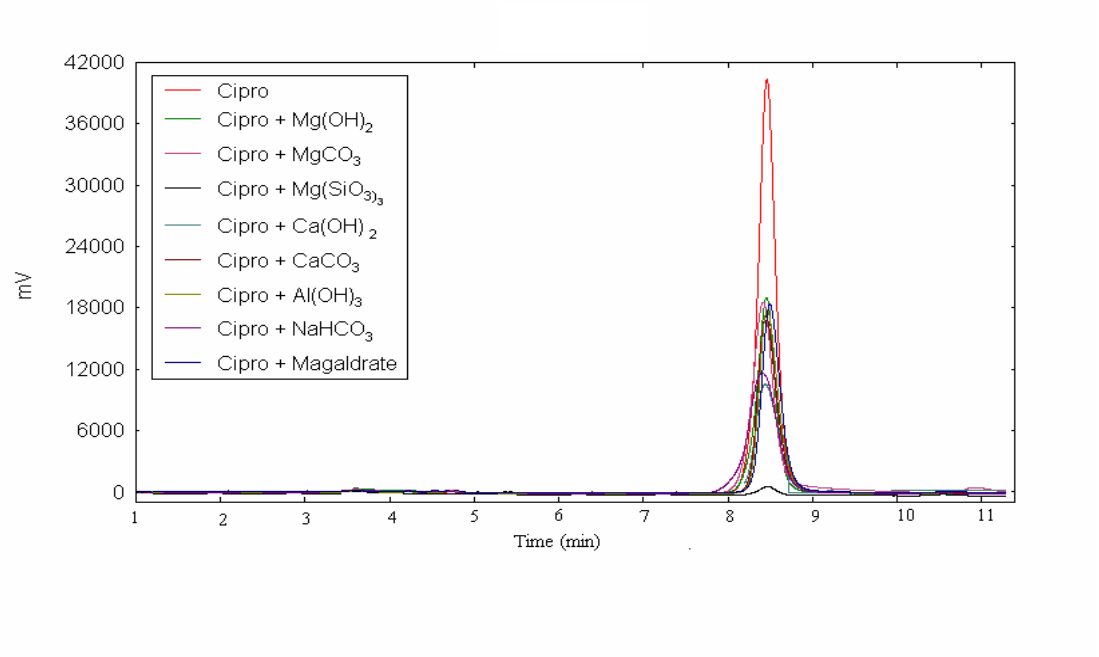


Fig. 3

RESULTS AND DISCUSSION

Ciprofloxacin is a widely used broad-spectrum oral quinolone antibiotic. In many clinical situations, oral ciprofloxacin has been used in place of intravenous antibiotics to facilitate the earlier discharge of patients and/or preventing the admission of patients. Like the tetracycline antibiotics, the interaction between oral ciprofloxacin and antacids is a chelation reaction. In order for the interaction to occur, the cation must be multivalent. As will be discussed, the antacids with which oral ciprofloxacin has been shown to interact are sodium bicarbonate, calcium hydroxide, calcium carbonate,

aluminum hydroxide, magnesium hydroxide, magnesium carbonate, magnesium trisilicate and magaldrate. It is postulated that the multivalent cations complex with the 3-ketone and 4-carboxylic acid groups on the ciprofloxacin molecule. The complex formed is an insoluble, non-absorbable compound.

The interactions between these antacids and ciprofloxacin are particularly dramatic when the two agents are given simultaneously. As shown in tables 1-4, the availability of ciprofloxacin in simulated gastric and intestinal juices at different time intervals is reduced to 54% when it is given simultaneously with aluminum and magnesium containing antacids. These reductions in ciprofloxacin availability by antacids may be due to the relative excess of aluminum and magnesium cations in a typical dose of antacid. The first-order dissolution constants, $T_{50\%}$ and $T_{90\%}$, of ciprofloxacin hydrochloride in presence of various antacids in simulated gastric and intestinal juices are given in table 5. Ciprofloxacin exhibits two λ_{max} one at 278 nm and the other at 316 nm, which are attributed to the carbonyl and carboxylic groups respectively. It was imperative to study changes in both of the λ_{max} so that possible site drug antacid interactions be positioned. Results given in tables 1-5 show these interactions at both wavelengths.

As can be seen from these profiles, the availability of ciprofloxacin hydrochloride decreased in presence of all antacids studied in both simulated gastric and intestinal juices except sodium hydrogen carbonate, which decreased merely in simulated intestinal juice. These interactions occur regardless of the dosage form of antacids (i.e., liquid suspension or tablets).

In our studies, when sodium hydrogen carbonate was added to the dissolution medium, in simulated gastric juice, the concentration of hydrogen ion decreased due to evolution of CO_2, which led to an increase in pH that may be responsible for increased rate of dissolution as compared with other antacids in simulated gastric juice. While it did not happen in simulated intestinal juice, that's why there was a decreased rate of dissolution similar to other antacids i.e. 49.7% and 57.9% after an interval of 90 min and at the end of experiment.

Frenning and Stromme (2003) concluded that all capsular medications were functionally inactive when given under conditions in which the contents of stomach were neutral or alkaline. He proposed an inhibitory effect of increased pH on dissolution of the capsule itself. According to Arayne *et al.* (1984) pH is probably not a major factor in dissolution of capsule medications. They found that at body temperature, varying pH did not affect the average release time of capsule, however at room temperature pH did affect the release time.

Magnesium trisilicate, which is insoluble in both dissolution media, exhibited a significant retardation effect on the dissolution of ciprofloxacin. After an interval of 90 minutes, 44% of the drug was present in the solution that was consistent up to 180 minutes. The T_{50} and T_{90} values of ciprofloxacin, in presence of magnesium trisilicate, were found to be 6.4min and 8.0 min respectively in both media.

In case of aluminum hydroxide 85% of the drug was present in the simulated gastric juice after the half interval of the experiment and at the end of the experiment 87 % was at 278 nm whilst 53 % and 69.7 % at 316 nm in the same dissolution medium respectively. In simulated intestinal juice the availability of the drug was 37.7 % and 40.2 % after 90 and 180 minutes while there was similar absorption at the both wavelengths of maximum absorptions. When aluminum hydroxide and magnesium trisilicate were added to the dissolution media, they remained in suspended and undissolved state. There are two possibilities for the slow rate of dissolution, either due to increase in pH or absorbent properties of these two antacids. According to Arayne *et al*. (1984[a]) from the pH studies it is quite clear that pH is not a major factor for prolonged dissolution behavior. The chelating effect of ciprofloxacin with Mg^{2+} and Al^{3+} may be responsible for the prolonged and incomplete dissolution.

From the results listed in tables 1-5, it is quite vivid that the availability of ciprofloxacin decreased in presence of calcium and magnesium carbonate (in a concentration of 0.2 % W/V). In presence of even lower levels of antacid, calcium carbonate also reduced ciprofloxacin availability; the amount dissolved after 90 min was 51.8 % and after 180 min 52.8 % with comparatively high values of T_{50} and T_{90}.

In magnesium carbonate case, merely 47.6 % of the drug was present in simulated gastric juice after an interval of 90 min and 49.4 % of the drug was present at end of the experiment with T_{50} and T_{90} values of 6.2 and 7.8 min, respectively, while in simulated intestinal juice the availability of the drug after intervals of 90 and 180 min was 40.6 and 43.9 %, respectively.

The availability of ciprofloxacin in presence of calcium hydroxide was 95% at half of interval and remained consistent till end of the experiment in simulated gastric juice at both wavelengths of maximum absorptions, whilst 37.1 and 47.2% at 90 and 180 minutes, respectively in simulated intestinal juice.

Magnesium hydroxide that is soluble in simulated gastric juice exhibited an insignificant effect on the availability of ciprofloxacin. After an interval of 90 min, 70% of the drug was present in solution, which was consistent up to end of the experiment, while in simulated intestinal juice 29 and 37% was present respectively.

Magaldrate, a combination of aluminum and magnesium hydroxides and sulphates showed insignificant effect on the availability of ciprofloxacin in simulated gastric juice. After an interval of mere 15 minutes, 80 % of the drug was present in simulated gastric juice and remained consistent till the end, while in simulated intestinal juice there was significant retardation in the availability of the drug. At half of the time, 36 % of the drug was available in the medium and in 180 min 43 % of the drug had been recovered.

Thus, it is clear that the availability of ciprofloxacin can be retarded by small amounts of antacids containing polyvalent cations. Although it had previously been suggested that antacids decrease the availability of other antibiotics by raising the pH of the medium (Arayne *et al.,* 2004) and the dissolution rate is markedly reduced at high pH values, there was no significant enhancement in pH by the addition of these antacids in the dissolution medium.

On the other hand, ciprofloxacin was found to be strongly adsorbed on various antacids. Figure1 is plotted according to the Langmuir equation (Jaroniec *et al.,* 1983) that may be written as

$$\frac{c}{x/m} = \frac{1}{ab} + \frac{c}{b}$$

where c is the equilibrium concentration of the solute, x/m is the amount of the solute adsorbed per unit weight of the adsorbent, and a and b are constants. The adsorption capacities of the antacids are also listed in table 6, which had been studied using RP-HPLC, their chromatograms are shown in figs. 2 and 3. It is evident from these studies that all antacids adsorbed ciprofloxacin to different extents. Magaldrate and calcium carbonate in simulated gastric juice exhibited relatively higher adsorption capacities, while in simulated intestinal juice magnesium trisilicate and calcium carbonate exhibited higher adsorption capacities.

It is thus clear that antacids containing polyvalent cations can retard the availability of ciprofloxacin. These studies indicate that ciprofloxacin is strongly adsorbed on antacids; magnesium trisilicate, calcium carbonate and magaldrate exhibited relatively higher adsorption capacities. The adsorption of ciprofloxacin by antacids may be responsible for the marked retardation of availability of ciprofloxacin.

CONCLUSIONS

The availability of oral ciprofloxacin can be affected by the concurrent ingestion of antacids containing multivalent cations. The most dramatic ciprofloxacin interactions are with antacids containing aluminum cation. However, significant interactions have been seen with antacids containing magnesium and calcium cations. It is important to avoid taking ciprofloxacin concurrently with multivalent cation containing medications. It is imperative to be aware of these interactions because they may so greatly affect ciprofloxacin availability that it may compromise the patient's outcome. When ciprofloxacin - antacid interaction is detected there are a number of alternatives that should be pursued so as to minimize or eliminate these interactions. Finally, patients receiving oral ciprofloxacin should be counseled about how to take this medication and how to avoid antacid-drug interactions.

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