

Comparative anti-ulcerogenic study of pantoprazole formulation with and without sodium bicarbonate buffer on pyloric ligated rat

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ABSTRACT

Objective: To compare the anti-ulcer activity of buffered pantoprazole tablet against plain pantoprazole in pyloric ligated rats. **Materials and Methods:** *In vivo* pyloric ligated ulcerogenesis model was used to assess the effect of buffered pantoprazole on the volume of the gastric content, pH, total and free acidity, and ulcerogenic lesion. Pantoprazole level in gastric content and concurrently in stomach tissue was assessed by High Performance Liquid Chromatography (HPLC) analysis. **Results:** Buffered tablet effectively increases the pH of the gastric content above 4 up to 6 h ($P < 0.001$) protecting pantoprazole from acid degradation resulting in high concentration in the gastric content and stomach tissue. **Conclusions:** This study substantiates better, faster and prolonged bioavailability of pantoprazole-buffered tablet compared to plain pantoprazole.

Key words: Buffered tablet, pantoprazole, proton pump inhibitors, pyloric-ligation

INTRODUCTION

Peptic ulcer disease comprises a group of chronic ulcerative conditions that primarily affect the gastric mucosa and proximal duodenum. H_2 -blockers like cimetidine, ranitidine and famotidine reduce the amount of acid produced by stomach. Proton pump inhibitors (PPIs) are a group of drugs whose main action is pronounced and long-lasting reduction of gastric acid production.

At neutral pH, PPIs are chemically stable, lipid-soluble weak bases devoid of acid-inhibitory activity. The PPIs are given in

an inactive form, which is neutrally charged or lipophilic and readily crosses cell membrane into intracellular compartments that have acidic environments. In an acidic environment, the inactive drug is protonated and rearranges into its active form.^[1] Most of the PPIs are formulated in an enteric-coated solid dosage form (either a delayed-release capsule or tablet) or as an intravenous solution (a product for reconstitution). The enteric dosage forms are employed because they are acid-labile, thus it is important that these drugs should not be exposed to low pH gastric acid prior to absorption. Although PPIs are stable at alkaline pH, they are destroyed rapidly as pH falls (e.g., by gastric acid).

The current frontier in PPI therapy is immediate-release forms combined with sodium bicarbonate buffer which prevent degradation before absorption. Such dosage forms are advantageously devoid of any enteric coating or delayed or sustained-release delivery mechanisms, and comprise a PPI and at least one buffering agent to protect the PPI against acid degradation.^[2]

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Ley *et al.*,^[3] in 2001, reported bioavailability of a crushed pantoprazole tablet after buffering with sodium hydrogencarbonate (bicarbonate) or magaldrate relative to the intact enteric-coated pantoprazole tablet in healthy male volunteers. Ferron *et al.*,^[4] in 2003, reported the bioavailability of pantoprazole administered as a suspension in sodium bicarbonate solution compared to enteric-coated tablet in an open-label, randomized, two-period crossover study on healthy fasting human subjects.

Till now to the best of our knowledge no such study has been reported on buffered formulations of esomeprazole, rabeprazole, omeprazole or pantoprazole to establish the therapeutic effectiveness comparative to plain drugs. The study was designed to compare plain pantoprazole sodium sesquihydrate with buffered pantoprazole sodium (sodium bicarbonate) on pH profile in stomach fluid, ulcer-protective efficacy and bioavailability at the active site.

MATERIALS AND METHODS

Sample

Marketed pantoprazole sodium 40 mg with 1680 mg sodium bicarbonate buffered tablets manufactured by a World Health Organization; Good Manufacturing Practices (WHO GMP) certified leading Indian pharmaceutical company was procured from the market. Pantoprazole sodium sesquihydrate bulk drug sample was obtained as gift sample from a pharmaceutical manufacturer.

In vitro studies

In vitro pH profile study of pantoprazole buffered formulation was carried out along with plain pantoprazole to check the stomach acid neutralizing capacity of buffered formulation compared with plain pantoprazole at different time intervals. This study was carried out in hydrochloric acid (HCl) buffer (pH=2) and artificial stimulated gastric fluid media.

pH Profile of formulation: HCl buffer (pH=2) was prepared by adding 50 ml of 0.2N KCl to 13 ml of 0.2N HCl and final volume was adjusted to 200 ml in a volumetric flask.^[5] Pantoprazole intact buffered tablet, crushed pantoprazole buffered tablet and plain pantoprazole 40 mg each was added to 100 ml of HCL (2 pH). pH of the resultant media was determined initially and at different time intervals after addition of formulation using a digital pH meter.

pH Profile of formulation in artificial gastric juice: Stimulated artificial gastric fluid was prepared by dissolving 2.0 g of NaCl and 3.2 g of pepsin (1:3000, Aristo Pharmaceuticals Ltd., Bhopal) in distilled water. To this 80 ml of 1M HCl was added and diluted up to 1000 ml with distilled water.^[6] Intact pantoprazole buffered tablet, crushed pantoprazole buffered tablet and plain pantoprazole, 40 mg each (equivalent weight)

was added in 100 ml of gastric juice and pH measured at different time intervals.

Test animals

Laboratory-bred Wistar albino rats of both sexes weighing between 150-200 g maintained under standard laboratory conditions at $22 \pm 2^\circ\text{C}$, relative humidity $50 \pm 15\%$ and photoperiod (12-h dark and light) were used for the experiment. Commercial pellet diet (Hindustan Lever, India) and water were provided *ad libitum*. Approval was obtained from Institutional Animal Ethical Committee before carrying out the experiments.

Pyloric ligation-induced gastric ulceration

Preparation of drug sample

Pantoprazole sodium was dissolved in normal saline and filtered. Pantoprazole buffered tablet was crushed in pestle mortar and dissolved in normal saline and filtered. The drug solutions were prepared immediately before administration.

Experimental model for antiulcer study

Twenty-four hour-fasted animals were divided into three groups of 15 rats each. Plain pantoprazole and buffered pantoprazole tablet dissolved in normal saline were administered orally at 40 mg/kg dose. Negative control group was treated with normal saline (0.5 ml/100 g) only.

Normal saline (0.5 ml/100 g), plain pantoprazole (40 mg/kg) and buffered pantoprazole (40 mg/kg) were administered orally 30 min before pyloric ligation. Under light ether anesthesia, the abdomen was opened by a small midline incision at one cm below the xiphoid process. Stomach was exposed and a tight knot was applied around the pyloric sphincter. During this process, care was taken to avoid traction to the pylorus or damage to its blood supply. The stomach was placed carefully and abdomen wall closed by interrupted sutures.^[7] Two, 4 and 6 h after pyloric ligation five animals of each group were sacrificed by decapitation, abdomen was opened and the stomach was isolated after suturing the lower esophageal end. The stomach was then cut open along the greater curvature, gastric contents were collected in a graduated centrifuge tube, volume measured, pH determined, and kept for pantoprazole analysis. Stomach surface was cleaned with cold normal saline, then ulcer index was determined using a hand lens and ulcer grading following the scoring system suggested by Puurunen.^[8] Stomach tissue was weighed and kept for estimation of pantoprazole.

Ulcer index was calculated with the following formula: $\text{Ulcer index} = 10/X$

Where, $X = \text{Total area of stomach mucosa} / \text{Total ulcerated area}$ ^[9]

Gastric fluid (one ml diluted with 9 ml of distilled water) was titrated against 0.01 NaOH using Topper's reagent till orange

color, which corresponds to free acidity and further titrated to pink color, and total volume of NaOH corresponds to total acidity.^[10]

Acidity expressed as Vol. of NaOH $\times$ Normality $\times$ 100 / 0.1 mEq/L/100 g

Estimation of pantoprazole in stomach content and stomach tissue

Preparation of stomach content sample

Stomach content was collected in graduated centrifuge tube and centrifuged at 10000 RPM for 10 min. The supernatant was collected, diluted 10 fold with 0.9% NaCl and kept on ice, and used for estimation of pantoprazole.

Preparation of stomach tissue homogenate

The finely excised stomach tissue was kept in chilled 0.9% NaCl after estimation of ulcer index; 500 mg of stomach tissue was homogenized with 5 ml of chilled 0.9% NaCl using a Teflon-glass tissue homogenizer and centrifuged at 3000 rpm (4°C) for 10 min. The supernatant was collected, kept on ice and used for estimation of pantoprazole.

Assay of pantoprazole by High Performance Liquid Chromatography (HPLC): Pantoprazole was estimated following HPLC assay method developed by Dentinger *et al.*^[11] The instrumentation included a constant-flow solvent-delivery system with a low-pressure gradient unit, a C₁₈ column maintained at room temperature, a variable-volume injector, a photo diode array detector set at 280 nm with sensitivity set at 0.01, and a system controller. The mobile phase consisted of acetonitrile and aqueous 0.05 M dibasic potassium phosphate buffer adjusted to pH 7.0 with dilute phosphoric acid (40:60, v/v). The mobile phase was filtered and degassed, and the flow rate was set at 1.0 mL/min (LC-20 AD, shimadzu, Japan). Ten μ l of each sample was injected into the HPLC system, and each sample was assayed in duplicate. Concentration of unknown sample was analyzed from the standard curve by noting the peak height.

Preparation of standard solutions and standard curve

A stock solution equivalent to one mg/ml of pantoprazole sodium was prepared from analytical grade pantoprazole sodium sesquihydrate in deionized, distilled water. Standard samples of pantoprazole sodium were prepared by diluting the stock solution with deionized, distilled water to 2, 20, 40, 60, 80, 100, 120, 140, 160, 180 and 200 μ g/ml and peak height was noted. A 20 μ g/ml concentration of pantoprazole sodium was assayed in duplicate after approximately every tenth sample as an external control. A linear regression concentration standard curve of pantoprazole was plotted against respective peak height. The standard curve was linear ($r^2 > 0.95$) over the working range of concentrations.

Statistical analysis

The results were expressed in terms of mean $\pm$ SEM. Experimental data of various physical and biochemical parameters were analyzed using one-way Analysis of Variance (ANOVA) followed by Turkey-Kramer multiple comparison test. *P* values < 0.05 were considered statistically significant.

RESULTS

Tables 1 and 2 represent the neutralizing capacity of pantoprazole buffered formulation in HCl buffer (pH=2) and artificial gastric fluid at different time intervals. Intact pantoprazole buffered tablet increases the pH of HCl buffer to 7.68 after 50 min whereas triturated buffered tablet showed pH 5.22 after 5 min, and 8.01 after 50 min compared to pH 3.12 of plain pantoprazole. In stimulated gastric juice pH was increased to 8.68, 8.50 and 3.40 respectively by pantoprazole intact buffered tablet, triturated tablet and plain pantoprazole after 45 min.

Effect of pantoprazole buffered tablet was assessed on pylorus-ligated gastric ulceration in rats. The parameters investigated were ulcer grading, volume of gastric content, pH of gastric content, free acidity, total acidity and concentration of pantoprazole in stomach content as well as stomach tissue homogenate.

Table 1: pH profile of sodium bicarbonate buffered pantoprazole tablet in 2 pH hydrochloric acid

Time interval (min)	pH of media		
	Intact buffered tablet	Triturated buffered tablet	Plain pantoprazole
0	2.01	2.01	2.01
5	3.54	5.22	2.02
15	4.65	7.24	2.02
25	5.21	9.03	3.01
30	5.78	8.50	3.05
45	6.04	7.92	3.04
50	7.68	8.01	3.12

Table 2: pH profile of sodium bicarbonate buffered pantoprazole tablet in stimulated gastric juice

Time interval (min)	Intact buffered tablet	Triturated buffered tablet	Plain pantoprazole
0	2.02	2.02	2.02
2	2.07	9.00	2.05
5	3.52	9.50	2.55
15	4.07	9.52	3.00
20	5.53	9.55	3.06
25	6.04	8.52	3.03
30	7.13	8.09	3.07
35	8.52	8.35	3.24
40	8.57	8.50	3.54
45	8.68	8.50	3.40

Buffered pantoprazole tablet prevented the formation of gastric lesion 2 h after pyloric ligation, which was highly significant ($P<0.01$) compared with plain pantoprazole. After 4 h of pyloric ligation the buffered tablet reduced the ulcer grading further to zero and after 6 h the ulcer grading was found zero in both the treated groups as tabulated in Table 3. Volume of gastric content was reduced extreme significantly ($P<0.001$) by buffered pantoprazole tablet as well as plain pantoprazole at 40 mg/kg dose after 6 h of pyloric ligation. Buffered pantoprazole tablet and plain pantoprazole at 40 mg/kg significantly also reduced total acidity ($P<0.001$) and free acidity ($P<0.001$) as compared to the control group. Buffered pantoprazole tablet showed extremely significant difference in values of gastric pH, volume of content, free and total acidity of stomach content when compared with plain pantoprazole ($P<0.001$) 6 h after pyloric ligation.

Concentration of pantoprazole in stomach content and stomach tissue homogenate after 2, 4 and 6 h of pyloric ligation was estimated by HPLC method in buffered pantoprazole tablet and plain pantoprazole-treated groups. The concentration of pantoprazole in stomach content of buffered tablet-treated

groups, was respectively 1605.62 ± 27.82 , 862.90 ± 9.15 and 450.05 ± 5.60 $\mu\text{g/ml}$ compared to 678.45 ± 7.31 , 160.34 ± 3.55 and 450.05 ± 5.60 $\mu\text{g/ml}$ of plain pantoprazole-treated groups respectively at 2, 4 and 6 h after pyloric ligation. The concentration of pantoprazole in stomach tissue homogenate of buffered tablet-treated groups was 164.20 ± 4.77 , 65.21 ± 4.09 and 33.44 ± 2.78 $\mu\text{g/ml}$ respectively compared to 86.56 ± 3.63 , 42.50 ± 2.81 and 8.70 ± 1.02 $\mu\text{g/ml}$ of plain pantoprazole-treated groups at 2, 4 and 6 h after pyloric ligation as represented in Table 4. The concentration of pantoprazole in stomach content and stomach tissue homogenate of buffered pantoprazole-treated groups was extremely high ($P<0.001$) at all the time intervals.

DISCUSSION

Pantoprazole sodium sesquihydrate is a white to off-white crystalline powder having weakly basic and acidic properties, freely soluble in water, stability in aqueous solution is pH-dependent and the rate of degradation increases with decreasing pH. Prodrug pantoprazole accumulates in the acidic compartment of parietal cells and is converted to the active

Table 3: Effect of different pantoprazole formulations on secretory parameters and ulcer index in pyloric ligated rats

Treatment (mg/kg, p.o)	Sacrifice time after pyloric ligation in h	pH of gastric content (Mean $\pm$ SEM)	Volume of gastric content in ml/100g (Mean $\pm$ SEM)	Free acidity in meq/L/ 100g (Mean $\pm$ SEM)	Total acidity in meq/L/ 100g (Mean $\pm$ SEM)	Ulcer Grading (Mean $\pm$ SEM)
Vehicle	2 h	2.10 ± 0.09	2.58 ± 0.14	133.63 ± 6.02	225.88 ± 5.76	2.37 ± 0.05
Plain pantoprazole		$3.8 \pm 0.06^*$	$1.98 \pm 0.22^*$	$70.93 \pm 4.51^{***}$	$131.29 \pm 4.72^{***}$	$0.62 \pm 0.01^{***}$
Pantoprazole buffered Tablet		$5.7 \pm 0.08^{***b}$	$1.65 \pm 0.12^{***}$	$73.77 \pm 3.09^{***}$	$84.92 \pm 3.48^{***c}$	$0.25 \pm 0.01^{***b}$
Vehicle	4 h	1.8 ± 0.02	3.43 ± 0.06	148.48 ± 6.32	296.97 ± 6.30	2.50 ± 0.08
Plain pantoprazole		$4.5 \pm 0.11^{***}$	$2.02 \pm 0.05^{***}$	$52.65 \pm 2.20^{***}$	$107.03 \pm 5.38^{***}$	$0.38 \pm 0.01^{***}$
Pantoprazole buffered Tablet		$6.2 \pm 0.12^{***a}$	$1.54 \pm 0.01^{***}$	$34.75 \pm 2.15^{***}$	$58.89 \pm 2.33^{***c}$	Nil
Vehicle	6 h	1.7 ± 0.04	3.57 ± 0.08	165.61 ± 5.22	326.67 ± 7.67	2.75 ± 0.11
Plain pantoprazole		$3.2 \pm 0.08^*$	$2.53 \pm 0.07^{***}$	$122.75 \pm 5.00^{***}$	$163.66 \pm 5.30^{***}$	Nil
Pantoprazole buffered Tablet		$6.8 \pm 0.14^{***c}$	$0.95 \pm 0.01^{***c}$	$44.55 \pm 2.43^{***c}$	$111.32 \pm 4.78^{***c}$	Nil

n = 5; * $P<0.05$ and *** $P<0.001$ compared to respective control groups. ^a $P<0.05$, ^b $P<0.01$, ^c $P<0.001$ for pantoprazole buffered tablet compared to plain pantoprazole for the respective time interval groups individually. All the values are expressed per 100 gm body weight of experimental rats

Table 4: Effect of different pantoprazole formulations on free pantoprazole level in stomach content and pyloric ligated rats

Treatment (mg/kg, p.o)	Sacrifice time after pyloric ligation in hrs	Concentration of pantoprazole in stomach content in $\mu\text{g/ml}/100\text{gm b.w}$ (Mean $\pm$ SEM)	Concentration of pantoprazole in stomach tissue homogenate in $\mu\text{g/gm}$ of stomach (Mean $\pm$ SEM)
Vehicle	2 hours	--	--
Plain pantoprazole		678.45 ± 7.31	86.56 ± 3.63
Pantoprazole buffered Tablet		$1605.62 \pm 27.82^{***}$	$164.20 \pm 4.77^{***}$
Vehicle	4 hours	--	--
Plain pantoprazole		160.34 ± 3.55	42.50 ± 2.81
Pantoprazole buffered Tablet		$862.90 \pm 9.15^{***}$	$65.21 \pm 4.09^{***}$
Vehicle	6 hours	--	--
Plain pantoprazole		34.43 ± 2.15	8.70 ± 1.02
Pantoprazole buffered Tablet		$450.05 \pm 5.60^{***}$	$33.44 \pm 2.78^{***}$

n = 5, *** $P<0.001$ when pantoprazole buffered tablets was compared with plain pantoprazole group for the respective time interval individually.

form, a sulfanilamide, which binds to hydrogen-potassium-ATP-ase at the secretory surface of gastric parietal cells. Inhibition of hydrogen-potassium-ATP-ase blocks the final step of gastric acid production, leading to inhibition of both basal and stimulated acid secretion.

At neutral pH pantoprazole is a weak base, non-ionized, lipid-soluble and thereby freely passes through physiologic membranes, including the cellular membranes of the parietal cells. It is believed that the non-ionized pantoprazole moves into the acid-secreting portion of the parietal cell, the secretory canaliculus. Once in the acidic milieu of the secretory canaliculus, the pantoprazole is apparently protonated (ionized) and converted to the active form of the drug. Ionized pantoprazole is membrane-impermeable and forms disulfide covalent bonds with cysteine residues in the alpha subunit of the proton pump.

The *in vitro* drug profile showed that the triturated buffered tablet immediately increases the pH of gastric content. Pantoprazole is rapidly absorbed orally, administered as a 40 mg enteric coated tablet, is quantitatively absorbed from the basic environment of the small intestine. Its absolute bioavailability is 77% and does not change upon multiple dosing.^[13] In the present study buffered pantoprazole tablet was shown to possess excellent acid-neutralizing activity in comparison to plain pantoprazole tablet *in vitro* by increasing pH of buffered HCl (2 pH) and stimulated gastric fluid above 3.5 within 5 min. The pH of the medium first increases to the highest point and then starts falling only with triturated buffered tablets. The crushed tablet led to a sharper rise in pH as the crushing made the buffered layer readily available to react with the acidic media and neutralization. The pH of media later falls and come close to neutral as may be the basic ions (anions) are not available to maintain the media pH on the higher side. The net increase in pH with crushed and uncrushed tablets was in the same range at the end of 50 min, as 7.68 and 8.01 in 2 pH HCl, and 8.68 and 8.50 in artificial gastric fluid respectively.

Increasing gastric pH has the potential to affect the bioavailability of any medication for which absorption is pH-dependent. Sodium bicarbonate employed as buffering agent protects the PPI against gastric acid degradation and in turn sufficiently preserves to increase the bioavailability. The buffering agent in the presence of the gastric acid elevates the pH of the stomach sufficiently to achieve adequate bioavailability of the drug to effect therapeutic action. Sodium bicarbonate acts as an antacid while pantoprazole is being absorbed and also acts as parietal cell activator (7 mEq to 25 mEq).^[13] Acid degradation of PPIs into their corresponding cyclic sulfonamide and dimer predominate at pH values 2-3. Amides are less acidic compared to free acids, which may be responsible for a slight increase in the pH (2.01 to 3.12) of artificial buffers treated with plain pantoprazole.

Understanding the pharmacodynamics of pantoprazole is more relevant than knowing its pharmacokinetic parameters, since the duration of action depends on the rate of *de novo* proton-pump regeneration, not on the duration of the circulation of drug in the body. Recovery of acid production after treatment with a proton pump inhibitor is driven by new pump synthesis, activation of existing cytoplasmic pumps, or reversal of proton pump inhibition.^[14] Although the mean plasma half-life ($t_{1/2}$) after a single 40-mg intravenous dose of pantoprazole is 1.0 h (range, 0.8 to 1.3 h), a steady state of acid secretion does not occur until after approximately three days of once-daily dosing because a balance develops between the synthesis of new enzyme and drug inhibition of existing ATPase. A clinical trial in healthy volunteers found equipotent inhibition of gastric acid secretion by equal doses of oral or intravenous pantoprazole. The primary parameter for the equivalence analysis was the percentage of time at which the intragastric pH was at least 4 or higher. The secondary parameter was the percentage of time at which the intragastric pH was at least 3 or higher.^[15] It implies that buffering will enhance the absorption of pantoprazole by increasing the pH of the stomach content ensuring its stability. Crushing the buffered tablet raises the pH fast and also up to the highest level of nearly in the range of pH 9. Highest achievable pH range does show much variation after 50 min duration, showing crushing does not have any adverse effect on pantoprazole bioavailability. When this study was carried out in pyloric-ligation antiulcer model the results were excellent in comparison to plain pantoprazole.

Bioavailability of crushed pantoprazole tablet in healthy male volunteers was reported by Ley *et al.*,^[3] after buffering with sodium bicarbonate or magaldrate relative to the intact enteric coated tablet. Total bioavailability was 93% compared with the intact enteric coated tablet. C_{max} was about 10% higher due to faster absorption. Comparative bioavailability study of pantoprazole sodium bicarbonate suspension against enteric coated tablet was reported by Ferron *et al.* in an open-label, randomized, two-period crossover study on healthy fasting human subjects.^[5] The suspension form of pantoprazole yielded C_{max} value similar to that of tablet formulation, but bioavailability was 25% less. Suspension of pantoprazole in sodium bicarbonate solution yielded a C_{max} similar to that of the tablet formulation, and the drug was quickly absorbed.

In pyloric ligation ulcer model buffered pantoprazole tablets showed faster and better bioavailability as compared to plain pantoprazole. Gastric content of pantoprazole was higher in buffered formulation compared to plain drug due to decreased degradation of drug in pH<5. The concentration of pantoprazole in gastric fluid and stomach tissue homogenate of buffered tablet-treated animals was significantly higher than plain pantoprazole. Pantoprazole buffered tablet *in vitro* and *in vivo* showed nearly the same pH profile. Buffered pantoprazole tablet also showed extremely significant decrease

in free and total acidity, and total protection from ulcer lesions compared to plain drug. The better gastric volume and ulcer score reduction was observed in 4 and 6 h treated animals may be due to the cumulative effect of pantoprazole over 4 and 6 h.

Gastric PPIs are substituted benzimidazole prodrugs that require an acid-induced activation and rate depends on the reactivity of the molecule relative to the environmental pH and determines the drug's tissue selectivity. Factors affecting the exposure of moderately acidic tissues to the activated PPI are the area under the serum concentration-time curve, serum protein binding, the partition coefficient and the serum elimination half-life relative to the chemical activation half-life at a critical tissue pH of about 5.^[16] The pH-dependent activation profile, i.e., activation at pH one versus activation at pH 4-6, is more favorable for pantoprazole than for the other PPIs currently available.^[17] Buffered pantoprazole tablet efficiently increases the pH of gastric media above 4 which protects it from acid degradation enhancing its bioavailability and the drug is quickly absorbed through the gastric mucosa. Inside the acidic environment of gastric mucosa the PPIs gets trapped and produces their pharmacological action. After diffusing in the parietal cells of the gastric mucosa PPIs gradually get tightly bound to the H⁺K⁺ATPase enzyme via covalent binding with -SH of enzyme. This may be a possible reason for the gradual decrease in the free pantoprazole availability in the mucosa from 2-6 h. In case of enteric coated tablets it gets absorbed from the small intestine and via the plasma it gets access to gastric tissue which is responsible for the faster action of buffered formulations.

CONCLUSIONS

Our current study indicates that buffered pantoprazole tablet effectively increases the pH of gastric content above 5 which protects it from acid degradation. The therapeutic efficacy of buffered pantoprazole on pH profile of artificial media and on ulcer induced by accumulated gastric fluid (pyloric ligation-induced) is assessed along with accumulated concentration in the gastric mucosa. These findings may throw light on not only the comparative therapeutic efficacy of pantoprazole but can also be extended to other drugs of this category.

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