Controlled release floating drug delivery system for proton pump inhibitors lansoprazole: *In-vitro, In-vivo* floating and pharmacokinetic evaluation

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**Abstract:** Lansoprazole (LPZ) show poor bioavailability because of first pass effect and absorption factors. The floating delivery systems could reduce fluctuations in plasma drug concentration through maintaining desirable plasma drug concentration. The objective of present study was to enhance bioavailability despite first pass effect through continuous availability of drug from floating system. Gum tragacanth (GT) and itaconic acid (IA) based floating hydrogels (FH) were synthesized. Parameters optimized were; microwave radiation exposure time, pH, GT:IA ratio and concentration of the glutaraldehyde. Optimized FH were evaluated for entrapment efficiency (% EE), *in-vitro* release, FTIR, SEM, and *in- vitro* and *in-vivo* floating study. Finally, pharmacokinetic was evaluated in ulcer-induced SD rats. Grafting percentage, swelling ratio and %EE of LPZ was 115%, 250% and 90%, respectively. Microwave radiation exposure time, pH of reaction medium, GT:IA ratios and cross linker concentration were 2 min, pH 5, ratios 2:1 and 0.02%, respectively. The optimized FH showed acceptable floating behavior. The X-ray images revealed that hydrogels remained floated over gastric contents up to 24 hours. The *in-vitro* release and pharmacokinetics revealed availability of LPZ upto 24h *in-vitro* and in ulcer-induced SD rats, respectively. The present hydrogels based floating system of lansoprazole is capable to extend the gastric residence time upto 24 hours.

**Keywords:** Floating hydrogels, gum tragacanth, itaconic acid, proton pump inhibitor, prolonged drug delivery, lansoprazole.

**INTRODUCTION**

Gastro esophageal reflux disease are hyper acid secretory disorders frequently occurs in older peoples. Such patients suffer reflux of stomach contents into esophagous which may cause mucosal injury. The major non-compliance with such diseases includes decrease in work productivity and sleep disturbance. The treatment option is to suppress acid secretion by providing drug at its therapeutic level over prolong period of time (Namdev and Jain, 2019). Several approaches have been used to achieve prolong gastric retention such as swelling controlled floating system, bio-adhesive, hydro-dynamically balanced system and high density systems (Singh et al., 2018). Amongst these, the floating drug delivery systems offer advantage over the others which include ease of preparation and providing prolong gastric transit time (Singh et al., 2018).

Lansoprazole (LPZ) is used for the treatment of gastric acid hyper-secretion (Yoshioka et al., 2019). Oral delivery of LPZ has shown lower bioavailability. In humans after oral administration, LPZ results in dose dependent reduction in acid secretion. It prevents experimentally induced ulcers and mucosal injury induced by aspirin in animals and humans. Once daily therapy is unable to control nocturnal acid breakthrough where acid secretory activity returns abruptly. This reflects the need for prolonged and steady state availability of LPZ in order to inhibit proton pump activity especially in the middle of night.

In the present study, floating hydrogels (FH) with floating lag time many folds compared to normal gastric transit time were targeted. Gum-tragacanth (TG) and itaconic acid (IA) were selected for present study. The critical quality parameters optimized include the microwave radiation exposure time, pH of reaction medium, GT:IA ratio and concentration of glutaraldehyde (GA). The grafting percentage and swelling behavior were key responses. LPZ as model drug was evaluated for percent entrapment efficiency (% EE) and *in-vitro* release study. FLT and TFT were determined. The *in-vivo* floating in rabbit stomach was investigated using radiographic imaging technique up to 24 hours. Finally, the pharmacokinetic performance was evaluated in ulcer induced SD-rats after the oral administration of the LPZ-loaded floated hydrogels.

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### MATERIALS AND METHODS

**Materials**

Gum tragacanth (GT), itaconic acid (IA), glutaraldehyde (GA), and potassium persulphate (KPS) were bought from Sigma Aldrich (Germany). Lansoprazole (LPZ) was a kind gift from GlaxoSmithKline (GSK) and Searle Pharma Pakistan. HPLC grade acetonitrile and analytical grade potassium dihydrogen phosphate were purchased from Merck, Darmstadt, Germany. High-quality pure water was prepared in-house by use of a Millipore (Billerica, MA, USA) Milli-Q water-purification system. All other materials used were of analytical grade.

**Methods**

**Gum tragacanth-g-itaconic acid Floating Hydrogel (GT-g-IA) FH**

**Synthesis**

The synthesis of GT-g-IA floating hydrogels (GT-g-IA)FH was performed after modification of procedure reported earlier (Pathania et al., 2018, Ranjha et al., 2008, Mudassir and Ranjha, 2008). GT (0.5g) was dissolved in 5 ml distilled water and stirred continuously for 2 hours and then 1gm IA and cross linker glutaraldehyde (GA) was added with continuous stirring. Latter on 0.5g potassium persulphate was added as initiator. Mixture was kept under continuous stirring until homogeneous mixture was obtained. Finally reaction mixture was exposed to microwave radiation. Formed hydrogels were allowed to cool and subsequently dried in hot air oven. Hydrogels were cut into disc for further use.

**Optimization parameters**

The parameters optimized during synthesis are presented in table 1. The observed responses were grafting and swelling percentage (Cruz et al., 2017).

**Physicochemical Characterization**

**Fourier transform infrared (FTIR) spectroscopy**

FTIR analysis of the (GT-g-IA)-FH were carried out using a Bruker IR affinity 1 model, Japan. FTIR spectra were observed in the region between 4000-400 cm\(^{-1}\).

**Scanning electron microscopy (SEM)**

SEM was performed using scanning electron microscope (Model: SEM JSM6100) (JOEL) to study the surface morphology of the optimized (GT-g-IA)-FH.

**Evaluation of Floating Behaviour**

**In-vitro floating lag time (FLT) and total floating time (TFT)**

In-vitro buoyancy study FLT and TFT was conducted by introducing weighed (GT-g-IA)-FH discs to 500ml phosphate buffer at pH 3 and maintained at 37°C in USP paddle apparatus at 50 rpm.

**X-ray imaging of rabbit’s stomach**

An in-vivo bouncy study was performed in albino rabbits (n = 3) using x-ray imaging (Razavi et al., 2015). Study protocols were approved from Animal Ethical Committee, BZU, Multan, (147/PEC dated 20-10-2018). Rabbits were orally administered with LPZ loaded (GT-g-IA)-FH containing 50 mg barium sulphate (Razavi et al., 2015). Animals were kept in the upright position during x-ray imaging (Siemens 300-MA with fluoroscopy, Munchen, Germany). Images were taken at a predetermined time of 1, 4, 8, 16 and 24 hours.

**Estimation of Lansoprazole**

**HPLC analysis of Lansoprazole**

In the present study Waters Acquity LC (Milford, MA, USA) with photodiode array was used as detector. Chromatographic separation was achieved using Waters Acquity BEH C18 (150 mm x 4.6 mm x 5 μm) column (Milford, MA, USA). The separation was performed by isocratic elution. Mobile phase constitute acetonitrile: water: triethyl amine (400ml: 600ml: 10ml). The mobile phase pH was maintained at 7.0 using 10 % phosphoric acid. The column temperature was kept at 40°C, and while 10μL injection volume was used. Flow rate was 1.0 ml/min while auto sampler temperature was 20°C. The chromatographic response was monitored at the wavelength of 285 nm.

**Entrapment efficiency (%EE)**

Entrapment of LPZ was performed by incubating weighed disc of FH in 5% w/v LPZ solution. After specified time hydrogels were removed from solutions and dried in oven at 40°C. The amount of LPZ left in solution was estimated using HPLC.

**In-vitro release**

The release of LPZ from optimized (GT-g-IA)-FH was performed using USP paddle method at 100 rpm of paddle speed maintained at 37°C upto 24 hours. At a predetermined time intervals (15, 30, 45min, 1hrs, 1.5, 2, 4, 6, 8, 12, 16, 20 and 24 hrs) 200μl release sample was withdrawn and concentration was determined HPLC. Fresh medium was added to replace the sample taken (Haneesha et al., 2020).

**In-Vivo Pharmacokinetic Study**

Pharmacokinetic was investigated in gastric ulcers induced SD rats. Ulcer was induced by oral administration of absolute ethanol (5ml/kg). The ethanol induced model of peptic ulcer is independent of gastric acid secretion and resembles acute peptic ulcers in humans Study was approved by Animal Ethical Committee BZU, Multan. The rats (n=5) were divided into two groups i.e., treatment and control groups and were administered with LPZ loaded FH (containing 5mg LPZ) and LPZ solution (5mg) respectively. Blood samples were collected from the tail veins of the rats prior to drug dosing and at predetermined time intervals (0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12 and 24 hours) after dosing. The blood samples were centrifuged at 10,500 rpm for 10-15
min and supernatant was separated. LPZ was extracted using acetonitrile. Finally, mixture was vortexed and then centrifuged. The supernatant was dried, and mixed with mobile phase for HPLC analysis. The pharmacokinetic parameters were obtained from the serum LPZ concentration time data (table 3). For this purpose a noncompartmental pharmacokinetic analysis model (WinNonlin software, version 5.3, Pharsight Corporation, CA, USA) was used. C<sub>max</sub> and T<sub>max</sub> were obtained directly from the observed concentration-time data. The area under the curve (AUC) to the last measurable concentration was calculated by the linear trapezoidal rule.

**STATISTICAL ANALYSIS**

Student’s t-test and one-way ANOVA was used for comparison. A post hoc Tukey’s HSD test was performed to find significant difference. Differences was statistically significant when p<0.05. Analysis was performed using a statistical software IBM, SPSS version 22. For pharmacokinetic analysis a noncompartmental model (WinNonlin software, version 5.3, Pharsight Corporation, CA, USA) was used.

**RESULTS**

**Gum tragacanth-g-itaconic acid floating hydrogel (GT-g-IA)FH**

**Synthesis**

The synthesis of FH was carried out by exposing components to microwave radiations. The reaction of GT and IA is predicted to proceed via following steps: upon exposure to microwave radiation, the initiator dissociates resulting in formation of free radicals which withdraw hydrogen atom from -OH groups on GT producing macro radicals. These macro radicals forms free radical and donor while the molecules (of IA or GT) become acceptors. The GT macro radicals attach to the monomer (IA) resulting in chain initiation. Subsequently, the radical active sites transfer to the monomers molecules which become free radical donors for the reacting monomers. This leads to the start of propagation step. Finally, the termination step becomes active through combining the grafted chains together to form graft copolymer (Gupta et al., 2018, Pathania et al., 2018, Ranjha et al., 2011).

**Optimization**

**Effect of microwave radiation exposure time**

The results (table 2) revealed a maximum graft percentage of 110±3.6% at 2 min exposure time. However, at 1 min or further increase in the radiation exposure time to 3 min, resulted in a slight drop in the graft percentage to 105±4.4%. The mild decrease in graft percentage may be due to (i) initially at the lower exposure time of 1 min, the FH active species could be still available for attachment through grafting; (ii) the rise in temperature upon increasing radiation exposure time to 3 min may result in rapid evaporation of reaction mixture and hence the reduced graft percentage (Pandey et al., 2014).

**Effect of pH of reaction medium**

The results (table 2) showed a maximum swelling of 246±4.2%, while synthesis performed at lower exposure time of 1 min and higher exposure time of 3 min showed 150±3.9 and 204±3.6% swelling, respectively. These results suggest that hydrogels with higher grafting shows increased swelling, which is in line with the results reported literature (Ibrahim et al., 2019).

The results of swelling percentages (table 2) prepared at 2 min exposure time showed a maximum swelling of 246±4.2%, while synthesis performed at lower exposure time of 1 min and higher exposure time of 3 min showed 150±3.9 and 204±3.6% swelling, respectively. These results suggest that hydrogels with higher grafting shows increased swelling, which is in line with the results reported literature (Ibrahim et al., 2019).

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Controlled release floating drug delivery system for proton pump inhibitors lansoprazole: In-vitro, in-vivo floating

Table 1: The feed compositions and reaction parameters for the synthesis of (GT-g-IA)FH.

<table>
<thead>
<tr>
<th>Sample</th>
<th>GT:IA (ratio)</th>
<th>Cross linker (% of total monomers)</th>
<th>Initiator (% of total monomers)</th>
<th>Microwave Radiation exposure time (min)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FH-1</td>
<td>2:1</td>
<td>0.02</td>
<td>0.3</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>FH-2</td>
<td>-do-</td>
<td>-do-</td>
<td>-do-</td>
<td>2</td>
<td>-do</td>
</tr>
<tr>
<td>FH-3</td>
<td>-do-</td>
<td>-do-</td>
<td>-do-</td>
<td>3</td>
<td>-do</td>
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</tbody>
</table>

Effect of microwave radiation exposure time

<table>
<thead>
<tr>
<th>Sample</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FH-4</td>
<td>2:1</td>
</tr>
<tr>
<td>FH-5</td>
<td>-do-</td>
</tr>
<tr>
<td>FH-6</td>
<td>-do-</td>
</tr>
<tr>
<td>FH-7</td>
<td>-do-</td>
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</table>

Effect of pH of reaction medium

<table>
<thead>
<tr>
<th>Sample</th>
<th>GT:IA ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>FH-8</td>
<td>2:1</td>
</tr>
<tr>
<td>FH-9</td>
<td>1:1</td>
</tr>
<tr>
<td>FH-10</td>
<td>1:2</td>
</tr>
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</table>

Effect of GT:IA ratio

<table>
<thead>
<tr>
<th>Sample</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FH-11</td>
<td>2:1</td>
</tr>
<tr>
<td>FH-12</td>
<td>-do-</td>
</tr>
<tr>
<td>FH-13</td>
<td>-do-</td>
</tr>
</tbody>
</table>

Effect of concentration of crosslinker

<table>
<thead>
<tr>
<th>Sample</th>
<th>GT:IA ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>FH-11</td>
<td>2:1</td>
</tr>
<tr>
<td>FH-12</td>
<td>-do-</td>
</tr>
<tr>
<td>FH-13</td>
<td>-do-</td>
</tr>
</tbody>
</table>

Effect of concentration of crosslinker

FH = gum tragacanth- itaconic acid floating hydrogels; Cross linker = glutaraldehyde

Table 2: Effect of different parameters on percentage grafting and swelling of (GT: IA)FH (x ± s)

<table>
<thead>
<tr>
<th>Microwave radiation exposure (Sec)</th>
<th>% Grafting</th>
<th>% Swelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH 60 (Sec) 120 (Sec) 180 (Sec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70±4.2 110±3.6 105±4.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>150±3.9 246±4.2 204±3.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH 3 4 5 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>78±3.7 90±5.2 120±3.9 118±3.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>180±3.4 210±2.9 240±3.7 248±3.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GT:IA ratios

<table>
<thead>
<tr>
<th>Cross linker conc</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.02</td>
<td>3</td>
</tr>
<tr>
<td>0.04</td>
<td>4</td>
</tr>
<tr>
<td>0.06</td>
<td>5</td>
</tr>
<tr>
<td>0.06</td>
<td>6</td>
</tr>
<tr>
<td>78±4.8</td>
<td>118±3.3</td>
</tr>
<tr>
<td>95±3.9</td>
<td>145±4.5</td>
</tr>
<tr>
<td>265±3.7</td>
<td>231±4.1</td>
</tr>
</tbody>
</table>

Table 3: Pharmacokinetic Parameters of LPZ after the oral administration of LPZ loaded FH in Ulcer-Induced SDRats at a Dose of 5 mg LPZ/kg (n=5) (x ± s)

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Pharmacokinetics Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC_{0-∞} (ng-h/mL)</td>
</tr>
<tr>
<td>LPZ loaded FH</td>
<td>12922.6±379.83</td>
</tr>
<tr>
<td>LPZ Solution</td>
<td>3254.5±345.7</td>
</tr>
</tbody>
</table>

Abbreviations: AUC_{0-∞}, area under the plasma concentration-time curve; C_{max}, maximum plasma concentration; T_{max}, time taken to reach maximum plasma concentration; t_{1/2}, elimination half-life; Ke, elimination rate.

the pH to 6 the graft percentage was mildly reduced to 118±3.3%. There was no significant (p>0.05) improvement in graft percentage changing the pH from 5 to 6. These results are in line with the findings reported by Pathania et al, where the authors reported that initially the percentage grafting was increased up to pH 5, then decreased upon further increase in pH (Pathania et al., 2018).

The swelling data (table 2) revealed that the synthesis performed at pH 5 showed maximum swelling of 240±3.7%. However, there was no significant (p>0.05)
difference in swelling for synthesis performed at pH 5 and at pH 6. The swelling results are in correlation with the percentage grafting observed at different pH. The samples that showed higher grafting percentage at pH 5 also displayed higher swelling (Pathania et al., 2018). Keeping in view the above results, a pH of 5 used for further studies.

Effect of GT: IA ratio
The results (table 2) revealed a graft percentage of 117±2.9, 96±4.3 and 76±3.6 for 2:1, 1:1 and 1:2, respectively. These results suggest that upon increasing the concentration of GT from 1:1 to 2:1, the graft percentage was increased. In contrast, the graft percentage was decreased when IA concentration was increased from 1:1 to 1:2. It is speculated that this behavior may be due to the increase in the radicals’ generation capacity upon increasing the concentration of GT, which subsequently results in an increase in the graft percentage. The concentration of IA presented a negative effect on grafting percentage, which may be due to the dominance of steric hindrance on account of IA monomer (Lanthong et al., 2006).

The results (table 2) demonstrated that swelling was higher for hydrogels with higher GT concentration i.e. 2:1, as compared to hydrogels with higher IA concentration i.e. 1:2. Based on these results, the GT:IA ratio of 2:1 was considered optimum and was chosen for further studies.

Effect of amount of cross linker
The results (table 2) revealed grafting percentage of 78±4.8%, 118±3.3% and 95±3.9% with 0.02g, 0.04g and 0.06, respectively. The results showed a maximum graft percentage at GA concentration of 0.04g. However, it did not significantly increase (p>0.05), rather it decrease upon further increasing the cross linker concentration to 0.06. It is speculated that the cross linking amongst the monomers is higher when the concentrations of reactants (GT or IA) was increased up to a certain limit, further cross linking decrease upon further increase in the cross linker concentration (Pandey et al., 2014).

The results (table 2) suggest that swelling percentage was 145±4.5%, 265±3.7% and 231±4.1% with 0.02g, 0.04g and 0.06, respectively. The increase in the amount of cross linking agent from 0.02g to 0.04g, showed an increase in swelling. Upon further increasing the amount of cross linker to 0.06g had shown decrease in swelling. The possible reason for this behavior could be the formation of dense and compact network which resists the swelling of hydrogels (Hosseini et al., 2016).

The optimized (GT-IA) FH-12 have the following parameters; microwave radiation exposure time is 2 min, pH of reaction medium is 5, GT: IA ratio is 2:1 and cross linker concentration is 0.02 % of the total monomers.

Physicochemical Characterization
Fourier transform infrared (FTIR) spectroscopy
The FTIR spectra of IA, GT and optimized (GT-g-IA)FH are presented in fig. 1a. IA showed a peak at 1695 cm\(^{-1}\) which likely corresponds to the carboxylic acid C=O stretching; a peak between 1600 cm\(^{-1}\) and 1700 cm\(^{-1}\) possibly from vinyl C=C double bond, and peaks between 2900 cm\(^{-1}\) and 3400 cm\(^{-1}\) likely due to the O-H stretching. The spectra of GT shows a peak at 3299 cm\(^{-1}\) possibly due to vibration of OH groups, a peak around 2900 cm\(^{-1}\) likely from the asymmetric methylene group. The reduced intensity of 1695 cm\(^{-1}\) is believed to be due to the involvement of vinyl bonds of IA and cross linker in co-polymerization. Moreover, the grafting of IA over GT is also evidenced due to the shifting of -OH peaks towards higher wave number and at lower intensity level (Gupta et al., 2018, Pathania et al., 2018).

Scanning electron microscopic (SEM)
The SEM results (fig. 1b) depict the porous surface morphology for network structure. The porous structure demonstrates the capability of (GT-g-IA) FH for sustained drug delivery and other biomedical applications. It also reflects the surface roughness which might be due to the synthesis carried out at various GT: IA ratios and at different concentrations of cross linkers.

Estimation of Lansoprazole
Estimation of Lansoprazole using HPLC
The HPLC assay was validated and was found linear between the concentrations 10 to 1,000ng/mL, and the coefficient of determination (R\(^2\)) was ≥0.9939. The lower limit of quantification was found to be at 10ng/mL. The accuracy was found to be 98.46-100.04%, and while precision was observed from 0.43-4.13%. The percentage recovery of loaded drug from serum samples was from 97.21-98.24%. The representative HPLC chromatogram is presented in fig. 2.

Entrapment Efficiency
The hydrogels discs were incubated for various time intervals such as 6, 12, 24 and 36 hours at optimal pH. The results reveals that maximum amount of LPZ (88.7±4.1%) was entrapped at pH 1.2. The pH facilitating higher swelling for hydrogels showed maximum swelling. The results suggest that entrapment was increased upon increasing the incubation time up to 24 hours. However, upon further increase in incubation time to 36 hours, there was no further increase in amount of LPZ entrapped. Based on these results the pH 1.2 and incubation time of 24 hour were considered optimum.

In-vitro lansoprazole release
The results presented in fig. 3 regarding the in-vitro release revealed that around 60% of LPZ was observed within initial 5 hours of administration and subsequent 40 % drug release was continued up to 24 hours. This
sustained delivery upto 24 hours ensured availability of LPZ at absorption site and thus may lead to improved bioavailability as well as reduced plasma fluctuation.

**Evaluation of floating characteristics**

*In-vitro floating lag time (FLT) and total floating time (TFT)*

The FLT and TFT analysis for the optimized (GT-g-IA)-FH were performed and the results revealed a FLT of 2 to 3 min and a TFT up to 10 hours in citrate phosphate buffer at pH 1.2. FLT may be explained as time required for external media to penetrate the hydrogel disc and develop swollen network. Swollen disc caused an increased in the volume of hydrogels. The combined effect of swollen network and reduced density prolongs the TFT up to 10 hours.

*In-vivo bouncy study using X-Ray imaging technique in rabbit's stomach*

The optimized (GT-g-IA)-FH were subjected to gastric floatation study using radiographic imaging technique. fig. 4 presents the X-ray images of FH in gastric contents of the rabbit stomach after 1, 4, 8, 16 and 24 hours. These images confirmed the prolonged residence of the prepared LPZ loaded (GT-g-IA)-FH in the upper gastric region even after 24 hours of administration. The results demonstrate the floating and gastro retentive capability of synthesized (GT-g-IA)-FH owing to their swelling nature in SGF, which possibly help in retaining hydrogels for longer duration of time and to provide sustained delivery of LPZ up to 24 hours.

**In vivo Pharmacokinetic Study**

*In vivo* pharmacokinetic characteristics of LPZ were evaluated in the ulcer-induced SD rats following the oral administration of LPZ loaded FH and LPZ solution. The pharmacokinetic responses are documented in table 3. The results revealed that after oral administration of LPZ solution, it was eliminated within 6 to 7 hours, however serum LPZ concentration was prolonged up to 24h following oral administration of LPZ loaded FH. The elimination half-life of LPZ from FH were significantly longer than those for LPZ solution. The peak plasma concentration from FH was reduced to (850.66±20.03 ng/ml) as compared to LPZ solution (2275.5±345.7).

**DISCUSSION**

The present gum tragacanth (GT) and itaconic acid (IA) based FH were synthesized using microwave irradiations and evaluated for the controlled delivery of lansoprazole. The cross linking of different polymeric chains resulted in increased graft percentage. The increase in monomer concentration (GT and IA) resulted in increased graft percentage due to increase availability of radicals generated from monomers.

The microwave radiations influenced the pace of chain transfer or termination reactions between monomer molecules and grafted chain, thus showed significant influence on grafting percentage of synthesized FH. During synthesis, active sites on backbone of monomers
are generated which ultimately increases the % grafting. When all active sites were occupied, a decrease in graft percentage is observed.

The in-vivo bouncy study using X-Ray imaging technique in rabbit’s stomach revealed the potential of FH to prolonged LPZ release. The present FH provided sustained release of LPZ with a long mean residence time as compared with LPZ solution in an ulcer-induced rat model. It has been reported that higher LPZ blood levels are generally associated with a higher incidence of side effect such as diarrhoea. However, the constant LPZ blood level observed by present FH could also benefit in reducing such side effects (Alai and Lin, 2015, Rashid et al., 2020).

CONCLUSION

In this study floating hydrogel (FH) based on GT and IA was synthesised using microwave irradiation for prolong delivery of LPZ. The optimised parameters include microwave radiation exposure time of 2 min, pH of reaction medium at 5, GT: IA ratio of 2:1 and cross linker concentration of 0.02. FTIR and SEM characterization confirmed the grafting and porous structure of the hydrogel respectively. The LPZ loaded FH showed floating lag time of 2 to 3 min and a total floating time (TFT) more than 10 hours. Radiographic images of rabbit’s stomach revealed floating time up to 24 hours. The present results of in-vivo bouncy study using X-Ray imaging technique in rabbit’s stomach and in-vivo pharmacokinetics in rat model indicate that the developed floating hydrogels have the potential to release LPZ for prolong duration and show improved oral bioavailability following oral administration.

REFERENCES


