

IN-VIVO EVALUATION OF MICROCAPSULE CONTAINING BCS CLASS II DRUGS FOR PEPTIC ULCER TREATMENT

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Abstract:

Gastroretentive drug delivery systems (GRDDS) have emerged as a promising approach to overcome these challenges by prolonging gastric residence time, enhancing drug dissolution, and improving the bioavailability of poorly soluble drugs. Among these systems, floating polymeric microcapsules provide sustained drug release, maintain therapeutic drug concentrations for an extended period, and reduce dosing frequency, thereby improving treatment outcomes and patient adherence. The present study focuses on the development and in vivo evaluation of polymeric gastroretentive floating microcapsules containing a BCS Class II drug as a potential alternative to conventional dosage forms for the treatment of peptic ulcer disease. The developed formulation is expected to prolong gastric retention, provide sustained drug release, enhance bioavailability, and improve the overall therapeutic efficacy in peptic ulcer management.

Keywords: Peptic ulcer disease, BCS Class II drug, Gastroretentive drug delivery system, Floating microcapsules, Sustained drug release, In-vivo evaluation.

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1. INTRODUCTION

Peptic ulcer disease (PUD) comprises gastric, duodenal, and esophageal ulcers and remains one of the most common gastrointestinal disorders worldwide. The most frequently reported symptom of PUD is epigastric pain, while other clinical manifestations include dyspepsia, bloating, nausea, vomiting, and weight loss. Gastric ulcers are associated with normal or reduced gastric acid secretion and may develop even in the absence of acid production. The major etiological factors responsible for PUD are chronic infection with *Helicobacter pylori* and prolonged use of non-steroidal anti-inflammatory drugs (NSAIDs). Gastric ulcers occur in the stomach and are more prevalent among the elderly population, whereas duodenal ulcers occur in the proximal part of the small intestine and are characterized by severe burning pain in the upper abdomen that frequently awakens patients from sleep. Duodenal ulcers are more common in younger individuals and predominantly affect males. [1]

Current treatment strategies primarily focus on the eradication of *H. pylori* infection using standard triple therapy comprising a proton pump inhibitor (PPI) in combination with two antibiotics, such as omeprazole, clarithromycin, and amoxicillin or pantoprazole, clarithromycin, and amoxicillin. However, many antiulcer drugs belong to Biopharmaceutics Classification System (BCS) Class

II, exhibiting poor aqueous solubility and variable oral bioavailability. These limitations often necessitate frequent dosing, resulting in reduced patient compliance and inconsistent therapeutic outcomes. Furthermore, conventional oral dosage forms are associated with rapid gastric emptying and limited gastric residence time, which can lead to incomplete drug release and suboptimal absorption, thereby reducing therapeutic efficacy. [2]

Gastroretentive drug delivery systems (GRDDS) have emerged as a promising approach to overcome these limitations by prolonging the residence time of dosage forms in the stomach, thereby enhancing drug dissolution, absorption, and bioavailability. Various gastroretentive approaches, including floating systems, bioadhesive systems, swellable systems, and high- and low-density systems, have been investigated to improve gastric retention and sustain drug release. Among these, gastroretentive microcapsule systems offer advantages such as controlled drug release, improved gastric retention, enhanced stability, and better patient compliance, making them suitable carriers for BCS Class II antiulcer drugs.

Since peptic ulcer disease is a treatable condition requiring sustained therapeutic drug concentrations at the site of absorption, the development of an effective gastroretentive microcapsule formulation is expected to improve treatment outcomes. Therefore, the

present study was designed to develop a gastroretentive microcapsule system containing a BCS Class II antiulcer drug and to evaluate its therapeutic performance through in-vivo studies. The in vivo investigations were undertaken to assess gastric retention, antiulcer efficacy, and overall pharmacodynamic performance of the developed formulation in suitable experimental animal models. The findings of these studies are expected to establish the potential of the gastroretentive microcapsule system as an effective strategy for improving the management of peptic ulcer disease. [3].

2. MATERIALS AND METHODS

Materials

Lafutidine was procured from Merck-Schuchardt, Mumbai, Maharashtra, India. Ciprofloxacin hydrochloride, HPMC- Hydroxypropyl methyl cellulose was purchased from Loba Chemical Pvt. Ltd., Maharashtra, India. Sodium Alginate was obtained from Sigma-Aldrich, Mumbai, Maharashtra, India. All chemicals and reagents utilized in the research were of analytical grade.

Methods

In-vivo evaluation of microcapsules

Wistar albino rats (150 - 200 g, both sex and aged 8–12 weeks) were used for the *in vivo* study of microcapsules. The animals were obtained from the CCSEA-approved animal house of School of Pharmacy, Chouksey Engineering College (Ref. No. 1275/PO/Re/S/09/CPCSEA). Animals were kept inside the same animal house at the temperature of 22 ± 3 °C and $55 \pm 5\%$ humidity under 12h/12h dark/light cycle. Free access to standard diet and water were provided to all the animals. The experimentations protocol was approved by IAEC, (SOP/IAEC/2024/11/04).

Toxicity Study

The toxicity evaluation of microcapsules was performed in Wistar albino rats. For conducting acute oral toxicity study (OECD 423) healthy female albino rats were selected and categorized into five groups (5 animals in each group). The normal saline was given to group I, Group II was treated with microcapsules 60 mg/kg body weight, animals in Group III were administered microcapsules 120 mg/kg body weight, Group IV received microcapsules 240 mg/kg body weight and Group V was treated with microcapsules of 480 mg/kg body weight. Acute toxicity was assessed using mortality rates, survival duration, clinical manifestations of intoxication, and responses to the behavioral changes. The animals under investigation were monitored for adverse reactions, including alterations in body weight, ocular and nasal condition, and motor activity for 14 days. After 14 days animals were humanely sacrificed and examined for internal disorders, including the dimensions and characteristics of the heart, lungs, liver, spleen, and kidneys during necropsy [4].

Biochemical analysis

Serum biochemical evaluation was conducted after collecting blood samples from the animals on the 14th day. The samples were centrifuged at 4000 rpm for 5 minutes and serum was kept at -20 °C prior to analysis. Various parameters like SGPT, SGOT, bilirubin content, total protein etc were examined using an automatic analytical instrument [5].

Histopathological analysis

After completion of 14 days, animals were euthanized to collect the tissues from different organs. Mainly heart, lungs, liver and kidney were separated and stored at 10% formalin solution for further histopathological study. Samples were prepared onto glass slides after slicing the organ from sample embedded paraffin blocks. The sample slides were stained and examined under microscope and photographs were captured [6].

Antiulcer Activity

The antiulcer effect of microcapsules was performed in Indomethacin induced ulcerative albino rats [16]. Male rats were randomized into five distinct groups, each comprising six animals. Group 1, designated as the normal control, were administered solely distilled water. Group 2, designated as the ulcerated control, received only Indomethacin at a dosage of 30 mg/kg of body weight. Animals in group 3 received a treatment regimen consisting of 30 mg/kg of Indomethacin and 100 mg/kg of native Lafutidine. Rats in group 4 were administered with 30 mg/kg Indomethacin and native Ciprofloxacin HCl 100 mg/kg. Group 5 animals were given Indomethacin 30 mg/kg and drug loaded microcapsules 200 mg/kg body weight. Drug loaded microcapsule were added to the animals for 21 days before administering Indomethacin. The drug was administered through oral route once daily with the help of oral incubator. Sufficient quantity of water and food were provided to the animals throughout the study. All the treatments were given 30 minutes before Indomethacin (30 mg/kg) administration.

Gastric juice collection from stomach

The stomachs of ulcerated rats were isolated on twenty-second day after humanely euthanized the animals by cervical dislocation. The stomach was surgically removed from the abdominal cavity and was subsequently incised along the greater curvature. The gastric contents from the stomach were collected in a centrifuge tube and 5 ml of freshly prepared distilled water was added to it. The resulting solution was centrifuged at 3000 rpm for 10 minutes and supernatant obtained was analyzed [7]. The titrimetric method was used to estimate the gastric acid volume from the supernatant using 0.0025 N NaOH and Toepfer's reagent as an indicator. A pH meter was used to determine the pH of gastric juice. Then phosphate saline buffer (pH 7.4) was prepared to preserve the stomach for further study.

Quantification of ulceration

IN-VIVO EVALUATION OF MICROCAPSULE CONTAINING BCS CLASS II DRUGS FOR PEPTIC ULCER TREATMENT

The ulcer was quantified by measuring the lesion length under a microscope following treatment of the cleaned stomach with a 2% formalin solution. The total lengths (mm) of all lesions for each rat were utilized in calculating the lesion index. Stomach lesions were rated on a scale from 0 to 5 as follows: [0 = Gray colored stomach, 1 = Pinkish to reddish stomach, 2 = Appearance of 1 to 2 lesions, 3 = More lesions (<5), 4 = Multiple lesions (>5) and 5 = Ulcer with bleeding]

The percentage mucosal damage was quantified from the total surface area of the stomach. The ulcer index (UI) and % ulcer inhibition in each animal were represented from mean value of ulcer scoring and was calculated using the following equations:

$$\text{Ulcer Index (UI)} = \frac{\text{Area of ulceration}}{\text{Total Area of Stomach}} \times 100$$

$$\% \text{ Ulcer inhibition} = \frac{\text{UI in control} - \text{UI in test}}{\text{UI in control}} \times 100$$

Histopathological analysis of ulcerated stomach

Following microscopic evaluation of the ulcer, the rat stomach was collected and subsequently histopathological study was conducted using previously described methods in toxicity evaluation section.

3. RESULTS AND DISCUSSION

Toxicity evaluation

The safety evaluation is the primary requirement for development of any pharmaceutical formulations. The toxicity study ensures the safety of drug or drug products for its future applications. The *in vivo* acute toxicity study of the drugs loaded microcapsules (F5) was performed using female albino rats. The results of the oral acute toxicity study demonstrated that no noticeable changes observed upto the dose level 240 mg/kg body weight. On the other hand, mortality was noted when animals were administered with the dose of 480 mg/kg body weight. Serum biochemical parameters exhibited no noteworthy variations between the test group (60, 120 and 240 mg/kg body weight) and the control group.

Table 1: Serum reports of control and treated Rats.

Parameter	Reference Value	Control (Distilled water)	60 mg/kg	120 mg/kg	240 mg/kg
Serum creatinine (mg/dL)	0.2 - 0.8	0.3 ± 0.08*	0.22 ± 0.07*	0.25 ± 0.01**	0.28 ± 0.09*
Total bilirubin (mg/dL)	0.3 - 0.8	0.5 ± 0.06***	0.61 ± 0.02**	0.69 ± 1.08	0.62 ± 0.3
Total proteins (g/dL)	5.6 - 7.6	5.9 ± 1.3*	5.8 ± 1.4*	6.3 ± 0.9**	6.4 ± 1.05*
ALT (SGPT)	17 - 30.2	24.5 ± 2.1**	25.9 ± 2.5**	24.8 ± 1.08**	24.5 ± 2.3**

U/L				*	
AST (SGOT) U/L	37 - 205	66.2 ± 2.06***	65.4 ± 3.1***	66.1 ± 4.01**	62.9 ± 2.4**
Glucose (mg/dL)	50 - 135	105.3 ± 2.7***	107.6 ± 3.3***	105.1 ± 2.03**	104.6 ± 3.6**
Sodium (mEq/L)	135 - 155	139.1 ± 7.9**	142.3 ± 6.3***	142.1 ± 8.03**	145.4 ± 4.9**
Potassium (mEq/L)	3.5 - 5.5	3.91 ± 2.2	4.6 ± 1.5*	4.53 ± 1.7*	5.15 ± 2.1

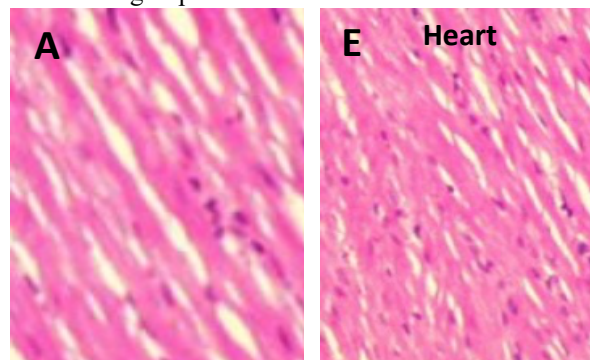
The values presented as Mean ± SD; (n=3)

This confirms that microcapsule formulation F5 has no influence on liver function. There were no sign of tremor, convulsion, salivation, lethargy, sleep, changes in skin, eyes, respiratory, circulation, autonomic and central nervous system of animals during the 14 days of observation period. The study also concluded that the formulation F5 does not have any impact on serum sodium, chloride and potassium.

Figure 1: Effect of drug loaded microcapsule (F5) on serum biochemical parameters in control and treated rats of acute toxicity studies.

Histopathological analysis

The histopathological study of heart, liver, kidney and lungs of Wistar albino rats was carried out under microscope. The dose level of 240 mg/kg body weight microcapsules was selected for the pathological examination. During examination of slides no alterations were observed in the histopathology of the glomerulus and tubules of the kidney. The hepatocytes were normal in the liver and no necrosis was observed while comparing with the control animals (Figure 5.35). The cells and tissues of heart, liver, kidney and lungs were also examined and did not exhibit any sign of abnormality following oral administration of the microcapsules, in comparison to the control groups.



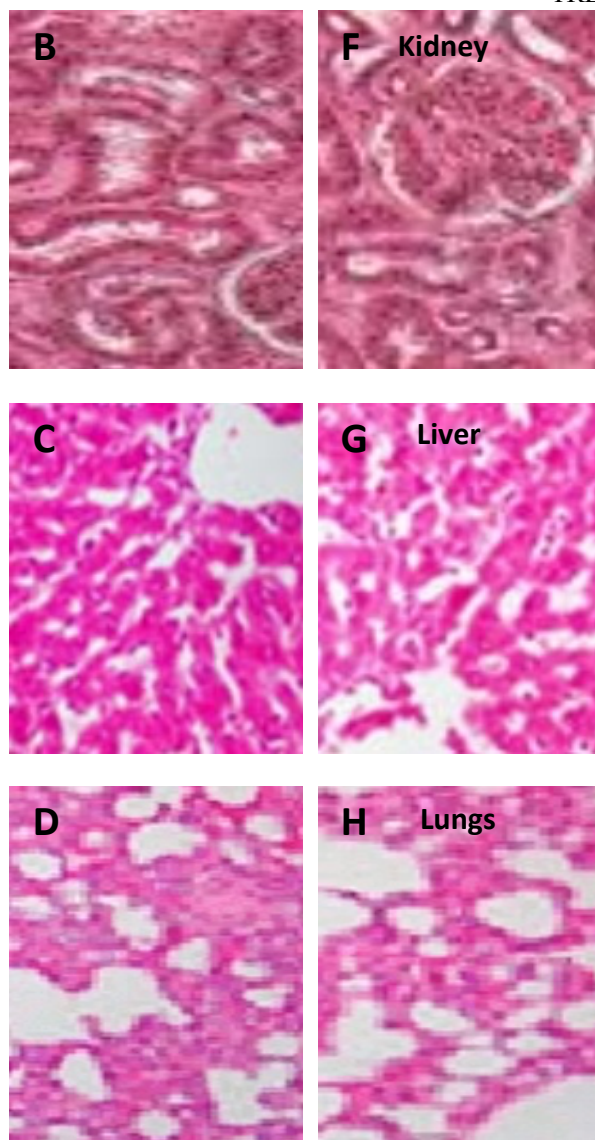


Figure 2: Histopathological slides of heart, kidney, liver and lungs of control rats and microcapsules treated rats. Slide (A to D) shows the heart, kidney, liver and lungs of control rats. Slide (E to H) shows the heart, kidney, liver and lungs of drug loaded microcapsule treated rats.

Antiulcer Activity

The antiulcer activity of microcapsules was conducted in Indomethacin induced ulcerative albino rats. The inhibitory effect of Indomethacin on production of prostaglandin, along with the formation of free radicals, is considered a significant biochemical event in the pathogenesis of ulceration. Biochemical analysis of gastric secretions, including pH and gastric volume, as well as assessment of mucosal integrity, is typically utilized to evaluate the status of the stomach after exposure to any pharmacological agents. The pH indicates the degree of acidity and the quantity of gastric secretions. The lower value of pH indicates a reduced concentration of H^+ ions in gastric medium. This phenomenon has

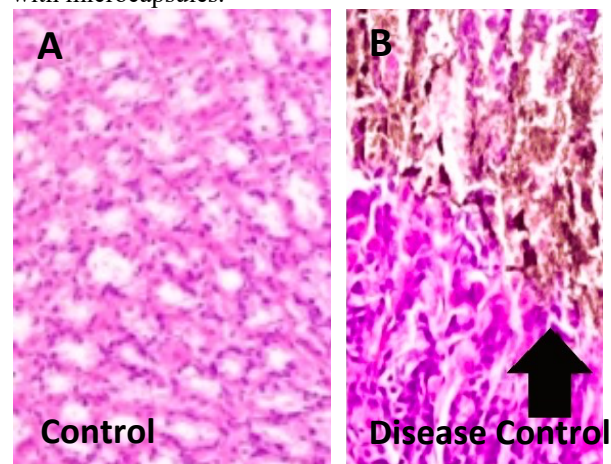
been linked to the underlying mechanisms contributing to the development of ulcers and gastric injury in experimental models. According to literature Indomethacin has been demonstrated to induce alteration in the gastric secretions of rats. In contrast, pretreatments utilizing the drug considerably lowered the pH and gastric volume.

Figure 3: Effect of drug loaded microcapsules on ulcer index of Indomethacin ulcerated rats (value represents Mean $\pm$ S.D. n= 6). IND: Indomethacin, LAFU: Lafutidine, CIPRO: Ciprofloxacin. The current study revealed that following a 21-day period, there was a reduction in both the ulcer index and gastric acid volume in the rats administered microcapsules, in contrast to those receiving the individual native drug treatment.

Figure 4: Effect of drug loaded microcapsules on Indomethacin induced ulcerated rats (value represents Mean $\pm$ S.D. n= 6). Bar represents % ulcer inhibition. IND: Indomethacin, LAFU: Lafutidine, CIPRO: Ciprofloxacin.

Figure 5: Effects of native Lafutidine, native Ciprofloxacin and drug loaded microcapsules on pH & gastric volume of ulcerated rats (value represents Mean $\pm$ S.D. n= 6). IND: Indomethacin, LAFU: Lafutidine, CIPRO: Ciprofloxacin.

The pH of gastric juice and the ulcer index were lower for drugs loaded microcapsule treated group when compared with native drug treated group (Figure 5.38). The histopathological analysis revealed that the damaged tissues in Indomethacin induced ulcerative rats were minimized after treating with microcapsules.



IN-VIVO EVALUATION OF MICROCAPSULE CONTAINING BCS CLASS II DRUGS FOR PEPTIC ULCER TREATMENT

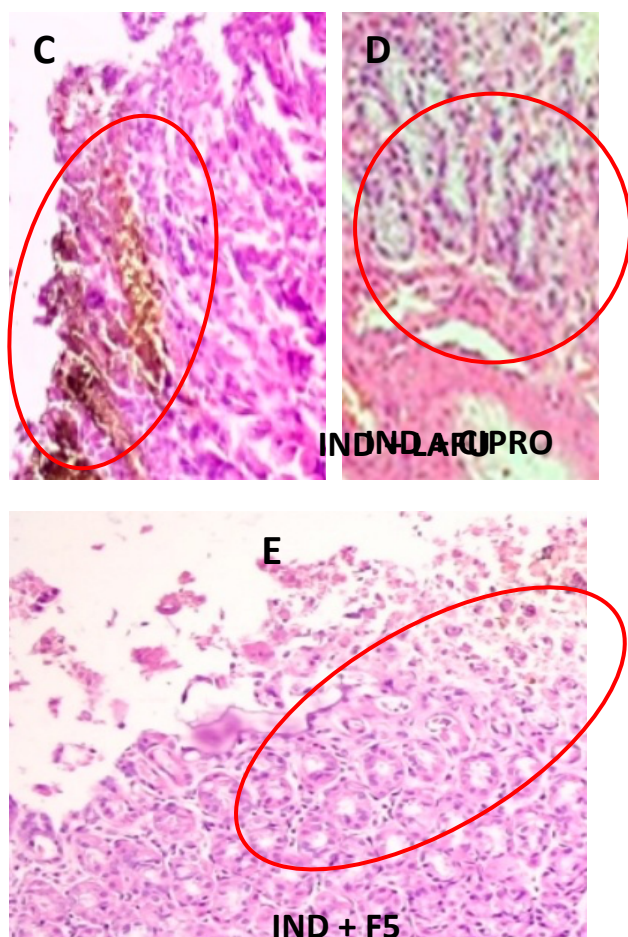
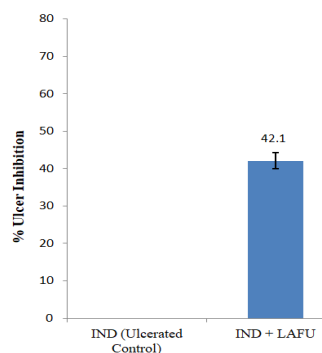


Figure 6: Histopathological slides of stomach of rats treated with distilled water, Indomethacin, Lafutidine, Ciprofloxacin and F5. IND: Indomethacin, LAFU: Lafutidine, CIPRO: Ciprofloxacin.

The combination of Lafutidine and Ciprofloxacin showed good antiulcer effect than the individual drug. The microcapsules will be helpful for effective management of ulcer which is caused either by pharmacological agents or by *H. Pylori* or by both in the stomach.

4. CONCLUSION

Peptic ulcer disease (PUD) is the silent killer for large population globally. If remain untreated the condition become worse leading to the death of patients. The predominant symptom of peptic ulcer disease is epigastric discomfort. The principal factors contributing to peptic ulcer disease include persistent infection with *Helicobacter pylori* and the inappropriate use of non-steroidal anti-inflammatory medications (NSAIDs). The majority of antiulcer medications fall under class II of BCS classification. They exhibits less solubility and variable bioavailability upon oral administration and also need frequent dosing. The Gastroretentive Drug Delivery System (GRDDS) is an effective approach to address the various issues associated with conventional orally administered drugs. To maintain the required therapeutic effect for the entire treatment period an attempt was made to develop stable microcapsule formulation of poorly soluble Lafutidine and Ciprofloxacin HCl with two polymers Sodium alginate and HPMC using ionic orifice gelation technique. Microcapsules showed improved *in vitro* and *in vivo* results as compared to pure drugs. The *in vitro* mucoadhesion test also supports the longer retention time of microcapsules inside the stomach. The stability studies showed no noticeable event in different temperature conditions confirming the stable microcapsules. The developed microcapsules of Lafutidine and Ciprofloxacin HCl exhibited great potential for the effective management of ulcer after single use. The promising microcapsules of Lafutidine and Ciprofloxacin HCl combination may further be explored for their suitability in human being.

REFERENCES

1. Jain, N.K., (2004). *Progress in Controlled and Drugs Delivery System* (1st Edition), CBS Publisher, Delhi: 77-95.
2. Chan, N.H., Chien, C.L., Lee, C.L., Yang, Y.C., Hung, C.S., Tu, T.C., Wu, C.H., (2015). *Comparison of 10-Day Sequential Therapy with 7-Day Standard Triple Therapy for Helicobacter Pylori Eradication in Inactive Peptic Ulcer Disease and the Efficiency of Sequential Therapy in Inactive Peptic Ulcer Disease and Non-Ulcer Dyspepsia*. BMC Gastroenterol.3, 15–170
3. Kawakami, E., Ogata, S.K., Aurea, C.M.P., Ana, M. Patricio, M., (2001). *Triple Therapy with Clarithromycin, Amoxicillin and Omeprazole for Helicobacter Pylori Eradication in Children and Adolescents*. Arq. Gastroenterol. 38(3).
4. Gelperina, S.E., Khalansky, A., Smirnova, Z.S., Bobruskin, A.L., Severin, S.E., (2002). *Toxicological Studies of Doxorubicin Bound to Polysorbate 80-Coated Poly (Butyl Cyanoacrylate) Nanoparticles in Healthy Rats and Rats with Intracranial Glioblastoma*. Toxicol. Lett. 126: 131-141.
5. Oberdorster, G., Oberdorster, E., Oberdorster, Jan., (2005). *Nanotoxicology: An Emerging Discipline*

IN-VIVO EVALUATION OF MICROCAPSULE CONTAINING BCS CLASS II DRUGS FOR PEPTIC ULCER
TREATMENT

Evolving from Studies of Ultrafine Particles.

Environmental Health Perspectives. 113, 823-839

6. Jana, U., Mohanty, A.K., Pal, S.L., Manna, P.K., Mohanta, G.P., (2014). *Felodipine Loaded PLGA Nanoparticles: Preparation, Physicochemical Characterization and In Vivo Toxicity Study.* Nano Convergence. 1:31.

7. Kodati, D., Surendra, P., Kartik, C.P., Kartik, A., (2010). *Antiulcer Activity of Ethanolic Extract of Buchanania Lanza Spreng Roots.* Ann. Biol. Res. 1(4): 234-239.