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DESIGN AND INVITRO CHARACTERIZATION OF GASTRO RETENTIVE FLOATING TABLETS OF CHLORPHENIRAMINE MALEATE

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ABSTRACT

Chlorpheniramine (INN), also called Chlorpheniramine , commonly marketed in the form of chlorpheniramine maleate, is a first-generation alkyl amine antihistamine used in the prevention of the symptoms of allergic conditions such as rhinitis and urticaria. In the present work, an attempt has been made to develop floating tablets of Chlorpheniramine by selecting natural polymers as retarding polymers. All the formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3 formulation showed maximum % drug release i.e., 97.33 % in 8 hours hence it is considered as optimized formulation. Whereas the formulations containing Xanthan gum showed more retarding with increasing concentration of polymer. The formulations with Guar gum were unable to produce the desired drug release pattern.

Keywords: Chlorpheniramine, Floating.

INTRODUCTION

`Oral administration is the most convenient mode of drug delivery and is associated with superior patient compliance as compared to other modes of drug intake. However, oral administration has only limited use for important drugs, from various pharmacological categories, that have poor oral bioavailability due to incomplete absorption and/or degradation in the gastrointestinal (GI) tract. Some of these drugs are characterized by a narrow absorption window (NAW) at the upper part of the gastrointestinal tract. This is because of proximal part of the small intestine exhibits extended absorption properties (including larger gaps between the tight junctions, and dense active transporters). Despite the extensive absorption properties of the duodenum and jejunum, the extent of absorption at these sites is limited because the passage through this region is rapid. Enhancing the gastric residence time (GRT) of a NAW the drug may significantly improve the net extent of its absorption [1].

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract. Drug absorption from the gastrointestinal tract is a complex procedure and is subject to many variables. It is widely acknowledged that the extent of gastrointestinal tract drug absorption is related to contact time with the small intestinal mucos [2]. Thus small intestinal transit time is an important parameter for drugs that are incompletely absorbed.

Floating drug delivery systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.

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The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion, modified shape systems, or by the simultaneous administration of pharmacological agent that delay gastric emptying [3-8].

Floating systems or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal (Figure 1). Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.

MATERIALS AND METHODS

Materials

Chlorpheniramine maleate was gift sample from Hetero labs, Hyderabad, India. Gum karaya, Xanthan gum, Guargum, Magnesium stearate, Talc were obtained from SD Fine chemicals Hyderabad, India and all other reagents used were of analytical grade and obtained from S.D. Fine chemicals. Mumbai. India.

Methods

Formulation of Chlorpheniramine Floating Tablet by Direct- Compression:

Composition of preliminary trials for Chlorpheniramine Floating Tablet by direct compression is shown in table 1. All the ingredients were weighed. Required quantity of drug and excipient mixed thoroughly in a polybag. The blend is compressed using rotary tablet machine-8 station with 12mm flat punch, B tooling. Each tablet contains 100mg of Quetiapine fumarate and other pharmaceutical ingredients.

Post compression parameters

Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table No. 2 [9].

Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2 [10].

Thickness

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper [11].

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at the height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

In-Vitro drug release

Invitro dissolution studies were carried out by using 900 ml of pH 6.8 phosphate buffer was added to the dissolution medium (900ml) and the dissolution was carried out for about 6 hours. The samples were withdrawn at regular time intervals of 30 min,1 hour,2 hr,3,,5,6,7 & 8 hours respectively [12].

Assay

10 tablets were weighed and triturated. The tablet triturate equivalent to 10 mg of the drug was weighed accurately, dissolved in pH 1.2 buffer and diluted to 100 ml with the same. Further dilutions were done suitably to get a concentration of 10 µg/ ml with simulated gastric fluid pH 1.2. Absorbance was read at 210 nm against the reagent blank, and the concentrations of Chlorphenamine in µg/ ml was determined by using the regression equation [13].

$$Y = 0.007x + 0.001$$

Drug content in mg / tablet = conc. µg/ml * dilution factor

% Drug content = drug content in mg * 100 / label claim.

Drug-Excipient Compatibility studies

The physico-chemical compatibility studies of Chlorpheniramine maleate and the various excipients used in the work were studied by IR spectroscopy. The samples were scanned under diffuse reflectance mold, plotted the graph by KBr pellet method and spectra were recorded in wavelength region between 4000 cm^{-1} to 400 cm^{-1}. The spectra obtained from various formulations were compared and reported.

RESULTS AND DISCUSSION

Post compression Parameters

Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 3. The average weight of the tablet is approximately in range

of 495 to 505 mg, so the permissible limit is ±5% (>220 mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

Hardness test

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 3. The results showed that the hardness of the tablets is in range of 4 to 4.5 kg/cm^2, which was within IP limits.

Thickness

Thickness of three tablets of each batch was checked by using Vernier Caliper and data shown in Table3. The result showed that thickness of the tablet is raging from 5.00 to 3 mm.

Friability

Tablets of each batch were evaluated for percentage friability and the data's were shown in the Table 3. The average friability of all the formulations lies in the range of 0.30 to 0.51% which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Assay

Assay studies were performed for the prepared formulations. From the assay studies it was concluded that all the formulations were showing the % drug content values within 97.23 -99.25 %.

Invitro Dissolution studies

Invitro dissolution studies were carried out by using 900ml of 0.1 N HCl in USP dissolution apparatus by using paddle method for about 2 hours. After 2 hours the dissolution medium was withdrawn keeping the tablet in the dissolution basket. Then pH 6.8 phosphate buffer was added to the dissolution medium (900ml) and the dissolution was carried out for about 6 hours. The samples were withdrawn at regular time intervals of 30 min,1 hour,2 hr,3,5,6,7 & 8 hours respectively. The results were displayed in table 4

From the tabular column 4 it was evident that the formulations prepared with GUM KARAYA as retarding polymer in low concentrations the polymer was unable to produce the required retarding action to the tablets. As the concentration of polymer increases the retarding nature was also increased. Gum karaya in the concentration of 30 mg showed good % drug release i.e., 97.3 in 8 hours. Where as in the concentration of 20 mg it showed less drug release due to increased retarding nature of polymer.

Where as in case of formulations prepared with xanthan gum as retarding polymer, the formulations with 10 mg concentration of polymer showed complete drug release in 6 hours only, whereas the concentration of polymer increases the retarding nature also increased. The Formulation Containing xanthan gum in 10 Mg Concentration Showed good retarding nature with required drug release in 8 hours i.e., 82.3%.

Where as in case formulations prepared with Guar gum as retarding polymer, as the concentration of polymer increases the retarding nature was also increased. When compared with HPMC polymers it was failed to produce desired drug release pattern.

From the above results it was evident that the formulation F3 is best formulation with desired drug release pattern extended up to 8 hours.

Application of Release Rate Kinetics to Dissolution Data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

From the above graphs it was evident that the formulation F3 was followed Zero order release mechanism

Table 1. Formulation of Chlorpheniramine Floating tablets

INGREDIENT	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F10	F11	F12
Chlorpheniramine	10	10	10	10	10	10	10	10	10	10	10	10
Gum karaya	10	20	30	-	-	-	-	-	-	10	10	-
Xanthan gum	-	-	-	10	20	30	-	-	-	-	10	10
Guar gum	-	-	-	-	-	-	10	20	30	10	-	-
Sodium bicarbonate	15	15	15	15	15	15	15	15	15	15	15	15
Talc	3	3	3	3	3	3	3	3	3	3	3	3
Mg. Stearate	3	3	3	3	3	3	3	3	3	3	3	3
MCC pH102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total	150	150	150	150	150	150	150	150	150	150	150	150

All ingredients are expressed in mg only.

Table 2. Weight Variation Specification as per IP

Average Weight of Tablets	%Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Table 3. Post compression parameters

Post-Compession parameters					
FD	**Weight variation(mg)**	**Hardness (kg/cm^2)**	**Thickness(mm)**	**Friability (%)**	**Assay (%)**
F_1	149	4.5	2.5	0.43	97.23
F_2	144	4.3	2.5	0.34	98.55
F_3	150	4.2	2.5	0.49	98.16
F_4	145	4.2	2.4	0.47	99.34
F_5	152	4.3	2.5	0.49	98.16
F_6	148	4.3	2.5	0.34	98.55
F_7	150	4.4	2.4	0.49	98.16
F_8	154	4.5	2.5	0.34	99.25
F_9	146	4.4	2.5	0.34	99.25
F10	151	4.4	2.5	0.43	98.6
F11	152	4.3	2.5	0.54	98.7
F12	154	4.5	2.5	0.43	98.5

Table 4. Invitro dissolution data

Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0.5	25.52	20.15	16.46	11.45	15.42	10.46	9.45	8.56	49.55	38.27	26.43	18.91
1	46.74	39.44	26.73	18.60	29.43	16.52	15.62	14.59	78.83	41.98	38.28	28.38
2	76.56	55.37	34.63	29.52	38.52	28.63	21.44	18.40	96.94	62.47	43.45	36.46
3	98.43	75.33	42.42	39.57	55.46	39.56	36.75	23.45	96.18	78.28	59.35	49.52
4		87.38	55.46	49.65	68.41	48.59	42.45	28.25		81.46	76.38	69.37
5		99.43	67.41	57.48	87.18	59.43	49.62	34.83		96.82	88.46	78.18
6			85.45	69.33	98.32	69.28	55.37	40.23			95.45	89.71
7			91.52	78.54		74.52	60.31	44.84			98.57	97.56

Fig 1. Mechanism of floating systems

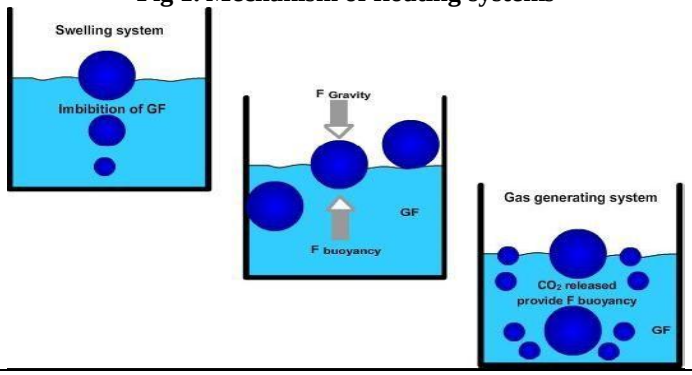


Fig 2. FT-IR spectra of Pure drug (Chlorpheniramine maleate)

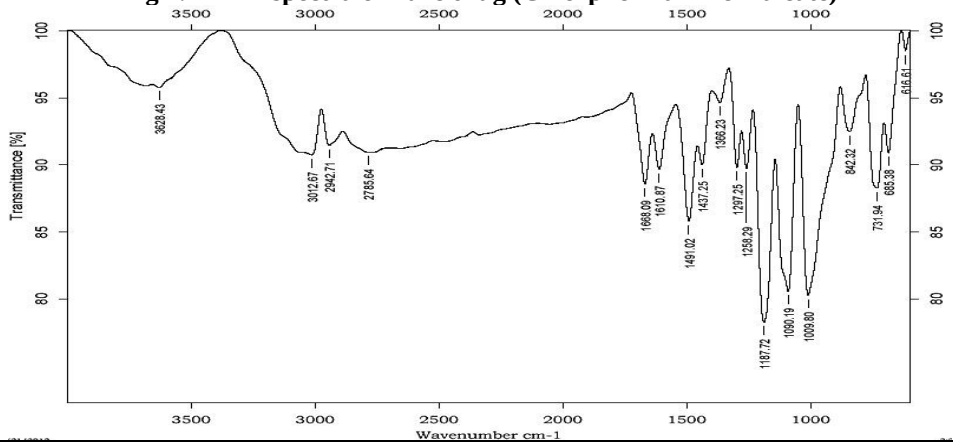


Fig 3. FT-IR spectra of drug +Gum karaya

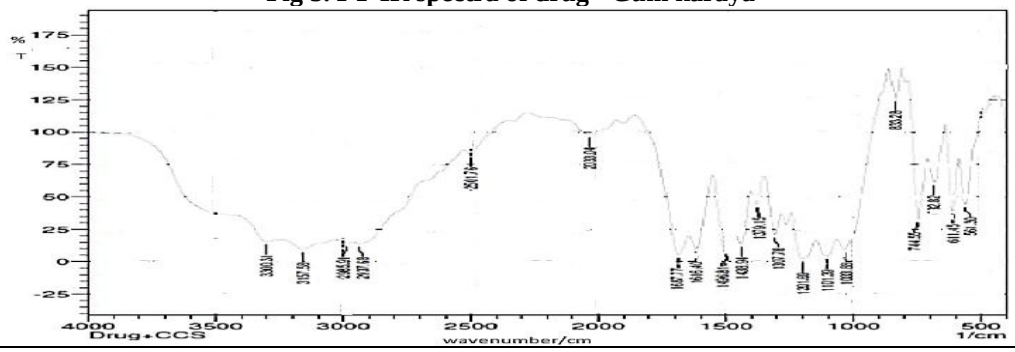


Fig 4. FT-IR spectra of drug + Xanthangum

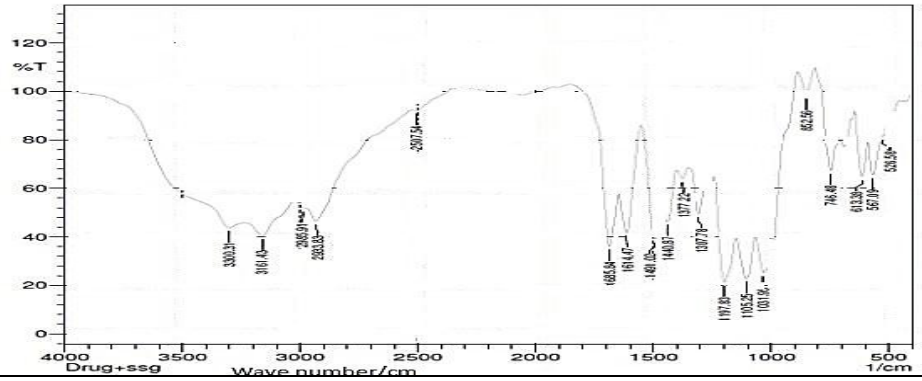


Fig 5. FT-IR spectra of drug + guargum

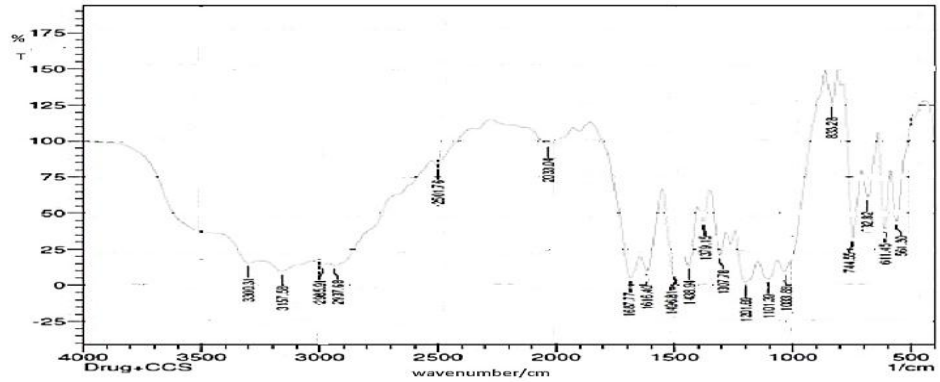


Fig 6. Dissolution profile of formulations prepared with GUM KARAYA polymer

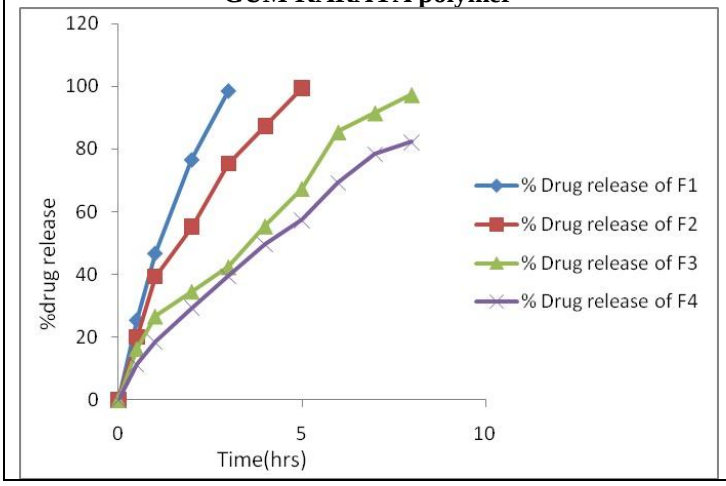


Fig 7. Dissolution profile of formulations prepared with xanthan gum polymer

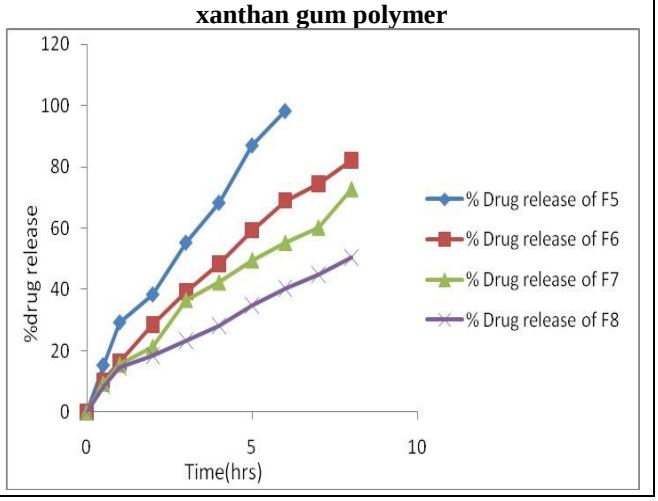


Fig 8. Dissolution profile of formulations prepared with Guar gum as polymer

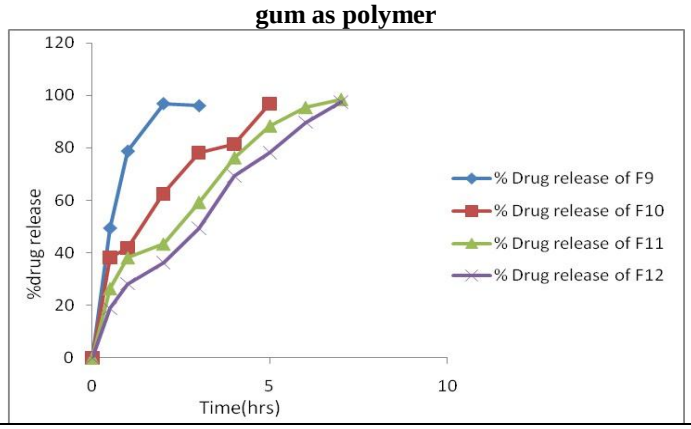


Fig 9 . Zero order release kinetics graph

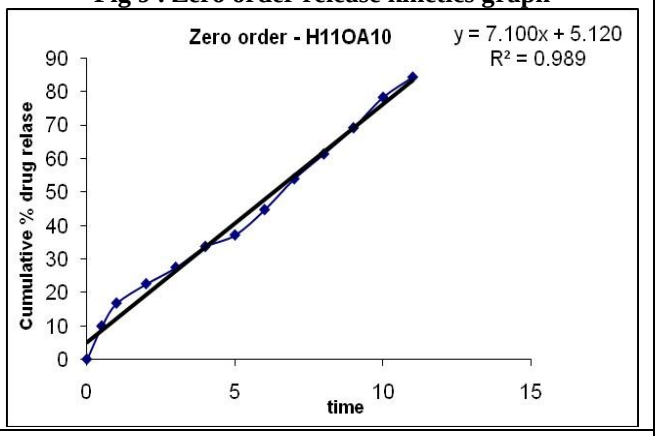


Fig 10. Higuchi release kinetics graph

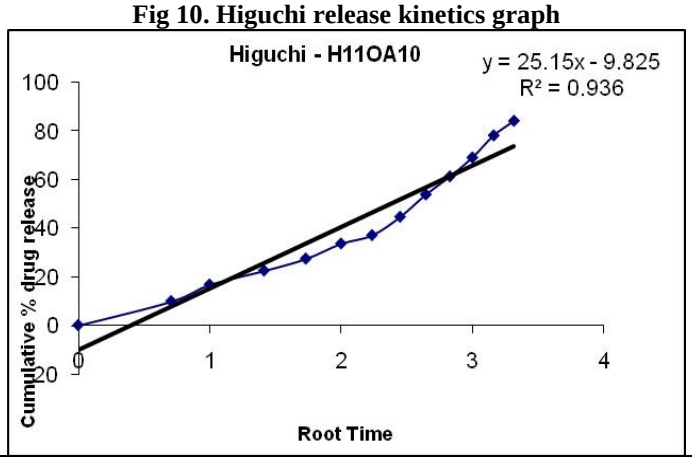


Fig 11. Koreys meyer peppas graph

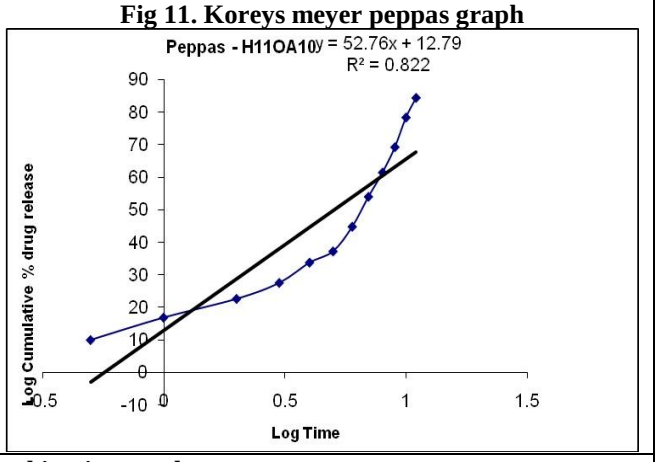
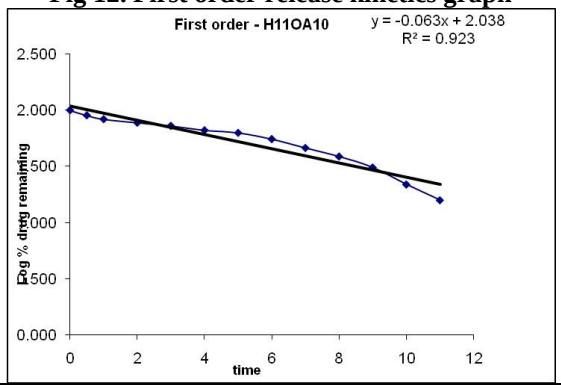


Fig 12. First order release kinetics graph



CONCLUSION

In the present work, an attempt has been made to develop extended release tablets of Chlorpheniramine by selecting natural polymers as retarding polymers. All the formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed god flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3 formulation showed maximum % drug release i.e., 97.33 % in 8 hours hence it is considered as optimized formulation. Whereas the formulations containing Xanthan gum showed more retarding with increasing concentration of polymer. The formulations with Guar gum were unable to produce the desired drug release pattern.

ACKNOWLEDGEMENT

Nil

CONFLICT OF INTEREST

None

REFERENCES

1. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system. *Expert Opin Drug Deliv*, 3(2), 2006, 217- 33.
2. Iannucelli V, Coppi G, Bernabei MT, Camerorni R. Air compertment multiple-unit system for prolonged gastric residence. Part-I. Formulation study. *Int J Pharm*., 174(1-2), 1998, 47-54.
3. Tortora GJ, Grabowski SR. Principles of anatomy and physiology. 8th ed. Harper Collins College Publishers, 1996, 658-669.
4. Wilson KJW, Waugh A. Anatomy and physiology in health and illness. 8th ed. (London): Churchill Livingstone, 1996.
5. Jain NK. Progress in Controlled and Novel Drug Delivery Systems, First Ed. CBS Publishers and Distributors, New Delhi, 2004, 84-85.
6. Wilson CG, Washington N. The stomach: its role in oral drug delivery. In: Rubinstein MH, ed. Physiological Pharmacetical: Biological Barriers to Drug Absorption. Chichester, 1989, 47-70.
7. Goyal M, Prajapati R, Purohit KK, Mehta SC. Floating Drug Delivery System. *J.Curr.Pharm.Res*, 5(1), 2011, 7-18.
8. Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. *Int J Pharm*, 136(1-2), 1996, 117 -139.
9. Hoichman D, Gromova LI, Sela J. Gastroretentive Controlled-Release Drugs. *Pharmaceutical Chemistry Journal*, 38, 2004, 621-4.
10. Mathur P, Saroha K, Syan N, Verma S, Nanda S, Valecha V. An overview on recent advancements and developments in gastro retentive buoyant drug delivery system. *Der Pharmacia Sinica*, 2(1), 2011, 161-169.
11. Vyas SP, Khar RK. Gastroretentive systems. In: Controlled drug Delivery. Delhi, Vallabh Prakashan editor, 2006, 197-217.
12. Bhowmik D, Chiranjib B, Chandira M, Jayakar,Kumar KPS. Floating Drug Delivery System-A Review. *Der Pharmacia Lettre*, 1(2), 2009, 199-218.