

Formulation and Evaluation of Hydrodynamically Balanced System of Labetalol Hydrochloride by Using Chitosan and *PlantagoOvata* for Sustained Stomach Delivery

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Received 28 May 2020; Accepted 16-June 2020

ABSTRACT: Labetalol Hydrochloride has been widely used as an anti-hypertensive drug. The present study concerns with the development and evaluation of Hydrodynamically balanced system of Labetalol Hydrochloride by using the different natural polymer such as chitosan (animal derived) and its different grades low medium and high molecular chitosan along with a plant derived polymer which is psyllium husk. We incorporated the natural polymer to eliminate the risk of toxicity. This formulation is designed to prolong the gastric residence time, increase the bioavailability and sustain the drug release pattern. The hydrodynamic ally balanced capsule was prepared by the help of ordered mixing technique and the evaluation is performed by the different study pattern such as in vitro drug release and buoyancy studies. And various identification tests such as DSC/DTG/TGA, FTIR were also performed. The drug release study was seen by using the USP type II apparatus and using pH 1.2 as dissolution medium. Different formulation batches were prepared by using the drug and different grades of chitosan polymer such as (LF1-LF3, MF1, MF3, HF1-HF3) and the other batch of formulations were incorporated along with natural polymer Psyllium husk in combination with chitosan such as (LF4-LF6, MF4, MF6, HF4, HF6) due to these formulation we can depict that the release pattern of the drug is retarded as the concentration of polymer is increased when the polymers were combined. The kinetics of these formulations followed the zero order kinetics which shows that the therapeutic efficacy of drug is more and less side effects.

Keywords: Hydrodynamically balanced system, labetalol hydrochloride, chitosan, *plantago ovata*, anti-hypertensive drug, toxicity, and bioavailability.

I. INTRODUCTION

The Gastroretentive systems owes very tremendous and curative benefits for the delivery of oral controlled release dosage systems and have wide properties in many aspects such as Its main role is to maintain the effective concentration in the system for longer period of time. Nextly, it has a wide aspect of providing easy dosage administration to patient. These systems can remain in the gastric region for the longer period of time as per for several hours and improves the bioavailability of drug by increasing the gastric residence time. And therefore reduces the drug wastage. This system improves the solubility of drug which are lesser soluble in higher pH and widely applicable for local as well as proximal small intestinal delivery. They also acquire various delivery patterns such as single delivery systems and multiple delivery systems. By prolonging the gastric retention time a greater therapeutic activity can be achieved without any repetition of the dose^[1]. (Sharma *et al.*, 2014).

HBS Mode of Action:

Hydro dynamically controlled systems are those which consist of sufficient buoyancy to float over the gastric contents as well as they are lesser in their densities and remain buoyant in the stomach and don't affect the gastric emptying rate for a prolonged period of time. Whereas the system remains in floating state on the gastric contents, the drug is released slowly and gradually at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This causes an increased Gastric residence time and a better control in the plasma drug concentration fluctuations. Moreover, besides the minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimum level of floating force

(F) is required to keep the dosage form buoyant on the surface of thermal. Hydrodynamically balanced systems have a bulk density less than gastric fluids and therefore they remain buoyant in the stomach without hindering the gastric emptying rate for a prolonged period of time. As the system is floating on the gastric contents, the drug is released slowly and gradually at the desired rate from the system. Afterwards when the drug is released, the residual system is emptied from the stomach. This results in an increased GRT and less fluctuations in the peak plasma concentration. Hydro dynamically balanced systems have the characteristics of hydrophilic matrices, since they are able to maintain their low apparent density, whereas the polymer gets hydrated and builds a gelled barrier at the outer surface. Then the drug is released progressively from the swollen matrix. These forms remains buoyant which is up to(3- 4 hours) on the gastric contents without causing any affect to the intrinsic rate of emptying because their bulk density is lesser than that of the gastric contents^[2,3].(**Dhaiyaet al.,2011**)(**Jain et al.,2011**)

$$F = F_{\text{buoyancy}} - F_{\text{gravity}}$$

$$= (D_f - D_s) gv \dots (1)$$

Where,

F= Total vertical force,

D_f = Fluid density,

D_s = Object density,

v = Volume, and

g = Acceleration due to gravity

II. METERIALS AND METHOD:

1. Materials Required

Insert Table 1

a) Equipment's Required

Insert Table 2

2. Methods

a) Pre-formulation Studies

i. Determination of Melting point

There will be taken an opened capillary tube; drug will be filled in it and record the temperature at which the drug will start melting by Digital melting point apparatus.

ii. Determination of λ max of drug

There will be studied λ max of drug by UV- visible spectrophotometer.

iii. Determination of drug content in formulation

The drug concentration in each formulation will be determined in triplicate form by emptying each formulation in 0.1 N HCl at 37±5°C. This mixture will be stirred for 2 hours at 200 rpm. The solution would be filtered through 0.45 m membrane filter diluted and would be analysed at suitable λ max.

iv. Solubility analysis

Solubility of drug will be determined in different media. There will be prepared saturated solution of drug in different media and kept in mechanical shaker for 24 h. After that it will be filtered and the supernatant diluted and will be studied by UV visible spectrophotometer.

v. Drug interaction studies using FTIR

FTIR were firstly performed by Parker Elmer BX2, Norwalk, and USA. FTIR will be done to carry out the analysis and compound qualitative analysis as well as identification to carry out that there is any drug excipient interaction or not which occurs between the compounds. It would help in confirming the presence of functional group in certain compounds and a fair comparison between the compendiums. The methods will include the direct compression technique by using potassium bromide (KBr). One KBr pellet of 1 mm diameter of the drug is prepared by grinding 3-5 mg of the sample along with 100-500 mg of KBr pressure compression machine. Then the sample pellet would be counted on FTIR compartment and scan was taken at 4000^{-1} - 400cm^{-1} .

vi. Thermoanalytical analysis

It would be on EXSTARTG/DTA 6300 and including Thermo-gravimetric analysis, DSC (differential scanning calorimetry) DTA (differential thermal analysis, DTG (derivative thermo gravimetric) analysis, which will have sensitivity of 0.2 for TGA and 0.06 volt for DTA. And will be carried out to study the determination of characteristic peaks basically endothermic and exothermic and heat of melting will be recorded of the excipient and drug expedients mixture in present era. The study would be carried out in $5^{\circ}\text{C}/\text{min}$ till melting point is achieved in the presence of inert nitrogen using the duplicate sample of 5mg in crumpled aluminium pan.

3. Preparation of formulations

Insert Table 3

III. RESULTS AND DISCUSSION

1. Pre-formulation Studies

a. Physical characteristics

The obtained Labetalol HCl sample was found white or almost white and was in accordance with Merck Index.

i. Melting point determination

To determine the melting point of the powdered drug was first filled in capillary tube with one end open and one end closed and then the capillary was placed in Digital melting point apparatus and the temperature at which the powdered API first start melting was noted as the melting point. It was found to be 188°C against the range of 188°C - 191°C (Table 4).

Insert Table 4

ii. Solubility profile of drug in 0.1N HCl

Solubility of (LH) in 0.1N HCl was found to be 0.00542mg/ml (Table 5).

Insert Table 5

iii. Partition coefficient of drug

The partition coefficient of drug was found to be 8.05. Thus, the drug is classified to be hydrophilic in nature.

iv. Determination of λ_{max} of drug in 0.1N HCl

In 0.1N HCl, the λ_{max} of the drug was found to be 301.7nm.

Insert Figure 1

Insert Table 6

Insert Figure 2

2. Thermal Characterization Using DSC/TGA/DTG

The differential scanning calorimeter was performed by using EXSTAR TG/DTA 6300. Thermal analysis was performed to find the characteristic peaks (exothermic and endothermic) and exact melting point of drug, excipient and the drug excipient sample used in the present investigation. The DSC analysis was carried out over melting point at the rate of $5^{\circ}\text{C}/\text{min}$, in the presence of the inert nitrogen using the duplicate samples over crimped aluminium pans.

a. Thermal analysis of Labetalol HCl

Insert Figure 3

Figure 3 shows the thermal behaviour of the drug labetalol hydrochloride under the experimental conditions. The DTG Thermogram shows that the drug is stable upto 282°C. The TG Thermogram shows the loss in mass takes place from 185-300°C and during this period approximately 42% of loss of mass takes place. Maximum degradation and maximum loss of mass takes place between the temperature of 185-300°C. The DSC Thermogram shows a small endothermic peak at 191°C (having enthalpy of 84.5mj/mg) which represents the melting point of labetalol hydrochloride. It has also broad endothermic peak at 295°C (enthalpy 435mj/mg) which represents the transition temperature. The broad exothermic peak at 570°C represents the degradation of labetalol hydrochloride under experimental conditions.

Insert Figure 4

Figure 4 shows the thermal behaviour of chitosan. DTG thermo gram shows that the chitosan is stable up to the temperature of 295°C which is characterized by the help of exothermic peak. It also shows a small exothermic peak at 77°C. this shows the vaporization of water molecules from the void spaces and from the surface of chitosan degradation and maximum loss of the water molecules represented by TG and it shows the biphasic curve maximum loss of mass takes place from temperature 200-300°C and this period about 61.6% loss of mass takes place. The DSC Thermogram of chitosan shows a broad exothermic peak 304°C (enthalpy - 6.31 j/mg) which results in slow degradation of chitosan.

Insert Figure 5

Figure 5 above shows the DTG Thermogram of Psyllium husk that it is stable up to the temperature 303°C. The maximum loss of mass occurs from 200-366°C (up to 43.4% loss of mass takes place) The DSC curve shows the broad exothermic peak at 310°C with enthalpy of -77mJ/g which shows the slow degradation of Psyllium husk in experimental conditions.

Insert Figure 6

The DTG Thermogram of the physical mixtures explains that the physical mixtures are stable up to 273°C where maximum loss of mass takes place from 200-300°C which is confirmed by TG Thermogram and 57.43% of loss of mass takes place from 300-400°C and during this during this interval of time 46.63% occurs the DSC Thermogram. The DSC Thermogram shows broad exothermic peaks at 280°C which is slow degradation under experimental conditions

From these we can conclude that there is no drug excipient interaction takes place between the systems.

3. FTIR Study

Insert Figure 7

Insert Figure 8

Insert Table 7

Insert Figure 9

Insert Table 8

Insert Figure 10

Insert Table 9

Insert Figure 11

Insert Table 10

4. Buoyancy and Lag Time Studies

Insert Table 11

5. In Vitro Drug Release

Insert Table 12

Insert Figure 12

Insert Table 13

Insert Figure 13

Insert Table 14

Insert Figure 14

The different drug release pattern showed that the different release pattern of the drug and the results showed that the drug release is retarded due to the various molecular weights of chitosan as well as the action of Psyllium husk helped in retardation of drug. Such as in formulation LF1-LF3(Fig.12),MF1-MF3 (Fig.13),HF1-HF3(Fig.14) (where the retardation of drug occurs due to the different molecular weights of polymer such as the drug retardation is low in low molecular chitosan due to its low degree of deacetylation and high in high molecular weight chitosan; then the formulations such as LF4-LF6 (Fig. 12), MF4-LF6 (Fig. 13), HF4-HF6 (Fig.14), were taken where the natural polymer is added along with the chitosan and its various grades and with the drug) here we can see that there is great retardation of drug due to the synergistic effect of chitosan and psyllium husk as chitosan being positively charged having high degree of deacetylation will bind with the negatively charged mucin layer and the psyllium husk having great swelling property will cause the formation of gelling structure as it will swell causing drug to liberate slowly.

Insert Table 15

In this release kinetics (Table 15) profile were fitted to various different models like Zero order, First order, Higuchi model, and the Korsmeyer-Peppas method. In order to know the release mechanism by using MS-Excel statistical functions, various release data were processed.

From the above kinetic drug release Table 15, it was concluded that all formulation follows zero order model, it means the drug release pattern is independent on the concentration of drug, so it depicts that if the concentration of polymers increases the retardation of drug release decreases and the diffusion of drug takes place from high conc. to the low concentration. Therefore, if maximum formulations follows Zero order model this lead the high therapeutic efficacy and minimum side effects. (Dubey *et al.*, 2015)

From the n value it was depicted that it follows super case II transport model because this n value which was observed is greater than 1. Hence it means that the drug release is through erosion of polymeric chain stresses and state-transition in hydrophilic polymers which swell in water or biological fluids

IV. CONCLUSION

The present study was aimed at formulation and evaluation of hydrodynamically balanced system of labetalol hydrochloride by using chitosan and psyllium husk, use of chitosan and psyllium husk proved to form an ideal formulation as it retarded the time period of the drug for the extended period of time. This formulation can help in retardation of drug for prolonged period of time due to the effect of polymer and it will cause no toxicity as we used natural polymer such as chitosan which we get from shrimp shells and psyllium husk which is plant based polymer, so when the polymer will bind with the mucin layer no side effect will happen to the layer. The psyllium husk will help in forming gel type structure when it will come in contact with intestinal fluid due to its swelling properties. A proper evaluation of the dosage form was carried out along with various studies such as DSC/DTG/DTA, FTIR, In vitro drug release, buoyancy, and release kinetics were found out.

REFERENCES

- [1]. Ali J, Arora S, Ahuja A, Babbar AK, Sharma RK, Khar RK, Baboota S. Formulation and development of hydrodynamically balanced system for metformin: in vitro and in vivo evaluation. *European journal of pharmaceuticals and biopharmaceutics*. 2007 Aug 31;67(1):196-201
- [2]. Ankur raj Sharma, Afroz khan *et al* (2014) a gastroretentive drug delivery: an approach to enhance gastric retention for prolong drug release. *International journal of pharmaceutical science's and research*, Vol 5 issue 4, page no. 1095

- [3]. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: a review. *AapsPharmSciTech*.2005 Sep 1;6(3):E372-90.
- [4]. oBhattarai N, Gunn J, Zhang M. Chitosan-based hydrogels for controlled, localized drug delivery. *Advanced drug delivery reviews*. 2010 Jan 31;62(1):83-99.
- [5]. oDhaiyaamarjeet, Rohilaankuret *et al.* (2011) Gastroretentive dosage forms: A review on floating drug delivery systems, *international research journal of pharmacy* ISSN page no. 72-73
- [6]. Drugbank.com
- [7]. oGarse H, Vij M, Yamgar M, Kadam V, Hirlekar R. Formulation and evaluation of a gastroretentive dosage form of labetalol hydrochloride. *Archives of pharmacal research*. 2010 Mar 1;33(3):405-10.
- [8]. oGavhaneYogeshkumar N. GuravAtul S *et al.*(2013)Chitosan and its applications: A Review of literature , *International journal of research inpharmaceutical and biomedical sciences*, ISSN2229-3701, page no.(312-325)
- [9]. oGohel MC, Mehta PR, Dave RK, Bariya NH. A More Relevant Dissolution Method for Evaluation of a Floating Drug Delivery System.*Dissolutiontechnologies*. 2004 Nov;11:22-6.
- [10]. oHejazi R, Amiji M. Chitosan-based gastrointestinal delivery systems. *Journal of Controlled Release*. 2003 Apr 29;89(2):151-65
- [11]. Jagdale SC, Ghorpade SA, Kuchekar BS, Chabukswar AR. Effect of polymer and gas forming agent on floating drug delivery of tramadol hydrochloride using response surface methodology: in vitro and in vivo evaluation. *Int J Pharm Appl*. 2011;2(3):181-94.
- [12]. Joel A. Formulation and Evaluation of Sustained Release Tablets of Labetalol Hydrochloride Using Hydrophilic Polymers. *Journal of drug discovery andtherapeutics*.2013 Jun 10;1(06).
- [13]. oKshirsagar RV, Jain V, Wattamwar S. Effect of different viscosity grade HPMC polymers on gastroretentive drug delivery of Metformin Hcl. technology. 2009;9:12.
- [14]. oKulkarni S.S*, Aloorkar N.H. Smart polymers in drug delievery: An overview. *Journal of pharmacy research* 2010, 3(), 100-108
- [15]. oLokendra pal Singh, Dr. Rajesh K.S *et al.* (2011) Floating Effervescent tablet: A review, *Journal of pharmaceutical and biomedical sciences*, ISSN page no 1-2
- [16]. oMundada A, Satturwar P, Fulzele S, Joshi S, Dorle A. Characterization and evaluation of novel film forming polymer for drug delivery. *Iranian journal of pharmaceutical research: IJPR*. 2011;10(1):35.
- [17]. Narayan Bhattarai, Jonathan Gunn *et al.*(2010) Chitosan-based hydrogels for controlled, *localized drug delivey*,*www.elsvier.com* page no 86
- [18]. oPawar VK, Kansal S, Garg G, Awasthi R, Singodia D, Kulkarni GT. Gastroretentive dosage forms: a review with special emphasis on floating drug delivery systems. *Drug delivery*.2011 Feb 1;18(2):97-110.
- [19]. oPrabaharan M, Mano JF. Chitosan-based particles as controlled drug delivery systems.*Drug delivery*. 2004 Jan 1;12(1):41-57.
- [20]. oPubChemNIH U.S. *National library of medicine National Centre forbiotechnology information Compound Summary for CID 3869*
- [21]. R Garg, GD Gupta (2008) Progress in controlled gastroretentive delivery
- [22]. oRabiaAslam, YasirMehmoodet *al.* (2014) technique and polymer used to design gastroretentive drug delivery system a review, *world journal of pharmacy andpharmaceutical sciences volume 3, issue 12, Page no. 97*
- [23]. oRajinikanth PS, Mishra B. Floating in situ gelling system for stomach site-specific delivery of clarithromycin to eradicate H. pylori. *Journal of controlled release*.2008 Jan 4;125(1):33-41
- [24]. oRaju DB, Sreenivas R, Varma MM. Formulation and evaluation of floating drug delivery system of Metformin Hydrochloride. *J. Chem. Pharm. Res*. 2010;2(2):274-8.
- [25]. Ravindra J, SalunkeSadhana R, ShahiSandeep C, AtramGajendra BN. Formulation and evaluation of the hydrodynamically balanced system of ciprofloxacin HCl. *Int J Pharm Res Dev*. 2009;7(1):1-7.
- [26]. Ray D, Prusty AK. Designing and in-vitro studies of gastric floating tablets of tramadol hydrochloride.*International Journal of Applied Pharmaceutics*.2010;2(4):12-6.
- [27]. ReetikaGanjoo, ShashankSoniet *al.*(2016)Medium molecular weight chitosan as a carrier for delivery of LincomycinHCl from intra-pocket dental film: Design, Development, *in vitro* and *ex vivo* characterisation. *Jouranal of applied pharmaceutical science*, Vol.6(10)
- [28]. Salve PS. Development and in vitro evaluation of gas generating floating tablets of metformin hydrochloride. *Asian Journal of Research in Pharmaceutical Science*.2011;1(4):105-12
- [29]. oSandinaSwettha, D.V Gowdaet *al.* (2012) a comprehensive Review on gastroretentive drug delivery systems, *International journal of research in pharmaceutical andbiomedical sciences* ISSN (1285) page no (1288-1291)

- [30]. oSenyigit ZA, Vetter A, Guneri T, Bernkop-Schnürch A. A comprehensive in vitro and in vivo evaluation of thiolated matrix tablets as a gastroretentive delivery system. *Drug delivery*.2011 Aug 1;18(6):405-14.
- [31]. Shah SH, Patil J.K *et al* (2009) stomach specific floating drug delivery system A review *international journal of pharmtech research* vol 1 no 3(64-65)
- [32]. Shalini, KopparamManjunath, Development and Evaluation of Floating Sustained Release Bilayer Tablets Containing Lamivudine, *International Journal for Pharmaceutical Research Scholars (IJPRS)*,vol 4, Issue 1,2015, ISSN No: 2277 – 7873
- [33]. Sharma VK, Bhattacharya A. Isabgol husk: a herbal remedy for human health. *J Pharm Res*. 2009;2:296-301.
- [34]. oStreubel A, Siepmann J, Bodmeier R. Floating matrix tablets based on low density foam powder: effects of formulation and processing parameters on drug release. *European journal of pharmaceutical sciences*.2003 Jan 31;18(1):37-45.
- [35]. Swapnila D. Vanshiv, Hemant P joshiet *al*(2012) gastroretentive drug delivery system a review, *journal of pharmacyresearch*, vol 2 issue 12 page 1881-1883.
- [36]. oVerma A, Mogra R. Psyllium (*Plantagoovata*) Husk: A Wonder Food for Good Health.
- [37]. Whitehead L, Fell JT, Collett JH, Sharma HL, Smith AM. Floating dosage forms: an in vivo study demonstrating prolonged gastric retention. *Journal ofcontrolled release*. 1998 Oct 30; 55(1):3-12.
- [38]. oYasir M, Asif M, Bhattacharya A, Bajpai M. Development and evaluation of gastroretentive drug delivery system for theopylline using psyllium husk. *International Journal of ChemTech Research*. 2010 Apr;2(2):792-9.
- [39]. Vinod KR, Rohit Reddy T, Sandhya S, David Banji VR. Critical review on mucoadhesive drug delivery systems. *Hygeia JD Med*. 2012;4(1):1-5.

TABLE 1: MATERIALS REQUIRED FOR THE EXPERIMENT.

S.NO	NAME OF CHEMICALS	SUPPLIERS
1	Labetalol	Yarrow chem
2	Chitosan	Aldrich 448869-50G
3	Calcium Chloride	CDH 026035
4	Syringe (5 ml)	Local market
5	Psyllium Husk	Local market

TABLE 2: EQUIPMENTS/INSTRUMENTS REQUIRED FOR THE EXPERIMENT

S.No.	Equipment's/ Instruments	Suppliers	Model
1.	Digital Weighing Balance	SHIMADZU	FLB 300
2.	Mechanical Stirrer	REMI ELECTROTECHNIK LIMITED	KFU25353
3.	Magnetic Stirrer	PERFIT	KFU25353
4.	U.S.P. Dissolution test apparatus	ELECTROLAB	1301014
5.	UV-Visible Double Beam Spectrophotometer	SHIMADZU	2101
6.	Digital pH meter	SYSTRONICS MK	886131
7.	Hardness Tester	Monsanto	EHO1P
9.	Fourier Transform Infra-Red (FTIR)	SHIMADZU, MUMBAI,INDIA	
10.	Scanning electron microscopy(SEM)	435 VF	LEO, India
11.	Digital Melting point apparatus	1013 A	PERFIT Instruments, Mumbai, India
12.	Hot Air Oven	NSW- 143	NARANG SCIENTIFIC WORK Pvt, ltd, India

TABLE 3: FORMULATION TABLE

Formulation code	Labetalol HCl	Low Molecular	Medium Molecular	High Molecular	Psyllium husk

	(mg)	Chitosan (mg)	Chitosan (mg)	Chitosan (mg)	(mg)
LF1	200	60	---	---	---
LF2	200	70	---	---	---
LF3	200	80	---	---	---
LF4	200	60	---	---	30
LF5	200	70	---	---	35
LF6	200	80	---	---	35
MF1	200	---	60	---	---
MF2	200	---	70	---	---
MF3	200	---	80	---	---
MF4	200	---	60	---	30
MF5	200	---	70	---	35
MF6	200	---	80	---	40
HF1	200	---	---	60	---
HF2	200	---	---	70	---
HF3	200	---	---	80	---
HF4	200	---	---	60	30
HF5	200	---	---	70	35
HF6	200	---	---	80	40

TABLE 4: OBSERVATION TABLE OF MELTING POINT

Observed value(°C)	Depicted value(drug bank.ca)
188°C	191°C

Table 5:OBSERVATION TABLE OF SOLUBILITY OF LH IN 0.1N HCL

Solvent	Solubility(drug bank.ca)
0.1N HCl	0.00548 mg/ml

TABLE 6:CALIBRATION CURVE DATA OF LABETALOL HYDROCHLORIDE IN 0.1N HCL

Concentration (µg/ml)	Absorbance 1	Absorbance 2	Absorbance 3	Average Absorbance	±S.D
2	0.177	0.178	0.179	0.178	0.001
4	0.352	0.350	0.351	0.351	0.001
6	0.512	0.519	0.519	0.516	0.004
8	0.689	0.692	0.691	0.690	0.001
10	0.843	0.846	0.847	0.845	0.002
12	0.937	0.939	0.939	0.939	0.101

TABLE 7:INTERPRETATION OF LABETALOL HCL

Functional group	Type of vibration	wavelength (cm ⁻¹)	Reported value (Bharathiet al,2015) (cm ⁻¹)	Peak characterization (cm ⁻¹)
N-H	Stretching	3353	3341.58	3400-3250
C=O	Stretching	1719	1739.58	1750-1735
C=C	Stretching	1678	1672.26	1680-1640
C-N	Aliphatic amines	1216	1208.79	1250-1020
C-H	Stretching	743	1028.63	900-675
C-O	Alcohols,carboxylic acids,esters,ethers	1015	819.06	1320-1000

TABLE 8:INTERPRETATION OF PSYLLIUM HUSK

Functional group	Type of vibration	Peak characterization (cm ⁻¹) (Mishra et al, 2013)	Wavelength(cm ⁻¹)
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OH-	Stretching	3500-3400	3031
CH-	Stretching	2500-3000	2936
C-O	Alcohols,carboxylic acids,esters,ethers	1000-1200	1022
C=C	Stretching	1750-1735	1722

TABLE 9:INTERPRETATION OF MIXTURE OF DRUG AND POLYMER

Functional group	Type of vibration	Peak characterization(cm ¹)	Wavelength(cm ¹)
OH	Stretching	3500-3400	3031
CH	Stretching	2500-3000	2936
C-O	Alcohols,carboxylicacids,esters,ethers	1000-1200	1022
C-O-C	Stretching	1000-1500	1722
C-H	Stretching	2500-3200	2920
NH	Stretching	3500-3250	3353
C-N	Aliphatic amines	1250-1020	1216
CH ₂	Stretching	1000-1500	1354

Table 10:INTERPRETATION OF CHITOSAN

Functional group	Type of vibration	Peak characterization(cm ¹) (Ganjooet al. 2016)	Wavelength(cm ¹)
C-H	Stretching	2500-3200	2920
O-H	Stretching	Near about 3000	3290-3000
C-H ₂	Stretching	1000-1500	1354
C-O-C	Stretching	1000-1500	1151
N-H	Stretching	Near about 3000	3500-3300

Table 11:TABLE SHOWING BUOYANCY STUDIES

FORMULATION	FLOATING TIME (Hours)
LF1	3
LF2	3
LF3	3
LF4	3
LF5	3
LF6	3.5
MF1	3
MF2	3.5
MF3	3.5
MF4	3.5
MF5	3
MF6	3.5
HF1	3
HF2	3.5
HF3	3
HF4	3
HF5	3
HF6	3.5

TABLE 12:DRUG RELEASE OF FORMULATIONS LF1-LF6

Time (hrs.)	Cumulative % Drug Release					
	LF1	LF2	LF3	LF4	LF5	LF6
0	0	0	0	0	0	0
1	25.45 ±0.12	23.12 ±0.46	22.68 ± 1.46	15.87 ±0.72	13.83 ± 1.14	12.94 ±0.40

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2	32.96±0.36	25.13 ±1.22	24.65±1.70	23.09± 0.78	22.87± 1.41	20.19±0.66
3	42.04±0.71	41.99±0.71	40.92±1.18	38.69±1.29	35.54± 0.83	33.57±0.76
4	47.62±1.09	45.15±2.09	44.6±0.64	37.68±0.91	36.96±0.75	34.49±1.18
5	58.59±1.41	56.22±1.66	55.23±1.86	53.26±1.31	52.62±1.30	47.87±3.17
6	65.46±1.20	64.82±1.69	61.11±0.78	58.73±1.77	56.43±0.78	54.4±1.18
7	74.04±1.23	73.92±1.55	72.3±0.86	65.6±1.36	64.58±0.98	62.46±0.87
8	77.05±1.60	76.22±0.77	75.27±0.97	68.56±1.32	66.48±1.55	64.23±1.10
9	84.28±1.94	82.83±1.30	80.48±0.76	76.91±1.14	75.12±0.69	74.91±0.88

TABLE 13:DRUG RELEASE OF FORMULATIONS MF1-MF6

Time(hrs.)	Cumulative % drug release					
	MF1	MF2	MF3	MF4	MF5	MF6
0	0	0	0	0	0	0
1	24.18±0.68	22.41±0.37	20.45±0.78	18.2±0.58	14.63±0.86	13.55±0.78
2	23.41±1.66	21.13±0.66	18.42±0.96	15.79±0.67	15.66±0.86	14.92±1.01
3	33.83±0.57	28.37±1.17	27.58±1.44	25.08±0.84	24.75±1.46	22.94±0.86
4	46.63±0.98	42.64±0.98	40.02±0.56	37.02±1.05	32.38±0.79	30.01±0.41
5	55.97±0.74	52.96±0.96	50.72±1.06	49.9±1.10	48.29±0.72	46.97±0.98
6	57.3±0.68	55.42±1.53	52.67±0.88	50.2±0.84	49.26±1.10	47.04±0.75
7	68.7±0.82	67.07±1.24	66.41±0.94	55.14±0.91	54.22±1.06	53.11±1.26
8	76.26±1.11	74.05±0.79	73.05±0.57	72.17±0.70	71.59±0.66	69±1.31
9	82.35±0.73	80.42±0.73	79.06±1.08	78.34±0.89	76.7±1.03	75.43±0.33

TABLE 14:DRUG RELEASE OF FORMULATIONS HF1-HF6

Cumulative % drug release						
Time(hrs.)	HF1	HF2	HF3	HF4	HF5	HF6
0	0	0	0	0	0	0
1	16.92±0.68	15.05±0.62	13.35±0.74	12.67±0.87	11.35±0.83	10.84±0.19
2	24.32±0.73	24.28±0.71	22.86±1.33	20.042±0.60	15.5±0.65	14.66±1.26
3	36.17±0.67	34.28±1.16	32.4±1.16	30.68±1.64	28.74±0.95	26.73±1.02
4	44.59±1.27	43.51±1.69	42.44±2.25	34.9±1.13	32.98±1.17	30.255±0.52
5	55.34±0.80	53.741±0.48	50.52±0.85	47.63±0.43	45.71±0.65	42.75±0.82
6	57.09±1.24	55.31±1.08	52.99±1.24	47.1±0.80	46.45±0.91	42.3±2.02
7	66.14±0.80	64.75±0.91	62.45±1.41	60.88±1.08	58.3±0.94	54.53±0.72
8	79.91±0.56	75.53±1.36	74.55±1.85	72.28±1.19	70.68±1.00	69.84±0.95
9	81.07±1.45	80.55±1.13	79.48±1.19	78.04±0.76	77.26±0.79	75.61±0.98

TABLE 15:DRUG RELEASE KINETICS TABLE

FORMULATION NO.	R ²				n value
	Zero order	First order	Higuchi	Korsmeyer-peppas	
LF1	0.9913	0.5924	0.9583	0.6509	1.25
LF2	0.9798	0.679	.9395	0.7656	1.41
LF3	0.9741	0.5829	0.9439	0.6329	1.24
LF4	0.9924	0.6669	0.9273	0.7291	1.33
LF5	0.9713	0.7733	0.9468	0.7691	1.44
LF6	0.9810	0.7139	0.8921	0.6509	1.25
MF1	0.9831	0.6879	0.8853	0.7198	1.31
M2	0.9761	0.6944	0.9359	0.9729	1.01
MF3	0.9854	0.6742	0.9431	0.7597	1.41
MF4	0.9882	0.7593	0.8774	0.8012	1.43

MF5	0.9839	0.7516	0.8743	0.7902	1.43
MF6	0.9922	0.6830	0.9332	0.7724	1.39
HF1	0.9865	0.6629	0.9416	0.7357	1.36
HF2	0.9744	0.6713	0.9446	0.7638	1.36
HF3	0.9913	0.7484	0.9077	0.7919	1.43
HF4	0.9806	0.7571	0.9077	0.7919	1.43
HF5	0.9881	0.6949	0.8855	0.7559	1.37
HF6	0.9741	0.6508	0.9207	0.7240	1.34

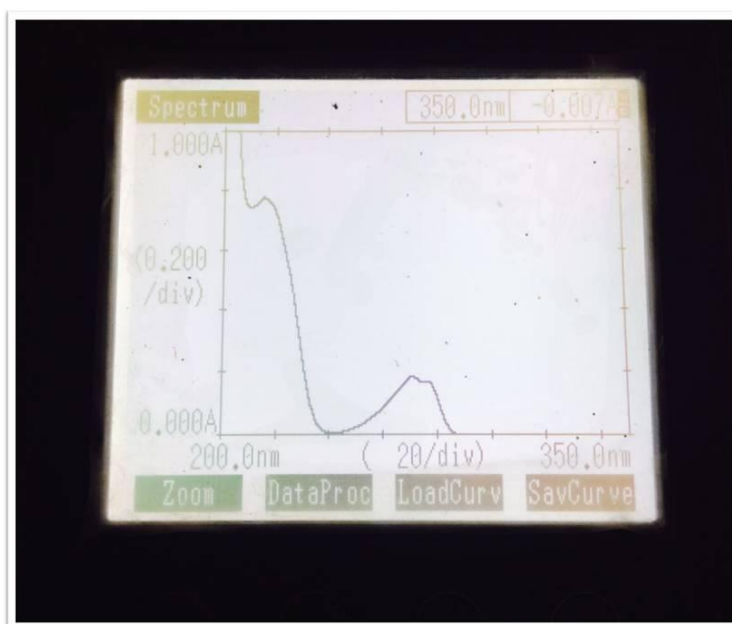


Fig. 1: Spectrum of Drug in 0.1 N HCl

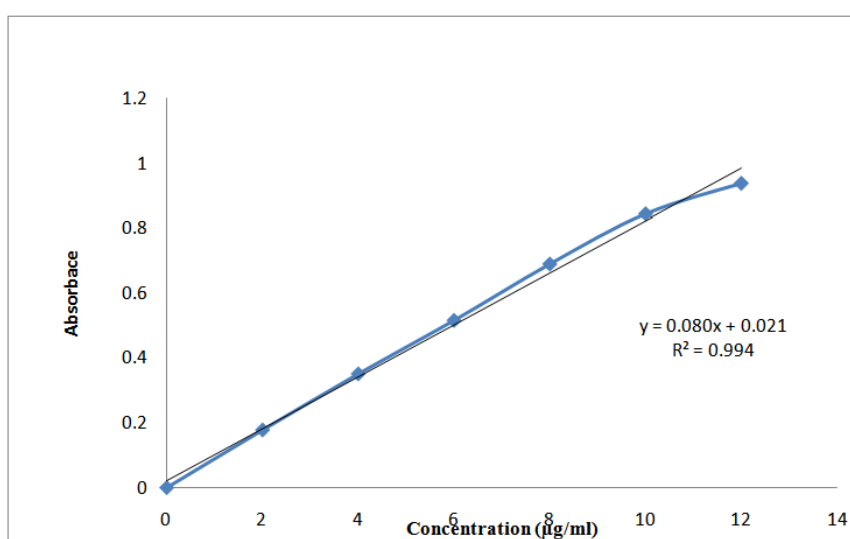


Fig. 2: Calibration curve data of Labetalol Hydrochloride in 0.1N HCl

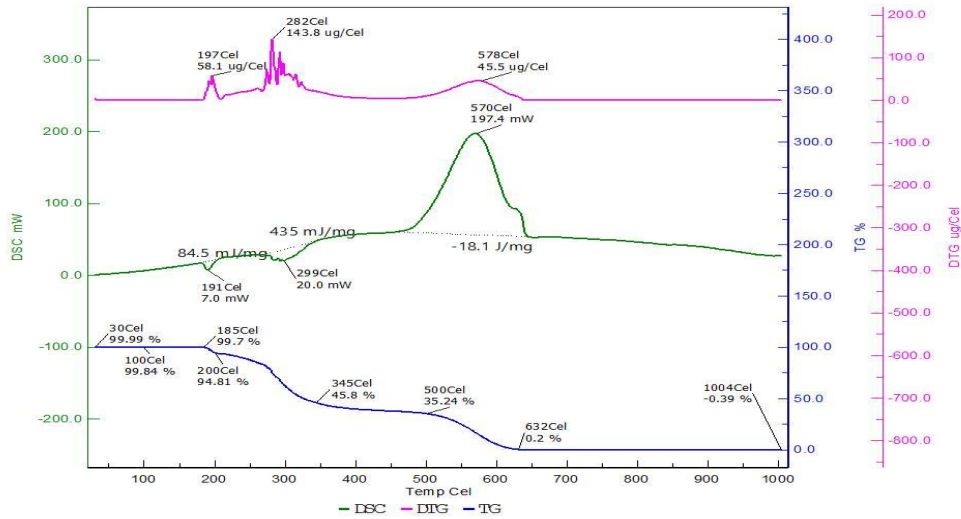


Fig. 3: Thermogram of Labetalol HCl

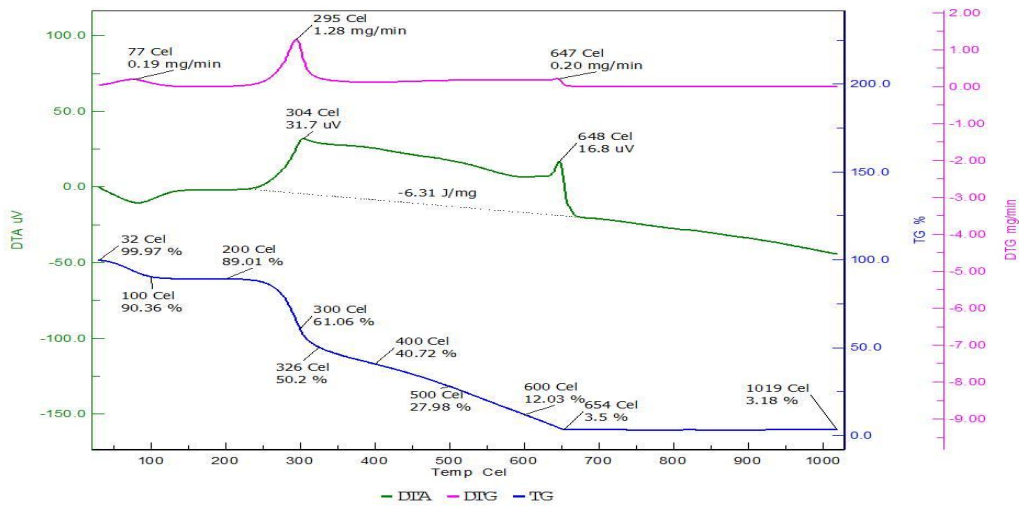


Fig. 4: Thermogram of Chitosan

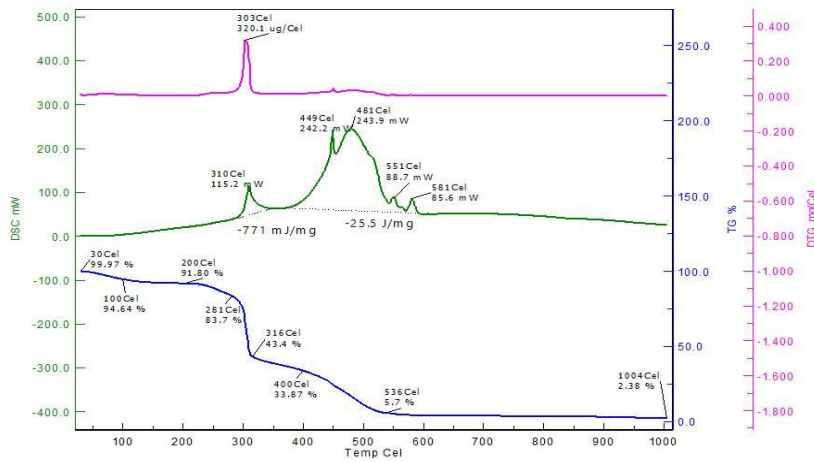


Fig. 5: Thermogram of Psyllium Husk

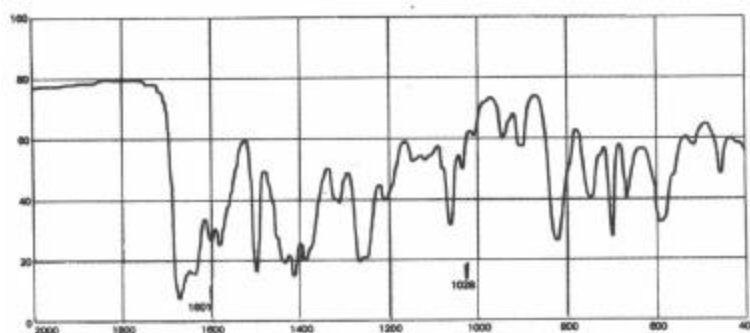


Fig. 8:FTIR of Labetalol HCl (Indian Pharmacopeia Volume I, 2014)

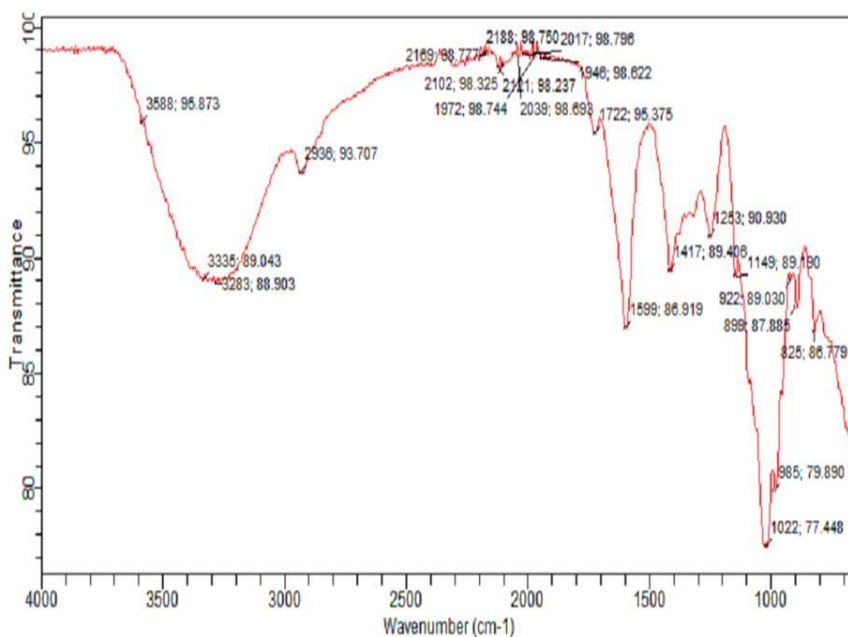


Fig. 9:FTIR of psyllium husk

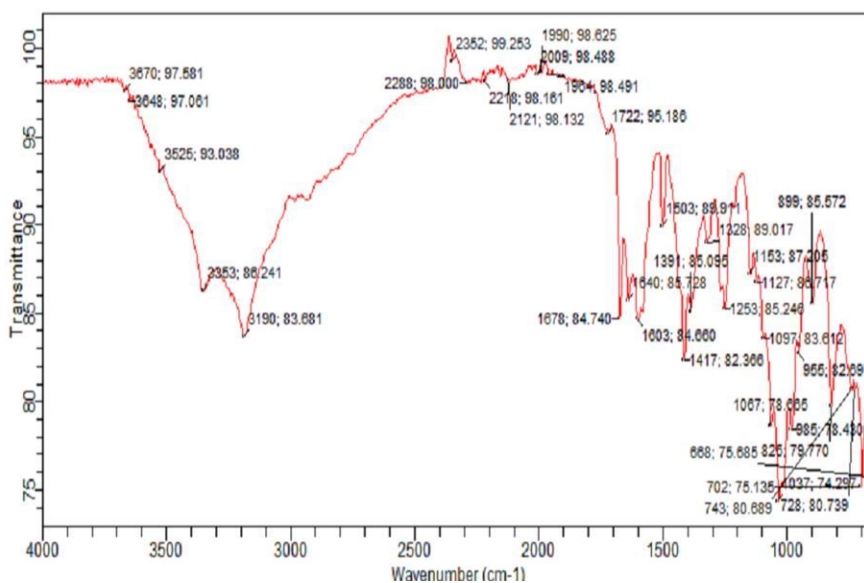


Fig. 10:FTIR of mixture of drug and polymer

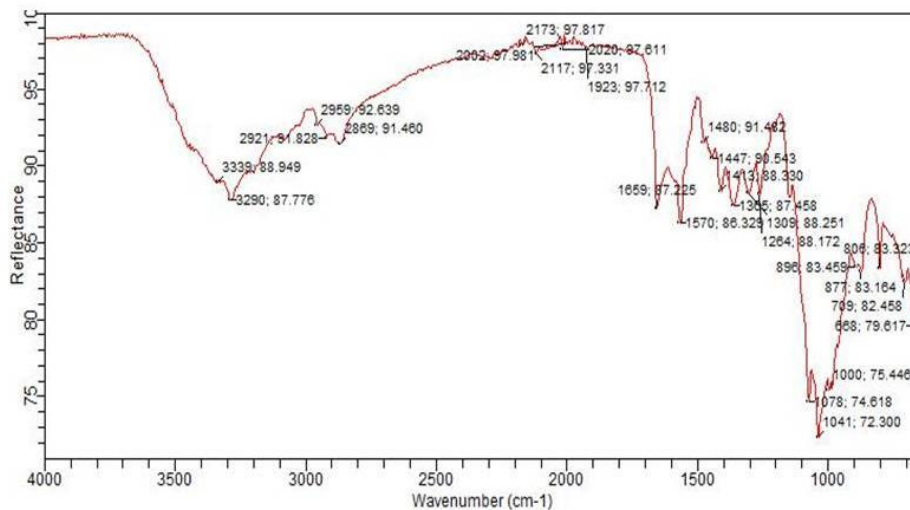


Fig. 11:FTIR of chitosan

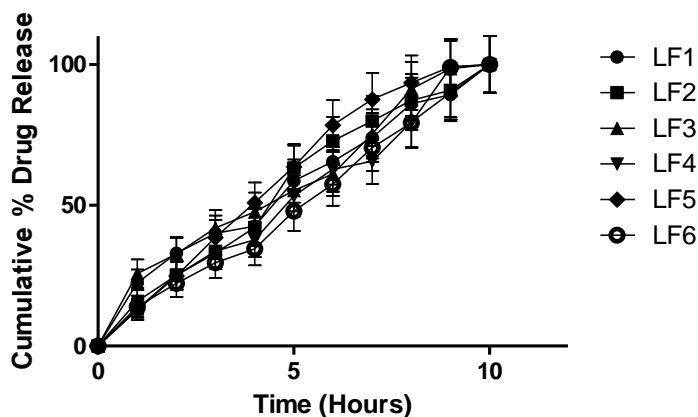


Fig. 12:Drug release of formulations LF1-LF6

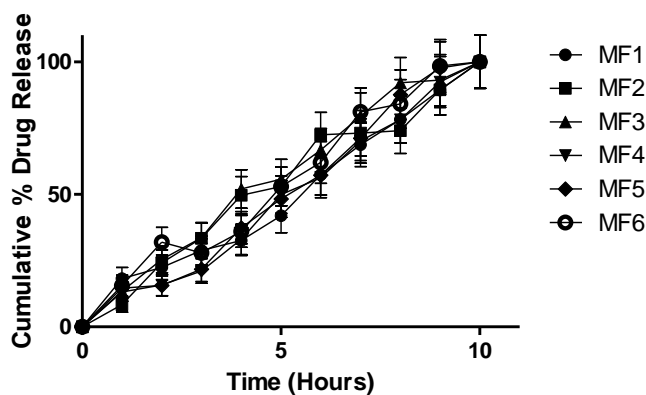


Fig. 13:Drug release of formulations MF1-MF6

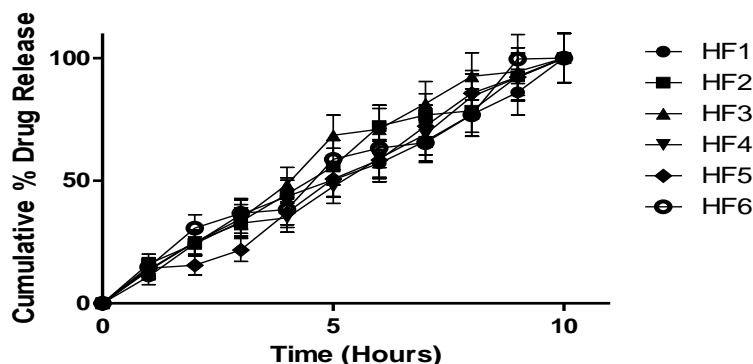


Fig. 14: Drug release of formulations HF1-HF6

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TABLE 1: MATERIALS REQUIRED FOR THE EXPERIMENT

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TABLE 5: OBSERVATION TABLE OF SOLUBILITY OF LH IN 0.1N HCL

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Fig. 1: Spectrum of drug in 0.1 N HCl

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Fig. 3: Thermogram of Labetalol HCl

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Fig. 6: Thermogram of physical mixtures

Fig. 7: FTIR of Labetalol HCl

Fig. 8: FTIR of Labetalol HCl (Indian Pharmacopeia Volume I, 2014)

Fig. 9: FTIR of psyllium husk

Fig. 10: FTIR of mixture of drug and polymer

Fig. 11: FTIR of chitosan

Fig. 12: Drug release of formulations LF1-LF6

Fig. 13: Drug release of formulations MF1-MF6

Fig. 14: Drug release of formulations HF1-HF6

Surabhi Ghildiyal, et. al. "Formulation and Evaluation of Hydrodynamically Balanced System of Labetalol Hydrochloride by Using Chitosan and PlantagoOvata for Sustained Stomach Delivery." *IOSR Journal of Pharmacy (IOSRPHR)*, 10(5), 2020, pp. 40-56.