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Research

Formulation And Evaluation Of Floating Microspheres Of Bromohexine HCL By Using Different Polymers

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Abstract

Objective: The primary objective of this study was to formulate and evaluate floating microspheres of bromhexine HCl to enhance its gastric retention time and achieve controlled drug release. The study aimed to explore the effects of different polymers on the microsphere characteristics and drug delivery profile.

Methods: Floating microspheres were prepared using various polymers, including Sodium Alginate, Guargum and Hydroxy propyl methyl cellulose through the solvent evaporation method. The formulations were characterized for their physicochemical properties, including particle size, drug entrapment efficiency, and floating behavior. In vitro drug release studies were conducted to assess the release kinetics and the ability of the microspheres to maintain floatation over time.

Results: The microspheres exhibited varying degrees of floating ability and controlled release characteristics depending on the polymer used. Among the different formulations, Guargum showed the optimal balance of prolonged floatation and sustained drug release. The drug entrapment efficiency was found to be 99.22%, and the microspheres demonstrated a zero-order, first-order release profile.

Conclusion: The study successfully developed floating microspheres of bromhexine HCl using different polymers, with Guargum showing the most promising results in terms of floating behavior and controlled drug release. These findings suggest that floating microsphere technology can significantly enhance the oral bioavailability and therapeutic efficacy of bromhexine HCl.

Keywords: Bromohexine

INTRODUCTION

The oral route is considered as the most promising route of drug delivery. Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range only when taken several times a day depending upon the dosage regimen. This result shows significant fluctuation in drug level. An approach overcome such fluctuations conventional led to the development of several novel drug delivery systems (NDDS) that could revolutionize methods of formulation and provide a number of therapeutic benefits. The main objectives of these new drug delivery systems are:

1) It would be single dose which releases the active ingredient over an extended period of time.
2) It should deliver the active entity directly to the site of action thus minimizing or eliminating the side effects.1

Controlled release, however, denotes that the system is able to provide some actual therapeutic control, whether this is of a temporal / spatial nature or both. By this the system attempts to control drug concentrations in target tissues for a controlled period of time.

Sustained release dosage forms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. In general, the goal of sustained release dosage forms is to maintain therapeutic concentration of drug for prolonged period of time. This is usually accomplished by attempting to obtain zero order release of drug from the dosage form which is independent of the concentration of drug in the delivery system (Fig. 1.1). Sustained release systems generally do not attain this type of release and usually try to mimic zero order release by providing drug in a slow first order fashion (i.e. concentration dependent). 2

Amongst the different routes of drug administration, the Oral route is the most widely used route of administration.It is considered to be most natural, unpredicted and safe due to its ease of administration, patient acceptance and cost effectiveness. The major drawback of oral drug delivery is that not all drug candidates are absorbed uniformly throughout the GIT. Unfortunately, in most cases, the vital variability of the gastrointestinal tract physiology and of its transit time leads to irregular bioavailability and non-reproducible therapeutic effects. Drug absorption from the gastrointestinal tract is a intricate procedure and is subject to many variables. Some drugs are absorbed in a particular section of GIT only or are absorbed to a different extent in various sections of GIT. Such drugs are assumed to have an “absorption window”. But, in case of „narrow absorption window“ drugs, the drug released in the region prior and in close vicinity to the absorption window is only available for absorption. Once more after crossing the absorption window, the released drug goes to waste with very little or no absorption. This phenomenon drastically diminishes the time available for drug absorption after it, which is then followed by lesser bioavailability. The other difficulties are related with physiological differences like short gastric residence time and unpredictable gastric emptying time. Many difficulties are faced in designing controlled release systems for improved absorption and enhanced bioavailability.

Most drugs are well absorbed throughout the entire intestinal tract, but some compounds, usually those that are polar in nature, are poorly absorbed from the large intestine. For such drugs, the main area from which absorption occurs is the small intestine. Some drugs may exploit a natural pathway, such as receptor-mediated transport, active transport or other specific transport mechanisms, and are known to have so-called “absorption windows” in the small intestine. Gastric emptying of dosage forms is an extremely variable process and the ability to prolong and control emptying time is a valuable asset for dosage forms that 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 associated with time of contact with the small intestinal mucosa.

Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolongation of gastric residence time (GRT) of a rate-controlled oral drug delivery system reduces inter-subject variability and the so-called “peak and valley” effect, leading to increased predictability and bioavailability of the dosage form, especially for molecules with a narrow absorption window. Moreover, the total gastrointestinal transit time is prolonged, thus, the number of dosage regimen can be reduced and solubility can be improved for drugs that are less soluble in a high pH environment.

Recent advances in novel drug delivery system to enhance the safety and efficacy of the drug molecule by formulating a dosage form being convenient for administration. The high level of patient compliance has been observed in taking oral dosage forms is due to the ease of administration and handling of these forms. There are lot of

advancements have been seen in oral controlled drug delivery system in the last few decades, this system has been of limited success in case of drugs with a poor absorption window throughout the GIT (Gastro Intestinal Tract).
To modify the GIT time is one of the main challenge in the development of oral controlled drug delivery system. Gastric emptying of dosage form is extremely variable process and ability to prolong and control the emptying time is valuable asset for dosage forms, which reside in the stomach for a long period of time than conventional dosage forms. Several difficulties are faced in designing controlled released systems for better absorption and enhanced the bioavailability.

Although single unit floating dosage forms have been extensively studied, these single unit dosage forms have the disadvantage of a release all or nothing emptying process while the multiple unit particulate system pass through the GIT to avoid the vagaries of gastric emptying and thus release the drug more uniformly. The uniform distribution of these multiple unit dosage forms along the GIT could result in more reproducible drug absorption and reduced risk of local irritation; this gave birth to oral controlled drug delivery and led to development of Gastro-retentive floating microspheres. Microspheres can be defined as solid, approximately spherical particles ranging in size from 1 to 1000 micro meter. The Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature. Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs. Microspheres are small in size and therefore have large surface to volume ratios. The concept of incorporating quantities of materials within microspheres dates back to the 1930s and to the work of Bungerberg de joing and coworkers on the entrapment of substances within coacervates. The potential uses of microspheres in the pharmaceutical have been considered since the 1960's and have a number of applications. The use of microspheres in pharmaceuticals have a number of advantages Viz., Taste and odour masking, conversion of oils and other liquids to solids for ease of handling, protection of drugs against environment (moisture, heat, light and oxidation), separation of incompatible materials, to improve flow of powders, production of sustained release, controlled release and targeted medications.

Gastroretentive Drug Delivery System

Oral controlled release (CR) dosage forms (DFs) have been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and flexibility in formulation. However, this approach is bedilled with several physiological difficulties such as inability to restrain and locate the controlled drug delivery system within the desired region of gastrointestinal tract (GIT) due to variable gastric emptying and motility.

Furthermore, the relatively brief gastric emptying time (GET) in humans which normally averages 2-3 h through the major absorption zone, i.e., stomach and upper part of the intestine, can result in incomplete drug release from the drug delivery system leading to reduced efficacy of the administered dose.
Therefore, control on placement of a variety of important drugs through appropriately designed drug delivery system (DDS) in a specific region of the GI tract offers advantages particularly for those having a narrow absorption window in the GIT or those with stability problems.

These considerations have led to the development of a unique oral controlled release dosage form with gastroretentive properties. After oral administration, such a DF would be retained in the stomach and release the drug there in a controlled and prolonged manner so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract.

Gastroretentive dosage form 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 of drugs that are less soluble in a high pH environment.

Drug candidates not suitable for Gastroretentive drug delivery systems

- Drugs that have very limited acid solubility e.g. phenytoin etc.
- Drugs that suffer instability in the gastric environment e.g. erythromycin etc.
- Drugs intended for selective release in the colon e.g. 5- amino salicylic acid and corticosteroids etc.

A number of systems have been applied to increase the GRT of dosage forms by employing a variety of concepts. These systems have been classified according to the basic principles of gastric retention (Fig. 1.3).

1. Floating drug delivery system (FDDS) with low density providing sufficient buoyancy to float over the gastric contents.
2. Bioadhesive systems enabling the localized retention of the drug in the stomach.
3. Swelling and expanding systems preventing transit from the gastric sphinctor.

4. High density systems remaining in the stomach for longer period of time by sedimenting to the folds of stomach. Fig no1.4: Illustrates the mechanism of these systems in stomach.

A number of other methods like use of passage-delaying agents and modified shape systems have also been used for gastro retention purposes.[7]

Floating microspheres (Hollow Microspheres) are gastroretentive drug delivery systems based on noneffervescen approach. The word Floating systems, first described by, have bulk density lower than that of the gastric fluid and thus remain buoyant in stomach without affecting the gastric emptying rate for a prolonged period of time. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations. While the system is floating on the gastric contents, the drug is released slowly at the desired rate and the system is eliminated from the stomach.

Many studies have demonstrated the validity of the concept of buoyancy in terms of prolonged GRT of the floating forms, improved bioavailability of drugs and improved effects in clinical situations. The results obtained have also demonstrated that the presence of gastric contents is needed to allow the proper achievement of the buoyancy retention effect.

Among the different hydrocolloids recommended for floating formulations, cellulose ether polymers are the most popular, especially hydroxypropylmethylcellulose (HPMC). Fatty material with a bulk density lower than 1 may be added to the formulation to decrease the water intake rate and increase buoyancy.

MATERIALS AND METHODS

Bromohexine Hcl-Procured From IPCA Laboratories Ltd., Mumbai, India Provided by SURA LABS, Dilsukhnagar, Hyderabad, Sodium alginate-Sd.Fine Chemicals, Mumbai, India, Guargum-Yarrow chemical products, India, Hydroxy propyl methyl cellulose-ONTOP Pharmaceuticals, Bangaloore, India, Sodium bicarbonate-CDH (P) Ltd, New Delhi, India, Calcium chloride-Merck Specialities Pvt Ltd, Mumbai, India, Acetic acid- Loba chemie Pvt Ltd. Mumbai , Glutaralde hyde-Merck Specialities Pvt Ltd, Mumbai, India

METHODOLOGY

Analytical method development

Determination of absorption maxima

100mg of Bromohexine Hcl pure drug was dissolved in 15ml of Methanol and make up to 100ml with 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with100ml by using 0.1 N HCL (stock solution-2 i.e 100µg/ml). From this 10ml was taken and make up with 100 ml of 0.1 N HCl (10µg/ml). Scan the 10µg/ml using Double beam UV/VIS spectrophotometer in the range of 200 – 400 nm.

Preparation calibration curve:

100mg of Bromohexine Hcl pure drug was dissolved in 15ml of Methanol and volume make up to 100ml with 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with100ml by using 0.1 N HCl (stock solution-2 i.e 100µg/ml). From this take 0.2, 0.4, 0.6, 0.8and 1.0ml of solution and make up to 10ml with 0.1N HCl to obtain 2, 4, 6 ,8, and 10 µg/ml of Bromohexine Hcl solution. The absorbance of the above dilutions was measured at 220 nm by using UV-Spectrophotometer taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The experiment was pre formed in triplicate and based on average absorbance; the equation for the best line was generated. The results of standard curve preparation are shown in table-5.1 & figure-6.3

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

Drug excipient interaction studies are significant for the successful formulation of every dosage form. Fourier Transform Infrared (FTIR) Spectroscopy studies were used for the assessment of physicochemical compatibility and interactions, which helps in the prediction of interaction between drug and other excipients. In the current study 1:1 ratio was used for preparation of physical mixtures used for analyzing of compatibility studies. FT-IR studies were carried out with a Bruker, ATR FTIR facility using direct sample technique

Preparation of microspheres

Microspheres are matrix systems that contains drug throughout their structure and are potential candidates for oral controlled release. Microspheres can be defined as solid spherical particles ranging from 1 to 1000µm in size. These particles contains of the drug which is the core material, and a coating material. The choice of methods for the preparation of microspheres depends on many factors such as the drug solubility, partition co efficient, Polymer composition, molecular weight etc.

The microsphere was prepared by solvent evaporation and ionic gelation technique. The 25 mg of Bromohexine Hcl was dispersed uniformly in aqueous mucilage of Sodium alginate. To this dispersion desired polymer was mixed in suitable proportion. Then, gas-forming agent such as Calcium carbonate and sodium bicarbonate was separately added to the solution. The resulting solution was dropped through a 26G syringe needle into 5% (w/v) glutaraldehyde/$CaCl_2$ solution which is prepared in water containing 10% (v/v) acetic acid. The process done with constant stirring (600rpm) at 60-70^oC. The solvent is slowly evaporated. The solution containing suspend microsphere was kept for 1.5 hr. To improve the mechanical strength of the microsphere and allowed to complete the reaction to produce gas. The fully formed microsphere were collected, washed with distilled water and subsequently air dried. The composition of floating microsphere are shown in Table 1.

Table 1: Composition of Floating Microspheres

INGREDIENTS	B1	B2	B3	B4	B5	B6	B7	B8	B9
Bromohexine Hcl	50	50	50	50	50	50	50	50	50
Sodium Alginate	15	30	45	-	-	-	-	-	-
Guargum	-	-	-	15	30	45	-	-	-
Hydroxy propyl methyl cellulose	-	-	-	-	-	-	15	30	45
Sodium bicarbonate (% w/w	30	30	30	30	30	30	30	30	30
Calcium chloride(% w/v	10	10	10	10	10	10	10	10	10
Acetic acid (%v/v)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Glutaralde hyde %	5	5	5	5	5	5	5	5	5

RESULT AND DISCUSSION

The present work was designed to developing Floating Microspheres of Bromohexine Hcl using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

Analytical Method

Standard graph of Bromohexine Hcl in 0.1N HCL

The scanning of the 10µg/ml solution of Bromohexine Hcl in the ultraviolet range (200-400 nm) against 0.1 N HCL the maximum peak observed at λ_{max} as 220 nm. The standard concentrations of Bromohexine Hcl (2-10 µg/ml) was prepared in 0.1N HCL showed good linearity with R^2 value of 0.999, which suggests that it obeys the Beer--Lamberts law.

Table 2: Standard curve of Bromohexine Hcl in 0.1N HCL

S.No	Concentration mcg/ml	Absorbance
1.	0	0
2.	2	0.111
3.	4	0.226
4.	6	0.335
5.	8	0.442
6.	10	0.551

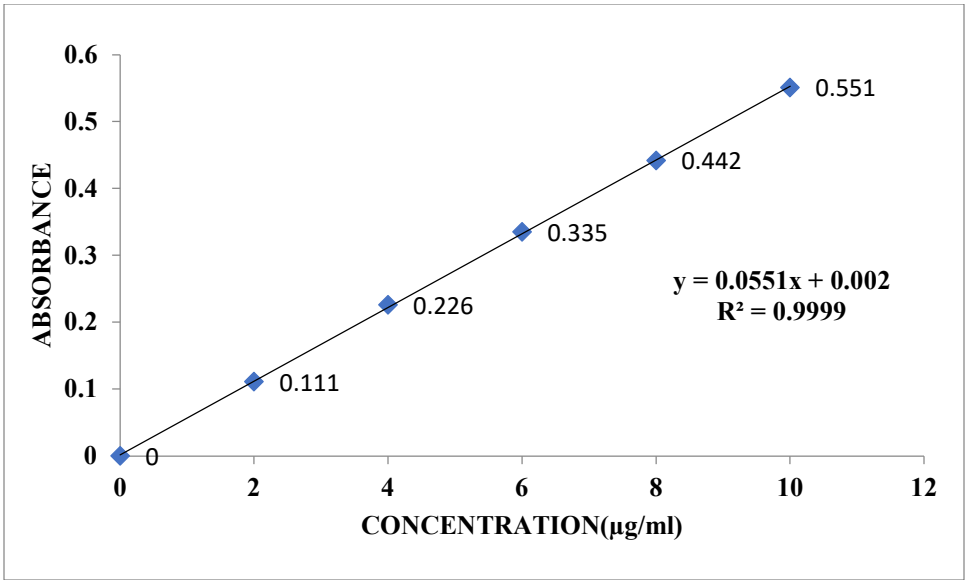

Fig 1: Calibration curve of Bromohexine Hcl in 0.1 N HCL at 220 nm

Evaluation parameters

Table 3: Evaluation of Floating Microspheres

Batch No	Mean Particle size(µm)	Bulk Density (gm/ml)	Tapped density (gm/ml)	Carr's Index	Hausner's ratio	Angle of repose (θ)
B1	410.32	0.525±0.11	0.619±0.02	15.32±0.09	1.197±0.07	35.24±0.07
B2	256.29	0.522±0.34	0.621±0.04	14.87±0.35	1.185±0.06	36.27±0.06
B3	453.81	0.526±0.65	0.614±0.01	15.62±0.72	1.187±0.13	34.65±0.08
B4	290.53	0.522±0.25	0.615±0.04	15.64±0.26	1.175±0.02	33.54±0.04
B5	338.56	0.516±0.24	0.622±0.05	14.96±0.15	1.186±0.03	32.21±0.01
B6	462.12	0.527±0.45	0.618±0.01	16.53±1.6	1.198±0.21	39.23±0.01
B7	459.87	0.522±0.36	0.623±0.02	14.56±0.20	1.170±0.01	31.10±0.02
B8	329.68	0.525±0.99	0.611±0.01	14.91±0.33	1.175±0.03	32.19±0.02
B9	337.61	0.517±1.05	0.617±0.03	15.66±0.10	1.185±0.15	33.28±0.01

Micromeritic properties of Microspheres

The Micromeritic properties of different batch are shown in above table. The mean diameter of the CNZ-loaded Sodium alginate cps microspheres, the mean diameter of batch 1 to 10 ranges between 256.29 and 462.12 µm. The average size of the microspheres increased slightly as the amount of polymer concentration increased. The hardening agent caused a decrease in bead size as it promoted the formation of cross-links between the alginate molecules. The tapped density of beads of different batch 1-12 ranges between 0.610±0.01 - 0.623±0.02 gm/ml respectively. The Compressibility Index ranges between 14.56±0.20 -16.53±1.6 gm/ml, shows that all the formulation preparations were good flowability. The Hausner's ratio of different batch ranges between 1.17±0.02 - 1.198±0.21. The Hausner's ratio result shows that all the preparations were good flowability.

Table 4: Result of mean Particle Size, *In vitro* Buoyancy and Encapsulation efficiency%

Batch No:	*In vitro* Buoyancy (in sec)	Encapsulation efficiency%
B1	58.01	98.36
B2	42.36	95.22
B3	39.12	99.35

B4	61.90	97.61
B5	48.64	98.20
B6	69.45	99.48
B7	56.39	97.69
B8	68.99	99.34
B9	36.24	96.75

Drug Entrapment Efficiency (EE) and Floating Property

The floating property of the microspheres was calculated from the fractional amount of drug and polymer density of the microspheres. As shown in above table the Floating efficiency of the sodium alginate microspheres. The floating agent sodium bicarbonate containing (batch 1-12) ranges from 36.24 and 69.45 % and floating agent Calcium chloride containing formulations (batch 1-12) shows from 97.43 – 99.61.

Table 5: *In vitro* drug release of containing Bromohexine Hcl B1 to B3 formulations

TIME	**CUMULATIVE PERCENT DRUG RELEASED**								
(hr)	**B1**	**B2**	**B3**	**B4**	**B5**	**B6**	**B7**	**B8**	**B9**
0	0	0	0	0	0	0	0	0	0
0.5	6.77	5.68	7.93	13.66	5.64	6.58	4.68	3.58	8.89
1	19.25	15.97	19.49	21.56	18.19	13.72	15.97	17.18	18.19
2	22.27	24.51	23.73	25.36	22.05	17.61	19.51	25.08	22.61
3	24.68	29.68	26.25	29.53	26.64	28.93	24.68	29.25	32.55
4	28.17	33.07	31.24	35.12	29.98	32.45	31.07	32.85	38.68
5	46.39	41.51	47.43	44.67	48.31	33.83	38.76	39.55	47.28
6	55.67	47.42	56.80	57.24	56.07	41.04	44.44	47.21	55.75
7	59.29	55.22	61.31	63.36	59.67	48.36	51.39	53.51	72.91
8	62.26	59.71	65.49	75.23	62.89	56.84	59.71	56.37	76.26
9	64.75	65.12	71.18	81.39	65.21	62.87	65.05	72.29	82.66
10	69.26	69.89	76.94	88.12	75.59	72.51	69.68	78.06	85.89
11	73.94	74.95	85.76	92.08	86.43	83.48	77.16	83.48	87.85
12	85.86	82.46	91.79	99.22	94.28	91.96	89.46	87.81	89.25

The % drug release of formulations (B1 to B3) containing Sodium Alginate depends on the concentration of polymer. The concentration of Sodium Alginate 1:1, 1:2 and 1:3 was able to retard the drug release up to desired time. When the concentration of polymer increased to was able to retard the drug up to 12 hours. In B3formulation 1:3 ratio (drug: polymer) ratio was maximum drug release was showed at 12 hours.

The % drug release of B4to B6formulations depends on polymer ratio Guargum. The concentration of Guargum 1:1, 1:2, and 1:3 ratios was excess retard the drug release up to desired time. In B4 formulations, Guargum **contain 1:1 ratio** showed maximum % drug release i.e 99.22% at 12 hours.

The % drug release of B7 to B9formulations depends on polymer ratio Guargum. The concentration of Guargum 1:1, 1:2, and 1:3 ratios was excess retard the drug release up to desired time. In B7 formulations, Hydroxy propyl Methyl Cellulose **contain 1:1ratio** showed maximum % drug release i.e 89.46% at 12 hours. Hence based on dissolution data of 9 formulations, B1, B2, B3, B5, B6, B7,B8,B 9,B10,B11,**B**12 formulations showed better release up to 12 hours. Among these formulations B4 formulation showed the drug release (99.22%) within the specified limits. So B4 formulation is optimised formulation.

Application of Release Rate Kinetics to Dissolution Data

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Bromohexine Hcl release. The data was fitted into various kinetic models such as zero, first order kinetics; higuchi and korsmeyer peppas mechanisms and the results were shown in below table**.**

Table 6: Release kinetics data for optimized formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE/ t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	**0**	0			2.000				100	4.642	4.642	0.000
13.66	0.5	0.707	1.135	-0.301	1.936	27.320	0.0732	-0.865	86.34	4.642	4.420	0.222
21.56	1	1.000	1.334	0.000	1.895	21.560	0.0464	-0.666	78.44	4.642	4.281	0.361
25.36	2	1.414	1.404	0.301	1.873	12.680	0.0394	-0.596	74.64	4.642	4.210	0.431
29.53	3	1.732	1.470	0.477	1.848	9.843	0.0339	-0.530	70.47	4.642	4.130	0.511
35.12	4	2.000	1.546	0.602	1.812	8.780	0.0285	-0.454	64.88	4.642	4.018	0.623
44.67	5	2.236	1.650	0.699	1.743	8.934	0.0224	-0.350	55.33	4.642	3.811	0.831
57.24	6	2.449	1.758	0.778	1.631	9.540	0.0175	-0.242	42.76	4.642	3.497	1.145
63.36	7	2.646	1.802	0.845	1.564	9.051	0.0158	-0.198	36.64	4.642	3.321	1.320
75.23	8	2.828	1.876	0.903	1.394	9.404	0.0133	-0.124	24.77	4.642	2.915	1.727
81.39	9	3.000	1.911	0.954	1.270	9.043	0.0123	-0.089	18.61	4.642	2.650	1.992
88.12	10	3.162	1.945	1.000	1.075	8.812	0.0113	-0.055	11.88	4.642	2.282	2.360
92.08	11	3.317	1.964	1.041	0.899	8.371	0.0109	-0.036	7.92	4.642	1.993	2.648
99.22	12	3.464	1.997	1.079	-0.108	8.268	0.0101	-0.003	0.78	4.642	0.921	3.721

Drug and Excipient Compatibility Studies

FTIR study

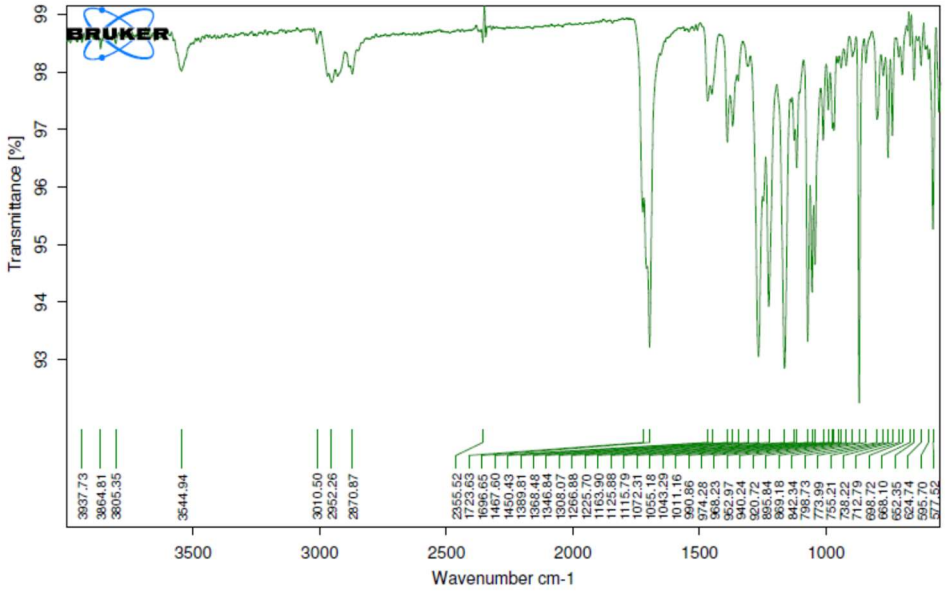

Fig 2: FTIR GRAPH OF PURE DRUG

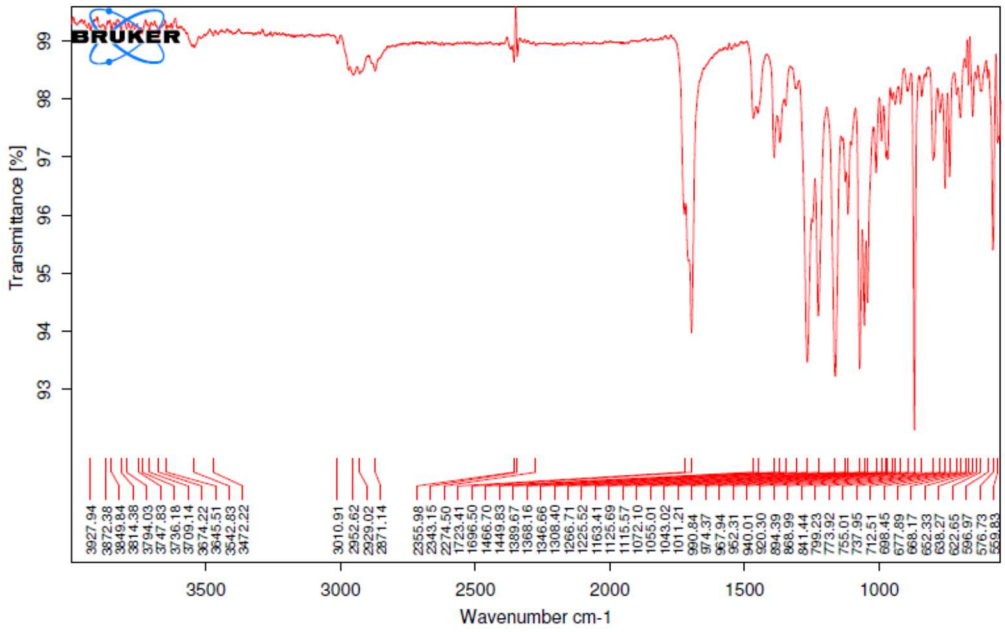

Fig 3: FTIR GRAPH OF OPTIMISED FORMULATION

From the FTIR data it was evident that the drug and excipients doses not have any interactions. Hence they were compatible.

CONCLUSION

The formulation and evaluation of floating microspheres containing bromhexine HCl using various polymers have demonstrated promising results in enhancing the drug's gastrointestinal retention time and controlled release profile. The study successfully developed microspheres with varying polymer compositions, including Sodium Alginate ,Guargum and Hydroxy propyl methyl cellulose each impacting the microsphere characteristics such as floating behavior, drug release kinetics. The microspheres formulated with Sodium Alginate, Guargum and Hydroxy propyl methyl cellulose exhibited the most favorable properties, including prolonged floatation and a consistent, controlled drug release, which is crucial for improving the therapeutic efficacy and patient compliance of bromhexine HCl. The in vitro release studies indicated that the optimized microspheres maintained their floating ability for an extended period and provided a sustained release of the drug, aligning with the desired pharmacokinetic profile. These findings underscore the potential of using floating microsphere technology to enhance the oral bioavailability of bromhexine HCl and other similar drugs. Future work could focus on further optimizing the formulation parameters, conducting in vivo studies to validate the clinical efficacy, and exploring the scalability of the manufacturing process.

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