ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 10| Issue: 4| April 2024|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2024: 8.402 || ISI Value: 1.188

FORMULATION AND EVALUATION OF CLINDAMYCIN HYDROCHLORIDE FLOATING DRUG DELIVERY

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Article DOI: https://doi.org/10.36713/epra16414
DOI No: 10.36713/epra16414

ABSTRACT

The Clindamycin Hydrochloride is a broad spectrum cephalosporin antibiotic. It is mainly used to treatment of bacterial infections. It is a suitable candidate for controlled release administration due to its short elimination time 1 hours. The main aim of present investigation is to increase the gastric residence time by preparing floating drug delivery by using raft forming approach thereby improving bioavailability. The prepared Clindamycin Hydrochloride floating drug delivery were evaluated for hardness, weight variation, thickness, friability, drug content uniformity, total floating time, In-vitro dissolution studies and buoyancy lag time. Floating tablets were formulated using direct compression technique. Various polymers are used in the formulation they Micro crystalline cellulose used as binder, HPMC K15M, Guargum used as hydrophilic polymers, Chitosan, Sodium bicarbonate was incorporated as an effervescent substance, Sodium alginate used as viscous gel forming agent, Magnesium streate used as lubrication, talc was used as diluent. The formulated Clindamycin Hydrochloride tablet to be evaluated the following parameters as follow Weight variation (mg), Hardness, Thickness, Friability, Drug content uniformity, Floating lag time, the in vitro cumulative amount of drug released was shown the F4 is 99% within 12 Hours the comparative studies with marketed formulations F4 show the better results. In vitro release rate studies showed that the maximum drug release was observed F4 formulation up to 12 hours.

KEYWORDS: *Clindamycin Hydrochloride, Direct compression, Floating drug delivery system.*

INTRODUCTION

The substances produced by microorganisms, they selectively suppress the development of or destroy other microorganisms at very low concentrations. The definition includes other natural substances which also inhibit microorganisms but are produced by higher forms (e.g. antibodies) or even those produced by microbes but are needed in high concentrations (ethanol, lactic acid, H_2O_2). Initially the term 'chemotherapeutic agent' was restricted to synthetic compounds, but now since many antibiotics and their analogues have been synthesized, this criterion has become irrelevant; both synthetic and microbiologically produced drugs need to be included together. It would be more meaningful to use the term Antimicrobial agent to designate synthetic as well as naturally obtained drugs that attenuate microorganisms. Oral controlled release dosage forms has not been suitable for a variety of important drugs, characterized by a narrow absorption window in the upper part ofthe gastrointestinal tract i.e. stomach and small intestine. This is due to the relatively short transit time of the dosage form in these anatomical segments. Thus, after only a short period of less than 6hrs, the control release dosage form has already left the upper gastrointestinal tract and the drug is released in non-absorbing

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distal segments of the gastrointestinal tract. This results in a short absorption phase that is often accompanied by lesser bioavailability.

MATERIALS AND METHODS

MATERIALS

The best sample Clindamycin hydrochloride is from Hetero Drugs LTD and other polymer mixtures such as Micro crystalline cellulose, Sodium alginate, HPMC K15M, Guar gum, Chitosan, Sodium bicarbonate, Talc, and Magnesium stearate are from Aurobindo pharma LTD. All these materials those were either AR/ LR grade or the best possible grade were used as supplied by the manufacture.

METHODS

PRE-FORMULATION

Drug and excipients interaction (FTIR) study

The compatibility between pure drug and polymer like Clindamycin Hydrochloride, HPMC K15M, guar gum, chitosan, Mcc, mixture of compounds prepared in the form of KBr Pellets and subjected for scanning from 4000 cm^{-1} to 400 cm^{-1} using FTIR spectroscopy.

Formulation of Floating Tablet of Clindamycin Hydrochloride

The Floating Raft forming approach tablets of Clindamycin Hydrochloride were prepared through direct compression method. The preparations of Clindamycin Hydrochloride by various steps involved in tablet production are sieving, mixing, lubrication and compression. Microcrystalline cellulose use as binder, HPMC K 15M used as synthetic hydrophilic polymer. Guar gum and chitosan used as natural hydrophilic polymer. Sodium alginate use as viscous gel forming, sodium bicarbonate used as gas generating agent. Talc is used as diluents, magnesium stearate used as lubricant. Finally, the powder mixture was compressed into tablets using rotator tablet punching machine at the weight of 500mg each. The below expressed gastro retentive drug delivery of Clindamycin Hydrochloride tablets performed a different formulation from F1 to F9 batches study with various concentrations of different polymers.

Table 1

Formulation of gastro retentive of Clindamycin Hydrochloride tablet prepared by using different polymers

Ingredients	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Clindamycin Hydrochloride (mg)	150	150	150	150	150	150	150	150	150
Micro crystalline cellulose (mg)	165	115	85	165	115	85	165	115	85
Sodium alginate (mg)	70	70	90	70	70	90	70	70	90
HPMC K15M (mg)	60	110	110	---	---	---	---	---	---
Guar gum (mg)	---	---	---	60	110	110	---	---	---
Chitosan (mg)	---	---	---	---	---	---	60	110	110
Sodium Bicarbonate (mg)	40	40	50	40	40	50	40	40	50
Talc (mg)	9	9	9	9	9	9	9	9	9
Magnesium stearate (mg)	6	6	6	6	6	6	6	6	6
Total (mg)	500	500	500	500	500	500	500	500	500

- **All formulation are shown in mg**

Parameters for Evaluation

Pre Compression Parameters

Angle of repose: Angle of repose is defined as the maximum angle between the surface of pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height (h), above a flat horizontal surface on which a graph paper was placed. Powder was carefully poured through the funnel until the apex of the conical pile formed just reached the tip of the funnel. These studies were carried out before and after incorporating lubricant/glidant. The angle of repose (ɵ) was then calculated.

$$\Theta = \tan^{-1}(h/r)$$

Bulk density: Bulk density was determined by using bulk density apparatus, during measurement accurately weighed quantity of the powder were taken in a measuring cylinder and recording the volume and weight of the total powder[61]. Bulk density is expressed in gm/ml and is given by,

$$BD = W/V_o$$

Tapped density: Tapped density was determined by using Tapped density apparatus during measurement accurately weighed quantity of the powder were taken in a measuring cylinder and recording the volume of powder after30 tapping and weight of the total powder.

$$TD = W/V_F$$

Compressibility index (or) Carr's index: Compressibility index is an important measure that can be obtained from the bulk and tap densities. A material having values less than 20 to 30% is defined as the free flowing material, based on the apparent bulk

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density and tapped density, the percentage compressibility of the bulk drug was determined by using the following formula.

Compressibility index = (TD – BD) × 100

Hausner's ratio: It indicates the flow properties of the powder. The ratio of tapped density to bulk density of the powder is called Hausner's ratio.

Hausner's Ratio=TD/BD

Table 2
Standard limits for flow properties of powder

S.NO.	Type of flow	Angle of repose	Carr's index	Hausner's ratio
1.	Excellent	25-30	10	1-1.11
2.	Good	31-35	11-15	1.12-1.18
3.	Fair	36-40	16-20	1.19-1.25
4.	Passable	41-45	21-25	1.26-1.34
5.	Poor	46-55	26-31	1.35-1.45
6.	Very poor	56-65	32-37	1.46-1.54
7.	Very Very poor	>65	>38	>1.60

Post Compression Parameters

Hardness: The hardness of ten tablets was measured using Monsanto tester. Resistance of the tablet during transportation or breakage under storage conditions and handling before usage depends on its hardness. The hardness was measured in terms of kg/cm^2. Five tablets were chosen randomly and tested for hardness. The average hardness of five tablets was recorded.

Thickness: Thickness was measured using a calibrated vernier calliper. It was determined for check the thickness of tablet. Five tablets of each formulation were picked randomly and thickness was measured individually.

Friability: The friability of the prepared tablets was determined using Roche friability apparatus. It is expressed in percentage (%). To calculate the percentage friability determines 10 tablets initial weight and transferred into friabilator. The friabilator was operated at 25 rpm for four mintues. After four minutes the tablets were weighed again. Then % friability was then calculated using formula.

$$\% \text{ Friability} = \frac{\text{initial weight} - \text{final weight} \times 100}{\text{Initial weight}}$$

Weight variation: The weight of the tablet being made was determined to ensure that a tablet contains the proper amount of drug. Twenty tablets were selected at random from each formulation and weighed on electronic weighing balance. The average weight of the tablets was determined. The weight of individual tablets was compared with the average weight variation.

Drug content uniformity: The drug content of prepared tablets was accurately weight and finely powered by pestle in a mortar. Weighed tablet of each powder equivalent to 400mg of Clindamycin Hydrochloride was transferred in to volumetric flask, dissolved in 60ml of 0.1N HCL and content of the flask were sonicated for 15 minutes. Then the volume was made up to100ml. The samples were analyzed UV-Visible spectrophotometer, and concentration of the drug in the sample was calculated.

***In-Vitro* Buoyancy Studies**: The in vitro buoyancy was determined by floating lag time (FLT). The time between introduce of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called floating lag time (FLT). Method described by the tablets was placed in a 100ml beaker containing 0.1 N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time.

***In-vitro* dissolution studies:** Dissolution of the tablets was carried out on USP XXXIII dissolution type II apparatus using paddle. The tablet was fixed to the paddle by hydration mechanism 900 ml of 0.1N HCL as dissolution medium was filled in a dissolution vessel and the temperature of the medium were set at 37± 0.5°c.The rotational speed of the paddle was set at 100 rpm. At particular intervals 5 ml of sample was withdrawn at predetermined time intervals of 2hr, 4hr, 6hr, 8hr, 10hr up to 12 hr and same volume of fresh medium was replaced. The withdrawn samples were diluted to 10 ml with 0.1N HCL, filtered and analyzed on UV spectrophotometer at 210 nm 0.1NHCL using buffer as a blank. Percentage cumulative drug release was calculated. The values and graphs are represented in tables and figure.

Raft strength measurement by in house method:

A tablet powder equivalent to unit dose was transferred to 150 ml of 0.1N HCL and maintained at 37°c in a 250 ml glass beaker. Each raft was allowed to form around an L- shaped wire probe (diameter: 1.2mm) held upright in the beaker throughout the whole period (30 min) of raft development. Raft strength was estimated using the modified balance method. Water was added drop wise to the pan and the weight of water required to break the raft was recorded.

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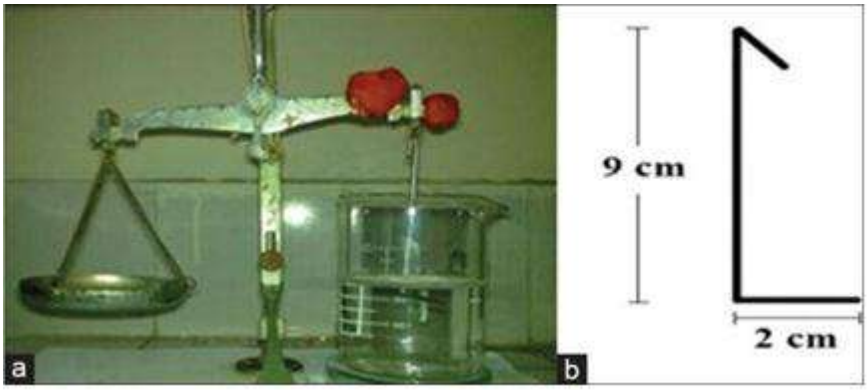

Figure 1
(a) Modified balance method. (b) Wire probe for raft strength measurement

Data analysis: To analyse the mechanism of release and release rate Zero order, first order, Higuchi matrix and Peppa's model. Based on the r-value, the best-fit model was selected

Zero order kinetics: Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, assuming that the area does not change and no equilibrium conditions are obtained can be represented by the following equation.

$$Qt = Q_o + K_o t$$

First order kinetics

To study the first order release rate kinetics, the release rate data were fitted to the following equation.

$$Log\ Qt = Log\ Q_o K_1\ t/2.303$$

Higuchi's model

Higuchi's developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semisolids and/or solid matrices. Mathematical expression were obtained for drug particles dispersed in a uniform matrix behaving as diffusion media. And the equation is,

$$Mt/M\infty = KH\ t1/2$$

Korsmeyer- Peppas Model:

The power law describes the fractional drug release is exponentially related to the release time and adequately describes the release of drug from slabs, cylinders and spheres, as expressed in following equation.

$$Mt / M\infty = Ktn$$

$$Log\ (Mt / M\infty) = log\ K + n\ log\ t$$

Stability Conditions

Stability study of tablets containing Clindamycin Hydrochloride was performed at following temperatures for one month and three months.

1. Long term testing : 25oC/ 60%RH (1Month)(3Month)
2. Accelerated testing : 40oC/75% RH (1Month)(3Month) Parameters estimated: Moisture content, assay and dissolution.

RESULTS AND DISCUSSION

Preformulation Studies

Drug and interaction (FTIR) study: From the spectra of Clindamycin Hydrochloride, excipients physical mixture of drug was observed that all characteristic peaks of Clindamycin Hydrochloride were present in the combination spectrum, thus indicating compatibility of the Clindamycin Hydrochloride and excipients. IR spectra of individual polymers and combination of Clindamycin Hydrochloride with all individual polymers shown in Figure 2 to 7, data as shown in table 3.

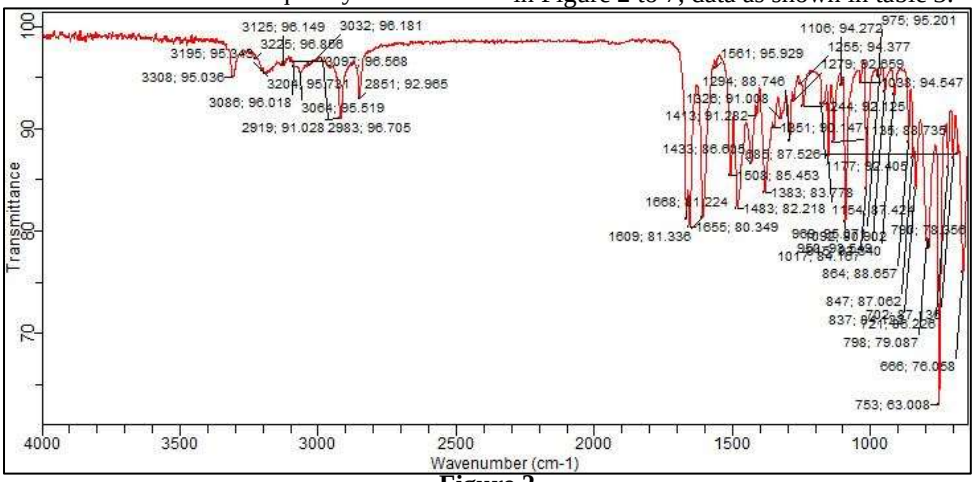

Figure 2
FTIR Spectrum of Clindamycin Hydrochloride

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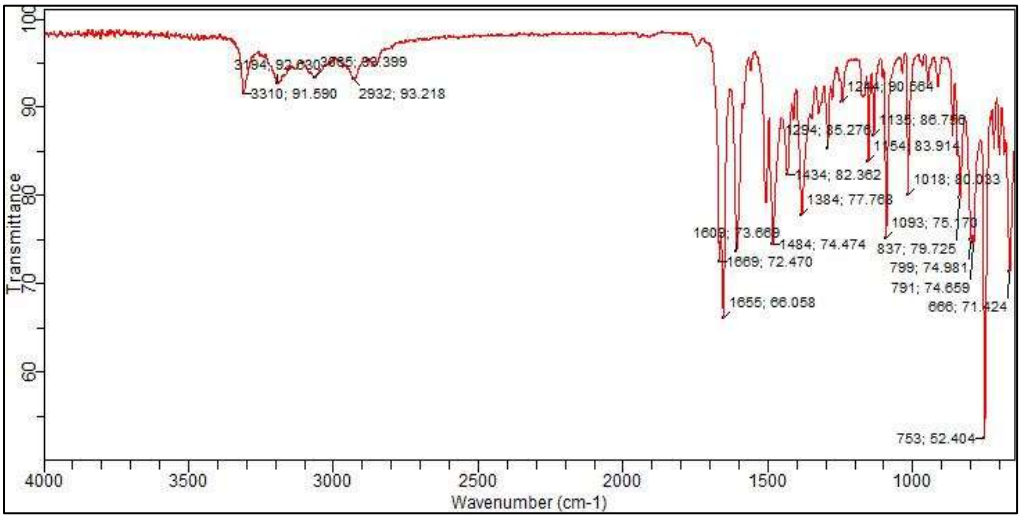

Figure 3
FTIR Spectrum of HPMC K15M

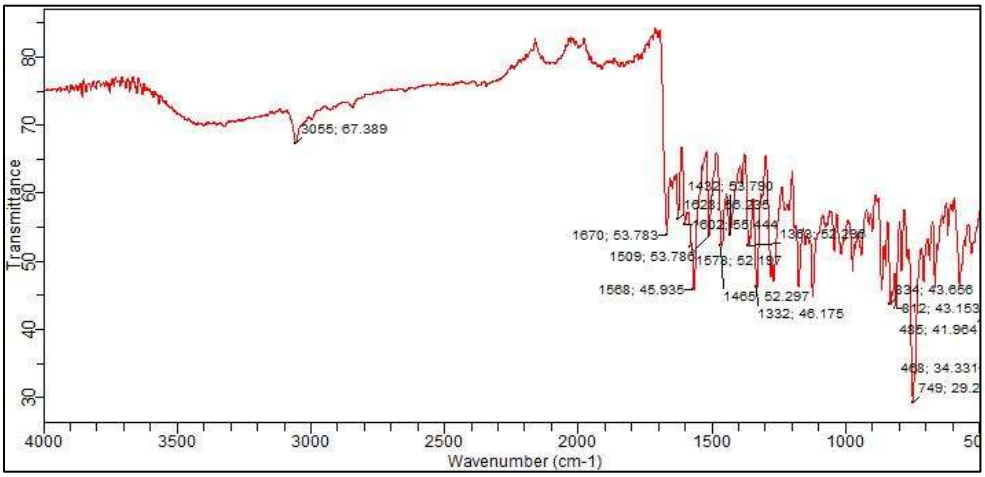

Figure 4
FTIR Spectrum of Guargum

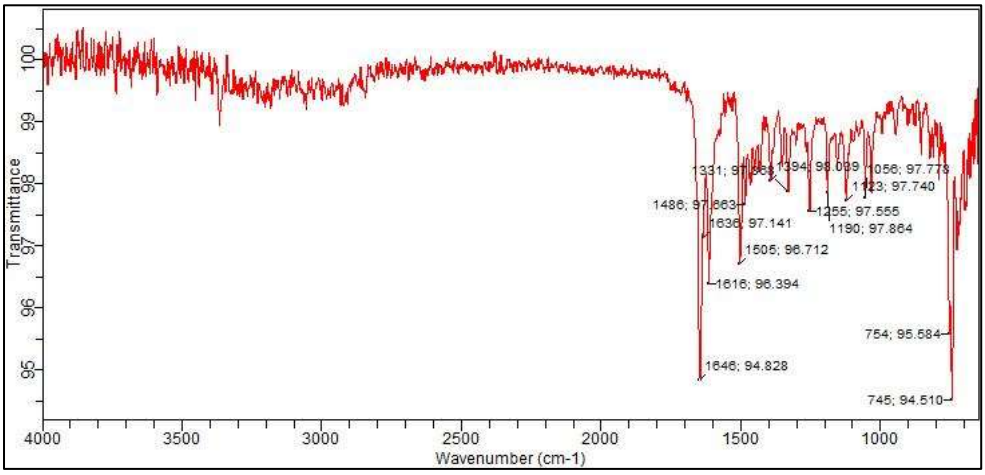

Figure 5
FTIR Spectrum of Chitosan

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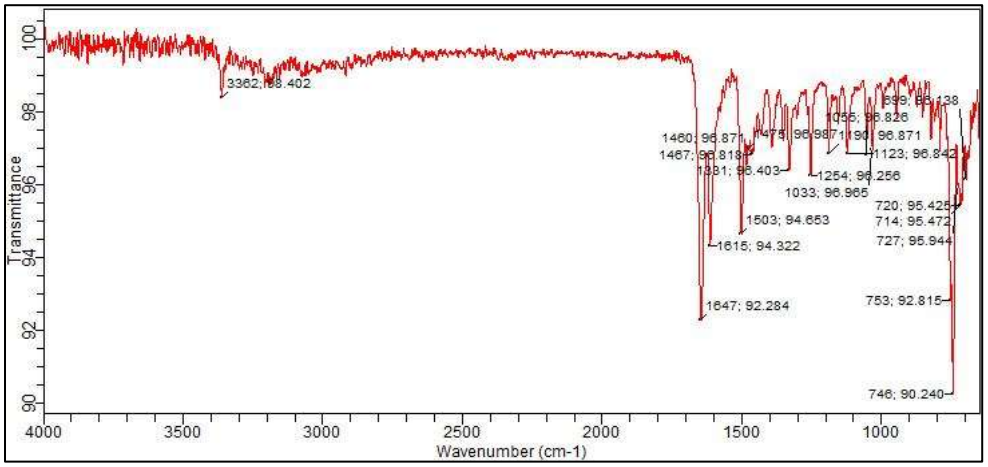

Figure 6
FTIR Spectrum of Microcrystalline cellulose

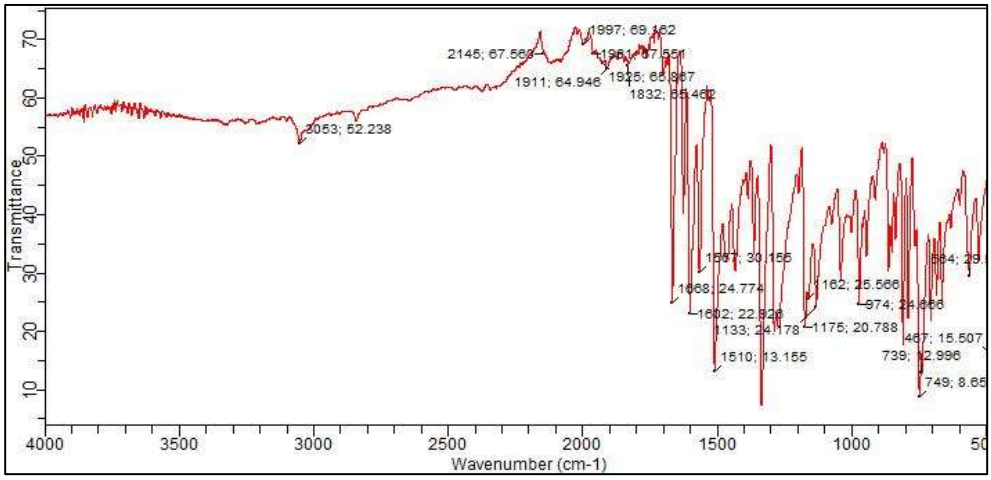

Figure 7
FTIR Spectrum of Mixtrue of compounds
Table 3
IR Interpretations for Pure drug and Polymers

Functional Group	Clindamycin Hydrochloride	HPMC K15M	Guar Gum	Chitosan	Microcrystalline Cellulose
(s)= C-H bend (Alkenes)	1106	3065	1363	1190	1140
(m)O-H bend (Carboxylic acid)	2851	2932	3055	1505	2996
(s, b) N-H wag (1^o,2^o amines)	1609	1609	1602	1616	1595
(m) C-Cl stretch (Alkyl halides)	847	799	834	1255	833
(s)C-O stretch (Nitro Compunds)	1017	1669	1670	1505	1670
(m)C-N stretch (Aromatic Amines)	1038	1609	1332	1486	1222

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Physical mixture of pure drug of Clindamycin Hydrochloride and polymer was characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the results, it was concluded that there was no interference in the functional group as the principal peaks of the Clindamycin Hydrochloride were found to be unaltered in the drug- polymer physical mixtures, indicating they were compatible chemically. IR spectra are shown in figures and interpretated values shown in the table respectively.

Physical properties of Clindamycin Hydrochloride

Inter particulate interactions influence the bulking properties of powder. A comparison of the bulk density and tapped density can give a measure of the relative importance of this interaction in a given powder; such a comparison is often used as an index of the ability of the powder to flow. The bulk density and tapped density were found to be 0.35gm/cm^{3}and 0.43gm/cm^3 respectively.

A simple indication of ease with which a material can be induced to flow is given by application of a compressibility index. The value for % compressibility index of Clindamycin Hydrochloride was found to be 12.79% and hausner's ratio of 1.16. The pre compression properties were tabulated.

Pre-Compression Parameters

Angle of repose: The results obtained for angle of repose for all the formulations. The values were found to be in the range of 27°.54' to 28°.82'. All the formulation showed the angle of repose below 30°, which indicates good flow.

Bulk density & Tapped density: The loose bulk density and tapped bulk density for all the formulations varied from 0.35gm/cm^3 to 0.43gm/cm^3 and 0.42gm/cm^3 to 0.44gm/cm^3 respectively. The values obtained lies within the acceptable range and no large difference found between loose bulk density and tapped density. These results help in calculating the % compressibility of the powder.

Percentage compressibility (carr's consolidation index): The percentage compressibility of powder mix was determined by the equation given for carr's consolidation index. The percentage compressibility lies within the range of 8.62 to 12.79 which indicates that the flow of the tablet mixture of various formulations is good to excellent.

Hausner's ratio: The Hausner's ratio of powder mix was determined by the data of loose bulk density and tapped bulk density. The Hausner's ratio for all the formulations lies within the range of 1.07 to 1.16, which indicates flow of powder is excellent.

Table 4
Evaluation of pre-compression parameters of Clindamycin Hydrochloride with different formulations

Formulation Code	Bulk density(g/cc) MEAN±SD	Tapped density(g/cc) MEAN±SD	Hausner's ratio MEAN±SD	Compressibility index (%) MEAN±SD	Angle of repose (θ) MEAN±SD
F1	0.35±0.03	0.42±0.06	1.07±0.03	8.62±0.05	27.54±0.05
F2	0.36±0.06	0.51±0.05	1.23±0.04	12.33±0.03	24.38±0.04
F3	0.38±0.04	0.44±0.03	1.21±0.06	11.49±0.06	23.32±0.03
F4	0.42±0.07	0.44±0.08	1.21±0.05	13.29±0.04	26.75±0.04
F5	0.37±0.03	0.45±0.03	1.09±0.03	8.72±0.03	25.64±0.03
F6	0.42±0.05	0.42±0.06	1.18±0.07	11.35±0.05	24.82±0.06
F7	0.44±0.04	0.46±0.04	1.15±0.03	11.57±0.06	23.38±0.03
F8	0.41±0.02	0.42±0.03	1.13±0.04	10.34±0.03	22.82±0.07
F9	0.43±0.05	0.44±0.07	1.16±0.07	12.79±0.05	28.82±0.06

Each value represents the mean ± standard deviation (n=3)

The evaluation studies of all the formulations were proved to be within limits and were shown good derived and flow properties.

Formulation development: Development of the formulation in the present study was mainly based on the type of polymers, different ranges of concentration of polymers used. Various polymers in different concentrations were used so as to get tablet with good physical properties and with minimum disintegration time. So, in the present study attempts were made to get good physical and analytical parameters of the tablets.

Total 9 formulations of gastro retentive drug delivery system of Clindamycin Hydrochloride tablet using raft forming approach by direct compression method. Different types of polymers in different concentrations and in different combinations were used and the tablets were prepared by the procedure described in the methodology section.

Post Compression Parameters

Shape and thickness: Macroscopic examination of the tablets from each formulation showed circular shape with no cracks. The thickness of tablet randomly was measured using vernier callipers.

Weight variation test: All the formulations passed weight variation test as the percent weight variation was within the pharmacopoeia limits of ±5%. It was found to be from 378.52 to 454.04 mg. None of the formulations were exceeding the limit

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±5% specified by IP. Thus all the formulations were found to comply with the IP standard as shows in table no 5.

Hardness and friability of the tablets: The tablet hardness of all the formulations was checked using Monsanto hardness tester, by the method described in methodology section. The average hardness of all the batches is in the range of 4.7 to 3.7 kg/m^2. The lower standard deviation values indicated that the hardness of each formulations were almost uniform in specific method and possess the good mechanical strength with sufficient hardness. The hardness of all formulations was found to be in acceptable range as shows in table no 5.

The friability test is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. A number of tables were weighed and placed in tumbling apparatus where they were exposed to rolling and 50 resolutions resulting from freefalls within the roche's apparatus. The percentage friability for all the formulations lies in the range of 0.22 % to 0.43 %, which was found to be in limit (i.e. <1%) as shows in table no 5.

Estimation of drug content: All the formulations were evaluated for the drug content estimation in 0.1NHCl sample of tablets using the procedure described in methodology section. The drug content values for all the formulations are in the range of 97 to 99% as shows in table no 5.

Table 5
Evaluation of Post Compression Parameters of Different Formulations Clindamycin Hydrochloride tablet floating drug delivery

Formulation code	Hardness (kg/cm^2) MEAN±SD (n=3)	Thickness (mm) MEAN±SD (n=3)	Weight variation(mg) MEAN±SD (n=20)	Friability (%) MEAN±SD (n=3)	Drug content (%) (n=2)
F1	4.7±0.3	5.2±0.4	378.52±0.32	0.22±0.19	97.35
F2	3.2±0.1	6.4±0.1	469.09±0.57	0.15±0.15	98.62
F3	4.2±0.3	6.7±0.2	455.56±0.24	0.37±0.16	97.65
F4	3.1±0.3	6.4±0.1	479.22±0.62	0.35±0.16	98.22
F5	4.8±0.2	6.6±0.2	475.34±0.24	0.32±0.18	99.34
F6	3.5±0.4	6.3±0.3	457.47±0.36	0.29±0.14	98.13
F7	3.3±0.2	6.7±0.3	445.74±0.48	0.42±0.15	99.14
F8	4.2±0.2	6.8±0.3	488.02±0.27	0.45±0.18	99.63
F9	3.7±0.3	6.9±0.2	454.04±0.42	0.43±0.16	99.64

Each value represents the mean ± standard deviation

***In-vitro* drug release studies:** The *In-vitro* dissolution study of Clindamycin Hydrochloride tablet floating drug delivery, 0.1N HCl as dissolution medium. The *In-vitro* drug release study of Clindamycin Hydrochloride tablets from each batch (F1 to F9) was carried out by using 0.1N HCl for 12 hours. The samples were withdrawn at specified time intervals and analyzed by UV-visible spectrophotometer. Percentage drug release was calculated on the basis of mean amount gastro retentive of Clindamycin Hydrochloride present in respective formulation. The cumulative percentage of drug release of floating drug delivery of Clindamycin Hydrochloride on y-axis was plotted against time on x-axis to obtain drug release profiles.

Drug Release Kinetics: The release constant was calculated from the slope of the appropriate plots, and the regression coefficient (r^2) was determined. The drug release data obtained were extrapolated by Zero order, First order, Higuchi model and Korsmeyer-Peppas plot for Best Formulation F6. The release kinetics shows that the release of drug followed zero order release in all the formulations as shown in table no.15 and figure 23.

Table 6
***In Vitro* dissolution Studies of Clindamycin Hydrochloride tablet floating drug delivery**

Sl.no	Time	% of Drug release								
		F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8	F 9
1	5	8.65	5.07	6.95	12.67	6.57	15.13	12.63	11.41	8.57
2	10	7.45	13.95	11.23	22.35	21.41	27.97	27.33	25.07	24.21
3	15	12.86	22.45	21.58	35.63	24.31	36.15	33.15	31.81	37.07
4	20	54.05	65.81	72.81	81.63	76.41	71.97	73.61	53.11	72.21
5	25	28.57	46.41	57.31	54.15	44.05	57.32	55.85	43.37	53.92
6	35	17.67	32.57	41.63	51.31	31.17	44.94	45.71	35.63	45.93
7	30	41.41	58.05	58.89	66.31	54.07	72.63	61.47	47.21	67.85
8	40	58.89	73.47	71.00	85.91	81.63	82.11	86.61	61.85	82.85
9	45	75.63	82.21	87.13	92.85	87.25	97.55	97.27	86.91	96.59

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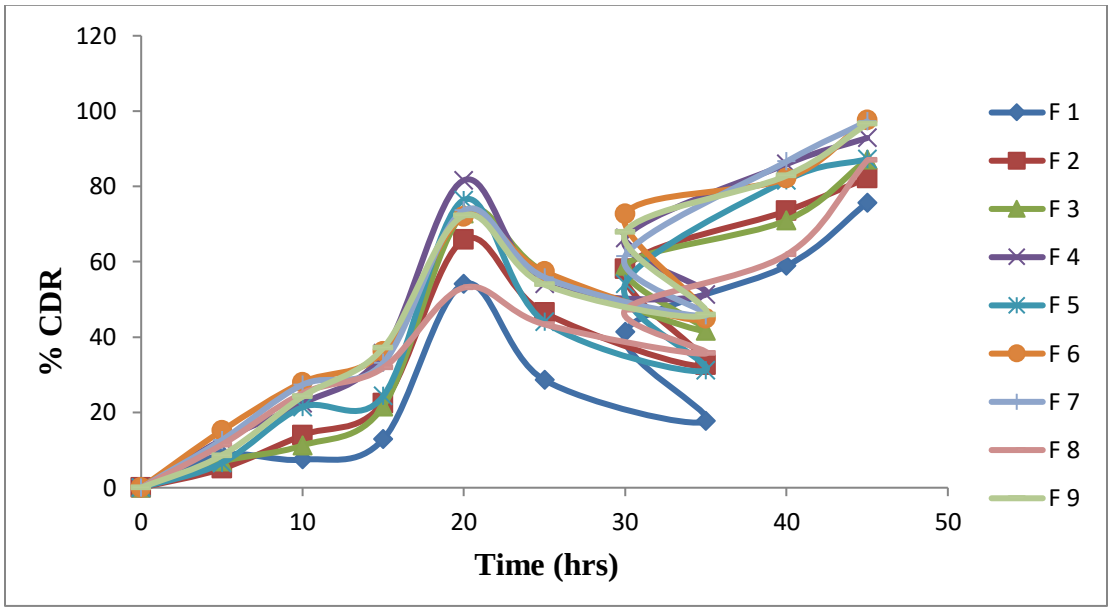

Figure 8

***In Vitro* dissolution Studies Clindamycin Hydrochloride tablet floating drug delivery**

Release Order Kinetics of Clindamycin Hydrochloride Floating Drug Delivery

Table 7

Release kinetics of Clindamycin Hydrochloride Floating Drug Delivery (F1 to F5)

Model	Equation	F 1		F 2		F 3		F 4		F 5	
		R^2	m	R^2	m	R^2	M	R^2	m	R^2	M
Zero order	Mo-Mt=kt	0.655	69.4	0.939	1123	0.007	15.93	0.202	72.88	0.928	1414
First order	InM=InMo	0.494	0.061	0.540	0.067	0.257	0.038	0.352	0.044	0.438	0.062
Higuchi's Matrix	$M_0 - M_t = kt1/2$	0.516	4508	0.767	7420	0.023	212.0	0.189	515.5	0.803	9618
Korsmeyer-Peppar	$\log (M_0\text{-}M_t) = \log k + n \log t$	0.835	2.354	0.884	2.545	0.572	1.709	0.663	1.813	0.806	2.517

Table 8

Release kinetics of Clindamycin Hydrochloride Floating Drug Delivery (F6 to F9)

Model	Equation	F 6		F 7		F 8	
		R^2	m	R^2	m	R^2	M
Zero order	Mo-Mt=kt	0.917	15.49	0.949	154.4	0.937	1593
First order	InM=InMo	0.481	0.052	0.465	0.051	0.399	0.061
Higuchi's Matrix	$M_0 - M_t = kt1/2$	0.798	1057	0.848	1067	0.899	11409
Korsmeyer -Peppar	$\log (M_0\text{-}M_t) = \log k + n \log t$	0.835	2.032	0.827	2.033	0.785	2.560

***In-vitro* Buoyancy Studies**

The all formulation were showed good floating lag time (FLT) and total floating time (TFT). The FLT and TFT of the tablets mainly depend on the type of polymer and their concentrate as shown in figure 9 and table 9.

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Figure 9
Buoyancy floating of formulated floating tablets

Table 9
Floating lag time of the gastro retentive tablets (F1-F9)

Formulation Code	Floating lag time (sec)	Total floating time (hour)
F1	23	12
F2	36	12
F3	28	12
F4	16	10
F5	10	10
F6	42	12
F7	18	12
F8	26	12
F9	31	12

STABILITY STUDY: Optimized formulation F4 was subjected to stability studies for 1 to 3 months and the tablets were tested for drug content and dissolution. The results obtained were as in the following table 10 and figure 10.

Table 10
Stability studies of the optimized formulation F4

Time in hrs	Cumulative % Drug Release		
	Standard	After 1 Month	After 3 Month
1	13.61	11.58	12.41
2	22.31	21.24	21.83
3	32.15	28.91	31.02
4	49.83	44.64	46.36
5	46.45	42.77	42.95
6	39.43	34.42	38.35
7	61.63	57.68	61.97
8	68.16	66.23	67.54
9	78.33	76.72	77.58
10	89.64	85.21	86.82
11	92.56	91.72	92.48
12	96.74	94.22	95.67

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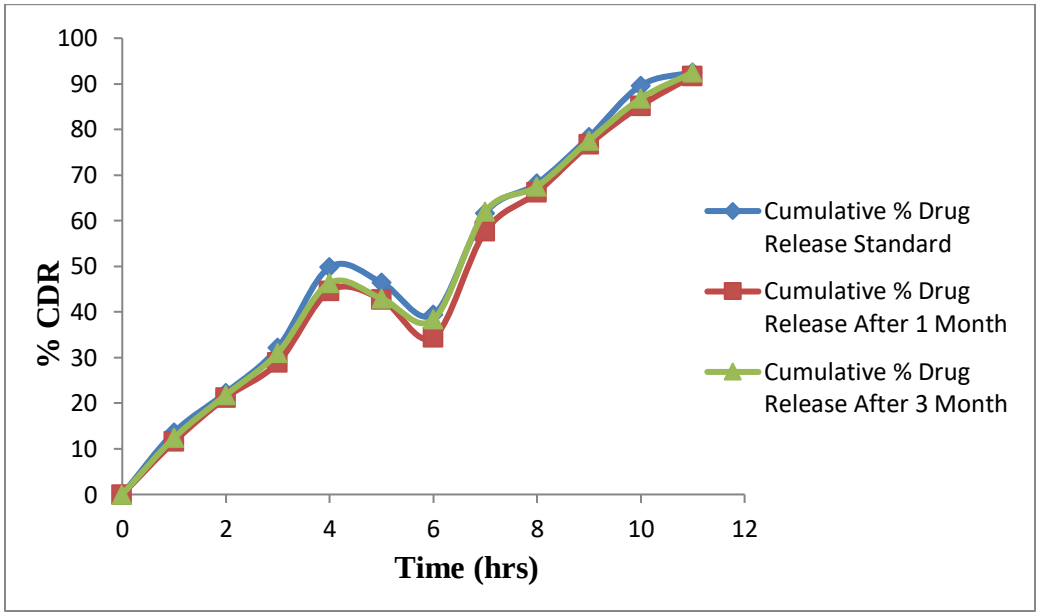

Figure 10
Stability studies of Optimized *In-vitro* Cumulative % Drug release of F4

Comparison of dissolution profile of optimized formulation (F4) with marketed product: The prepared all F4 formulations, the tablets made with combination of chitosan F4 showed better results of dissolution. It has showed 99.8% dissolution in 12 hours. This formulation was compared with marketed formulation shown in table 11 and figure 11.

Table 11
Comparison of dissolution profile of F4 and marketed product
Brand name: - Claforan

Time (H)	Marketed product	Optimized formulation F4
2	13.7	24.1
4	32.2	46.2
6	64.3	64.8
8	86.4	82.3
10	92.5	93.2
12	98.6	99.8

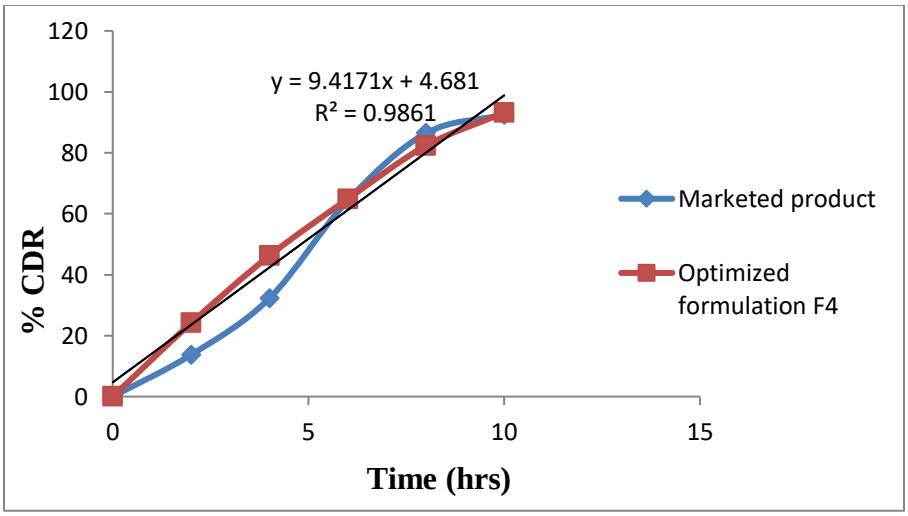

Figure 11
Comparison of dissolution profile of F4 and Marketed product

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CONCLUSION

From the experimental results, it can be concluded that the sodium bicarbonate and sodium alginate has shown a predominant effect on the buoyancy lag time, while HPMC K15M and Guar gum have the predominant effect on drug release. Floating drug delivery of Clindamycin Hydrochloride tablet has controlled release. In vitro release rate studies showed that the maximum drug release was observed F4 formulation upto 12 hours.

From the study it is evident that promising controlled release tablets of Clindamycin Hydrochloride can be developed. Further detailed investigations are required to establish efficacy of these formulations.

Acknowledgement

I would like to thank Principal sir (Dr. Kamal Has-san) St. Mary's Group of Institutions, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvana-giri (Dist), Telangana-508284, India.

Conflict of Interest: The authors attest that they have no conflict of interest in this study.

Funding Support: The authors declare that there is no financial support for the current study.

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