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FORMULATION AND DEVELOPMENT OF CYPROHEPTADINE HCL EXTENDED-RELEASE TABLET BY USING NATURAL POLYMERS

Udithyavath Divya[1], Dr. Madhusudhan Reddy A

[1]Department Of Pharmaceutics, Princeton College Of Pharmacy, Pocharam, Hyderabad, Telangana 500088.

Abstract:

The present research work focuses on the formulation and development of extended-release tablets of Cyproheptadine Hydrochloride using natural polymers with the objective of achieving prolonged drug release, reducing dosing frequency, and enhancing patient compliance. Natural polymers such as guar gum, xanthan gum, and gum karaya were selected as release-retarding agents due to their biocompatibility, cost-effectiveness, and safety.

Pre-formulation studies, including drug-excipient compatibility tests, were carried out to ensure stability of the formulation. Extended-release tablets were prepared by the direct compression/wet granulation method and evaluated for various pre-compression parameters (bulk density, tapped density, angle of repose) and post-compression parameters (hardness, friability, weight variation, and drug content), all of which were found within pharmacopeial limits.

In-vitro dissolution studies revealed that the drug release rate varied with the type and concentration of natural polymers used. Among the formulations, the optimized batch exhibited a sustained drug release up to 12 hours, following near first-order release kinetics with a non-Fickian diffusion mechanism.

The study concludes that natural polymers can be effectively utilized in the design of extended-release matrix tablets of Cyproheptadine Hydrochloride, providing a promising alternative to synthetic polymers for achieving controlled drug delivery, better therapeutic efficacy, and improved patient compliance.

Keywords: *Cyproheptadine Hydrochloride, Extended-Release Tablets*

Corresponding author:

Udithyavath Divya,

Department of Pharmaceutics,, Princeton college of Pharmacy, Pocharam, Hyderabad

Mobile:

Email Id: *princeton.pharmacy@gmail.com*

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INTRODUCTION:

Historically, oral drug administration has been the predominant route for drug delivery. It is known to be the most popular route of drug administration due to the fact the gastrointestinal physiology offers more flexibility in dosage form design than most other routes. A major challenge for the pharmaceutical industry in drug development is to produce safe and efficient drugs, therefore properties of drugs and the way in which they are delivered must be optimized.

A controlled release drug delivery system delivers the drug locally or systemically at a predetermined rate for a specified period of time. The goal of such systems is to provide desirable delivery profiles that can achieve therapeutic plasma levels. Drug release is dependent on polymer properties; thus the application of these properties can produce well characterized and reproducible dosage forms.

Oral route still remains the most popular for drug administration by virtue of its convenience to the patient. A sizable portion of orally administered dosage forms, so called conventional, are designed to achieve maximal drug bioavailability by maximizing the rate and extent of absorption. While such dosage forms have been useful, frequent daily administration is necessary, particularly when the drug has a short biological half-life. This may result in wide fluctuation in peak and trough steady-state drug levels, which is undesirable for drugs with marginal therapeutic indices. Moreover, patient compliance is likely to be poor when patients need to take their medication three to four times daily on chronic basis. Fortunately, these short comings have been circumvented with the introduction of controlled release dosage forms. These dosage forms are capable of controlling the rate of drug delivery, leading to more sustained drug levels and hence therapeutic action.

Hydrophilic matrix systems are among the most commonly used means for oral controlled drug delivery as they can reproduce a desirable drug profile and are cost effective. The primary mechanism of drug release from hydrophilic matrices occurs when the polymer swells on contact with the aqueous medium to form a gel layer on the surface of the system. The drug then releases by dissolution, diffusion and/or erosion.

TERMINOLOGY:

A list of important terms that describe different modified release dosage forms are defined below.

Modified release dosage forms (MRDF): Defined as those dosage forms whose drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms.

Controlled release (CR): The drug is released at a constant (zero order) rate and the drug concentration obtained after administration is invariant with time.

Delayed release: The drug is released at a time other than immediately after administration.

Extended release (ER): Slow release of the drug so that plasma concentrations are maintained at a therapeutic level for a prolonged period of time (usually between 8 and 12 hours).

Prolonged release: The drug is provided for absorption over a longer period of time than from a conventional dosage form. However, there is an implication that onset is delayed because of an overall slower release rate from the dosage form.

Repeat action: Indicates that an individual dose is released fairly soon after administration, and second or third doses are subsequently released at intermittent intervals.

Sustained release (SR): The drug is released slowly at a rate governed by the delivery system.[1]

ZERO ORDER DELIVERY:

Zero order, or constant rate release of drug is desirable in order to minimize swings in drug concentration in the blood. In conventional dosage forms rapid increase in concentration is followed by a rapid decrease, and little time is spent inside the so-called therapeutic range, which is bounded below by a minimum effective concentration (MEC) and above by a minimum toxic concentration (MTC). Frequent repetitive dosing is required to maintain concentration within these limits, and compliance and control are difficult [2].

Dosage forms that prolong release can maintain drug concentration within the therapeutic range for extended periods and minimize episodes of underexposure or toxicity. A well designed system displays a narrow, predictable residence time distribution in the gastrointestinal (GI) tract, and releases drug by a controlled mechanism. Zero order release leads, in principle, to the best control of plasma concentration. Such control leads to constant drug effect, provided the drug's pharmacokinetic and pharmacodynamic properties, including absorption, distribution, metabolism, and excretion (ADME), and its pharmacodynamic properties relating plasma concentration to drug effect, are stationary.

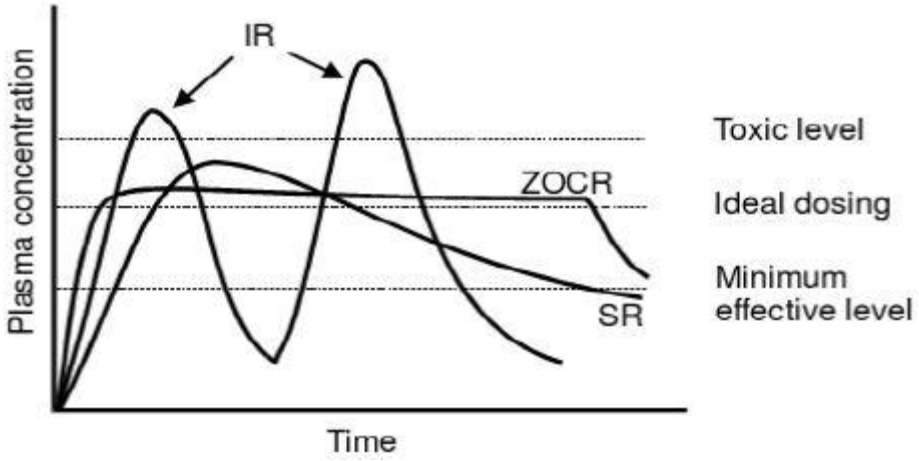


Fig.1.1 Diagram shows characteristic representation of plasma concentrations of a conventional immediate relese dosage form (IR), a sustained release dosage form (SR) and an idealized zero-order controlled release (ZOCR) dosage form (in combination with a start-up dose).

Zero order oral drug release can be achieved, in principle, by surrounding a core tablet with a membrane that is permeable to both drug and water, as illustrated in. After swallowing, the core becomes hydrated, and drug dissolves until it reaches its saturation concentration or solubility. The core serves as a saturated reservoir of drug. Drug release proceeds by partitioning from the reservoir into the membrane, followed by diffusion across the membrane into the gastrointestinal fluid. So long as saturation is maintained in the core, there will be a stationary concentration gradient across the membrane, and release will proceed at constant rate. Eventually, the dissolved drug's concentration in the core falls below saturation, reducing the concentration gradient and hence the release rate, which decays to zero. If the membrane consists of a water-soluble polymer of high molecular weight, then it will initially swell into a gel, through which drug diffuses. The thickness of the gel layer initially increases with time due to swelling, but ultimately it decreases due to disentanglement and dissolution of polymer chains. At intermediate times, the gel layer may be of approximately constant thickness, and release occurs at a relatively constant rate [2].

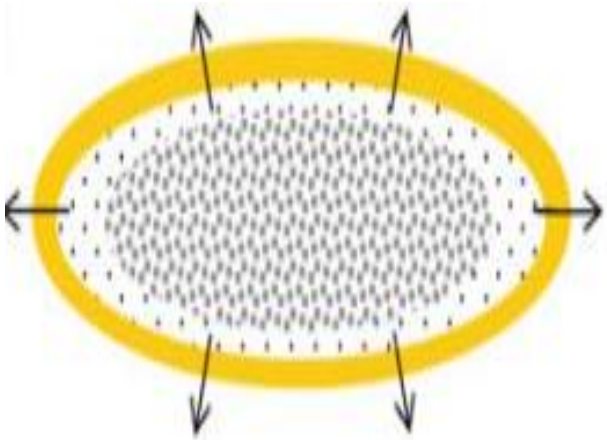


Fig.1.2 Membrane diffusion controlled release. Drug in core (granulated pattern) dissolves to form saturated solution (dilute dots). Drug then diffuses across membrane (thin tipped arrows). Zero order release persists as long as there is sufficient drug in core to form saturated solution.[2]

Drawbacks of Conventional Dosage Forms [3,4]

- Poor patient compliance, increased chances of missing the dose of a drug with short half life for which frequent administration is necessary.
- The unavoidable fluctuations of drug concentration may lead to under medication or over medication.
- A typical peak-valley plasma concentration time profile is obtained which makes attainment of steady-state condition difficult.

- The fluctuations in drug levels may lead to precipitation of adverse effects especially of a drug with small Therapeutic Index (TI) whenever over medication occur.

Advantages of Extended Release Delivery System [5,6]

- Extended release products have many advantages.
- The extended release formulations reduce dosing frequency of drugs.
- The extended release formulations may maintain therapeutic concentrations.
- Reduce the toxicity by slowing drug absorption.
- The use of these formulations avoids the high blood concentration.
- Extended release formulations have the potential to improve the patient compliance and convenience.
- Minimize the local and systemic side effects.
- Increase the stability by protecting the drug from hydrolysis or other degradative changes in gastrointestinal tract.
- Improvement in treatment efficacy.
- Minimize drug accumulation with chronic dosing.
- Improve the bioavailability of some drugs.
- Usage of less total drug.
- Improve the ability to provide special effects. For example, Morning relief of arthritis through bed time dosing.

7. METHODOLOGY:

7.1 Characterization of Cyproheptadine Hcl

Organoleptic properties:

Take a small quantity of sample and spread it on the white paper and examine it visually for color, odour and texture.

Determination of Cyproheptadine Hcl Melting point

The melting point of Cyproheptadine Hcl was determined by capillary tube method according to the USP. A sufficient quantity of Cyproheptadine Hcl powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Cyproheptadine Hcl in the tube passed into liquid phase**.**

Determination of Cyproheptadine Hcl Solubility

Determination of solubility of drug by visual observation, an excess quantity of Cyproheptadine Hcl was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Table.

7.2. Analytical method development:

7.2.1 Determination of Wavelength:

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution - 10µg/ml). The working solution was taken for determining the wavelength.

7.2.2 Determination of Calibration Curve:

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 8.1 and 8.2) and those concentrations absorbance were found out at required wavelength.

7.3. Pre formulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose:

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$\tan \theta = h / r$ θ = Angle of repose

h = Height of the cone,

r = Radius of the cone base

Table 7.1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density:

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / V_o$$

Where, M = weight of sample

V_o = apparent volume of powder

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

$$\text{Tap} = M / V$$

Where, Tap= Tapped Density

M = Weight of sample

V= Tapped volume of powder

Measures of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticle interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

$$\text{Carr's Index} = [(\text{tap} - b) / \text{tap}] \times 100$$

Where, b = Bulk Density

Tap = Tapped Density

Table 7.2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

7.4. Formulation development of Tablets:

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 7.3. The tablets were prepared as per the procedure given below and aim is to prolong the release of Cyproheptadine Hcl. Total weight of the tablet was considered as 100mg.

Procedure:

1) Cyproheptadine Hcl and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method.

Table 7.3: Formulation composition for tablets

INGREDIENTS	FORMULATION CHART								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Cyproheptadine Hcl	4	4	4	4	4	4	4	4	4
Xanthan Gum	4	8	12	-	-	-	-	-	-
Guar Gum	-	-	-	4	8	12	-	-	-
Karya Gum	-	-	-	-	-	-	4	8	12
PVP K 30	5	5	5	5	5	5	5	5	5
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2	2	2	2
MCC	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total Weight	100	100	100	100	100	100	100	100	100

All the quantities were in mg

8. RESULTS & DISCUSSION:

Organoleptic properties

Table 8.1: Organoleptic properties

S NO.	Properties	Results
1	State	Solid
2	Colour	White
3	Odour	Odourless
4	Melting point	152 °C

Solubility studies

Table 8.2: Solubility studies of drug in different solvents

S NO.	Solvents	Solubility of Cyproheptadine Hcl
1	Ethanol	Soluble
2	Acetonitrile	Sparingly soluble
3	Water	Freely Soluble
4	Dimethyl sulfoxide	Soluble

The present study was aimed to develop extended-release tablets of Cyproheptadine Hcl using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

8.1. Analytical Method

Graphs of Cyproheptadine Hcl were taken in 0.1N HCl and in pH 6.8 phosphate buffer at 286 nm and 288 nm respectively.

Table 8.3: Observations for graph of Cyproheptadine Hcl in 0.1N HCl (286 nm)

Conc. [µg/ml]	Absorbance
0	0
5	0.124
10	0.244
15	0.362
20	0.481
25	0.597

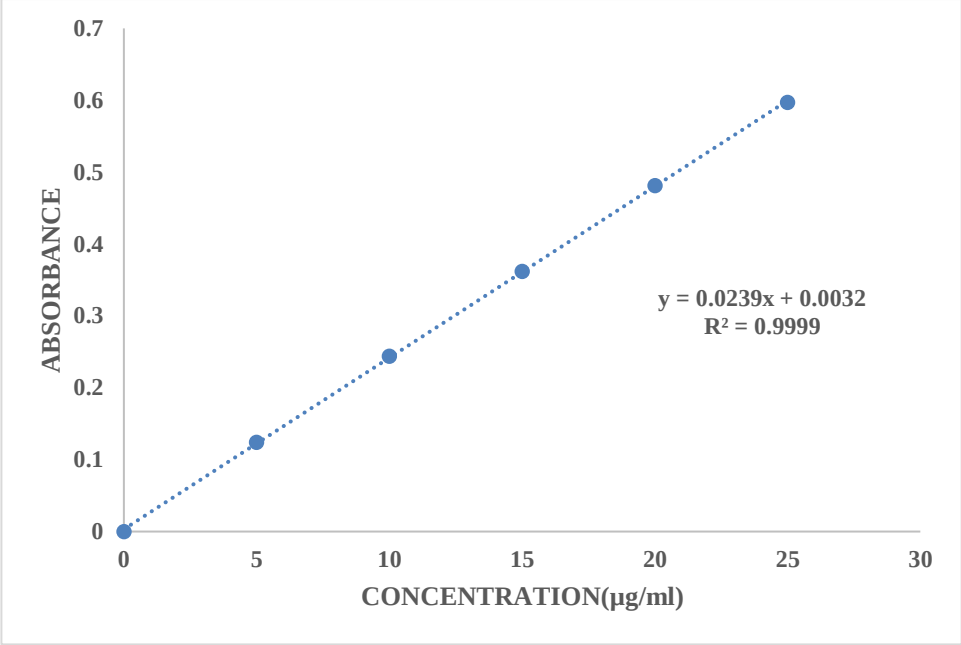


Figure 8.1: Standard graph of Cyproheptadine Hcl in 0.1N HCl

Table 8.4: Observations for graph of Cyproheptadine Hcl in pH 6.8 phosphate buffer (288nm)

Concentration [µg/ml]	Absorbance
0	0
5	0.116
10	0.237
15	0.358
20	0.472
25	0.601

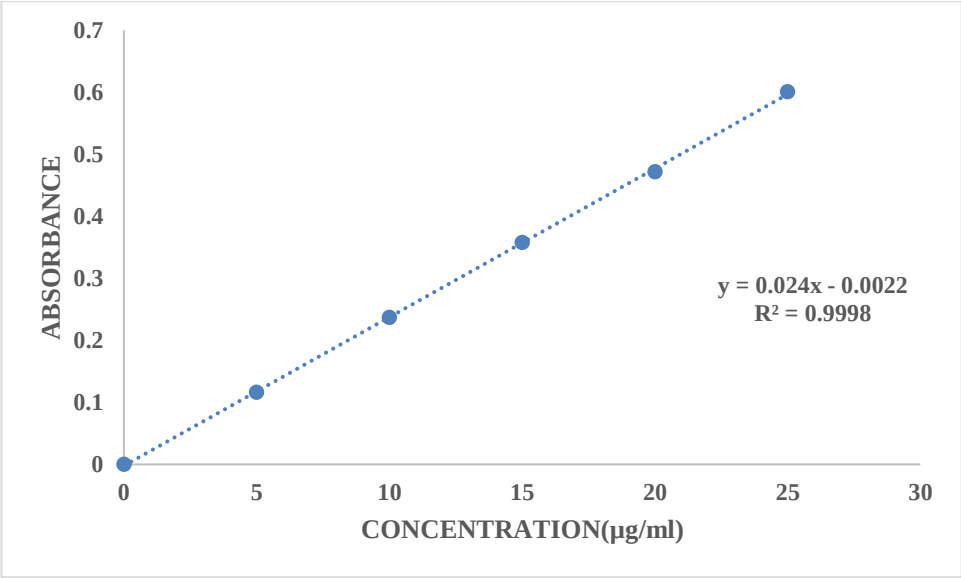


Figure 8.2: Standard graph of Cyproheptadine Hcl pH 6.8 phosphate buffer (288 nm)

8.3. Pre formulation parameters of powder blend

Table 8.5: Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	27.22±1.31	0.410±0.069	0.496±0.020	17.33±0.320	1.20±0.013
F1	28.35±1.64	0.382±0.032	0.462±0.015	17.31±0.208	1.20±0.015
F3	28.23±1.6	0.405±0.05	0.470±0.032	13.82±0.198	1.16±0.016
F4	29°76′±0.02	0.536±0.05	0.593±0.03	15.96±0.01	1.18±0.02
F5	26°49′±0.01	0.492±0.06	0.542±0.04	9.22±0.06	1.1±0.02
F6	28°63′±0.02	0.521±0.03	0.596±0.02	12.5±0.03	1.14±0.03
F7	27°09′±0.03	0.528±0.02	0.586±0.06	9.89±0.04	1.1±0.02
F8	27°01′±0.02	0.498±0.03	0.549±0.02	9.22±0.02	1.1±0.06
F9	26°14′±0.03	0.477±0.04	0.542±0.02	11.99±0.01	1.13±0.02

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.382±0.032 to 0.536±0.05 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.462±0.015 to 0.596±0.02 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 17 which show that the powder has good flow properties. All the formulations have shown the Hausner ratio below 1.20 indicating the powder has good flow properties.

8.4. Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

8.6. *In vitro* quality control parameters for tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	99.25	2.9	0.56	1.14	98.49
F1	101.52	2.4	0.43	1.69	99.60
F3	100.10	2.6	0.31	1.41	97.34
F4	98.01	2.0	0.50	1.97	97.58
F5	100.96	2.7	0.41	1.52	99.62
F6	99.58	3.1	0.35	1.47	99.24
F7	98.72	2.8	0.43	1.66	98.10
F8	101.18	2.3	0.34	1.87	99.24
F9	97.34	3.0	0.30	1.21	99.71

Weight variation test:

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 8.4. The average weight of the tablet is approximately in range of 97.34 to 101.52 mg, so the permissible limit is ±7.5% (>100 mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

Hardness test:

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data were shown in Table 10.4. The results showed that the hardness of the tablets is in range of 2.0 to 3.1 kg/cm^2, which was within IP limits.

Thickness:

Thickness of three tablets of each batch was checked by using Micrometer and data shown in Table-10.4. The result showed that thickness of the tablet is raging from 1.14 to 1.97 mm.

Friability:

Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 10.4. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Drug content:

Drug content studies were performed for the prepared formulations. From the drug content studies it was concluded that all the formulations were showing the % drug content values within 97.10 - 99.71 %.

All the parameters such as Weight Variation, Friability, Hardness, Thickness and Drug Content were found to be within limits.

***8.5. In Vitro* Drug Release Studies**

Table 8.7: Dissolution Data of Cyproheptadine Hcl Tablets

Time (HRS)	% of Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	16.58	13.76	12.73	19.39	11.64	12.61	22.01	14.08	17.89
1	21.43	18.05	16.37	24.96	18.58	19.26	26.23	19.22	21.24
2	25.16	28.29	25.96	29.57	28.24	31.37	30.76	25.12	24.68
3	30.27	37.11	31.47	34.41	39.22	35.52	42.35	32.68	32.07
4	37.15	41.67	37.51	41.93	44.65	41.19	51.29	36.27	39.41
5	43.03	48.53	44.27	48.66	51.12	49.46	57.68	42.56	45.95
6	48.08	52.98	49.32	51.19	58.39	55.12	65.09	48.91	57.52
7	57.11	58.43	55.71	61.71	68.57	59.03	72.68	63.45	59.37
8	64.17	68.12	61.87	67.75	75.92	64.48	79.54	74.98	63.41
9	71.94	73.42	66.21	72.97	79.19	69.96	84.21	77.23	74.25
10	79.53	77.79	72.95	87.15	87.52	74.12	91.52	82.89	85.94
11	84.62	82.07	76.01	92.56	94.44	79.07	95.26	86.23	87.02
12	98.24	89.41	82.19	99.82	97.22	88.71	98.13	91.21	94.15

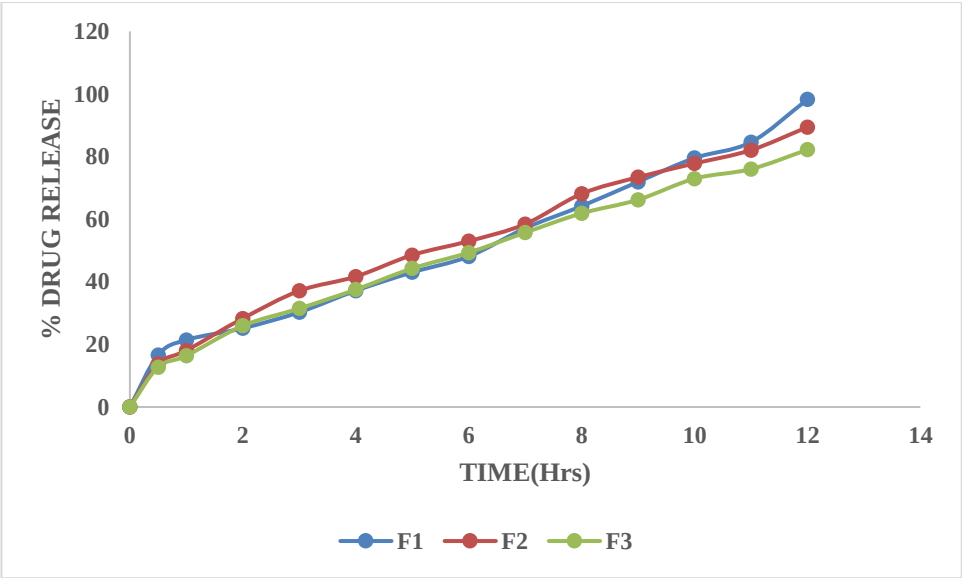


Fig 8.3: Dissolution profile of Cyproheptadine Hcl (F1, F2, F3 formulations)

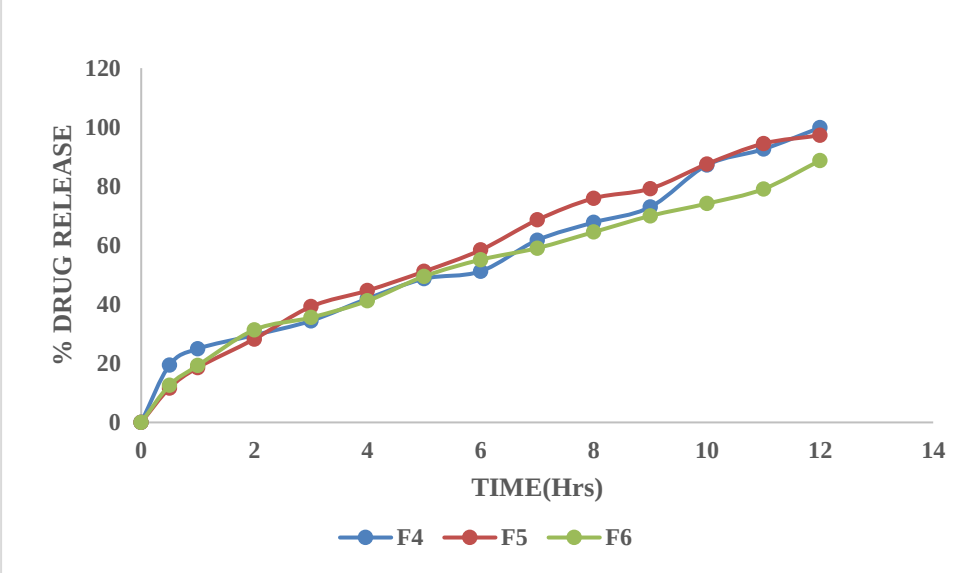


Fig 8.4: Dissolution profile of Cyproheptadine Hcl (F4, F5, F6 formulations)

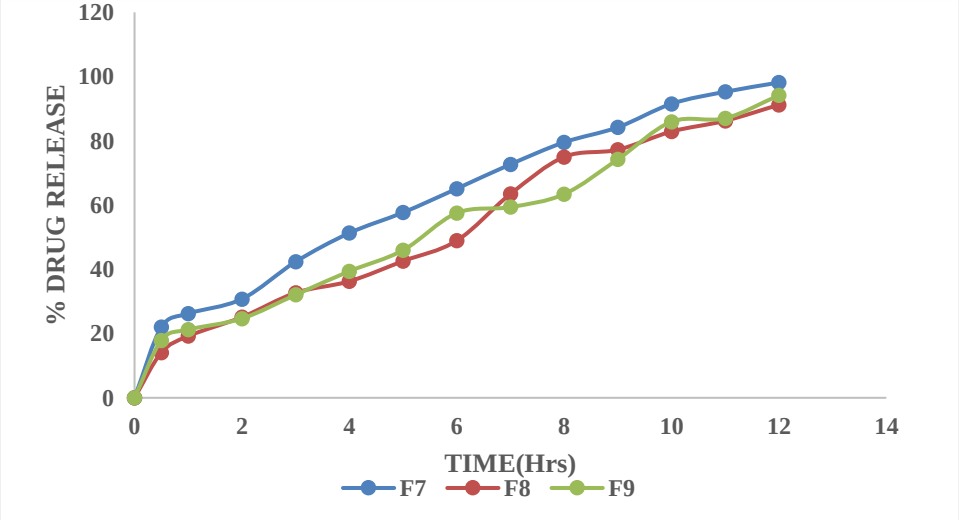


Fig 8.5: Dissolution profile of Cyproheptadine Hcl (F7, F8, F9 formulations)

From the dissolution data it was evident that the formulations prepared with Xanthan Gum as polymer were retarding the drug release up to desired time period i.e., 12 hours.

Formulations prepared with Guar Gum retarded the drug release in the concentration of 4mg (F4 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.82% in 12 hours with good drug release.

The Formulation Containing Karya Gum in 4mg Concentration Showed good retarding nature with required drug release in 12 hours i.e., 98.13%.

From the above results it was evident that the formulation F4 is best formulation with desired drug release pattern extended up to 12 hours.

Application of Release Rate Kinetics to Dissolution Data:

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

Table 8.8: Release kinetics data for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	%) REL	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	0	0	0	0	0	0	0	0	0	0
19.39	0.5	0.707	0.841	0.917	0.958	0.979	0.989	0.995	0.997	0.999	0.999	-0.001
24.96	1	1.000	1.397	0.000	1.875	24.960	0.0401	-0.603	75.04	4.642	4.218	0.424
29.57	2	1.414	1.471	0.301	1.848	14.785	0.0338	-0.529	70.43	4.642	4.130	0.512
34.41	3	1.732	1.537	0.477	1.817	11.470	0.0291	-0.463	65.59	4.642	4.033	0.609
41.93	4	2.000	1.623	0.602	1.764	10.483	0.0238	-0.377	58.07	4.642	3.872	0.769
48.66	5	2.236	1.687	0.699	1.710	9.732	0.0206	-0.313	51.34	4.642	3.717	0.925
51.19	6	2.449	1.709	0.778	1.689	8.532	0.0195	-0.291	48.81	4.642	3.655	0.987
61.71	7	2.646	1.790	0.845	1.583	8.816	0.0162	-0.210	38.29	4.642	3.371	1.271
67.75	8	2.828	1.831	0.903	0.452	8.469	0.0148	-0.169	32.25	4.642	3.183	1.459
72.97	9	3.000	1.863	0.954	0.477	8.108	0.0137	-0.137	27.03	4.642	3.001	1.640
87.15	10	3.162	1.940	1.000	0.500	8.715	0.0115	-0.060	12.85	4.642	2.342	2.299
92.56	11	3.317	1.966	1.041	0.521	8.415	0.0108	-0.034	7.44	4.642	1.952	2.689
99.82	12	3.464	1.999	1.079	0.540	8.318	0.0100	-0.001	0.18	4.642	0.565	4.077

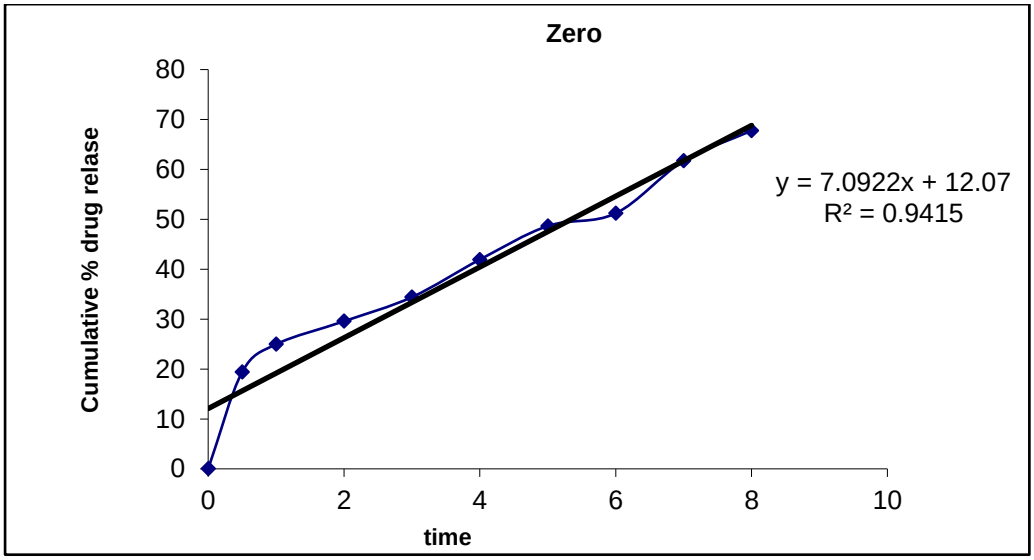


Fig 8.6 : Zero order release kinetics graph

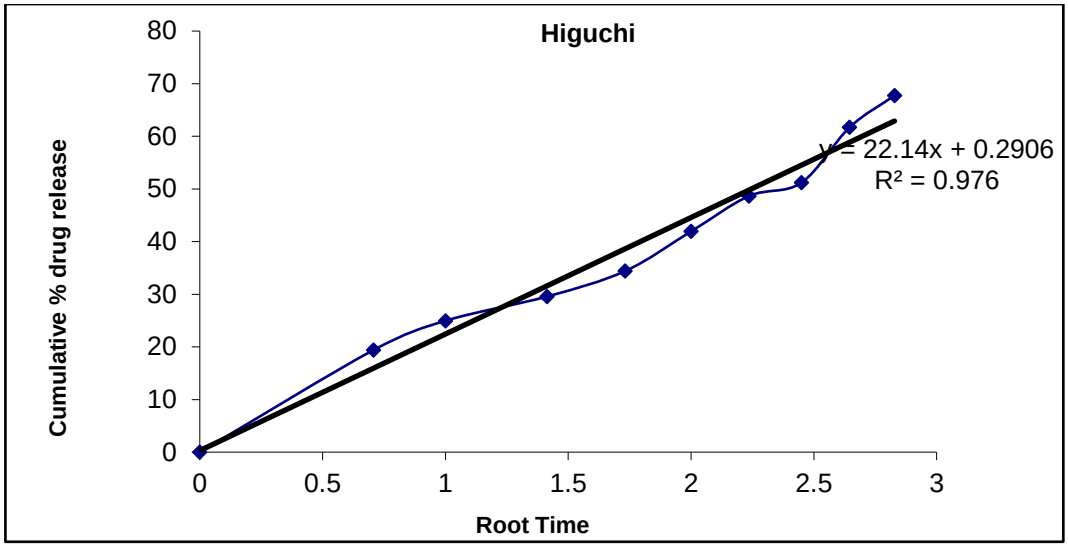


Fig 8.7 : Higuchi release kinetics graph

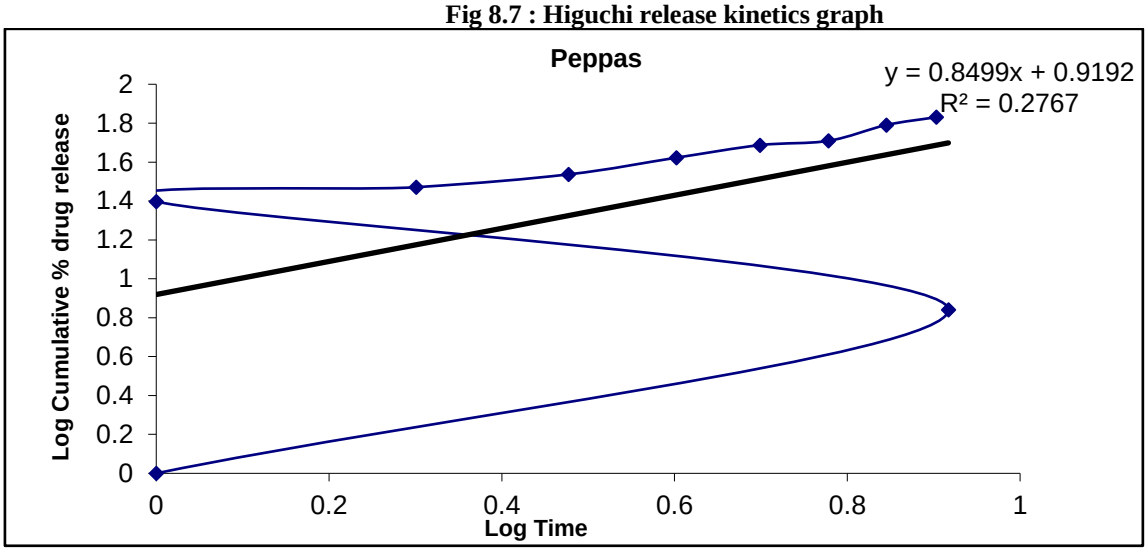


Fig 8.8: Kars mayer peppas graph

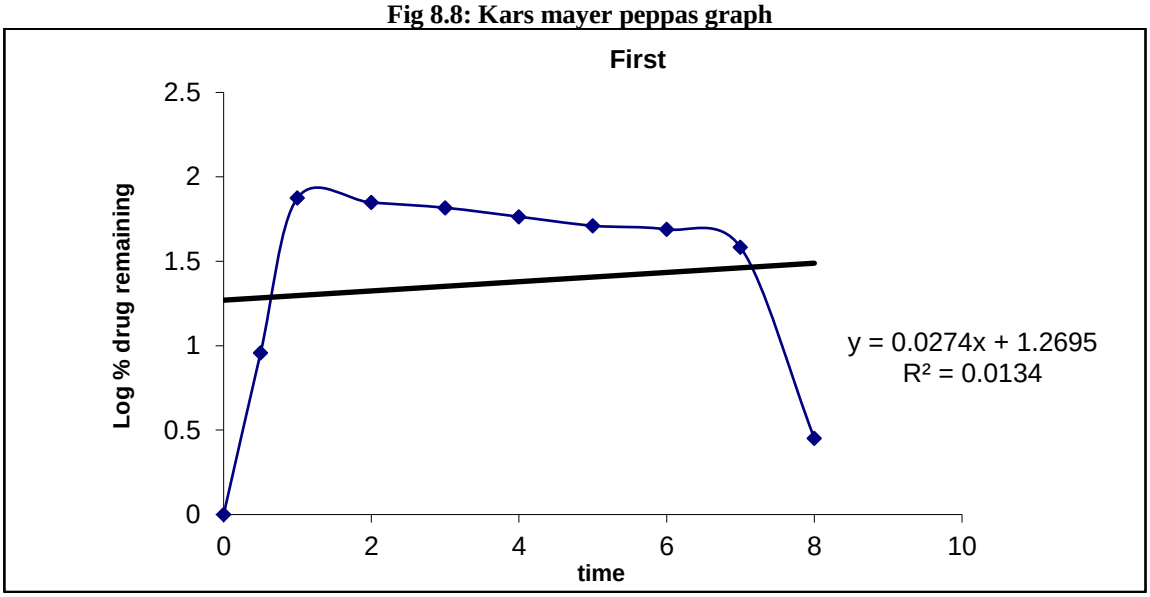


Fig 8.9: First order release kinetics graph

From the above graphs it was evident that the formulation F4 was followed Zero order release kinetics.

Table 8.9: kinetics Correlation coefficient values

Release Kinetics	Correlation coefficient values
Zero order release kinetics	$R^2 = 0.9415$
Higuchi release kinetics	$R^2 = 0.976$
Peppas release kinetics	$R^2 = 0.2767$
First order release kinetics	$R^2 = 0.0134$

8.2. Drug – Excipient compatibility studies
Fourier Transform-Infrared Spectroscopy:

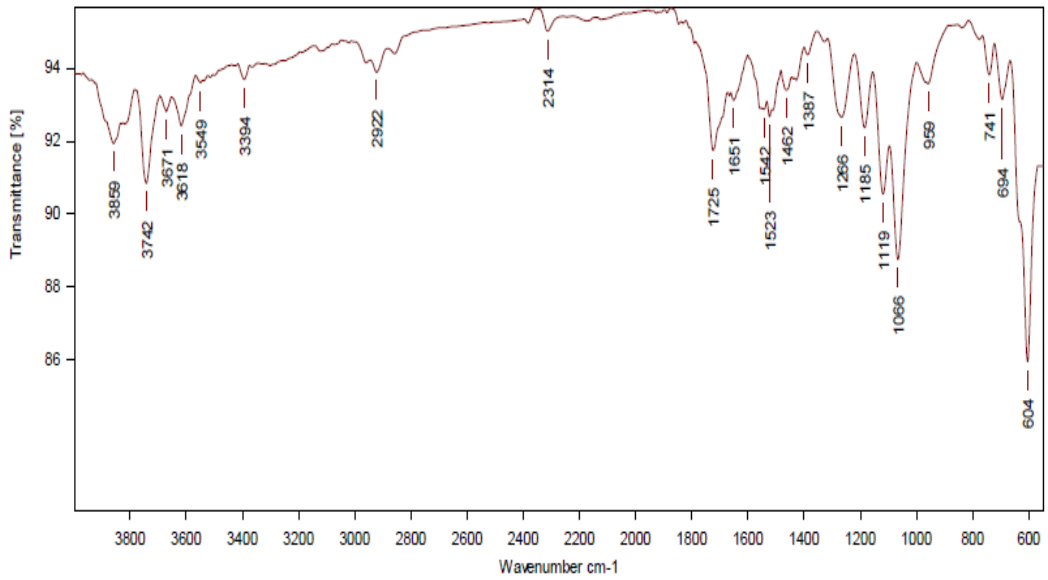


Figure 8.10: FT-TR Spectrum of Cyproheptadine Hcl pure drug

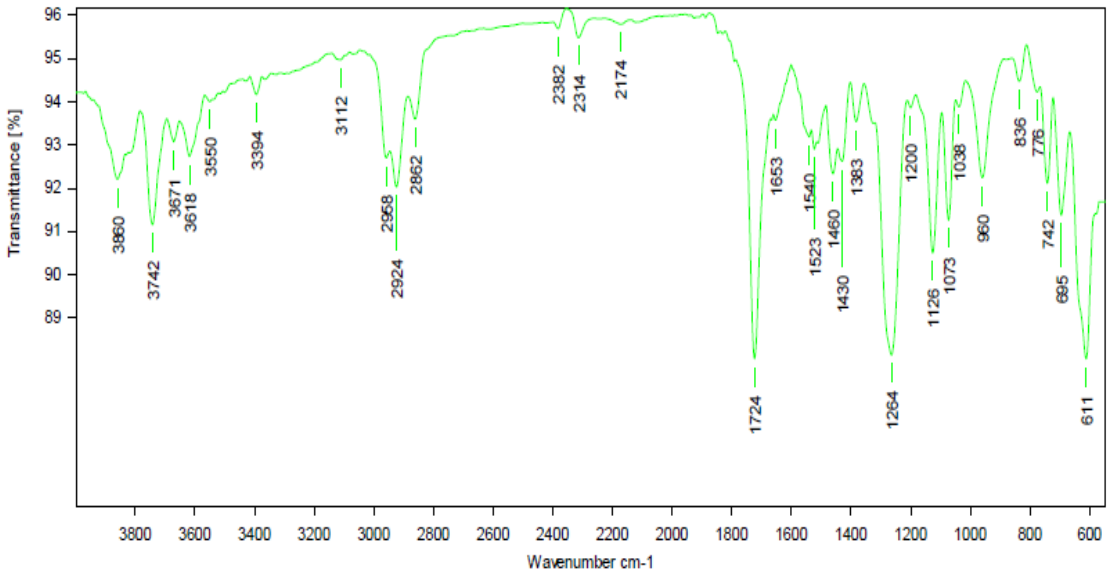


Figure 8.11: FT-IR Spectrum of Optimized Formulation

From the above studies it was found that there was no shifting in the major peaks which indicated that there were no significant interactions occurred between the Cyproheptadine Hcl and excipients used in the preparation of different Cyproheptadine Hcl extended-release tablets formulations. Therefore, the drug and excipients are compatible to form stable.

Formulations under study The FTIR spectra of extended-release tablets and physical mixture used for optimized formulation were obtained and these are depicted in above figures. From the FTIR data

it was evident that the drug and excipients does not have any interactions. Hence, they were compatible.

CONCLUSION:

The present study was successfully carried out for the formulation and development of Cyproheptadine Hydrochloride extended-release tablets using natural polymers. Various natural polymers were employed to design matrix tablets with the goal of achieving sustained drug release, minimizing dosing frequency, and improving patient compliance. All the pre-compression and post-compression parameters of the prepared formulations were found to be within the acceptable limits as per pharmacopeial standards.

Among the different batches, the optimized formulation demonstrated a controlled and sustained drug release profile, following the desired release kinetics over an extended period of time when compared to other formulations. The results revealed that natural polymers such as guar gum, xanthan gum, and gum karaya are effective release-retarding agents and can be successfully used in the design of extended-release dosage forms.

Hence, it can be concluded that Cyproheptadine HCl extended-release tablets formulated with natural polymers are a promising approach to enhance therapeutic efficacy, reduce dosing frequency, and improve overall patient compliance.

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