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Formulation and Evaluation of sustained release tablet chlorpromazine

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ABSTRACT

The treatment of acute or chronic disease has been primarily achieved by administering drugs to patients using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, liquids, sprays and injectables , as a drugs. carriers. this sort of drug delivery system is understood to supply rapid release of drug or immediate release product. Such immediate release products end in relatively rapid drug absorption and associated pharmacodynamic effects. However, once drug absorption from the dosage form is complete, the plasma concentrations of the drug decrease supported the pharmacokinetic profile of the drug. Eventually, the plasma concentrations of the drug drop below the minimum effective plasma concentration (MEC), leading to a loss of therapeutic activity. Before now is reached, another dose is typically given if a protracted therapeutic effect is desired. an alternate to administering another dose is to use a dosage form that gives sustained release of the drug and thereby maintains plasma drug concentrations beyond what's typically seen with immediate-release dosage forms. In recent years, several modified versions and / or the time of release of the drug. After the 20th century, the look for a replacement drug remained thanks to the value of researching the new drug. Therefore, pharmaceutical industries and academic laboratories have focused on creating a replacement drug delivery system / or modified release dosage forms instead of research and development of a replacement drug. The rationale for a protracted drug delivery system is to optimize the biopharmaceutical, pharmacokinetic and pharmacodynamic properties of a drug such its usefulness is maximized by reducing side effects and treating or controlling the disease as quickly as possible using the foremost little ones.

Key Words: chlorpromazine, Microcrystalline Cellulose, Magnesium Stearate.

INTRODUCTION

For many decades, the treatment of acute or chronic disease has been primarily achieved by administering drugs to patients using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, liquids, sprays and injectables , as a drugs. carriers. this sort of drug delivery system is understood to supply rapid release of drug or immediate release product. Such immediate release products end in relatively rapid drug absorption and associated pharmacodynamic effects. However, once drug absorption from the dosage form is complete, the plasma concentrations of the drug decrease supported the pharmacokinetic profile of the drug. Eventually, the plasma concentrations of the drug drop below the minimum effective plasma concentration (MEC), leading to a loss of therapeutic activity. Before now is reached, another dose is typically given if a protracted therapeutic effect is desired. an alternate to administering another dose is to use a dosage form that gives sustained release of the drug and thereby maintains plasma drug concentrations beyond what's typically seen with immediate-release dosage forms. In recent years, several modified versions and / or the time of release of the drug. After the 20th century, the look for a replacement drug remained thanks to the value of researching the new drug. Therefore, pharmaceutical industries and academic laboratories have focused on creating a replacement drug delivery system / or modified release dosage forms instead of research and development of a replacement drug. The rationale for a protracted drug delivery system is to optimize the biopharmaceutical, pharmacokinetic and pharmacodynamic properties of a drug such its usefulness is maximized by reducing side effects and treating or controlling the disease as quickly as possible using the foremost little ones. amount of drug,

administered by the foremost appropriate route. The novel drug delivery system offers a way of accelerating the therapeutic efficacy of incorporated drugs by providing a controlled and sustained release and / or by targeting the drug to the specified site. The goal of any drug administration : The system consists of administering a therapeutic amount of drug within the correct position of the body to rapidly reach and thus maintain the specified drug concentration. There is a growing interest in the pharmaceutical industry for extended-release oral drug delivery systems. There is also a great deal of interest in designing a dosage formulation that allows for a high drug load, particularly for active ingredients with high water solubility.

AIM

Aim: The aim of present investigation was to formulation and Evaluation of sustained release tablet chlorpromazine.

Objectives:

a) Formulate and evaluate of tablet of chlorpromazine.
b) Select stable and compatible excipients with chlorpromazine by carrying out a pharmacological compatibility study of the excipients.
c) To characterize pure medicine for intrinsic physico-chemical properties such as M.P., λmax, Solubility, etc.
d) Evaluate the powder for compression for its rheological parameters.
e) Evaluate the compressed tablets for post-compression characteristics.
f) Study the effect of different combinations of polymers on: myself.
g) Study the in vitro release profile of tablet of chlorpromazine.

MATERIALS AND EQUIPMENTS

Materials Used

Table 5.1: Material Used in study

Sr.No	MATERIALS USED	MANUFACTURED BY
1.	chlorpromazine HCl	R.L.fine chem, Karnataka
2.	Microcrystalline cellulose	Maa Saptashrungi chemicals Mumbai
3.	PVP	N Shashikant & co Mumbai
4.	HPMC	Amnem , Mumbai
5.	Magnesium Stearate	Ozone International, Mumbai
6.	colloidal Silicon dioxide	Ozone International, Mumbai

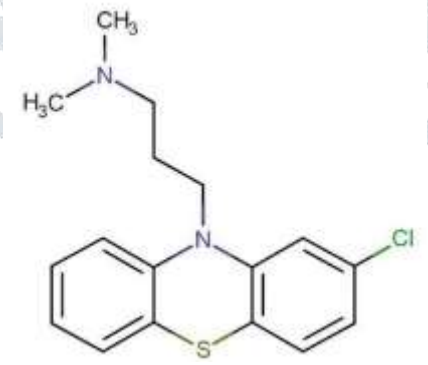
Instruments Used

Table 5.2: Instruments used in study

Sr. No	Instruments	Manufacturer
1	Electronic Balance & Top loading Balance,	Shimadzu Corporation, AW 220 and BX 6205
2	Tray Dryer	Erweka Pvt. Ltd.
3	Coating machine	Erweka Pvt. Ltd.
4	Dissolution Apparatus (USP) Auto Sampler	Electrolab Pvt. Ltd.
5	Shaking Water Bath	Equitron
6	Tablet Hardness tester	Monsanto
7	Friability test apparatus	Electrolab Pvt. Ltd. EF 2 USP
8	Ultra Violet Visible spectro photometer	Shimadzu Corporation UV-1700
9	FT-IR Spectrophotometer	Shimadzu Corporation,8400S
10	Tap density Appratus	Erweka Pvt. Ltd.
11	Granulate Flow Tester	Erweka Pvt. Ltd.
12	Vernier Caliper	Digimatic
13	pH Meter,	Systronics (335)
14	Tablet punching machine	CADMACH 16 station

Drug Profile

Chlorpromazine HCl
Structure:



Molecular Formula : C17H19ClN2S.HCl
Molecular Weight : 318.86 g/mol
IUPAC Name: [3-(2-Chloro-phenothiazin-10-yl)-propyl]-dimethyl-amine
Categories : antipsychotic and antieme
Indications: For the treatment of schizophrenia; to control nausea and vomiting; for relief of restlessness and apprehension before surgery; for acute intermittent porphyria; as an adjunct in the treatment of tetanus; to control the manifestations of the manic type of manic-depressive illness; for relief of intractable hiccups; for the treatment of severe.

Pharmacodynamics: Chlorpromazine is a psychotropic agent indicated for the treatment of schizophrenia. It also exerts sedative and antiemetic activity. Chlorpromazine has actions at all levels of the central nervous system-primarily at subcortical levels-as well as on multiple organ systems. Chlorpromazine has strong antiadrenergic and weaker peripheral anticholinergic activity; ganglionic blocking action is relatively slight. It also possesses slight antihistaminic and antiserotonin activity.

EXPERIMENTAL WORK

Preformulation Studies The preformulation test is the first step in the rational development of dosage forms of a drug substance. It can be defined as an investigation of the physical and chemical properties of a drug alone and when combined with excipients. The overall goal of preformulation testing is to generate information useful to the formulator in the development ofstable and bioavailable dosage forms that can be mass produced.

Analytical method used in the determination of Chlorpromazine HCl.

The UV spectrophotometric method was developed for drug analysis using the Shimadzu 1800 spectrophotometer.

Preparation of the phosphate buffer solution at pH 6.8:

A) Preparation of 0.2 M potassium dihydrogen phosphate 27.22 g of potassium dihydrogen phosphate were weighed out and diluted to 1000 ml with distilled water to obtain 0.2 M of potassium dihydrogen phosphate.

B) **Preparation of the phosphate buffer solution at pH 6.8:**

50 ml of the 0.2 M potassium dihydrogen phosphate solution were extracted from the stock solution in a 200 ml volumetric flask, and 22.4 ml of sodium hydroxide solution was added from the sodium hydroxide solution or stock solution, 2M and then distilled water was used to make the volume.

Determination of λmax

1% w / v Chlorpromazine HCl was prepared in water and the maximum absorbance was scanned on the double beam UV spectrophotometer (Shimandzu-1800) in the range of 200 to 400 nm, using 0.1 N as a blank. The λmax of the drug was found to be 250 nm.

Standard curve for Chlorpromazine HCl

100 mg of Chlorpromazine HCl was carefully weighed out and dissolved in 100 ml of water to prepare the first stock solution. 10 ml of the above solution were taken and diluted to 100 ml with the same solvent to prepare the stock solution II. The aliquot of stock solution II was further diluted with water to obtain 5 µg, 10 µg, 15 µg, 20 µg, 25 µg and 30 µg of drug per ml of the final solution. The absorbance was then measured on a UV spectrophotometer at 249 nm against water as a blank. The graph was plotted for absorbance versus concentration.

Compatibility study using FT-IR:

A successful formulation of a stable and effective solid dosage form depends on a careful selection of excipients that are added for ease of administration that promote steady release and bioavailability of the drug and protect it from degradation. Infrared spectroscopy was performed using a Thermo Nicolet FTIR and the spectrum was recorded in the region of 4000 to 400 cm -1. Drug-excipient interaction was observed from IR-spectral studies by observing any changes in drug peaks in the physical spectrum of the drug mixture.

Procedure:

The weighed amount of drug (3 mg) was mixed with 100 mg of potassium bromide (dried at 40-50 ° C). The mixture was taken and compressed at a pressure of 10 tons in a hydraulic press to form a transparent tablet. The sediment was scanned by the IR spectrophotometer. A similar procedure is followed for all relevant excipients used.

EVALUATION OF PREFORMULATION PARAMETERS

Determination of angle of repose

The angle of repose is an indication of the excited frictional forces between the granular particles. It is the maximum possible angle between the surface of the grain pile and the horizontal plane:

$$\tan \theta = h / r$$

Where,

θ = the angle of repose,
h = height of the dust heap and
r = radius of the dust heap

Table no.4 : ANGLE OF REPOSE

SL.NO	ANGLE OF REPOSE(θ)	TYPE OF FLOW
1.	< 20	Excellent
2.	20-30	Good
3.	30-40	Passable
4.	>40	Very poor

Procedure:

Heavy amounts of powder (mix mix) were poured through the funnel from a fixed height onto the graph paper. The height of the pile was measured. The circumference of the pile was marked with a pencil. The area of the formed circle was calculated on the basis of the large and small squares present within the circle and then the angle of repose was calculated on the parameter "r" which was identified by the area of the circle.

Determination of apparent density and derived density

20 g of the mixed mixture (W) were placed in a 100 ml graduated cylinder and the initial volume was observed. The cylinder was dropped under its own weight onto a hard surface from a height of 2.5 cm at 2 second intervals. Tapping continued until no further volume changes were observed.

Bulk density = W / VO

Tapped density = W / VF

Bulk density and density under pressure were calculated using the following formulas.

Where W = weight of the powder mixture,
VO = initial volume of the powder mixture
VF = final volume of powder mix 52

Carr's compressibility index (CI):

The compressibility index is an important measure that can be obtained from bulk and exploited densities. In theory, the less compressible a material is, the more fluid it is. A material with values below 20% has good flow property.

$$CI = \frac{(\text{Tapped Density} - \text{Bulk Density}) \times 100}{\text{Tapped Density}}$$

Table no. 5 : Compressibility Index

SL NO	% COMPRESSIBILITY INDEX	PROPERTIES
1.	5-12	Free flowing
2.	12-16	Good
3.	18-21	Fair
4.	23-35	Poor
5.	33-38	Very poor
6.	>40	Extremely poor

Hausner's Ratio:

It indicates the flow properties of the granules and is measured by the relationship between the threading density and the apparent density.

Hausner‟s Ratio = Tapped density/Bulk density

Table No. 06 : Hausner's Ratio

SL.NO	HAUSNER'S RATIO	PROPERTY
1.	0-1.2	Free flowing
2.	1.2-1.6	Cohesive flowing

Preparation of sustained-release matrix tablets by direct compression method

Sustained release tablets of Chlorpromazine HCl were prepared by direct compression method. The corresponding amount of drug and excipients was carefully weigh ed and mixed properly and the matrix tablets were prepared by direct compression using a drilling machine. Each tablet contains 100 mg of Chlorpromazine HCl.

Table no 7: Selected excipients for prototype formulation

Sl.NO	EXCIPIENT	FUNCTION
1	HPMC	Release rate retardant
2	Polyvinylpyrrolidone	Binder
3	Micro Crystalline Cellulose	Diluent
4	Magnesium stearate	Lubricant
5	colloidal Silicon Dioxide	Glidant

Table no 8: Formulation development of Chlorpromazine HCl by direct compression technique

FORMULA CODE(mg)	F1	F2	F3	F4	F5	F6	F7
Chlorpromazine HCl	100	100	100	100	100	100	100
HPMC	30	40	50	60	70	80	100
Colloidal Silicon dioxide	5	10	15	20	25	30	35
PVP	5	6	7	8	9	10	11
Magnesium Stearate	3	3	3	3	3	3	3
Micro crystalline cellulose QS to	250	250	250	250	250	250	250

POST-COMPRESSION EVALUATION PARAMETERS

Evaluation of Chlorpromazine HCl sustains release tablets: The tablets were subjected to various evaluation parameters, including drug content uniformity, weight change, tablet hardness, friability, and thickness, and in vitro drug release with different media.

Weight shift

The weight of the tablet produced has been routinely determined to ensure that a tablet contains the correct amount of drug. The USP weight variation test is performed by weighing 20 tablets individually, calculating the average weight, and comparing the individual weights with the average. The tablets met the USP specification that no more than 2 tablets are outside the percentage limits and no tablet differs by more than twice the percentage limit. The tablet's official USP percent deviation limits are presented

Table no 9: Weight Variation Limit

Sr. No.	Average weight of tablet (mg)	Maximum % difference allowed
1.	130 or less	10
2.	130-324	7.5
3.	324<	5

Tablet hardness:

The resistance of tablets to shipping or breakage under the conditions of storage transport and handling before use depends on their hardness. The hardness of each batch of tablets was tested using the Monsanto hardness tester. Hardness was measured in terms of kg / cm2. 5 tablets were chosen at random and tested for hardness. The mean hardness of 5 determinations was recorded.

Friability:

Friability generally refers to the loss of weight of packaged tablets due to the removal of fine particles from the tablet surface. Friability generally reflects the poor cohesion of the tablet ingredients.

Method:

20 tablets were weighed and the initial weight of these tablets was recorded and placed in the Roche crusher and rotated at the speed of 25 rpm for 100 rpm. The tablets were then removed from the shredder, the fine particles were dusted off and weighed again and the weight was recorded.52 The percent friability was calculated using the formula: % Friability = Initial weight of the tablets – Final weight of the tablets X 100 Initial weight of the tablets

Tablet thickness:

The thickness of the tablet is important for uniformity in the size of the tablet. The thickness was measured using vernier calipers. It was determined by checking the thickness of ten tablets from each batch of formulation.

Uniformity of drug content:
10 tablets from each batch were weighed and the average weight was calculated. All tablets were crushed and a powder equivalent to 80 mg of the drug was dissolved in 6.8 phosphate buffer and the volume made up to 100 ml with pH 6.8 phosphate buffer. From the warehouse solution, 1 ml of solution was collected in a 10 ml volumetric flask and the volume was made up with phosphate buffers at pH 6.8. The solution was filtered and the absorbance was measured spectrophotometrically at 250 nm against phosphate buffer at pH 6.8 as a blank. The amount of drug in one tablet was calculated.

In vitro dissolution studies:
In vitro dissolution studies were performed using the USP-II dissolution apparatus (Paddle) at 50 rpm. The dissolution medium was 0.1 N HCl during the first 2 hours and the phosphate buffer at pH 6.8 during the remaining hours and the temperature was maintained at 37 ± 0.50 ° C. 5 ml were taken at intervals of time specific and the same volume of fresh medium was replaced. The collected samples were diluted with pH 6.8, filtered and analyzed in a UV spectrophotometer at 250 nm using pH 6.8 as a blank. The cumulative drug release rate was calculated.

RESULTS AND DISCUSSION

Determination of Chlorpromazine HCl λ max
Chlorpromazine HCl λ max was found to be 250 nm in water.

Chlorpromazine HCl calibration curve
The absorbance of Chlorpromazine HCl was measured on a UV spectrophotometer at 250 nm against water as a blank. The absorbance thus obtained was tabulated (table No. 12) and the graph was obtained by plotting the concentration of the absorbance

Table no.12: Spectrophotometric data for the estimation of Chlorpromazine HCl in water

SL. No.	Concentration (µg/ml)	Absorbance at 250 nm				
		Trail-1	Trail-2	Trail-3	Average	S.D.
1	0	0	0	0	0	0
2	5	0.0124	0.0153	0.0153	0.00952	0.00306
3	10	0.0222	0.022	0.0219	0.0189	0.0088
4	15	0.0258	0.0258	0.0252	0.0258	0.00077
5	20	0.0320	0.0331	0.0329	0.0360	0.00350
6	25	0.0369	0.0376	0.0378	0.04174	0.00422
7	30	0.0431	0.0433	0.0434	0.0533	0.00412

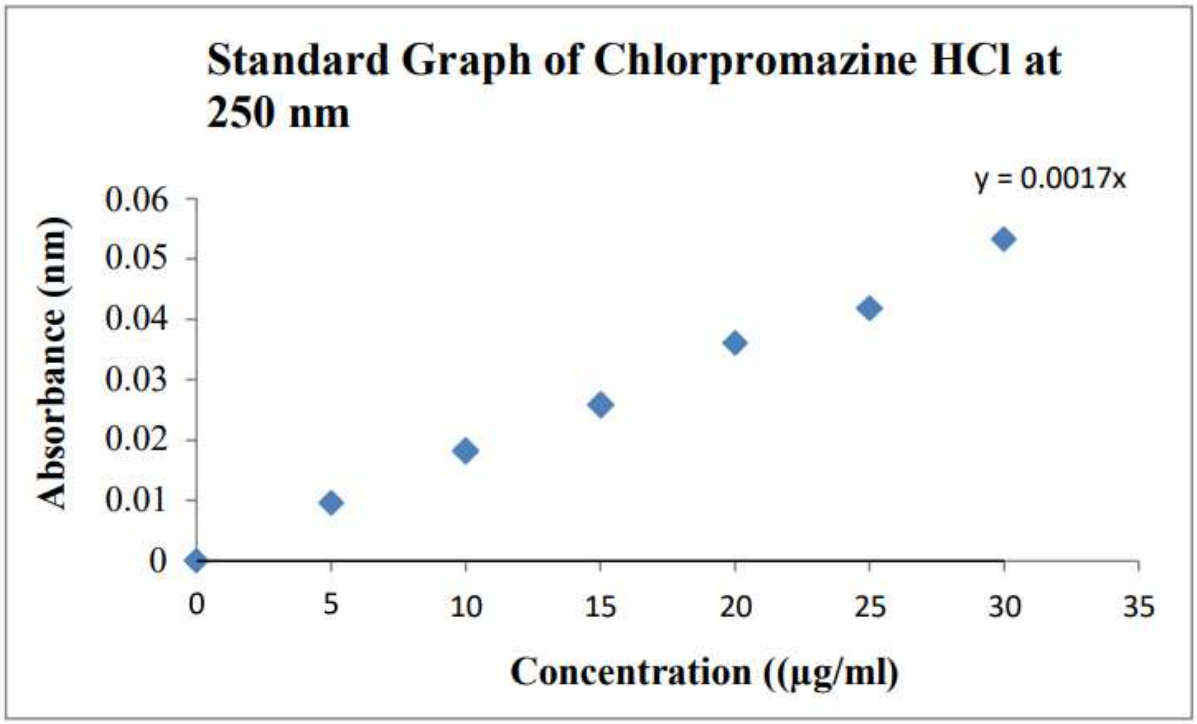


Figure 6: Calibration Curve of Chlorpromazine HCl in water

Compatibility studies using FT-IR

The infrared spectrum of the drug, the polymers and the mixture of both were determined by the KBr disk method. The samples were prepared in KBr discs using a hydrostatic press at a pressure of 5 tons for 5 min. All characteristic peaks of Chlorpromazine HCl were present in the spectrum of the drug polymer mixture, indicating drug-polymer compatibility. From the results it was concluded that there was no functional group interference since the main Chlorpromazine HCl peaks were not altered in the physical drug-polymer mixtures, indicating that they were chemically compatible. The spectrum confirmed that there is no significant change in the chemical integrity of the drug.

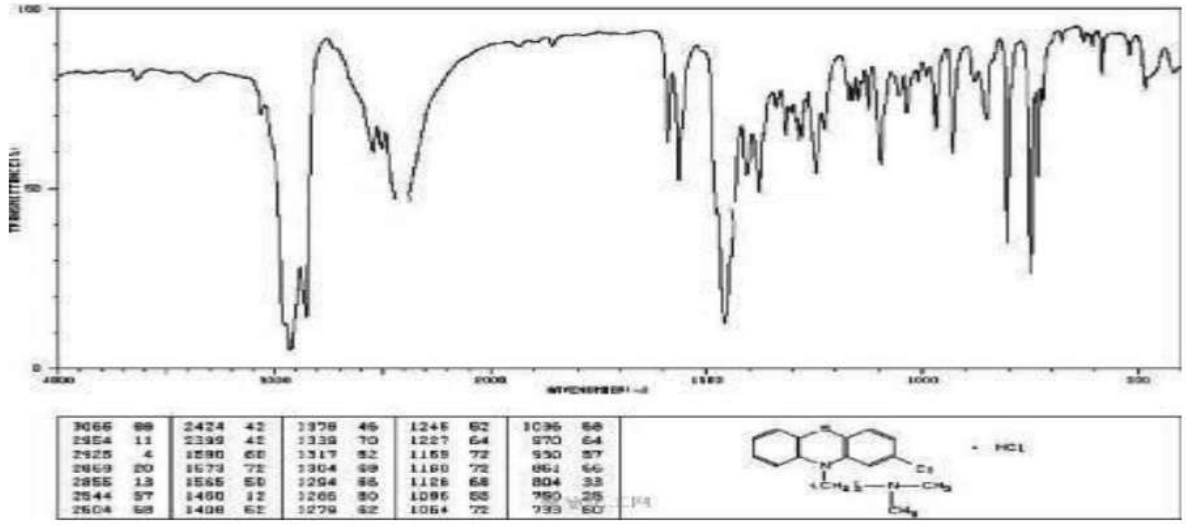


Figure 7: IR Spectrum of Pure Drug Chlorpromazine HCl

FORMULATION DESIGN

The main objective of the present study was to formulate Chlorpromazine HCl sustained release matrix tablets using HPMC to improve its therapeutic efficacy and decrease adverse effects by minimizing the frequency of dosing. In this case, nine sustained release matrix tablet formulations were prepared using different polymers such as HPMC, MCC and PVP in different proportions. The detailed composition of each formulation is shown in table no. 5. The powder mixture was subjected to pre-compression and post-compression evaluation before and after compression.

Evaluation parameters:

Evaluation of the characteristics of the powder mixture of the Chlorpromazine HCl matrix tablet formulation For each type of formulation, mixtures of Chlorpromazine HCl and other excipients were prepared and evaluated for various parameters such as bulk density, plugging density, compressibility index of Carr, Hausner relationship and rest corner. The apparent density was found in the range of 0.355-0.3850 g / cm3 and the derived density between 0.4101 and 0.4880 g / cm3 indicates that both parameters were within the limits. Using the two density data reported above, the Carr compressibility index was calculated.

The compressibility index and the Hausner relationship were found in the range of 7.27-18.42% and 1.053-1.24 respectively, which indicates that all mixtures of powder exhibited excellent to acceptable flow properties. The flow property of all powder mixtures is best explained by the angle of repose. The angle of repose was found in the range of 25.33 to 31.43 °. The angle of repose results showed that all the powder mixtures had good to fair flow properties.

Table no.14: Evaluation parameters of pre-formulation characteristics of powder blend

Formulations Number	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (θ)
F1	0.3712±0.011	0.4101±0.025	7.27±0.659	1.177±0.076	29.73± 0.41
F2	0.3803±0.05	0.4120±0.026	7.58±0.514	1.053± 0.060	25.33 ±0.63
F3	0.3843±0.015	0.4120±0.05	7.43±0.760	1.059±0.088	28.44 ±0.35
F4	0.376±0.020	0.4270±0.037	13.74±0.386	1.073±0.053	27.44 ±0.52
F5	0.355±0.017	0.4600±0.024	15.31±0.794	1.224±0.011	31.34± 0.13
F6	0.3810±0.045	0.4780±0.065	18.42±0.120	1.24±0.020	28.26 ±0.43
F7	0.3850±0.081	0.4384±0.133	10.88±0.301	1.113±0.021	27.27±0.42

Physical evaluation of tablets

After compression, several quality control tests were carried out, which demonstrated the following organoleptic properties viz. color, smell and shape. All formulations (F1 to F7) were white, odorless and concave, rounded and flat with a break line on one side.

Table no.15: Organoleptic properties of prepared tablets

Formulation code	Color	Odour	Shape
F1	White color	odourless	Concave, round and flat with break-line on one side
F2	White color	odourless	Concave, round and flat with break-line on one side
F3	White color	odourless	Concave, round and flat with break-line on one side
F4	White color	odourless	Concave, round and flat with break-line on one side
F5	White color	odourless	Concave, round and flat with break-line on one side
F6	White color	odourless	Concave, round and flat with break-line on one side
F7	White color	odourless	Concave, round and flat with break-line on one side

Table no.16: Post-compression parameters results

Formulation	Diameter (mm) ± SD	Thickness (mm) ± SD	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	5.82±0.12	3.9±0.91	250.89±0.12	7.3±0.41	0.61±0.17	98.25±0.44
F2	5.80±0.20	4.0±0.21	253.88±0.60	7.8±0.32	0.52±0.22	96.31±0.37
F3	5.85±0.30	4.2±0.12	251.12±0.54	8.0±0.75	0.58±0.11	98.54±0.71
F4	5.84±0.22	3.9±0.73	249.81±0.13	6.5±0.44	0.72±0.16	99.67±0.87
F5	5.90±0.15	4.0±0.41	250.80±0.32	6.8±0.83	0.665±0.19	99.37±0.52
F6	5.94±0.10	3.8±0.93	248.92±0.41	7.1±0.32	0.714±0.12	98.97±0.73
F7	5.97±0.16	4.1±0.17	252.61±0.60	6.0±0.51	0.447±0.01	98.61±0.81

Discussion of physical parameters such as

A. Thickness of tablets
B. hardness
C. friability
D. Weight change

Thickness of tablets

All the formulations have been evaluated regarding their thickness using "Calipers" according to the procedure of methodological section 4. The average thickness for all formulations was found in the range of 3.8-4.2 mm which is within the limit of allowable deviation, which is 5% of the standard value. The crown diameter of the entire tablet formulation was also between 8.0 and 7.8 mm.

hardness

The hardness of the tablets is one of the critical parameters to evaluate the resistance of the tablets to plugging, abrasion or breakage in conditions of storage, transport and handling before administration. All Chlorpromazine HCl controlled release matrix tablet formulations were evaluated for their hardness according to the procedure in section 4 of the methodology and the results were dissipated. The hardness test was performed by the "Monsanto hardness tester". All the formulations have an average hardness between 6.0 and 8.0 kg / cm2. This ensures good handling characteristics for all formulation batches.

Friability

Friability is determined to assess the ability of tablets to resist abrasion during packaging, handling, and shipping. The friability of the prepared tablets was determined with the "Roche friabilizer". The percent friability of all the controlled release matrix tablet formulations was evaluated. The mean percent friability for all formulations was found to be between 0.447% and 0.72%, which is within the limit of the pharmacopoeia (ie, below 1%). Therefore, the maximum friability was 0.72% observed for F4 and the minimum friability observed was 0.447% for F7.

Weight variation test:

Thickness of tablets All the formulations have been evaluated regarding their thickness using "Calipers" according to the procedure of methodological section 4. The average thickness for all formulations was found in the range of 3.8-4.2 mm which is within the limit of allowable deviation, which is 5% of the standard value. The crown diameter of the entire tablet formulation was also between 8.0 and 7.8 mm. B. hardness The hardness of the tablets is one of the critical parameters to evaluate the resistance of the tablets to plugging, abrasion or breakage in conditions of storage, transport and handling before administration. All Chlorpromazine HCl controlled release matrix tablet formulations were evaluated for their hardness according to the procedure in section 4 of the methodology.The hardness test was performed by the "Monsanto hardness tester". All the formulations have an average hardness between 6.0 and 8.0 kg / cm2. This ensures good handling characteristics for all formulation batches. C. friability is determined to assess the ability of tablets to resist abrasion during packaging, handling, and shipping. The friability of the prepared tablets was determined with the "Roche friabilizer". The percent friability of all the controlled release matrix tablet formulations was evaluated and the results are shown in Table No. . The mean percent friability

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Weight variation test:

Since the powder material flowed freely, the obtained tablets had a uniform weight due to the uniform filling of the mold with acceptable variations according to IP standards. The weight change for all the formulations was found in the range of 249.92 to 253.88 mg and the results were dissipated in Table No. 16. All the formulated tablets passed the weight change test since the% of weight change was within the limits of the pharmacopoeia.

Drug content

The percent drug content for formulations F1 to F7 was found to be between 98.25% w / w and 99.61% w / w. Meets official specifications. The results are shown in table no. 16.

In vitro drug release study

In this study, HPMC was chosen as the polymer and combined with PVP and MCC to explore its sustained release ability. In vitro release data of Chlorpromazine HCl PVP-HPMC and MCC sustained release matrix tablets are presented in Table 17 and illustrated in Figure 10. In vitro release of Chlorpromazine HCl, from formulations of tablets in the matrix, was mainly affected by dissolution medium, PVP concentration, MCC concentration, and polymer concentration. The in vitro release of matrix tablets prepared in the form of Chlorpromazine HCl also depends on the swelling behavior of the tablets, the greater the swelling of the tablet compared to the lower amount of drug release. The in vitro release study was performed in 0.1 N HCl for the initial first 2 hours, then the medium was replaced with phosphate buffer (pH 6.8) and the study continued for 24 hours. The in vitro release of Chlorpromazine HCl was highest in the first 6-7 hours in all formulations. After 1 hour, approximately 10.29% - 18.34% of Chlorpromazine HCl was released from the PVP-HPMC tablets, 16.90% - 21.91% from MCC and HPMC, 25.12% from the tablets containing only release retardant polymer. Initially, the amount of drug released was higher, but after 6-7 hours the release of the drug was delayed. Formulation F1 does not contain any crosslinking agents, so almost all drugs were released at the end of 12 hours.

Table. : In-vitro drug release profile of Chlorpromazine HCl sustain release tablet

Time (Hrs)	Cumulative Percentage Drug Release						
	F_1	F_2	F_3	F_4	F_5	F_6	F_7
0	0	0	0	0	0	0	0
1	25.12±0.19	18.34±0.43	15.386±0.33	10.29±0.55	21.91±0.54	18.25±0.32	16.90±0.85
2	40.02±0.12	29.24±0.21	26.905±0.45	25.64±0.62	30.92±0.43	29.25±0.22	25.99±0.42
4	58.82±0.12	35.45±0.33	31.465±0.21	30.94±0.53	39.33±0.54	35.20±0.64	33.71±0.79
6	72.41±0.14	48.71±0.20	46.137±0.13	41.54±0.45	51.64±0.51	48.82±0.73	41.55±0.54
8	80.03±0.28	59.99±0.54	52.186±0.43	48.96±0.33	63.93±0.65	61.73±0.83	54.08±0.64
10	91.61±0.34	68.41±0.55	63.97±0.42	59.68±0.42	72.96±0.72	69.40±0.88	61.27±0.53
12	99.07±0.12	77.09±0.22	71.33±0.54	63.38±0.38	81.23±0.42	77.73±0.95	75.14±0.43
14	--	85.86±0.26	76.50±0.65	74.11±0.43	89.37±0.44	86.24±0.76	82.67±0.42
16	--	92.15±0.33	85.96±0.66	83.39±0.14	95.39±0.62	91.28±0.87	88.75±0.48
18	--	99.71±0.42	90.88±0.59	85.21±0.11	99.77±0.11	95.62±0.73	92.23±0.48
20	--	--	98.54±0.43	93.39±0.14	--	97.99±0.61	94.54±0.48
24	--	--	--	99.54±0.11	--	--	98.78±0.48

CONCLUSION

The aim of the present study was to investigate the possibility of supporting the release of Chlorpromazine HCl from the prepared tablet using different concentrations of crosslinking agents and polymers. From the result obtained, the following conclusions can be drawn.

1. Pre-formulation studies, such as angle of repose, bulk density, Haunser ratio of thread density, and Carr's index of all formulations were found to be within standard limits.
2. FTIR studies revealed that there was no chemical interaction between the drug and other excipients.
3. The powder mixtures were compressed into tablets and evaluated for postcompression parameters such as weight, thickness, hardness, friability, and change in drug content. All formulation batches showed acceptable results.

4. In vitro drug release was studied with a USP type II dissolution apparatus in both simulated gastric fluid and intestinal fluid over a 24-hour period. The results showed that formulations containing a higher concentration of HPMC, i.e., F4 (99.54%) and MCC, i.e., F7 (98.78%), maintained drug release for a period of 24 hours.

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