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ORIGINAL ARTICLE **OPEN ACCESS**

Development and Evaluation of Sustained Released Tablet Formulation Containing Fiuphenazine HCl

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ABSTRACT
The aim of the present work was to develop pharmaceutical dosage treatment of many patients with Dementia – related psychosis with at high risk of antipsychotic . Fluphenazine HCl drug to treat the psychotic Patient. drug to treat the high risk central nervous system disease simultaneous. In this formulation three batches are prepared by direct compression method preformulation parameter such as identification, solubility, melting point, compatibility studies and precompression parameter bulk density, tapped density, angle of repose, Hausner ratio, compressibility index and post compression parameter weight uniformity, hardness, drug content, thickness, in vitro drug release. In vitro drug release Fluphenazine HCL of all formulation B1, B2, B3 was carried out in 2hrs 0.1Hcl and the 10 hrs in phosphate buffer P^{H} dissolution media. Among all the formulation B3 was optimized as best formulation. B3 formulations B3 showed 85% for Fluphenazine hydrochloride maximum drug release at 12hrs.
Keywords: *Sustained release tablet, Fluphenazine HCl.*

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INTRODUCTION

Sustained-release oral delivery systems are designed to achieve therapeutically effective concentrations of drug in the systemic circulation over an extended period of time. Possible therapeutic benefits of properly designed SR dosage form include low cost, simple processing, improved efficacy, reduced adverse events, flexibility in terms of the range profiles attainable, increased convenience and patient compliance[1].

Currently Fluphenazine hydrochloride available as separate tablet for the treatment of dementia-related psychosis. The formulation were prepared by granulation compression method. Single tablet containing only one drugs such as Fluphenazine Hcl release the compassion typically done by using Lactose monohydrate and microcrystalline cellulose. The compatibility parameter preformulation study compression parameter and in vivo parameters were performed with pharmaceutical expectable [2]. The aim of the present work was to develop pharmaceutical dosage treatment of many patients with Dementia – related psychosis with at high risk of antipsychotic.

MATERIAL AND METHODS

Materials

Fluphenazine HCl gifted sample (flamingo pharmaceutical) HPMCK4, (Thermmosil fine chem), microcrystalline cellulose (research lab), magnesium stearate (Hilab chemicals) were sample is analytical grade) [3, 4].

Preparation of Tablet

The Fluphenazine hydrochloride were prepared by Granulation compression method using varying proportion of polymers either alone or combination. The ingredients were passed through 40 and 60 mesh sieve calculated amount of drug polymer (Lactose monohydrate, Starch 1500,Avicel PH 102, Super tab 14 SD microcrystalline Cellulose) was mixed thoroughly. Then it make a dry mix. Add purified water until wet granulation. Dry it. magnesium stearate was added as lubricant. The appropriate amount of the mixture was weighed and the compression machine(MAKE CREATE INDUSTRIES,MODEL-LP-8GMP).

Table No.1: Formulation of Fluphenazine HCL tablet:

Sr. No	Ingredients	B1	B2	B3
1	Fluphenazine Hcl	14.00	14.00	14.00
2	Microcrystalline cellulose(Avicel PH101)	248.626	244.166	242.144
3	Lactose monohydrate(pharm 200M)	56.00	56.00	56.00
4	Starch 1500	21.00	21.00	21.00
5	Hydroxy propyl cellulose (HPC SL)	1.974	4.200	4.200
6	Polysorbate 80	4.200	4.200	-
7	Purified water		q.s	
8	Microcrystalline cellulose (Avicel PH 102)			
9	Super tab 14 SD	56.00	56.00	56.00
10	Magnesium stearate	4.200	4.200	4.200
	Total			400.00

Preformulation Study:

Identification test by UV- Spectrophotometer:

a) Fluphenazine hcl

Determination of λ max of Fluphenazine HCl in pH 6.8 phosphate buffer From the stock 1 mL was taken and diluted to 100 mL with pH 6.8 phosphate buffer. Spectrum of this solution was seen from 200-400 nm range on UV-Visible spectrophotometer for determination of λ max. And the λ max was found to be 231 nm. From the above mentioned stock solution subsequent dilutions were made with pH 6.8 phosphate buffer to obtain the series of dilutions containing 2, 4, 6, 8, 10, 12, 14µg/mL of solution. The absorbance of the above dilutions was measured at 231nm by using the UV-Spectrophotometer using pH 6.8 phosphate buffer as the blank. Then a graph was plotted by taking concentration on X-axis and absorbance on Y-axis which gives a straight line.

Melting point determination [5]

The melting points of Fluphenazine Hcl were determined by melting point apparatus. The melting point was determined by introducing small amount of substance in the capillary attached to graduated thermometer.

Determination of solubility:

Qualitative solubility

Qualitative solubility analysis of drugs were done by dissolving 5mg of drug in 5ml solvent such as distilled Aqueous solution, chloroethane .

Compatibility study (FTIR):

The powdered substance of the tablet were mix, dried potassium bromide ratio of sample is should be 1:100mg, are compressed to form transparent pellets. The sample scanned from 4000 to 400cm at ambient temperature [6,7].

Pre-compression Evaluation:

Bulk density:

Bulk density was determined by placing the power blend into measuring cylinder and total volume was measured and also total powder weight was measured and also total powder weight was measured. The bulk density was calculated by using formula.

Bulk density = weight of powder/ bulk volume.

Tapped density:

Tapped density was obtained by tapping the cylinder by using tapped density apparatus. Tapped the cylinder up to 100 times and then measure the tapped volume and calculate the tapped density by using formula,

Tapped density = weight of powder/tapped volume

Hausners ratio:

Hausner's ratio is the number that is correlated to the flowablity of powder or powder blend. It is calculated using formula,

Hausner's ratio = tapped density –bulk density/tapped density*100.

Compressibility index

Compressibility index was calculated by formula,

Carr's index (%) = tapped density/bulk density*100

Angle of repose

The angle of repose of powder blend of each layer of each formulation was determined by fix funnel method. The blend was poured through funnel separately until apex of pile so formed just touch the tip of the funnel. The angle of repose was calculated by using formula

$\theta = \tan h/r$

h is height of piler is radius of pile

Post compression evaluation [8, 9]

Uniformity weight:

Average weight of the tablet was determined by selecting 20tablet randomly. This selected tablet weighing individually and the weight of individual tablet was compared with average weight.

Thickness:

Thickness of the tablet was measured by using vernier calliper. 5 tablets were selected and thickness was measured in (mm).

Hardness:

Hardness is important parameter of evaluation of tablet. The resistance of the tablet to break under condition of handling, transportation and storage depend upon hardness. The hardness of tablet was measured by using Monsanto hardness tester. The unit of hardness is expressed in term of kg/cm^2.

Friability:

Friction and shock are the forces that most often cause tablets to chip, cap or break. 20 tablets are weighed and placed in the roche friabilator apparatus they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked. The percentage friability was determined by the formula;

% friability = [initial weight – final weight/initial weight]*100n

Drug content:

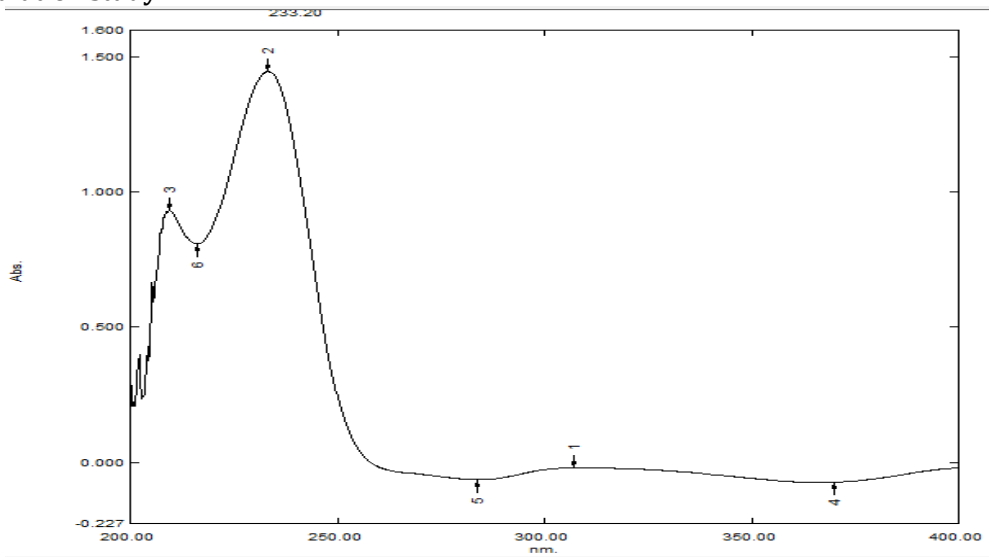
5 tablets were taken and powdered. The quantity of powder equivalent to100 mg of Fluphenazine HCL was dissolved in 100ml volumetric flask containing 6.8 phosphate buffer. This solution was filtered through 0.45µm membrane filter. 1ml of above solution was diluted 100ml 6.8 phosphate buffer. The absorbance were measured at 231 nm using UV visible spectrophotometer.

***In Vitro* Drug Release Study:**

The release of tablets was determined using USP Type II (Paddle) dissolution apparatus under sink condition. The dissolution medium was 900 ml of a 0.1N HCl solution (pH=1.2), at 37˚c ±0.2cº for 2 hour. Then dissolution media replace by phosphate buffer (6.8pH). The stirring speed was 50 rpm. Aliquot of the solution was collected at specific interval were replaced with fresh dissolution medium. The Fluphenazine HCL were analyzed spectrophotometrically at 231 nm respectively using simultaneous equation method.

RESULTS AND DISCUSSION

Preformulation study



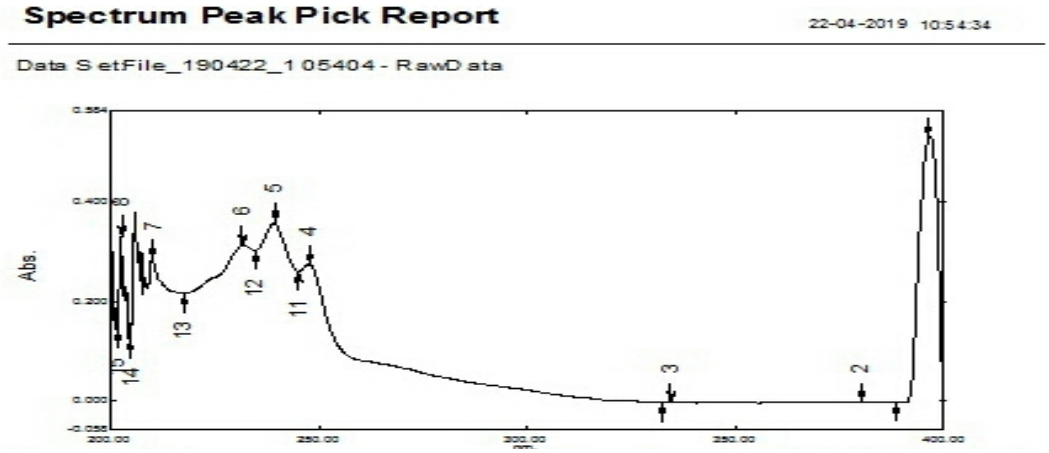


Figure 2: Spectrum peak report of

Table 1: Preformulation studies of Fluphenazine HCL

Sr. No	Parameter	Observation
1	Identification by UV spectrophotometer.	231.
2	Melting point	235-237cº
3	Solubility	Very soluble in chloroethane, freely soluble in aqueous solution.
4	Compatibility study(FTIR)	compatible

Compatibility Study (FTIR):

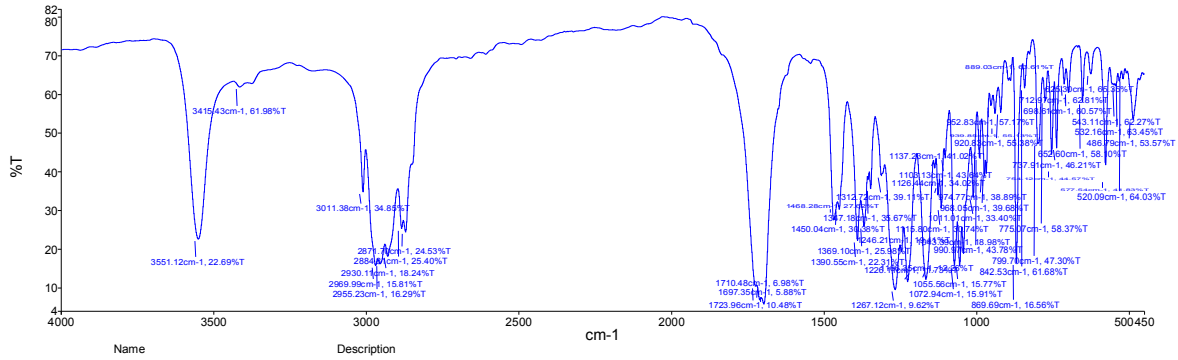


Fig 2: FTIR Spectrum of Fluphenazine HCL

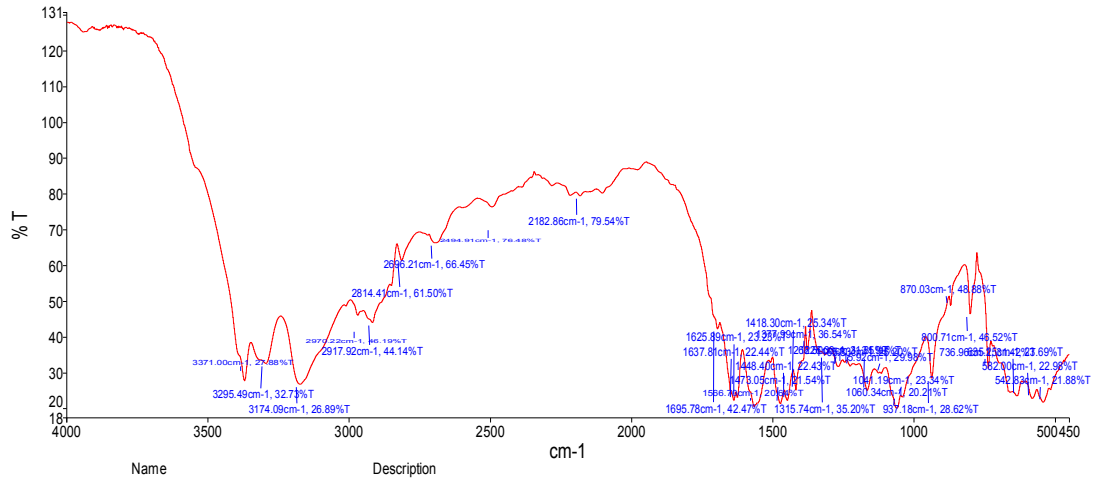


Fig 3: FTIR Spectrum of formulation

Pre-compression Evaluation:

Pre-compression parameters like angle of repose, bulk density, tapped density, hausner ratio of all batches was represented Table 3. Flow properties also found to be passable flow properties for all batches.

Table 3.Precompression Evaluation of tablet

Sr. No	Parameter	B1	B2	B3
1	Bulk density(g/ml)	0.476	0.465	0.470
2	Tapped density(g/ml)	0.625	0.58	0.66
3	Compressibility index (%)	26.76	21.62	16.66
4	Hausner's ratio	1.23	1.20	1.25
5	Angle of repose(degree)	36.80	38.60	37.56

Post-Compression Evaluation of Tablet

The prepared tablets were evaluated for weight variation, dissolution test, thickness, hardness uniformity of dosage units and friability. The weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The hardness of each batch of tablet was checked by using Monsanto hardness tester. The hardness was measured in terms of kg/cm^2. The hardness of 6 tablets was determined using . The Friability was determined by first weighing 10 tablets after dusting and placing them in a friability tester (Roche friabilator), which was rotated for 4 min at 25 rpm. After dusting, the total remaining mass of tablet was recorded and the percent friability was calculated. The drug content determined. The test value are include in table 4,5.

Table 4: Post-Compression Evaluation

Sr. No	**Parameter**	**B1**	**B2**	**B3**
1	Uniformity weight(mg)	999.5	998.5	998
2	Thickness(mm)	4.47	4.49	4.46
3	Hardness(kg/cm(kg/cm$^{2)}$	70	71	72
4	Friability (%)	0.5	0.3	0.2
5	Drug content of metformin (%)	85.56	86.58	83.56

Table 5: % Drug Release Data of Fluphenazine Hydrochloride Sustained-Release

Time(Hrs)	B1	B2	B3
1	4.58	6.6	7.36
2	9.51	11.8	10.65
3	16.14	17.1	20.25
4	24.51	25.82	27.56
5	30.22	32.82	32.4
6	35.22	38.03	40.23
7	43.22	44.13	46.23
8	50.25	52.66	55.27
9	60.58	58.96	63.32
10	68.56	69.42	72.36
11	72.47	74.85	77.25
12	81.63	83.29	85

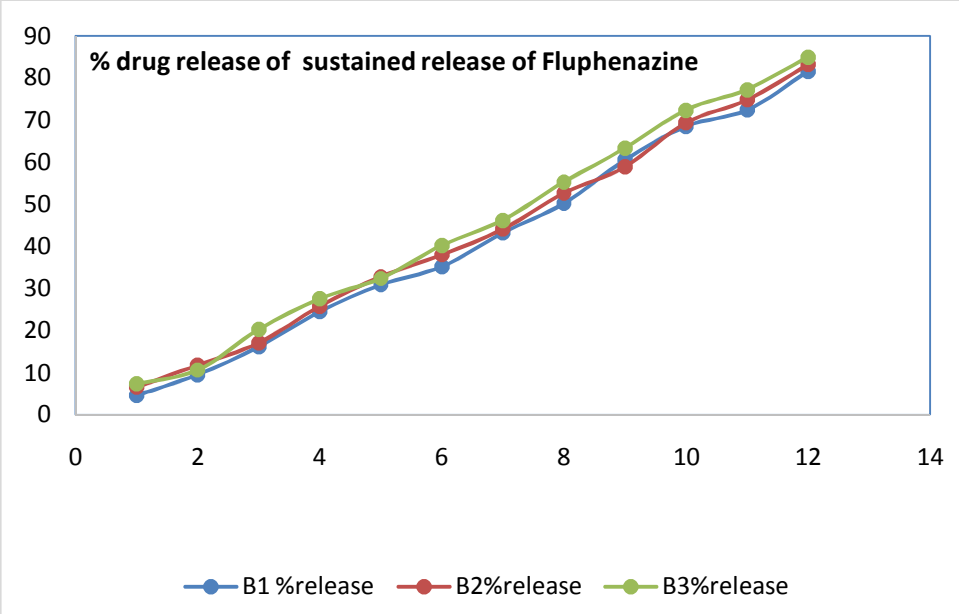


Fig 3: % Drug Release of Sustained Release of Fluphenazine HCL

CONCLUSION

The prepared tablets showed satisfactory results for various evaluation tests such as tablet hardness, friability, weight uniformity, drug content and in vitro dissolution study. The optimized formulation based on all the parameter B3 batch useful for the patient disease .

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