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FORMULATION AND EVALUATION OF PH INDEPENDENT FORMULATION OF FELODIPINE

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ABSTRACT

All active pharmaceutical ingredients are having good therapeutic activity and show poor oral bioavailability , because of poor solubility .The present study is to investigate to improve the solubility of Felodipine using different carriers and different methods of preparation of techniques to identify that which carrier and suitable method of preparation. All formulation are evaluated for hardness, friability, drug content uniformity, and in vitro dissolution studies. Among all the formulations three formulation shows good drug release and the formulation with direct compression method shows good drug release compared to other formulation among all the formulation (Eudragit RLPO, Eudragit RSPO and Ethyl cellulose N50) with direct compression is considered as ideal formulation from the study.

INTRODUCTION

Felodipine is used to treat high blood pressure (hypertension). Lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems. Felodipine is known as a calcium channel blocker. By blocking calcium, this medication relaxes and widens blood vessels so blood can flow more easily.

METHODOLOGY:

Analytical Method Development:

Preparation of 6.8 Sodium phosphate buffer containins 2% SLS: 12gms of sodium di hydrogen ortho phosphate was taken in a 100ml volumetric flask and dissolved with distilled water and make up to 100 ml. Add 2 gms of SLS to the above solution (100ml 6.8 sodium phosphate buffer) and dissolved.

Determination of λ_{max} of Felodipine 6.8 Sodium phosphate buffer contains 2% SLS:

Procedure:

Working standard:50mg of Felodipine was weighed and dissolved in 50ml **6.8 Sodium phosphate buffer contains 2% SLS** and then made up to a volume of 50ml with**6.8 Sodium phosphate buffer contains 2% SLS** it give 1000µg/ml ppm concentrated stock solution.

Dilution 1:From the working standard solution 10ml was diluted to 100ml with **6.8 Sodium phosphate buffer containins 2% SLS** it will give 10µg/ml concentrated solution.

Dilution 2: From the working standard solution 10ml was diluted to 100ml with **6.8 Sodium phosphate buffer containins 2% SLS** it will give 10µg/ml concentrated solution.

This solutions was scanned at range of 200-400nm wavelength light corresponding scan spectrum curve was noted .the corresponding wavelength having highest absorbance is noted as $\lambda_{max.}$

Formulation of Felodipine ER tablets by Wet granulation method

Processing steps involved in Wet granulation method:

The Felodipine ER tablets were prepared by following the General Methodology as given below:

1. ll ingredients (Felodipine+ Avicel PH 102 + polymer) were weighed accurately and co-sifted by passing through #22 sieve, blended in a Poly Bag for 5 min.
2. bove blend were granulated with Iso propyl alcohol.
3. he above granules were lubricated with # 40 Sieve passed Magnesium stearate, Aerosil and Cros carmellose sodium.
4. he final blend was then compressed into tablets using 16 station tablet compression machine with an average hardness of 4.0kg/cm^2,by using 8mm to 12mm dies
5. Evaluation Of Tablets
6. The formulated tablets were evaluated for the following Pre, post compression quality control studies & In vitro Buoyancy studies and dissolution studies

A) Pre Compression studies:

Angle of Repose: It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

Angle of Repose of granules was determined by the funnel method. Accurately weighed powder blend was taken in the funnel. Height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel freely on to the surface. Diameter of the powder cone was measured and angle of repose was calculated using the following equation.

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

Where

θ = angle of repose

h = height in cms

r = radius in cms

Assay Procedure

Weigh and finely powder not less than 20 tablets. Transfer an accurately weighed portion of the powder equivalent to about 10mg Of model drug a 10 ml volumetric flask. Add approximately 6ml of **6.8** Sodium phosphate buffer containins A2% SLS and shake and sonicate for 10 min to complete the extraction. Dilute the methanol to volume and mix. Pipette 1ml aliquot into a 10ml volumetric flask, dilute with mobile phase to volume, mix and filter. From it withdraw take 1ml aliquot and make up to mark with buffer A

Calculate the quantity in mg of model drug Hydrochloride in the portion taken by the formula

assay = T test absorbance/standard absorbance*standard concentration/sample concentration*purity of drug/100*100

Parameter	Details
Dissolution T apparatus	USP -Type II (paddle)
Medium	0.1N HCl.
Volume	900 ml
Speed	50rpm
Temperature	37± 0.5 ºC
Sample volume withdrawn	5ml
Time points	1,2,4,6,8,10,12, 16 and 20hr
Analytical method	Ultraviolet Visible Spectroscopy
λ_{max}	282 nm

In vitro Dissolution Study:

900 ml of **6.8 Sodium phosphate buffer containins 2% SLS** was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of $37^0C \pm 0.5^0C$. A tablet was placed in the vessel and was covered; the apparatus was operated up to 12 hrs at 50 rpm. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium and were analyzed spectrophotometrically at λ_{max} =282 nm using a UV-spectrophotometer (Lab India)

Table 1: Flow Properties and Corresponding Angles of Repose

Flow Property	Angle of Repose (degrees)

Parameter	Details
Dissolution apparatus	USP -Type II (paddle)
Medium	0.1N HCl.
Volume	900 ml
Speed	50rpm
Temperature	37± 0.5 ºC
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Time points	1,2,4,6,8,10,12, 16 and 20hr
Analytical method	Ultraviolet Visible Spectroscopy
λ_{max}	282 nm

Excellent	25–30
Good	31–35
Fair—aid not needed	36–40
Passable—may hang up	41–45
Poor—must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

Table 2: Standard calibration values of felodipine

Standard plot of **Felodipine** plotted by taking absorbance on Y – axis and concentration (µg/ml) on X – axis.

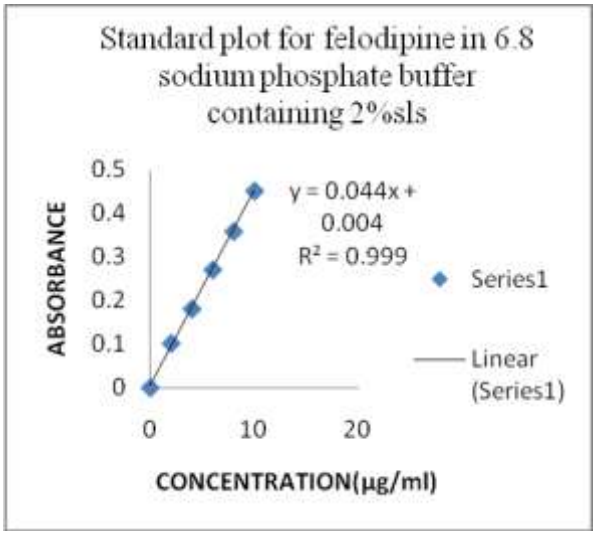

Fig. 1: standard calibration curve of felodipine

Inference: The standard calibration curve of **Felodipine** in **6.8 sodium phosphate buffer** showed good correlation with regression value of 0.9993

Evaluation of Tablets:

Table 3: Pre Compression studies

Formulation Code	Bulk density (Kg/cm^3)	Tapped density (Kg/cm^3)	Cars index	Hausners ratio	Angle of repose (˚)
F1	0.43	0.52	17.3	1.41	12.62
F2	0.40	0.46	13.0	1.5	12.29
F3	0.50	0.58	13	1.16	11.58
F4	0.44	0.51	13.7	1.25	9.29
F5	0.39	0.47	17.0	1.56	18.23
F6	0.42	0.52	19.2	1.45	13.24
F7	0.36	0.39	7.6	1.0	11.03
F8	0.41	0.50	18	1.5	17.4
F9	0.39	0.48	18	1.23	11.96
F10	0.41	0.51	19.6	1.53	12.26
F11	0.44	0.52	15.3	1.40	13.62
F12	0.41	0.45	8.8	1.0	11.85

Inference:

- The Felodipine ER tablets were evaluated for their flow properties; the results for the blends of compression tablets were shown in Table:10
- The bulk density and the tapped density for all formulations were found to be almost similar.

- The Carr's index and Hausner's ratio were found to be in the range of ≤ 18 and 1.0 to 1.56 respectively, indicating good flow and compressibility of the blends.
- The angle of repose for all the formulations was found to be in the range of 11.03-18.23˚ which indicating passable flow (i.e. incorporation of glidant will enhance its flow).

Table 4: Post compression studies

Formulation Code	% weight vaiation	Thickness	% Friability	%Drug Content	Hardness (Kg/cm^2)
F1	pass	3.16±0.11	0.22	102.0 ±1.1	4.68 ±0.17
F2	pass	3.53±0.15	0.15	101.3 ±1.5	5.13 ±0.15
F3	pass	4.06±0.057	0.12	99.8±1.3	5.58 ±0.13
F4	pass	5.1±0.1	0.43	101.7 ±0.8	5.98 ±0.04
F5	pass	3.03±0.05	0.32	100.6±1.2	4.63 ±0.05
F6	pass	3.83±0.15	0.14	98.9 ±2.1	5.2 ±0.02
F7	pass	4.93±0.05	0.20	99.2± 1.7	5.7 ±0.10
F8	pass	5.26±0.1	0.33	99.5± 1.4	5.93 ±0.05
F9	pass	3.02±0.2	0.18	99.2±1.3	4.39 ±0.02
F10	pass	3.48±0.14	0.21	100.3 ±1.4	4.86 ±0.03
F11	pass	4.91±0.18	0.32	101.2± 1.6	5.72 ±0.12
F12	pass	5.14±0.12	0.16	100.3 ±1.8	5.89 ±0.13

Post compression studies of Felodipine ER tablets

*Test for Friability was performed on single batch of 20 tablets

Inference

- The variation in weight was within the limit
- The thickness of tablets was found to be between 3.03 -5.26 mm.
- The hardness for different formulations was found to be between 4.39 to 5.98 kg/cm^2, indicating satisfactory mechanical strength
- The friability was < 1.0% W/W for all the formulations, which is an indication of good mechanical resistance of the tablet.
- The drug content was found to be within limits 98 to 102 %.

INVITRO DISSOLUTION STUDIES OF FELODIPINE ER TABLETS

Table 5: Dissolution profile:

Parameter	Details
Dissolution apparatus	USP -Type II (paddle)
Medium	6.8 sodium phosphate buffer
Volume	900 ml
Speed	50rpm
Temperature	37± 0.5 ºC
Sample volume withdrawn	5ml
Time points	1,2,4,6,8,10,12, 16 and 20hr
Analytical method	Ultraviolet Visible Spectroscopy
λ_{max}	282 nm

STABILITY STUDIES OF PHYSICAL AND CHEMICAL PARAMETERS:

Selected formulation F3 was stored at 40°C ± 2°C / 75% ± 5% RH and 25°C ± 2°C / 60% ± 5% RH or a period of 3 months. Samples were analyzed after storage for 1,2and 3 months and evaluated.

SUMMARY AND CONCLUSION

The approach of the present study was to make a comparative evaluation among these polymers (Eudragit RLPO, Eudragit RSPO and Ethyl cellulose N50) and to assess the effect of physico-chemical nature of the active ingredients on the drug release profile.

The angle of repose, compressibility index and sieve analysis results shown that the formulation is suitable for wet granulation.

This study have been showed that Felodipine could be used in extended release drug delivery system by formulating it has extended drug delivery system, provides extend duration of action in therapeutic range without reaching toxic levels as in the case of conventional dosage forms. These dosage forms have the ability to reduce the dosing frequency and increasing.

The technique employed in the preparation of matrix system i.e. wet granulation, is highly practical and economical from the industry point of view.

By the results we can confirm that order of drug release first order and the mechanism of drug release from sustained release matrix tablets is Higuchi model.

Success of the *In vitro* drug release studies recommends the product for further *In vivo* studies, it may improve patient compliance.

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