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Formulation and Evaluation of Nicardipine Sustained Release Tablets

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ABSTRACT

Nicardipine supported discharge tablets were planned by utilizing distinctive excipients by wet granulation strategy. All the physicochemical tests were performed and the outcomes were in the points of confinement according to ICH rules. The detailed granules were under taken for all the post pressure tests and the outcomes were in limits according to IP. Add up to 13 definitions were readied, disintegration was performed for 12 hrs, as the % tranquilize discharge by disintegration for F7 detailing is most extreme, thus F7 plan is chosen as improved among F1 – F13.

Keywords: Nicardipine, ICH rules, Post pressure Optimized.

1. INTRODUCTION

To the date, for each disease or disorder state of the patient, correct medication is of prime importance to take care of the patient in healthiness. To realize this, the medication or drug is run conventionally by one or additional of many well outlined and widespread routes of drug administration as well as oral, parental, rectal, alveolar, ocular and topical. Among subsequently previously mentioned prevalent courses oral conventional route of drug administration lies at the top of the hierarchy of the conventional routes. It is sensible presumption that medication fixation at the site of activity is identified with sedate plasma level and that, in the immense lion's share of cases, the force of impact is a couple of perform of medication focus at the objective site. The target of the most restorative regimens is to quickly raise the plasma fixation to the required level and after that to hold it consistent for the coveted term of treatment. The extent to that this case will be achieved depends on several factors, together with the minimum effective concentration of the drug the amount at that aspect effects occur, the dose administered, the speed of drug unharness from the indefinite quantity kind, the speed of elimination and also the frequency of dosing [1] only if the dose size and frequency of administration square measure correct, therapeutic 'steady state' levels of the drug will be achieved quickly and maintained by the repetitive administration of standard oral dosage forms [2].

Nicardipine might be an intense Ca channel blockader with stamped dilator activity. Its therapeutic medication properties and is successful inside the treatment of angina and coronary fits while not demonstrating cardiodepressant impacts. It is conjointly been used in the treatment of respiratory issue and upgrades the activity of particular antineoplastic operators.

Nicardipine experiences broad initially pass digestion. Along these lines the pinnacle plasma focus happens 1 to 3 hrs. after a solitary oral measurements. The half existence of disposal ranges from 3 to 4.5 hrs. In typical subject. The most widely recognized reaction watched are GIT unsettling influences, sickness, regurgitating and so forth [3].

Subsequently it is required to plan a medication conveyance framework which may convey hostile to hypertensive specialists like Nicardipine in controlled way for a drawn out timeframe to bypass the medication related symptoms. Considering every one of these issues related with oral organization of hostile to

hypertensive specialists i.e. Nicardipine endeavor has been made to create lattice tablet with a specific end goal to accomplish a superior discharge design.

2. MATERIALS AND METHODS

Nicardipine was procured from Chandra labs, Hyderabad. Guar gum,Xanthan Gum, Poly vinyl pyriolidone were purchased from S.D. Fine Chem. Ltd, Mumbai, India.

Formulation Development

The pharmaceutical development studies have to be carried out with the purpose of selecting right dosage form and a stable formulation. These studies give detailed description of all the steps involved in the process of formulation development. Such details are intended towards identifying critical parameters involved in the process, which have to be controlled in order to give reliable and reproducible quality product [4].

Formulation of SR tablets:

This sustained release tablets was prepared by wet granulation method.

Sieving: The active ingredient was passed through the sieve#40 followed by the other ingredients were passed the same sieve [5-6].

Dry mixing: Nicardipine, Micro Crystalline Cellulose and natural polymers were taken in a poly bag and mixed for 5minutes to ensure uniform mixing of the ingredients with the drug.

Preparation of binder solution [7-10]

PVP-K_{30}

IPA: Weigh PVP K-30 accurately and it is mixed with IPA to form a solution is used as binder solution and kept separately.

Then the granulation, drying and sieving were followed by lubrication for final compression. Magnesium stearate and talc were weighed and they were passed through sieve#20.Then mixed with dried granules of Nicardipine in a polybag for 5minutes to get a uniform blend. Then the lubricated granules of Nicardipine were weighed accurately and fed into the die of single punch machinery and compressed. For this 9mm round punch was used for compression.

Formulation of Sustained release tablets:

Development of sustained release tablets of Nicardipine was carried out. Sustained release tablets were prepared using formulae given below. Sustained release tablets were prepared on 16 station tablet compression machine by wet granulation. The tablets of different formulations were punched with 9mm round punch on compression machine.

Prior to the formulation the flow properties of the formulations have to be evaluated for angle of repose, bilk density, tapped density, carr's index and hausner's ratio.

EVALUATION OF TABLETS [11-15]

The quantitative evaluation and assessment of a tablets chemical, physical and bioavailability properties are important in the design of tablets and to monitor product quality. There are various standards that have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets. These include the diameter, size, shape, thickness, weight, hardness, Friability and *in vitro*-dissolution characters.

1. Physical Appearance:

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, colour, presence or absence of odour, taste etc.

2. Size & Shape:

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micro-meter or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

3. Weight variation test:

This is an in process quality control test to ensure that the manufacturers control the variation in the weight of the compressed tablets, different pharmacopoeia specify these weight variation tests.

Friability:

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. It is usually measured by the use of the Roche friabilator.

The percentage friability was determined by the formula:

$$\% \text{ friability} = (W_1 - W_2) / W_1 \times 100$$

W_1 = Weight of tablets before test

W_2 = Weight of tablets after test

***In vitro* Dissolution Studies**

In vitro drug release studies were carried out using USP XXIV dissolution apparatus type II, with 900ml of dissolution medium maintained at 37±1°C for 12 hr, at 50 rpm, pH 6.8 phosphate buffer for 12hrs for sustained release tablets. 5ml of sample was withdrawn at predetermined time intervals replacing with an equal quantity of drug free dissolution fluid. The samples withdrawn were filtered through 0.45µ membrane filter, and drug content in each sample was analyzed after suitable dilution by UV/Vis Spectrophotometer and cumulative percent drug release was calculated.

Drug release kinetics and mechanism

To analyze the mechanism of drug release from the formulation, the dissolution profile of all the batches were fitted to zero order, first order, Higuchi and Peppas models to ascertain the kinetic modelling of drug release.

3. RESULTS AND DISCUSSION

Composition of Sustained Release Tablets

Table 1: Formulation table for sustained release tablets

Formulation	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F9	F10	F11	F12	F13
Nicardipine	20	20	20	20	20	20	20	20	20	20	20	20	20
Ethyl cellulose	30	-	-	45	-	-	30	30		45	45		30
HPMC	-	30	-	-	45	-	30	-	30	45		45	30
Xanthum gum	-	-	30	-	-	45	-	30	30		45	45	30
MCC	190	150	110	70	190	150	110	70	70	40	40	40	40
PVP K-30	15	15	15	15	15	15	15	15	15	15	15	15	15
Magnesium stearate	9	2	2	2	2	2	2	2	2	2	2	2	2
Talc	9	8	8	8	8	8	8	8	8	8	8	8	8
Total weight	300	300	300	300	300	300	300	300	300	300	300	300	300

Pre Compression Parameters

Table 2: Pre Compression Parameters

Formulations	Angle of Repose (θ)	Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	%Compressibility	Hausner's ratio	RESULT
F1	28.38±0.06	0.614±0.01	0.754±0.04	18.56±0.05	1.22±0.03	Excellent
F2	27.36±0.04	0.661±0.01	0.812±0.03	18.59±0.06	1.22±0.02	Excellent
F3	25.55±0.03	0.648±0.02	0.793±0.02	18.27±0.03	1.23±0.03	Excellent
F4	29.11±0.06	0.612±0.01	0.766±0.03	20.12±0.03	1.25±0.02	Excellent
F5	27.72±0.07	0.668±0.01	0.828±0.02	19.34±0.03	1.23±0.02	Excellent
F6	28.14±0.07	0.663±0.03	0.820±0.03	19.19±0.05	1.23±0.02	Excellent
F7	28.39±0.06	0.676±0.02	0.847±0.03	20.19±0.02	1.25±0.04	Excellent
F8	26.31±0.02	0.659±0.02	0.831±0.02	20.67±0.01	1.26±0.04	Excellent
F9	26.51±0.02	0.682±0.01	0.893±0.02	17.34±0.03	1.53±0.02	Excellent
F10	25.65±0.03	0.671±0.01	0.720±0.03	21.12±0.03	1.18±0.02	Excellent
F11	27.14±0.07	0.686±0.02	0.821±0.02	17.19±0.05	1.46±0.04	Excellent
F12	28.51±0.02	0.658±0.01	0.654±0.04	18.34±0.03	1.43±0.02	Excellent
F13	24.65±0.03	0.666±0.02	0.827±0.03	22.14±0.03	1.28±0.02	Excellent

From the above pre-compression parameters it was clear evidence that granules have excellent flow properties.

Post Compression Parameters

Table 3: Post Compression Parameters

F.Code	Hardness (kg/cm²)	Thickness (mm)	Weight (mg)	Friability (%)
F1	7.25±0.02	3.40±0.03	300±0.01	0.58±0.05
F2	7.53±0.02	3.32±0.03	300±0.03	0.50±0.05
F3	7.46±0.01	3.40±002	300±0.03	0.52±0.05
F4	7.31±0.03	3.40±0.01	300±0.02	0.33±0.05
F5	7.59±0.03	3.41±0.01	300±0.03	0.31±0.03
F6	7.87±0.02	3.41±0.01	300±0.03	0.32±0.05
F7	7.94±0.05	3.11±0.02	300±0.05	0.45±0.04

F8	7.81±0.06	3.11±0.03	300±0.04	0.49±0.01
F9	7.15±0.02	3.20±0.03	300±0.06	0.58±0.04
F10	7.43±0.02	3.12±0.03	300±0.02	0.50±0.02
F11	7.56±0.01	3.50±002	300±0.04	0.52±0.04
F12	7.21±0.03	3.30±0.01	300±0.01	0.33±0.05
F13	7.29±0.03	3.51±0.01	300±0.05	0.31±0.03

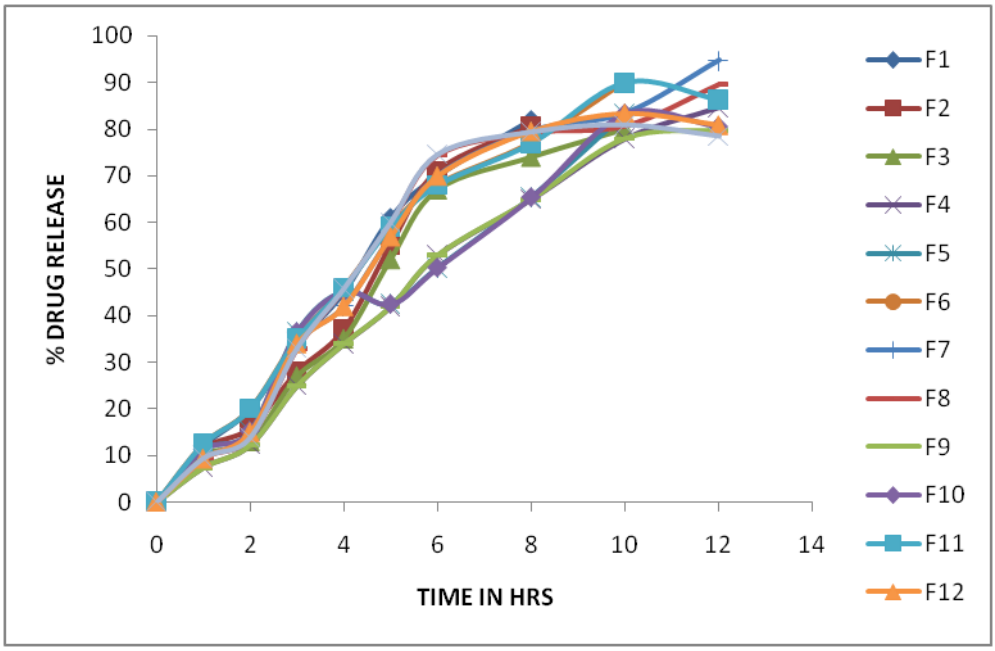

Figure 1: *In Vitro* drug release of Nicardipine sustained release tablets

***In-vitro* release of Nicardipine sustained release tablets**

From the table, it was confirmed that the F7 formulation SR tablets fulfill the sustained release theory, In that the Guar gum was used separately in the formulations, but increasing the polymer concentration, it was clearly identified that the drug release was retarded. And also from the table, it was also confirmed that the formulation made with guar gum (F4 and F8) showed sustained drug release compared to the formulations made with xanthum gum (F1 to F4).

4. CONCLUSION

- The Sustained released tablets containing Nicardipine SR tablets were successfully prepared by wet granulation method.
- The physiochemical evaluation results for the granules of all trials pass the official limits in angle of repose, compressibility index.
- The prepared granules were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability. The optimized formulation contains the average thickness of 3.11±0.02, average hardness of 7.94±0.05, average weight of 300±0.05, friability of 0.45.
- The optimized formulation F7 which releases the Nicardipine in sustained manner in 1st hour it releases 9.3% but the remaining drug release was sustained up to 12 hours.

"Hence it may be summarized that the F7 tablets prepared by wet granulation method for sustained release tablets might be a perfect and effective formulation to treat the hypertension".

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