DOI: 10.55522/jmpas.v3i5.0060 **ISSN NO. 2320 – 7418**

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research article

Design, development and optimization of fast dissolving tablet of nebivolol HCL

Isha Shah*, Alpesh Yadav, Shailendra Bhatt

Maharishi Arvind Institute of Pharmacy, Jaipur, Rajsthan, India

Corresponding author: Isha Shah, ✉ Isha21.shah@gmail.com,

College of Pharmaceutical Sciences, Govt. Medical College, Calicut, Kerala, India

Received – 20 September 2014**, Revised** – 20 October 2014, **Accepted** – 25 October 2014 **(DD-MM-YYYY)**

Refer This Article

Isha Shah, Alpesh Yadav, Shailendra Bhatt, 2014. Design, development and optimization of fast dissolving tablet of nebivolol HCL. Journal of medical pharmaceutical and allied sciences, V 3 - I 5, Pages -229 – 232. Doi: https://doi.org/10.55522/jmpas.V3I5.00.60.

ABSTRACT

The current research work involves preparation of fast dissolving tablets of nebivolol by direct compression method using different concentrations of superdisintegrants. A two-factor three- level (3^2) factorial design is being used to optimize the formulation. A total of 39 experimental done with 3 Centre points were performed at all possible combination. The amount of % Disintegrating agent X_1, Diluents concentration X_2 and Disintigration agent X_3, were selected as independent variable three levels (+1, 0, −1). The disintegration time and hardness were selected as dependent variable. All the active blends the tablets were evaluated for post compression parameters (weight variation, hardness, and friability, wetting time, disintegration time, water absorption ratio, and *in vitro* drug release studies). Formulation was selected by the Design- Expert software which exhibited DT (26 sec) and hardness (4 kg/cm^2). It was concluded that fast dissolving tablets with high mechanical strength and rapid disintegration without the use of superdisintegrants could be prepared, which provide better patient compliance.

Keywords: Fast dissolving tablet, Optimization, Factorial design, direct compression technique.

INTRODUCTION

The oral route of administration is considered as the most widely accepted route. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leadin to patients incompliance particularly in case of pediatric and geriatric patients. Thus, a new delivery system known as oral fast dissolving/disintegrating (FDDS)/melt-in- mouth tablets gaining importance. These oral dosage forms dissolve rapidly in saliva and can be swallowed without the need of drinking water. Elimination of bitterness is an important criterion in product formulation of mouth dissolving tablets. The dissolution and bioavailability parameters of poorly soluble drug in a solid dosage form mainly depend upon excipients added to the formulation and their characteristics. According to these parameters the present study was proposed to formulate oral drug delivery dosage form in the form of fast dissolving tablet of nebivolol to increase its bioavailability. In the present investigation FDTs were prepared by direct compression method by using two approaches namely superdisintegrants and effervescent agent. The prepared tablets were subjected to both pre and post compression parameters. The main intention of present study was to prepare fast dissolving tablet of nebivolol using superdisintegrants and effervescent agent is to enhance the onset of action, improve dissolution and bioavailability. The present study aims to formulate such a tablet that disintegrates rapidly and provides rapid dissolution of drug.

MATERIALAND METHOD

Nebivolol HCl was kindly gifted by Glen mark Generics Limited (Colvale) Goa, PEG 6000, PVP K 30, methanol, Avicel, lactose spray dried, mannitol, Magnesium stearate, Saccharin sodium used in the study were obtained commercially.

Methods for Preparation of solid dispersion

Solid dispersions of nebivolol: PVP K30 in different weight ratio (1:1, 1:3, 1:5, and 1:7) was prepared and characterized.

Preparation of tablets by direct compression method

Fast dissolving tablets containing 5 mg of nebivolol were

prepared by direct compression method and the formula used in the study is shown in Table 1. Different superdisintegrants such as polyplasdone xl- 10, kyron T-314 and L-hpc were used. Saccharin sodium is a sweetening agent. Nebivolol was mixed in geometric proportions with sweeteners, diluents and lubricants. All the raw material were passed through a screen (60 mesh) prior to mixing. Tablets were compressed on a 10 station mini press tablet machine (Ratnakar Machinery Pvt. Ltd., Ahmedabad, India.) equipped with 9 mm concave punch [2].

Experimental Design of Nebivolol Hcl Fast Dissolving Tablets

A randomized 3 level full factorial design using two factors was adopted to systematically study the formulation of FDT of Nebivolol HCL. A total of 39 experimental run with 3 centre points were performed at all possible combination (Table 3). The amount of % Disintegrating agent (X_1), diluents concentration (X_2) and Disintigration agent (X_3) were selected as independent variable (Table 2). The disintegration time and hardness were selected as dependent variable. The responses were analyzed for analysis of variance (ANOVA) using Design Expert version 8.0software.

A statistical model incorporating interactive and polynomial terms was utilized to evaluate the response.

$Y = b_0 + b_1X_1+b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b22X22$

Where, Y is the dependent variables, b_0 is

the arithmetic mean response of the nine runs, and b_1 is the estimated coefficient for the factor X_1. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1X_2) show how the response changes when two factors are

simultaneously changed. The polynomial terms (X_1^2 and X_2^2) are included to investigate non-linearity.

Validation of Statistical Model

Levels of both the factors were selected at three different points and responses predicted by the statistical models were calculated. Fast dissolving tablets were prepared using these levels and responses were measured practically. The predicted responses were compared against observed responses and closeness between them was checked.

Response surface plots

Response surface plots were generated for each response to study the effect of both factors on each response.

Evaluation of tablet properties

Weight variation test

Weight variation test was performed as per specification given in I.P. on 20 tablets. The average weight of one tablet was determined from the collective weight. The maximum acceptable limit is ± 5% deviation of an individual mass from average mass.

Hardness

Hardness measured by using a Pfizer hardness tester. Five tablets were chosen randomly and tested for hardness and the average was calculated. The limit for crushing strength of the tablets was kept in range of 3-4 kg.

Friability

The friability was determined by Roche friabilator (Electro lab EF-2). Twenty tablets were weighed and at 25 rpm for 4min. the percentage of weight loss was calculated. The limit of the percent friability was kept below 1%.

% Friability = $(W_0-W) / W \times 100$

Where, W_0 is initial weight of the tablets before the test and W is the weight of the tablets after test.

Wetting time

Twice folded tissue paper was kept in a culture dish (internal diameter 5 cm) containing 6 mL of purified water. A tablet having a methyl red was added to Petri dish and tablet was carefully placed on the surface of the tissue paper. Three trials required for water to reach upper surface of the tablet was noted.

Disintegration test

The disintegration test of FDTs was studied using a modified disintegration method. A petri dish of 10 cm diameter was filled with 10 ml of distilled water, the tablet was carefully places at the center and the time of complete disintegration in to fine particles was noted as disintegration time [3].

Drug content

Drug content was determined by taking twenty tablets. Randomly selected tablets were weighed and powdered in a glass mortar pestle. The weight equivalent to 5 mg nebivolol was weighed and dissolved in 5 ml of methanol in volumetric flask, the volume was adjusted to 100 ml with phosphate buffer (pH 6.8) and the solution was filtered. An aliquot of 1.0 ml of solution were diluted to 10 ml phosphate buffer (pH 6.8) in separate volumetric flask. The content in was determined spectrophotometrically at 280 nm.

***In vitro* drug release study**

The release rate nebivolol from fast dissolving tablets was determined using dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of pH 6.8 phosphate buffers, at 37 ±0.5°C and 50 rpm. A sample (10 ml) of the solution was withdrawn at 5, 10, 15, 20, 25 and 30 min. with attain sink condition. The samples were filtered through a 0.45 µm membrane filter. Absorbance of these solutions was measured at 280 nm using a Shimadzu UV-1800 UV/Vis double beam spectrophotometer [4].

RESULTS AND DISCUSSION

Evaluation of tablet properties

Nebivolol tablets were prepared by direct compression method using different concentration of superdisintegrants (0 - 6%). To study the effect of different superdisintegrant types (polyplasdone xl-10, kyron t-314 and L-hpc) with different concentrations (0 - 6%), Kyron T-314 displays best results among all superdisintegrants, tablet disintegrated in 26.09 seconds and drug release was found to be 95.37%. The hardness, friability, disintegration time, drug content

and weight of formulated tablets are described.

All the parameters are within the acceptable range. Good uniformity in drug content was found amongst different batches.

The optimization was carried out in different groups and each group consists of 39 formulations.

Response surface plots were generated for each response to study the behavior of the system. The groups are tabulated. It shows responses for each experimental run.

Analysis of variance (ANOVA) was carried out to identify the insignificant factors, which were then removed from the full 43.50 implies the model is significant [5].

There is only a 0.01% chance that a "Model F- Value" this large could occur due to noise. "Adequate Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable. The ratio of 20.128 indicates an adequate signal. This model can be used to navigate the design space: It shows summary of result of regression analysis for disintegration time. Summary of result of regression analysis for hardness.

Validation of statistical model

To validate the statistical model checkpoint batches, CP1 and CP2 were prepared according to the formula. From the response surface plot and the calculations from the statistical equation obtained by regression, the results revealed the close match of the experimental results. Different constraints were applied; solution with desirability 1 was selected.

Friability of optimized tablet was below 1% which showed good mechanical resistance. All the parameters i.e. thickness, diameter, weight, friability, drug content and wetting time were under acceptable limits in table 12: It shows characterization of optimized tablet (FDT).

From the results of dissolution study of the optimized tablet revealed rapid release of drug in phosphate buffer pH 6.8 compared with pure drug. From *in vitro* dissolution data it was concluded that there may be rapid absorption (98.27%) of the drug formulation as compared with the pure drug [6, 7].

CONCLUSION

Fast dissolving tablets of nebivolol were formulated and optimized using 3^2 factorial designs. Two independent variables, that is, amount of Kyron T-314 and amount of lactose at three levels were selected on the basis of preliminary studies. Addition of superdisintegrant Kyron T-314 leads to significant effect on disintegration characteristics as well as drug release. But higher concentrations of Kyron T-314 had negative impact on drug release and disintegration time. In the present investigation Fast dissolving tablets of Nebivolol HCl having rapid disintegration and good mechanical strength was prepared using direct compression technique. Result of the study showed that disintegration time and hardness was strongly dependent on concentration of Kyron T-314 and mannitol. Comparison of predicted responses and observed values for the same showed close agreement, and the models were found to be valid. Hence, 3 level full factorial desigen and statistical models can be successfully used to optimize the formulations.

REFERENCES

1. Sastry SV, Nyshdham JR, Fix JA, 2000. Formulation and evaluation of fast dissolving tablet of nebivolol hcl. Res Focus Pharma Technol. 3, Pages 138-45.

2. Redkar MR, Gore SP, Devrajan PV, 2002. Formulation and evaluation of fast dissolving tablet. Indian J Pharm Sci. 64, Pages 291-292.

3. B Yunxia, Y Yorinobu, S Hisakozu, 1999. Formulation and evaluation of mouth dissolving tablets of metformin. J Pharm Sci. 88, Pages 1004-1010.

4. Abdul Ahad H, Anuradha CM, Kumar C Suresh, 2010. Novel approach in formulation and evaluation of mouth dissolving tablets of ondansetron HCl. Int J app Bio Pharmaceut Tech. 1(2), Pages 582-585.

5. Bi y, Sunada H, Yonezawa Y, 1996. Preparation and evaluation of a compressed tablet rapidly disintegrating in oral cavity. Chem Pharm Bull. 44, Pages 2121-2127.

6. Shah Isha, Bhatt Shailendra, Yadav Alpesh, 2014. Enhancement of solubility and dissolution of nebivolol by solid dispersion technique. Int J of Pharmacy and Pharmaceutical Sciences. 6(7), Pages 566-571.

7. Patel D, Shah R, Jogani D, 2004. Tablet formulation of paroxysm containing PVPK 30 and sodium laurel soleplate. Ind J Pharm Sci. 66(1), Pages 49-55.