International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 12 (B); December 2020; Page No.23472-23474
DOI: http://dx.doi.org/10.24327/ijcar.2020.23474.4649

Research Article

NOVEL IN HOUSE PROCESS FOR ENTERIC COATING OF RANOLAZINE PELLETS BY WURSTER TECHNIQUE

Devashish Rathore* and Rashmi Dahima

School of Pharmacy, Devi Ahilya Vishwavidyalaya, Takshashila Campus, Ring Road, Indore, India

A R T I C L E I N F O

Article History:

Received 06th September, 2020
Received in revised form 14th October, 2020
Accepted 23rd November, 2020
Published online 28th December, 2020

Key words:

Ranolazine, Eudragit L100-55, controlled release pellets, enteric coating process, fluidized bed coater.

A B S T R A C T

Ranolazine, an approved antianginal drug, provides remarkable differences in solubility profile at different pH conditions. Due to its higher solubility characteristics at low pH, it rapidly absorbs from stomach, produces undesirable plasma drug concentration and clears from the body. This necessitates formulating a delayed release dosage form that provides desired drug release profile. The enteric coated pellets were prepared by fluid bed coater using pH dependent and independent polymer. All the process parameters were perfectly optimized and the process runs smoothly throughout the time course. The prepared pellets were evaluated for percentage yield, particle size distribution, surface morphology and dissolution study to confirm adequate enteric coating. This novel method achieved pellets, with percentage yield of 97.21%, free from agglomeration and fine particle development. It is concluded that this novel in house process can help provide an alternative approach to formulate enteric coated ranolazine pellets and the process can also be used by the pharmaceutical industries for enteric coating of other drugs.

INTRODUCTION

Ranolazine, an approved second line drug for chronic stable angina pectoris, provides many benefits compare to other antianginal drugs. This drug emerged as therapeutically effective moiety, lacks effect on heart rate and blood pressure (Mathew *et al.,* 2012) however, other drugs like calcium channel blockers, beta blockers and nitrates, show changes in heart rate and blood pressure besides their therapeutic activity. This distinct property provides an alternative to the patient faces problem with traditional agents, moreover, it can also be used as adjunctive agent which does not add to the side effects of traditional agents. The unique character may be due to the mechanism of action of ranolazine. Drug selectively inhibits late inward sodium currents, which reduces calcium overload and so the diastolic wall stress. This results in an improvement in coronary blood flow.

Additionally, this novel drug ranolazine finds beneficial results in acute coronary syndrome (ACS), Microvascular Corronary Dysfunction (MCS), Arrhythmia and Glycemic Control (Rayner-Hartley *et al.*, 2016). Drug also reduces nitroglycerine consumption and the frequency of angina attack. The immediate release dosage formulation of ranolazine shows bioavailability of around 35% (Jerling, 2006). This lower bioavailability value is linked with the solubility problem associated with the drug.

Corresponding author:* **Devashish Rathore
School of Pharmacy, Devi Ahilya Vishwavidyalaya, Takshashila Campus, Ring Road, Indore, India

At different pH conditions, remarkable differences in the solubility profile of drug are observed. It is highly soluble at low pH. This high solubility results in rapid absorption and clearance, provides undesirable plasma drug concentration (Wolff *et al.,* 2003). Moreover, short duration of action requires to optimize the dosage regimen for the treatment.

In order to overcome this problem, a pelletized controlled drug delivery system was planned to reduce fluctuation in plasma drug concentration and to enhance the patient compliance and bioavailability of the drug. Based on rate and extent of drug absorption behaviour, if plasma drug concentration remains below minimum effective concentration and above maximum safe concentration, then desired therapeutic drug concentration profile will never be achieved. Moreover, the toxic effects may get precipitated, which may lead to an increased undesirable risk associated with the drug. Proposed pellet formulations achieve sustained release profile in such a manner that the plasma drug concentration remains in between therapeutic range for longer period of time.

Pellets are an assortment of systematically manufactured, geometrically characterized agglomerate acquired from various starting materials using distinctive handling conditions. They are free-flowing, round or semi-round solid units which are tiny (0.5 mm to 1.5 mm) and are mostly intended for oral administration. Notwithstanding which fabricating process is utilized, pellets need to meet the following prerequisites- (Samineni *et al.,* 2013)

- Circular shape and smooth surface are considered as wanted attributes for uniform film coating.
- The size of pellets ought to be 600-1000 µm.
- The amount of the API in pellets ought to be greatest keeping in mind the end goal to keep up size of pellet.

The pellets were prepared using combination of pH dependent polymer (Methacrylic acid copolymer - Type C viz Eudragit L100-55) and pH independent polymer (Hypromellose 5 cps viz HPMC-E5). The rate of drug release across the range in stomach and in intestine is controlled by eudragit L100-55. Partial neutralization of polymer is achieved by using base (sodium hydroxide) which can start dissolution at certain pH. HPMC-E5 is selected to achieve the initial drug release at lower pH. All the excipients are selected in the formulation to obtained desired drug release profile.

The enteric coating is done using wurster technique or fluid bed coater. Wurster technique, also referred to as bottom spraying, enables film coating to be applied to pellets. The dry fluidized air carries the uncoated pellets in upward direction and drops back down slowly so that a uniform flow pattern can be achieved inside the container. The coating is done through a spray nozzle attached to the bottom of container at adequate temperature. Pam Glatt GPCG 1.1 laboratory model was used for performing experiment.

MATERIAL AND METHOD

Material Ranolazine was procured from SunPharma, Gudgao (India). All the materials like Hydroxypropyl Methylcellulose-E5 IP (Samsung Fine Chemical Co. Ltd. Korea), Polyethylene Glycol 6000 IP (Viswaat Chemicals Ltd.), Methacrylic acid and Ethyl acrylate Copolymer (Type C) USP-NF (Evonik Rohm Gmbh), Sodium hydroxide BP (Gujrati Alkalies and Chemicals), Titanium Dioxide IP (Travancore Titanium Products Ltd.), Quinolline Yellow Lake IPA IP(Lcy Chemicals Corp-Taiwan), DCM (Standard Reagent, Spectrum chemical Mfg Corp, Merck) were of high grade and standard.

Method

Previously 3% HPMC E-5 base coated sugar nonpareil core were layered with drug ranolazine in 1:0.9 ratios. These drug loaded pellets were then provided with a seal coat (10%) with HPMC E-5. These seal coated pellets (200 g) were coated by freshly prepared enteric coating solution using fluid bed coater.

Enteric layer

Eudragit L100-55 generates unstable solution with large particle, when added directly in water. In order to overcome this problem, a novel in house method was established for enteric coating using hydroalcoholic solution (isopropyl alcohol and water in ratio 40:60). The percentage of eudragit L100-55 was 6%w/v in the coating dispersion.

Procedure for the preparation of coating solution

1.8% w/v solution was prepared by dissolving sodium hydroxide pellets in water (20%). In another beaker, 30% w/v dispersion prepared by adding polymer in water (30%) under stirring, plasticizer PEG 6000 (12% w/v) solution in water (7%) was then mixed with polymer solution. Now isopropyl alcohol was added to this solution and previously prepared NaOH solution was added to it. In another beaker, HPMC E5 (4.2% w/v), Talc (1.5% w/v), TiO_2 (0.1% w/v) and color (0.2% w/v) were dispersed in remaining quantity of water. Both the prepared solutions were mixed under stirring and then homogenized for 20 minutes. The dispersion (5% w/v) having pH 6.32 was ready to use as coating solution.

Machine parameter and process

After fitting air distribution plate (B type) and spray nozzle (0.8 mm) in the bottom of container, the seal coated pellets were allowed to reach product temperature of 40 ^{0}C at low air flow rate of 25 cfm. As the temperature reaches, the height of inner cylinder (18), atomization pressure (1 bar) and airflow rate (78-88 cfm) were adjusted so that to achieve proper bubbling and flow pattern. The coating solution (under stirring) was gradually allowed to flow through spray nozzle to maintain a constant spray rate of 4 g/min. The product temperature was maintained at 38-39 ^{0}C. After achieving 25% weight gain, the process stopped and the drying continued for 1 h at 50 ^{0}C to evaporate solvents.

Characterization

The prepared pellets were evaluated for percentage yield, particle size distribution, DSC studies, surface morphology and dissolution study to confirm adequate enteric coating.

The particle size distribution was analyzed using electromagnetic sieve shaker EMS-8, DSC study of drug and pellets were performed using a differential scanning calorimeter (PerkinElmer Jade DSC), surface morphology of pellet formulation was examined using scanning electron microscopy (JEOL JSM 5600) and the dissolution study was carried out using USP type II dissolution tester (Electrolab TDT-08L) operated at 50 rpm in 0.1 N HCl media for 2 h.

RESULTS AND DISCUSSION

This novel method achieved enteric coated pellets, with percentage yield of 97.21%, free from agglomeration and fine particle development. The process runs smoothly throughout the time course. The sizes of pellets were found to be in the range of 840-1190 micron. DSC curve of drug (Fig 1) showed a single endothermic peak at around 120^{0}C, which denotes melting point of drug, while the DSC curve of pellet formulation (Fig 2) showed no change in peak, which depicts that there is no change in the drug sample in formulation form.

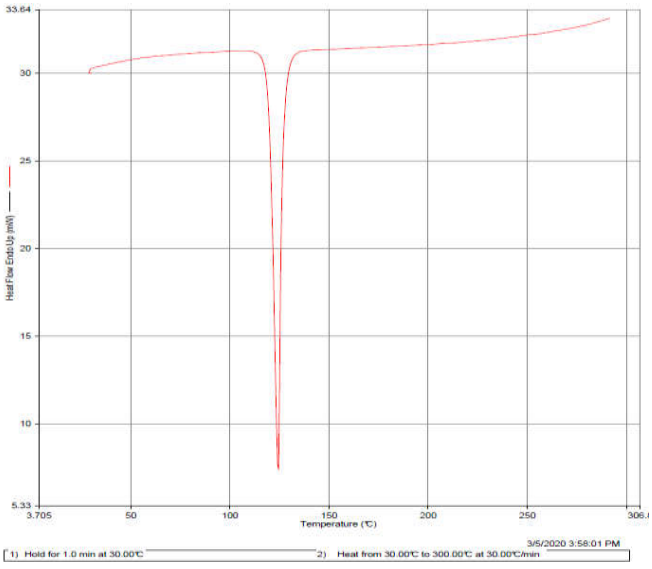

Figure 1 DSC thermogram of Ranolazine hydrochloride

The SEM image (Fig 3) of pellets showed the spherical and uniform morphological characteristics with smooth surface. The drug release of 8.85% in 2 hr confirmed the enteric coating behaviour of the pellet formulation.

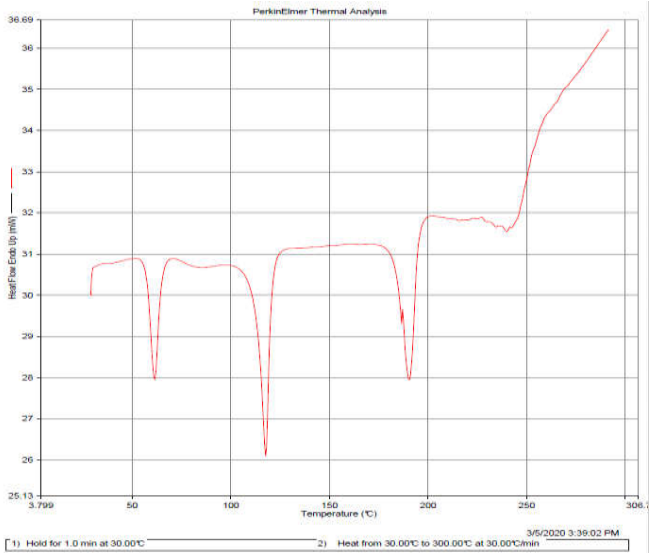

Figure 2 DSC thermogram of enteric salus pellets

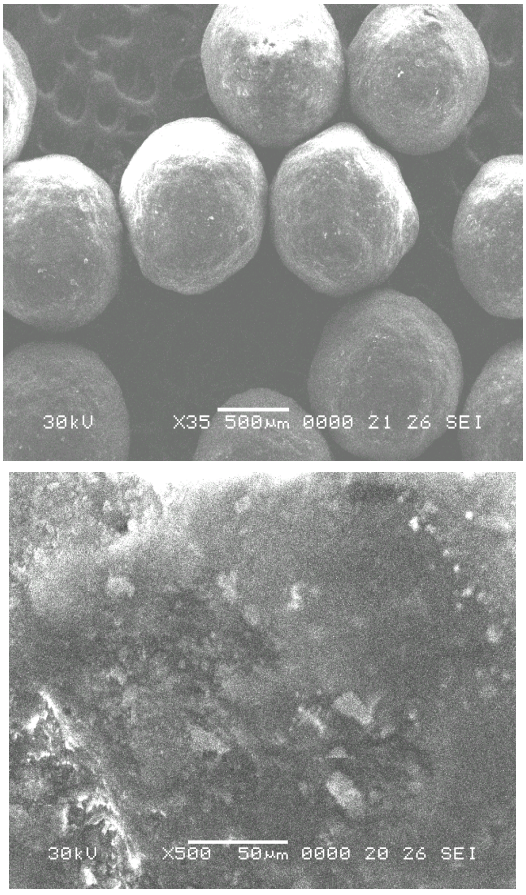

Figure 3 Scanning electron photomicrograph of pellet formulation

It is concluded that this novel in house process can help provide an alternative approach to formulate enteric coated ranolazine pellets and the process can also be used by the pharmaceutical industries for enteric coating of other drugs.

Acknowledgement

The author greatly acknowledges Aristo Pharmaceuticals Limited, Mandideep, M.P. India for providing lab facility to accomplish this research work. The author would also like to thank UGC-DAE Consortium, Indore, M.P. for providing SEM facility.

References

Han M, Yu Q, Liu X, Hu F, Yuan H. 2018. Preparation and characterization of a novel aqueous dispersion for enteric coating of pantoprazole sodium pellets. Acta Pharmaceutica 68(4): 441-455.

Jerling M. 2006. Clinical pharmacokinetics of ranolazine. Clinical Pharmacokinetics 45(5): 469-491.

Mathew M, Sajeeth CI, Santhi K, Madhu EN. 2012. Ranolazine, a new addition to angina treatment. *International Journal of Pharmacy and Biological Sciences* 2(1); 157-165.

Nastruzzi C, Cortesi R, Esposito E, Genovesi A, Spadoni A, Vecchio C, Menegatti E. 2000. Influence of formulation and process parameters on pellet production by powder layering technique. AAPS PharmSci Tech 1(2): article 9.

Rayner-Hartley E, Sedlak T. 2016. Ranolazine: A contemporary review. *Journal of the American Heart Association* 5(3): e-003196.

Samineni R, Ramakrishna G, Balaji M, Rao KK, Reddy SH, Kumar DP. 2013. Multiple unit drug delivery system: pelletization techniques. *American Journal of Advanced Drug Delivery* 1: 11-21.

Tan X, Hu J. 2016. Investigation for the quality factors on the tablets containing medicated pellets. *Saudi Pharmaceutical Journal* 24(5): 507-514.

Wolff AA, Baker F, Langridge J. 2003. Sustained release ranolazine formulations. United States Patent; US 6617328 B2.

How to cite this article:

Devashish Rathore and Rashmi Dahima (2020) 'Novel in House Process for Enteric Coating of Ranolazine Pellets by Wurster Technique', *International Journal of Current Advanced Research,* 09(12), pp. 23472-23474.
DOI: http://dx.doi.org/10.24327/ijcar.2020.23474.4649

****