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Short communication

Suitability of Wurster-Fluid Bed technique for functional Eudragit L-100 coating on tablet cores

Sanja Dukovska[1], Elizabeta Atanaskova[2], Maja Simonoska Crcarevska[1], Marija Glavas Dodov[1], Katerina Goracinova[1], Nikola Geskovski[1]

[1]*University Ss Cyril and Methodius in Skopje, Faculty of Pharmacy, Institute of Pharmaceutical technology, ul. Majka Tereza 47, 1000 Skopje, N. Macedonia*
[2]*Research & Development, Alkaloid AD, bul. Aleksandar Makedonski 12, 1000 Skopje, N. Macedonia*

Introduction

Film coating of solid dosage forms in pharmaceutical manufacturing is carried out using range of equipment, process parameters and coating formulations to achieve the quality target profile of the dosage form. Besides for aesthetic reasons, film coatings are mostly applied to modify the dissolution behaviour of active pharmaceutical ingredients. Currently, a number of coater types are used in pharmaceutical industry, including drum, fluid bed, rotary and continuous coaters. The end-point of coating process is usually defined by the amount of applied coating dispersion or weight gain of coated dosage forms. However, these measurements provide little information on coating quality attributes such as coating thickness, uniformity etc. Other monitoring techniques are scanning electron microscopy, Near infrared (NIR) or Fourier transform infrared spectroscopy (FTIR) (Hasar et al., 2013).

The aim of this research was to examine the suitability of Wurster-Fluid bed technique for functional Eudragit L-100 coating on tablet cores by monitoring critical attributes during the process.

Materials and methods

Coating: Eudragit L-100 is an anionic copolymer of methacrylic acid and methyl methacrylate, insoluble at pH<6, therefore it is suitable for enteric-coating. Triethyl citrate (TEC) and Polyethylene glycol (PEG 400) were used as plasticizers, to improve the flexibility and processability of the polymer film. Ammonia Solution 25% was used to promote dispersion of the anionic copolymer in water.

Preparation of Aqueous Enteric Coating Dispersion: Eudragit L-100 (20g) was added in purified water (108,53g) slowly, with constant stirring and suspension was stirred approximately for 10 minutes. Strong Ammonia Solution (1.20g) was slowly added to dispersion and the mixture was stirred for 30 minutes. Triethyl citrate (4.99g) and Polyethylene glycol (0.71g) were added to dispersion and moderately stirred for 20 minutes. (United States of America Patent No. US 6,224,911 B1, 2001)

Production of tablet cores: A mixture of 65% α-Lactose monohydrate (FlowLac 100, MEGGLE Wasserburg GmbH & Co. KG), 33% Microcrystalline cellulose (Avicel PH102, DuPont Nutrition & Health), and 2% Magnesium stearate (Faci S.p.A) was prepared using Erweka AR 400 drum hoop mixer (ERWEKA GmbH).

The lubricated final blend was tablet compressed on Korsch Xl 100 Pro rotary tablet press (Korsch AG), equipped with four 6 mm flat punches and gravity feeder configuration, at a production rate of 50 rpm. The main compression pressure was 6 kN and the pre-compression was fixed at 0.1 kN. Tablet compressing was performed on constant production speed and compression pressure. The filling depth was adjusted so that the resulting tablets have an average mass of 80 mg. Tablet cores weight was measured by use of analytical balance Sartorius model SECURA224-1CEU (Sartorius AG), and hardness and thickness were measured using Erweka TBH 425 multitester (ERWEKA GmbH).

Fluid bed coating procedure: Coating procedure was performed in Fluid bed - Wurster coater VFC-LAB

*dukovskasanja@gmail.com

MICRO FLO-COATER, (Freund-Vector Corporation, USA) with a process chamber, equipped with a classical air-distributor plate and Wurster column. The tablet cores (150g) were preheated (5 min) at an inlet air temperature of 90°C and afterwards the coating was performed using the following parameters: inlet air temperature of 70°C, airflow of 183 LPM, exhaust temperature of 60°C, nozzle air of 550 mBar and pump speed of 8 RPM (1g/min). The process was stopped at predefined intervals (after using 50% and 75% of the coating dispersion) for sampling purposes. After the spraying stage, the coated tablets were dried in the apparatus for additional 5 minutes.

Film thickness measurements: The thickness of the obtained film was confirmed and measured by microscopic method. Cross-sections of coated tablets withdrawn in different stages of the process were observed using stereo microscope Stemi 305 (Zeiss,, Germany) and film thickness was measured using Zeiss Zen 3.8 software, under 5x magnification.

Fourier transform infrared spectroscopy (FTIR): FTIR spectroscopy was performed by using Diamond ATR-FTIR, Carry 600 (Agilent, Germany) under the following conditions: resolution 4 cm^{-1}, 32 scans per spectrum, and range of 4000 to 650 cm^{-1}.

Disintegration: Disintegration test was performed in accordance with Ph.Eur requirements for gastro-resistant tablets (Ph.Eur. 2.9.1). The examination was performed on 6 tablets, individually, in 0.1 M hydrochloric acid as a liquid medium, on a temperature of 37°C, using ERWEKA ZT72 Apparatus (European Pharmacopoeia 11th ed., 2022).

Results and discussion

The tablet cores were with smooth surface, average diameter of 6.01±0.01 mm and average hardness of 2.44 kP±0.33. The coating process was performed continuously with minute adaptations in the process parameters in order to maintain the exhaust temperature and appropriate fluidization of tablet cores. The coated tablet samples demonstrated smooth, homogenous film with increasing thickness ranging from 90.51±1.99 µm to 192.23±11.42 µm for 50 and 100% used coating dispersion, respectively, which is probably due to the continuous increasing of concentrations of the Eudragit L-100 on the tablet cores during the coating process. This could be confirmed by the continuous increase of the intensity of the Eudragit L-100 characteristic bands in the FTIR spectrum of the coated tablets (Fig. 1). The most intensive bands at 1716 cm^{-1} originating from–C=O stretching and 1154 cm^{-1}, 1189cm^{-1} and 1254 cm^{-1}, originating from –C-O stretching vibrations, as well as the less intensive ones at 1387 cm^{-1}, 1456 $cm^{-1,}$ 1473 cm^{-1} and 1488 cm^{-1} were following the abovementioned pattern. The disintegration time has increased from 15 to 42 minutes for 50 to 100% coated tablet cores, respectively. These results clearly confirm the relation among the thickness of the Eudragit L-100 layer and the disintegration time at pH 1.

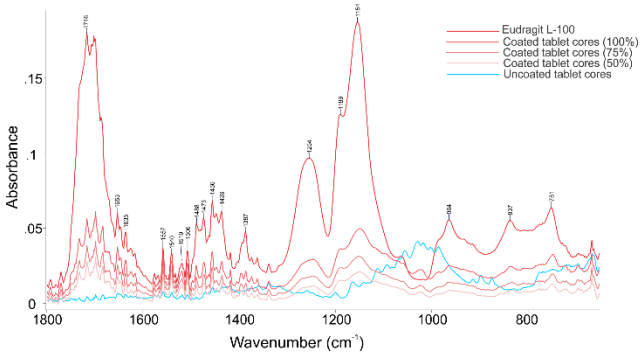

Fig. 1. FTIR spectra of pure Eudragit L-100 and 50%, 75% and 100% coated tablet cores.

Conclusion

Tablet cores were coated with gastro-resistant coating with anionic copolymer Eudragit L-100 by using Fluid bed - Wurster technique, by monitoring critical attributes of the film related to its functionality. It can be concluded that the process is suitable and can provide tablet coating with appropriate resistance in acidic medium. In addition FTIR spectroscopy demonstrated potential for film thickness monitoring. Further work on the development of quantification models based on multivariate analysis is needed to promote FTIR into a viable PAT tool for monitoring of film thickness during the coating procedure

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