DEVELOPING IN VITRO RELEASE TESTS FOR SEMISOLID DOSAGE FORMS CONTAINING DEXPANTHENOL AND METRONIDAZOL

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INTRODUCTION

Semisolid dosage forms are complex formulations, their drug release is a reflection of both physical and chemical properties and depends largely on formulation and manufacturing process. In vitro release test is useful performance test for semisolid dosage forms in assessment of product sameness after postaproval changes.

SUBJECT AND METODS

Table 1. Changes introduced to drug products

DRUG PRODUCT	POSTAPPROVAL CHANGE	REGULATORY DEMANDS
Dexpanthenol cream	Type and amount of excipient	In vitro release test and documentation
Metronidazol cream	API particle size distribution	

It was necessary to develop reliable methods to determinate in vitro release rate for Dexpanthenol cream and Metronidazol cream to meet regulatory demands (**Table 1.**). Starting point was choosing receptor media, after that, other key parameters shown in **Table 2**. were established during method development.

Table 2. Parameters defined in method development

PARAMETER	DEXPANTHENOL CREAM	METRONIDAZOL CREAM
Apparatus	mini paddles	paddles
Media	phosphate buffer pH 5.8	water
Media volume	200 mL	500 mL
Stirring rate	100 rpm	60 rpm
Temperature	32°C	32°C
Membrane	Cuprophane	Cuprophane
Sampling volume	2 mL	2 mL
Sampling points	15 ' 30 ' 45 '* 60' 120' 240' 360'	

*point 45' was included only for metronidazol cream

Tests were performed in dissolution apparatus Varian VK7010 with on-line autosamper Varian VK8000, using immersion cells with variable depth reservoir. Assay of dexpanthenol and metronidazol was determinated with validated HPLC methods.

RESULTS

After method development, two-stage test was carried following SUPAC-SS guideline.

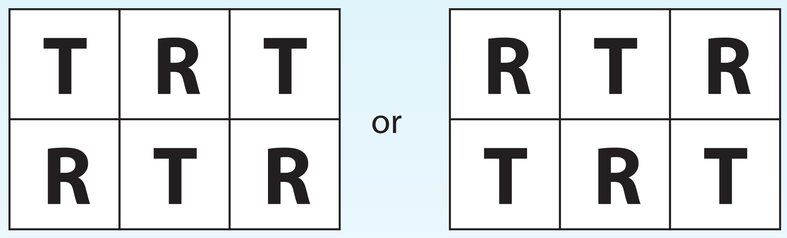

Figure 1. Assignment of two products for each run in six cell apparatus; R – prechange lot, T – postchange lot

With obtained results, release rate of prechange lot was compared with release rate of postchange lot and Mann-Whitney U test was used to calculate the 90% confidance interval for both drug products.

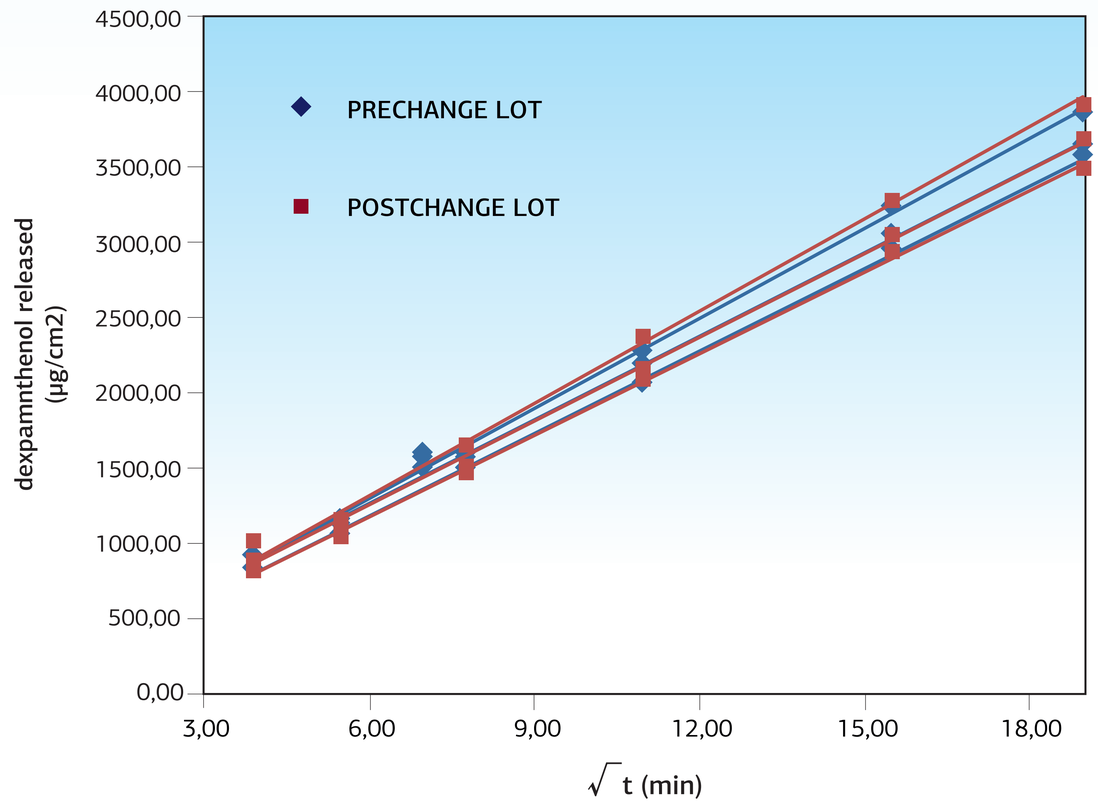

Figure 2. Amount of dexpanthenol released per unit area (µg/cm^2) against the square root of time ($\sqrt{t}$) – results of 1st stage of release testing

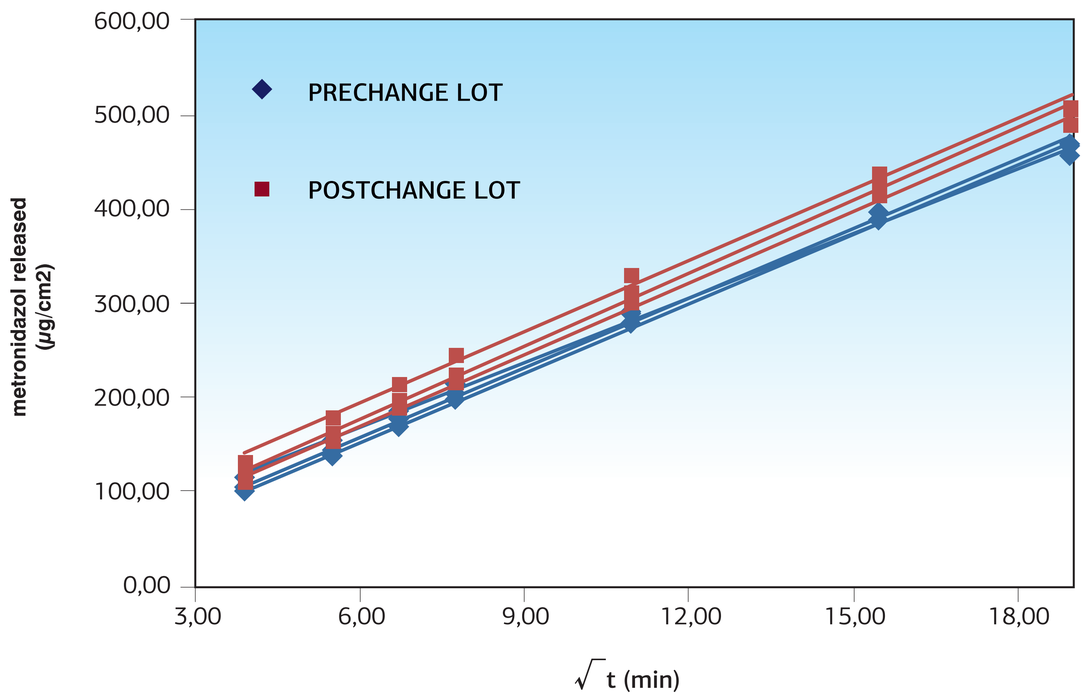

Figure 2. Amount of metronidazol released per unit area (µg/cm^2) against the square root of time ($\sqrt{t}$) – results of 1st stage of release testing

CONCLUSION

Results have shown that in vitro release rates of prechange and postchange formulation of dexpanthenol cream and prechange and postchange formulation of metronidazol cream are within 90% confidence interval, therefore their equivalence was proven

REFERENCES

[1] Food and Drug Administration (FDA), Guidance for Industry. Nonsterile semisolid dosage forms, scale-up and postapproval changes: chemistry, manufacturing, and controls; in vitro release testing and in vivo bioequivalence documentation. Rockville, US. Center for Drug Evaluation and Research (CDER), 1997.