

NRobe™ Technology: A simplified approach to controlled release formulation

Introduction

NRobe technology is a novel oral dose form technology based on a process consisting of light compression of a drug loaded fill which is enrobed between two dry, pre-formed films and sealed to provide a non-friable, coated dosage form.

The NRobe™ process overview is given in figure 1.

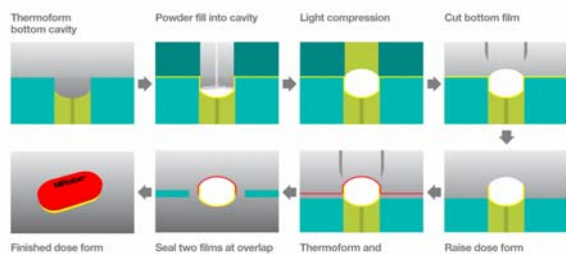


Figure 1 - NRobe process steps

The aim of this work was to investigate whether the technology affords some formulation and processing advantages such as simplicity and flexibility when formulating controlled release matrix oral dose forms. Specifically formulations containing high drug loadings and high viscosity grades of HPMC were considered. The potential to achieve zero order release with these formulations is shown. In addition, a two layered NRobe dose form concept was investigated to ascertain whether an immediate 'fast onset' followed by controlled release type profile could be achieved. Equipment capable of manufacturing this layering concept is currently in development.

Materials and methods

NRobe™ dose forms were filled with a blended formulation of 1) 1-a: 5% of HPMC K100M and 95% of theophylline, 1-b: 10% of HPMC K4M and 90% theophylline; 2) 2-a: 20% of HPMC K4M and 80%

of theophylline, 2-b: 20% HPMC K100M and 80% theophylline; 3) layer 1: theophylline 98% and 2% Ac-Di-Sol® and layer 2: 40% HPMC K4M and 60% of theophylline were manufactured and apparent powder compact densities were calculated.

The drug release from these NRobe dose forms (using USP 24 method for Theophylline IR tablets and SR capsules) was measured.

Figure 2 shows the 10 hours release profile of the high drug-loaded (95%) NRobe dose forms. The second curve of this figure represents the zero order release from the NRobe dose forms containing a simple compressed blend (90% of Theophylline and 10% of HPMC K100M).

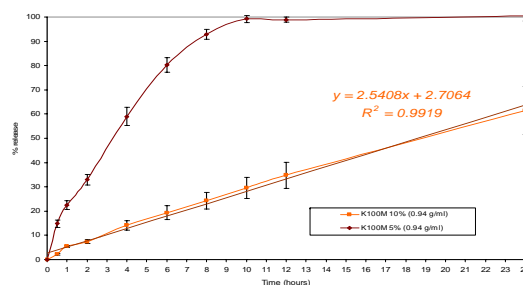


Figure 2 – High drug loading (95%) and zero order release in NRobe dose form

Figure 3 depicts the influence of the viscosity grades of NRobe dose forms matrix formers on the drug release rate at constant polymer content (20%) and fill compact densities (0.83 g/ml).

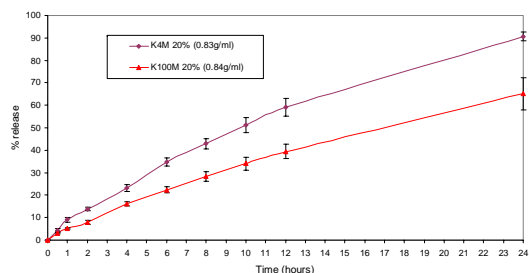


Figure 3 – Matrix former polymer viscosity influence on NRobe drug release profile

The drug release profiles of NRobe dose forms containing the combination of IR and SR layers in one dose form are shown in figure 4.

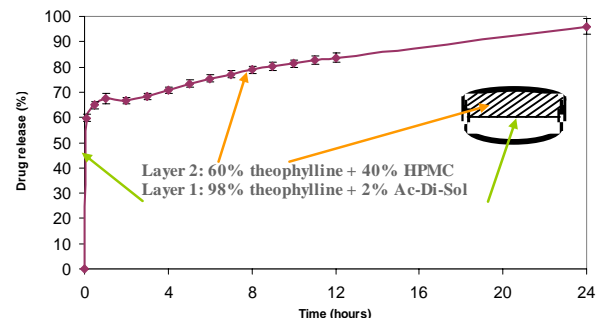


Figure 4 – Enrobing immediate and sustained release materials

The relatively low density powder fill enables the use of small amounts of high viscosity polymers to achieve desired release profiles without the need for additional pore formers. In addition the enrobing film provides the dose forms with sufficient tensile strength thus eliminating the need for inclusion of binding excipients. Thus the formulation approach is significantly simplified.

In addition, no burst effect was observed as it was reported for conventional matrices when using pure high viscosity grade of HPMC^{1,2}. A hypothesis for this is that the enrobing HPMC film provides an effective initial protection of the powder compact until a thin protecting gel layer is formed unlike in conventional matrices where time is required for the formation of an efficient gel layer¹. The combination of this and high compact porosity enables the achievement of zero-order release ($R^2=0.9919$; fig2) from HPMC matrices in NRobe dose forms.

The drug release from the immediate/CR concept NRobe dosage forms (fig4) occurred in 2 stages: an immediate release of 65% of the drug, followed by a prolonged release of the remaining drug in 24 hours time period.

Conclusions

Simplified formulation and processing to easily obtain zero order release was demonstrated using NRobe technology. Flexibility was also shown by obtaining tailored release profiles when immediate and sustained release layers were combined.

References

- Colombo P., Bettini R., Santi P. and Peppas N.A. (2000). Swellable matrices for controlled drug delivery: gel layer behavior, mechanisms and optimal performance, PSTT 3
- Giunchedi P., Maggi L. And Conte U. (1994). Modification of the dissolution behavior of a water-insoluble drug, Nafazone, for zero-order release matrix preparation, J. Pharm. Pharmacol. (46) 476-480.

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Laboratory and pilot-scale production
capabilities are available

Full-scale production equipment
is in progress

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