

# NRobe™ Dose Form: Influence of fill compact porosity on the drug release from the NRobe dose form

## Introduction

NRobe™ is a novel oral dose form technology with a high fill porosity and inherent tensile strength given by the enrobing film, not the compact density. The NRobe™ process overview is shown in Figure 1: the drug-loaded fill is lightly compressed between two dry, preformed, non-gelatin films and then sealed to provide a non-friable coated dose form.

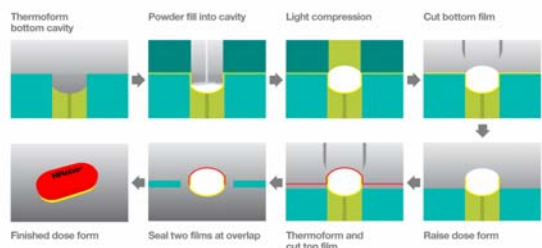


Figure 1 - NRobe process steps

Compaction pressures typically used in this process are significantly lower (up to 50 MPa) than in conventional tableting. Tye et al.<sup>(1)</sup> identified the importance of the porosity and associated compactibility of tablets as a means of defining tablet attributes that were insensitive to scale-up. Sun<sup>(2)</sup> identified a distinct relationship between compact porosity and end product performance such as dissolution.

Our work aims to determine whether the fill compact porosity in NRobe Dose Form influences drug release and whether targeted levels of porosity could be utilized advantageously to optimize the dose form or process.

## Materials and Methods

Formulations of 76% Ibuprofen (Shasun Chemicals & Drugs Ltd) and (a) 23% Avicel® PH200 microcrystalline cellulose and 1% talc (VWR) or (b) 20% Avicel PH200, 1% talc and 3% Ac-Di-Sol® were compacted at several pressures in the range 5-68 MPa on an ESH compaction simulator.

The compact thicknesses were measured using a micrometer and porosities calculated by measuring the powders true densities using a helium pycnometer. The relationship between compact porosity and a. compaction pressure and b. compact dissolution (using USP 24 method for IR Ibuprofen tablets) was investigated.

In a separate study, NRobe dose forms were manufactured from a granulated proprietary formulation including more than 70% of a freely soluble drug. The dissolution from NRobes made at 3 different compaction levels was compared using dissolution baskets (preferred method for NRobe) in 900 ml of 0.1N HCl. Lower porosity (10%) tablets of the same formulation were manufactured and tested using USP 24 method (paddles).

## Results and Discussion

Figure 2 shows the linear decrease of Ibuprofen compact porosity with increasing compaction pressure within the studied range (5-36 MPa), which is typical of values used for NRobe. The decrease in porosity at higher pressures (36-68 MPa) was less significant. The apparent porosity of the non-compacted powder was 60%.

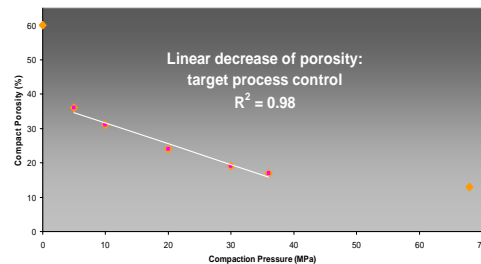


Figure 2. Relationship between compaction pressure and porosity in Ibuprofen-based compacts.

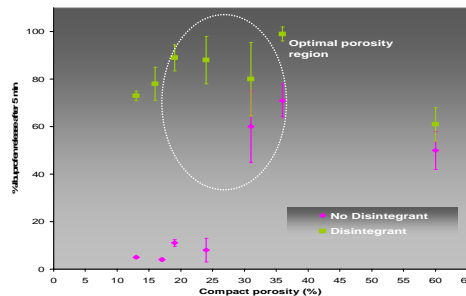


Figure 3. Influence of compact porosity on Ibuprofen release at 5 minutes.

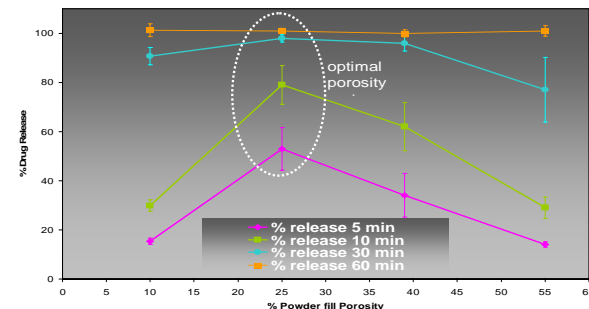


Figure 4. Release of freely soluble drug from tablets and NRobes filled with compacts of various porosity.

For both drugs, dissolution was faster within a defined high porosity range (around 19-36% for Ibuprofen, see fig. 3 and 20-30% for the freely soluble drug, see fig. 4) and significantly slower at lower or higher porosities.

Such high porosities cannot be exploited using a conventional tableting approach due to insufficient tensile strength. At porosities typical for conventional hard capsules (higher than 55%<sup>(3)</sup>), the dissolution of both drugs was significantly slower.

## Conclusion

This study suggests that within the relatively high porosities achievable with NRobe™ there exists specific porosity 'windows' in which the dissolution is enhanced. This effect was shown for compacts but also shown to translate to the film enrobed dose forms. This compact porosity 'window' that exists lies between that typically seen in tablets (low porosity) and hard capsules (higher porosity). It appears wide enough to be utilizable as a process control parameter. The next steps will be to assess whether control of a compaction process to target specific compact densities at such low pressures is viable.

## References

- 1) C.K. Tye, C. Sun, G.E. Amidon (2005), Evaluation of the effects of tableting speed on the relationships between compaction pressure, tablet tensile strength and tablet solid fraction, *J. Pharm. Sci.* 94(3), 465-472
- 2) C. Sun (2005), Critical Roles of Porosity in Tableting Properties Characterization and Solids Formulation Development, *American Pharmaceutical Review*, p102-107
- 3) B.C. Hancock, J.T. Colvin, M.P. Mullarney and A. V. Zinchuk (2003), The relative densities of pharmaceutical powders, blends, dry granulations, and immediate-release tablets, *Pharm. Tech.* 27 (4), 64-80

FMC Corporation conducts NRobe  
Technical development at :  
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Laboratory and pilot-scale production  
capabilities are available

Full-scale production equipment  
is in progress

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