Fuji Chemical Industries

Solving Puzzles since 1946.

Creativity and Contribution

# PHARMACEUTICAL NEWSLETTER

## Harnessing the Power of Neusilin® in HPMC Matrix Tablets

# OVERVIEW

Hydrophilic matrices, particularly those formulated with hypromellose (HPMC), are essential for controlled drug release in pharmaceutical formulations. While HPMC offers numerous advantages, its propensity to exhibit a burst release effect remains a significant challenge.

While this can be beneficial in certain cases, it often leads to suboptimal therapeutic outcomes and increased adverse effects. To ensure consistent drug delivery and optimize therapeutic efficacy, minimizing initial burst release is crucial in controlled-release formulations. Traditional excipients like microcrystalline cellulose (MCC) have been employed to mitigate this effect, but the pursuit of novel excipients with superior properties for controlled drug release continues.

## NEUSILIN®: THE GAME-CHANGER

Neusilin®, an amorphous magnesium aluminometasilicate, has gained prominence as a versatile excipient in pharmaceutical formulations. Its distinctive characteristics, including a high specific surface area and adsorption capacity, make it well-suited for modulating drug release profiles.
A recent study by Bilik et al., featured in this newsletter, elucidated the effectiveness of incorporating Neusilin® into HPMC matrix tablets. The inclusion of Neusilin® significantly reduced the initial burst release of soluble drugs, such as caffeine, providing a more controlled and sustained release profile from matrices with 10-20% of HPMC content.

## OPTIMIZATION OF POWDER BLENDS FOR TABLET PRODUCTION

1

### Mixing and Characterization

- All ingredients, as specified in Table 1, were thoroughly mixed using a three-axial homogenizer turbula for 10 minutes.
- Prior to tablet preparation, the powder blends were characterized for their flow properties.

2

### Tablet Preparation

- Convex-faced HPMC matrices were directly compressed using an eccentric tablet press to achieve maximum hardness.

3

### Evaluation

- The prepared tablets were subjected to a comprehensive evaluation, including assessments of weight, content uniformity, hardness, friability and dissolution
- Dissolution studies were conducted to assess the rate and extent of drug release from the tablets.

## TABLE 1:MATRIX TABLETS COMPOSITION *

| Sample* | Caffeine | | HPMC K4M | | MCC PH 102 | | Neusilin® US2 | |
|---|---|---|---|---|---|---|---|---|
| | (mg) | (%) | (mg) | (%) | (mg) | (%) | (mg) | (%) |
| M100 | 100.0 | 38.8 | 50.0 | 19.5 | 100.0 | 38.8 | 0.0 | 0.0 |
| M125 | 100.0 | 38.8 | 25.0 | 9.7 | 125.0 | 48.5 | 0.0 | 0.0 |
| M75 | 100.0 | 38.8 | 75.0 | 29.1 | 75.0 | 29.1 | 0.0 | 0.0 |
| N125 | 100.0 | 38.8 | 25.0 | 9.7 | 0.0 | 0.0 | 125.0 | 48.5 |
| N100 | 100.0 | 38.8 | 50.0 | 19.4 | 0.0 | 0.0 | 100.0 | 38.8 |
| N75 | 100.0 | 38.8 | 75.0 | 29.1 | 0.0 | 0.0 | 75.0 | 29.1 |
| N75M50 | 100.0 | 38.8 | 25.0 | 9.7 | 50.0 | 19.4 | 75.0 | 29.1 |
| N50M50 | 100.0 | 38.8 | 50.0 | 19.4 | 50.0 | 19.4 | 50.0 | 19.4 |
| N25M50 | 100.0 | 38.8 | 75.0 | 29.1 | 50.0 | 19.4 | 25.0 | 9.7 |

*Each sample contains 0.5% of Aerosil® 200 and 2.5% of magnesium stearate for better flowability and compression feasibility. ** HPMC amount always corresponds to 150 minus the numeric value or the sum of the numeric values in the sample designation.

# IMPACT OF NEUSILIN®

### NEUSILIN® US2 ON TABLET FORMULATION AND MECHANICAL PROPERTIES

**Enhanced Tablet Hardness and Compressibility: Neusilin®** US2, when incorporated as a filler, significantly improved the mechanical properties of the tablets.
This was manifested by enhanced tablet hardness and excellent compression characteristics.

### NEUSILIN® ON THE FORMATION OF HPMC GEL LAYER

**Neusilin® matrices formed thicker gel layers than MCC matrices but required less penetration force** due to Neusilin®'s higher adsorption capacity, which allowed for deeper penetration of the dissolution medium and promoted HPMC swelling.
However, individual Neusilin® particles disrupted the gel layer more significantly than MCC alone or Neusilin® / MCC combinations, leading to faster drug release. This is depicted in figure no. 2.

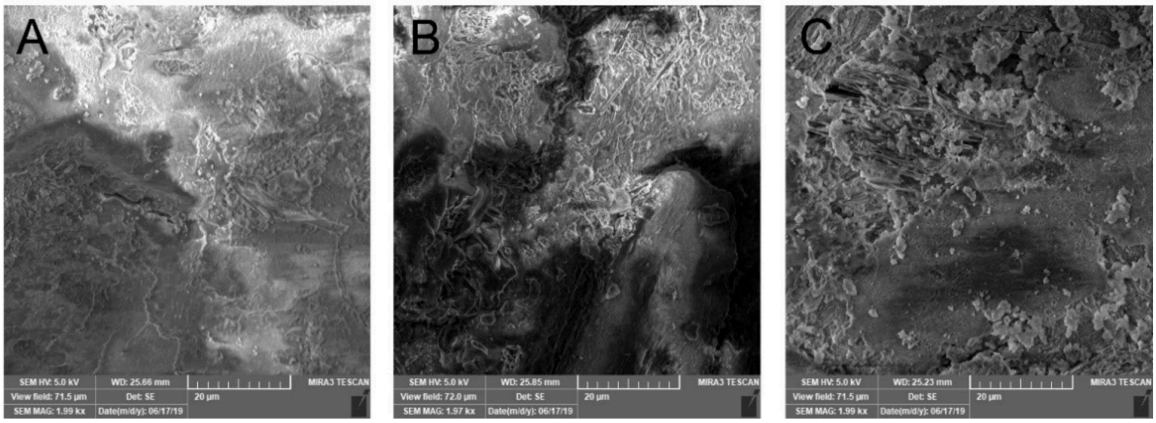



**Figure 1**: SEM surface topography of the selected samples of matrix tablets: (A) N75M50, (B) M125, (C) N125

SEM analysis revealed a more compact surface structure for sample N75M25 compared to the furrowed surfaces of samples M125 and N125.

## THE FORMATION OF HPMC GEL LAYER

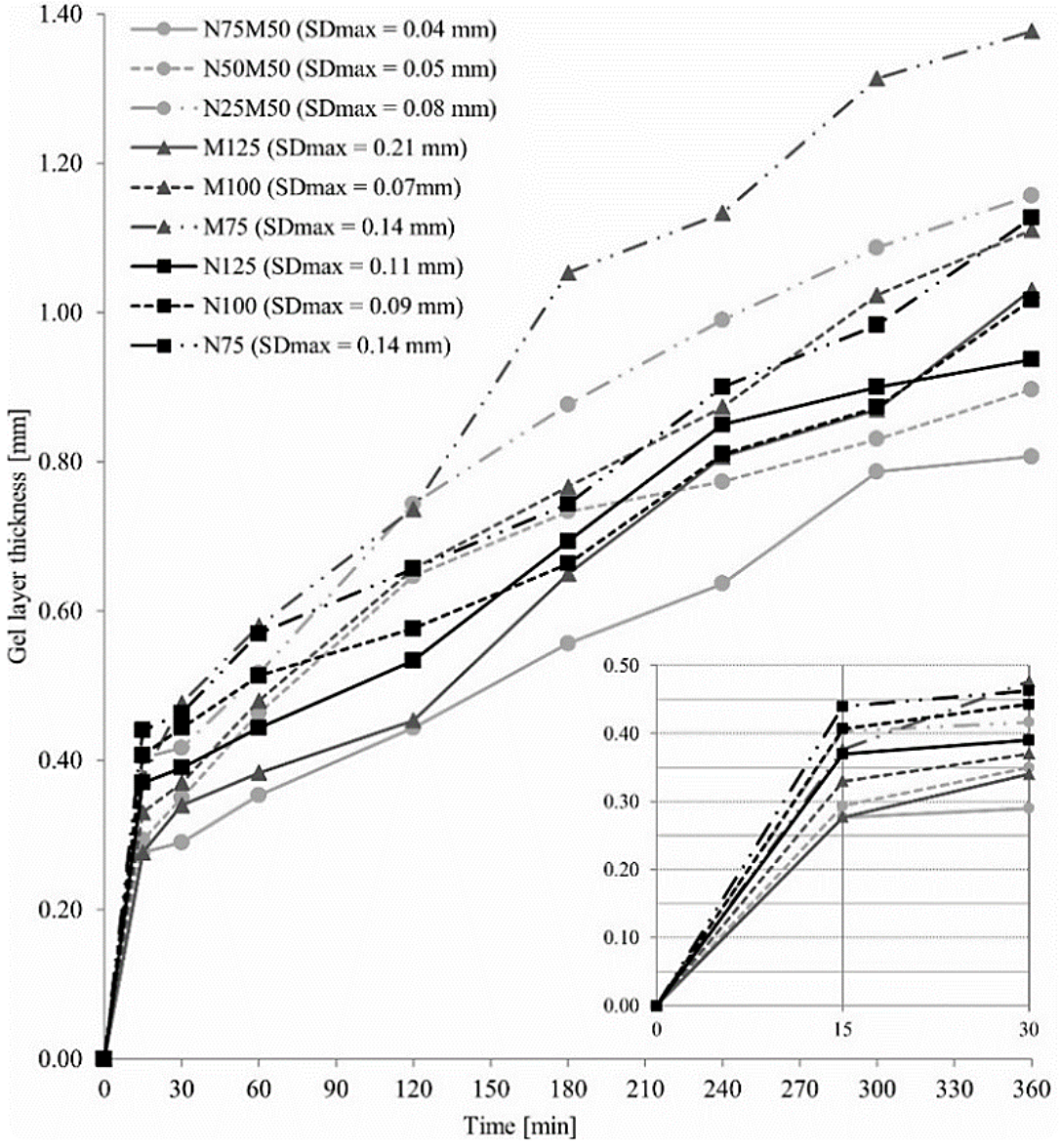



**Figure 2: The gel layer thickness of the HPMC matrix tablets**

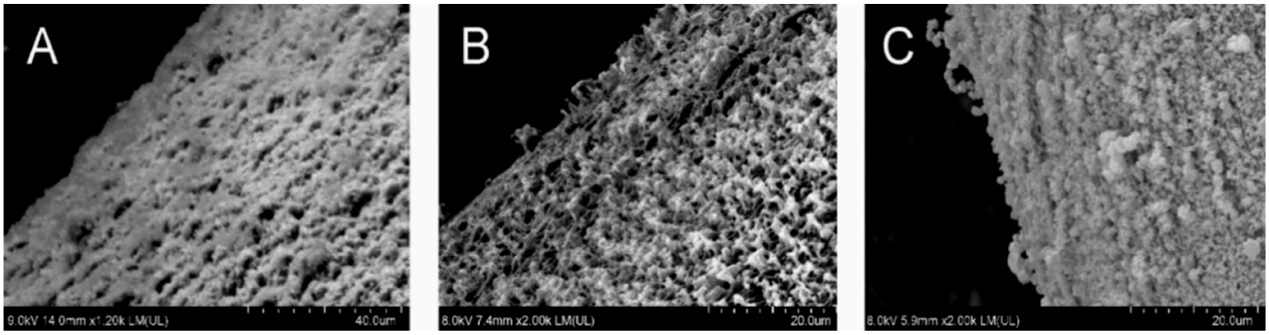



**Figure 3:** Cryo-SEM images showing gel layer of swollen tablet samples in the 30th min of the dissolution test: (A) M100, (B) N100, (C) M50N50.

Figure 3 shows cryo-SEM images of the swollen tablets' gel layers after 30 minutes. The gel layers were less compact in the order of M50N50, M100, N100, which aligns with the burst effect.

# INFLUENCE OF NEUSILIN®

## NEUSILIN® US2 ON THE INITIAL BURST RELEASE OF CAFFEINE FROM HPMC MATRICES

Dissolution studies demonstrated that the incorporation of Neusilin® US2 / MCC into HPMC matrices significantly reduced the initial burst release of caffeine. This effect was attributed to the immobilization of caffeine within the swollen matrix structure.

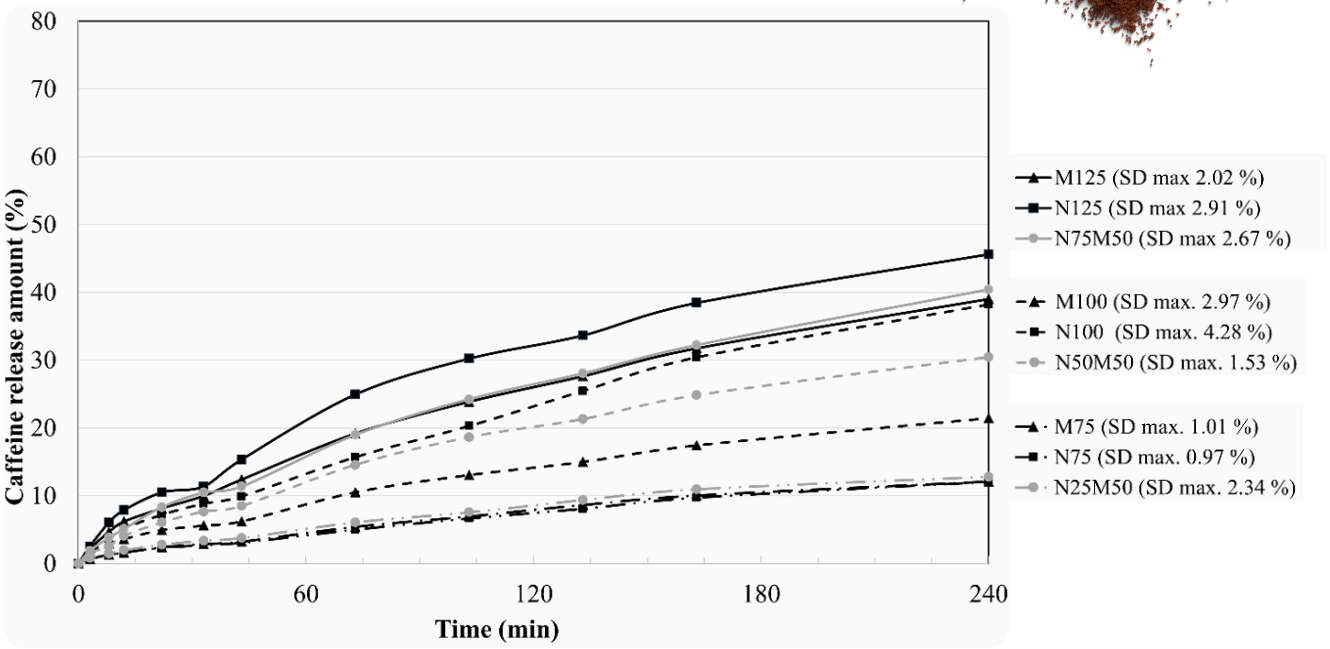
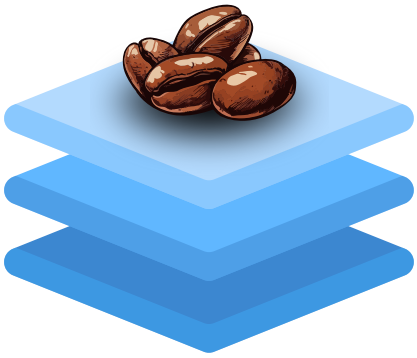



**Figure 2: Cumulative dissolution data from all four phases of the dynamic dissolution test**

## NEUSILIN® ON CAFFEINE RELEASE FROM HPMC MATRICES: POTENTIAL MECHANISMS

- Enhanced Gel Layer: **Neusilin®** can form a thicker gel layer in HPMC matrices, slowing drug release.
- Drug Adsorption: **Neusilin®**'s high surface area can adsorb caffeine, reducing its immediate availability.
- Matrix Interaction: **Neusilin®** may alter HPMC swelling and gel strength, controlling matrix hydration.
- Improved Matrix Integrity: Addition of **Neusilin®** can enhance matrix integrity, leading to slower erosion and reduced initial burst release.



# REASONS TO CHOOSE NEUSILIN®

### Biorelevant Dissolution
Biorelevant dissolution tests were more effective than USP tests in assessing the differences between **Neusilin®** and MCC.

### Slower Release
**Neusilin®**/MCC combinations in 10-20% HPMC matrices slowed drug release compared to MCC alone.

### Improved Predictability
Only **Neusilin®**/MCC samples showed similar results in both USP and biorelevant tests, suggesting better prediction of *in vivo* behavior.

### Potential Applications
**Neusilin®**/MCC combinations may be useful for developing matrix or self-emulsifying systems due to their improved predictability.

REFERENCES
- Bílik, T., Vysloužil, J., Naiserová, M., Muselík, J., Pavelková, M., Mašek, J., Čopová, D., Čulen, M., Kubová, K. (2022). "Exploration of Neusilin® US2 as an Acceptable Filler in HPMC Matrix Systems-Comparison of Pharmacopoeial and Dynamic Biorelevant Dissolution Study." Pharmaceutics, 14(1), 127.

Fuji Chemical Industries

Solving Puzzles Since 1946.

Creativity and Contribution

## CONTACT US


**India**
AstaReal (India) Private Limited
(A Fuji Chemical Group Company)
Unit No. 606/6th floor, Sunteck
Crest, Behind Mukund Hospital,
Near Leela Business Park,
Andheri East, Mumbai – 400059
Tel. +91-22-62369998
Email: pharma@fujichemical.co.jp

**Europe**
AstaReal AB
(A Fuji Chemical Group Company)
Forumvägen 14, Level 16,
131 53, Nacka, SWEDEN
Tel. +46-8-570-139-50
Email: pharma@fujichemical.co.jp

**USA**
Fuji Chemical Industries USA, Inc.
3 Terri Lane, Unit 12
Burlington, NJ 08016 USA
Tel. +1-609-386-3030
Email: contact@fujichemicalusa.com
www.fujichemicalusa.com

**Japan**
Fuji Chemical Industries Co., Ltd.
Shibakoen Ridge Building 2nd Floor,
1-8-21 Shiba Koen, Minato-ku,
Tokyo 105-0011 JAPAN
Tel. +81-3-3437-2350
Fax: +81-3-3437-2347
Email: pharma@fujichemical.co.jp
www.fujichemical.co.jp/english


*Regulations may vary from one region to another. Please contact your local distributor or sales person for more information.