



Make harder tablets and protect it from humidity by adding 2% Neusilin® UFL2 to a lactose or mannitol formulation

Does your team face difficulty in maintaining tablet strength during stability studies? Adding a small amount of Neusilin®UFL2 could be the simple solution.

Neusilin® UFL2 is ultra fine powder of magnesium aluminometasilicate and is widely accepted as multi-problem solver excipient for oral solid dosage forms. In this newsletter, we introduce you a new study where Neusilin® UFL2 is used as excipient to improve hardness of acetaminophen tablets and to protect the tablets from deterioration by moisture. Tablet hardness does not decrease significantly even under humid conditions.

Investigated formulations are showed in Table 1. In these formulations, acetaminophen was set at 10%, and lactose and mannitol were used as excipients at 67-69% and 62-64%, respectively. Microcrystalline cellulose (MCC) was used as molding agent at 20%, and hydroxypropyl cellulose was used as disintegrant at 5%. Finally, magnesium stearate was used as lubricant at 1% of tablet formulations.

Component	Lot				
	#1	#2	#3	#4	#5
Acetaminophen (mg)	15	15	15	15	15
Lactose (Super-Tab) (mg)	103.5	100.5	93	-	-
Mannitol (Parateck M200) (mg)	-	-	-	96	93
MCC (Ceolus UF-711) (mg)	30	30	30	30	30
Hydroxypropyl cellulose(L-HPC LH-B1) (mg)	-	-	7.5	7.5	7.5
Neusilin® UFL2 (mg)	-	3	3	-	3
Magnesium stearate (mg)	1.5	1.5	1.5	1.5	1.5
Total (mg)	150	150	150	150	150

Table 1: Investigated formulations

The batch size of formulation was set at 1000 tablets (150 g). The materials were placed in a polyethylene bag and mixed thoroughly. Tablets were produced by single punch tableting equipment (N-30EX model, Okada Seiko Co., Ltd.; tablet diameter: 7.0 mm, compression force: 700 kgf). Tablet properties including weight, thickness and hardness were measured using 10, 5, and 5 tablets respectively. The dissolution test was carried out by the paddle method (50 rpm), using 3 tablets in 900 ml of water. The dissolution rate was measured spectrophotometrically at wavelength of 244 nm.

Parameters	Lot				
	#1	#2	#3	#4	#5
Excipient	Super-Tab	Super-Tab	Super-Tab	Pardeck M200	Pardeck M200
Addition of 2% Neusilin®	No	Yes	Yes	No	Yes
Tablet weight (mg) (CV: %)	149.6 (1.34%)	148.3 (0.78%)	152.9 (0.9%)	148.0 (1.1%)	148.7 (1.1%)
Thickness (mm)	3.8	3.81	3.83	3.77	3.73
Hardness (N)	77.9	100.2	108.5	139.3	151.8
Dissolution rate (% value at 15 min.)	90.8	86.0	102.2	95.3	94.6

Table 2: Hardness and dissolution profiles of tablets

The results are shown in Table 2. Addition of 2% Neusilin®UFL2 increased the tablet hardness irrespective of the filler-binder excipients used (formulations #2, #3 and #5). Furthermore, with Super-tab as excipient, Neusilin®UFL2 reduced the coefficient of variation (CV) of tablet weight from 1.34% to 0.78% and 0.9% (formulations #1-#3). The dissolution rate met a criterion of 85% or more in 15 minutes in all formulations.

Accelerated stability tests and stability test at room temperature were performed for a period of one month with 30 tablets in high-density polyethylene (HDPE) bottles (sealed or open). The hardness and dissolution profiles of tablets are shown in Table 3. In formulations #1 and #4 in which Neusilin® UFL2 was not added, the hardness decreased significantly under accelerated stability test (bottle/open) and in stability test (bottle/open) conditions. In formulations #2 and #3 in which Neusilin® UFL2 was added and Super-tab was used as excipient, the hardness slightly decreased under accelerated stability condition (bottle/open) but remained at 80.2 N and 87.3 N respectively. In rest of the conditions, a decrease in hardness was not observed. In formulation #5 where Neusilin®UFL2 was added with Pardeck M200 as excipient, the hardness remained above 100 N at all stability test conditions. However the same formulation without Neusilin® showed significant reduction of tablet hardness (Fig. 1).

	Formulation	Measurement item	Initial value	40°C/75% RH Bottle/Sealed	40°C/75% RH Bottle/Open	25°C/75% RH Bottle/Open	Note
- Disintegrant	#1 (without Neusilin®)	Hardness (N)	77.9	72.4	40.1	53.2	Not good
		Dissolution rate (% value at 15 min.)	90.8	57.9	52.3	48.9	
	#2 (with 2% of Neusilin®)	Hardness (N)	100.2	112.0	80.2	113.0	Poor dissolution rate
		Dissolution rate (% value at 15 min.)	86.0	49.6	30.8	36.6	
+ Disintegrant	#3 (with 2% of Neusilin®)	Hardness (N)	108.5	110.3	87.3	105.4	Good hardness and dissolution rate
		Dissolution rate (% value at 15 min.)	102.2	100.2	98.4	101.3	
	#4 (without Neusilin®)	Hardness (N)	139.3	80.3	60.7	50.3	Drop in hardness
		Dissolution rate (% value at 15 min.)	95.3	98.3	92.1	93.3	
	#5 (with 2% of Neusilin®)	Hardness (N)	151.8	143.2	126.4	135.7	Hardness is maintained
Dissolution rate (% value at 15 min.)		94.6	95.5	93.1	93.4		

Table 3: Hardness and dissolution profiles of tablets stored under humid conditions for one month

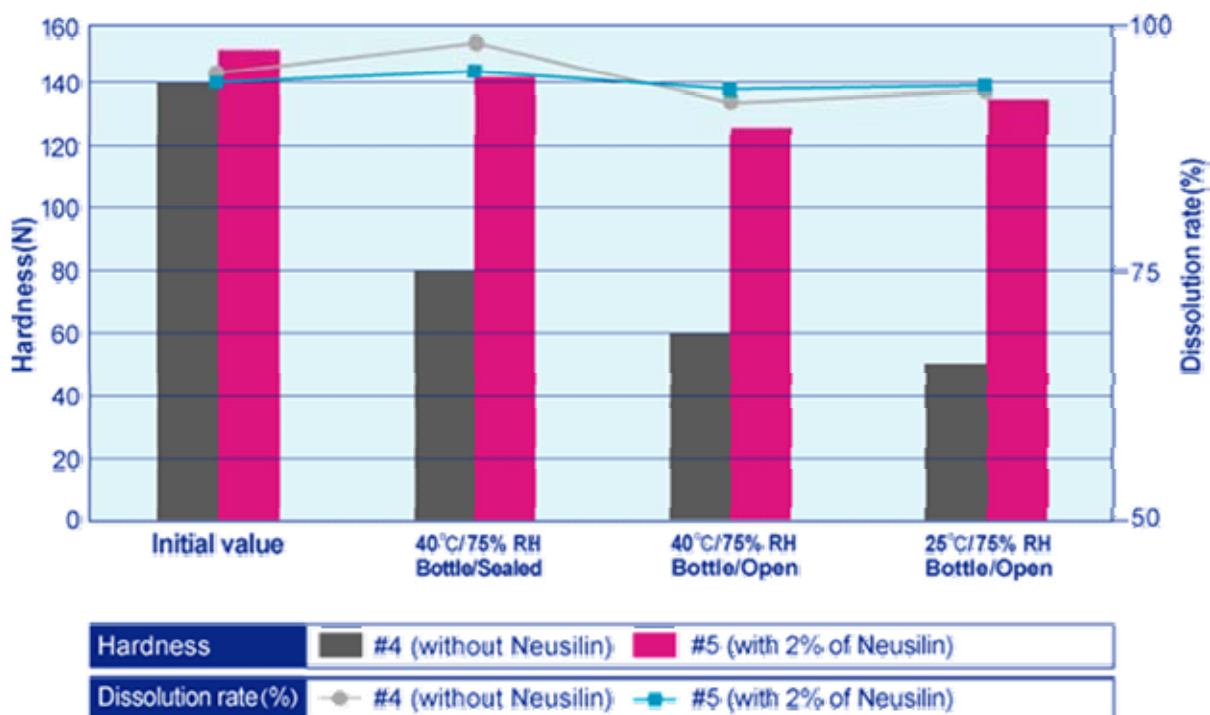


Fig. 1 Hardness and dissolution profiles of tablets stored under humid conditions for one month

Conclusions:

This study demonstrated that addition of 2% Neusilin®UFL2 would allow:

1. Improvement of the tablet hardness.
2. Maintenance of tablet hardness under humid conditions.

Furthermore, adding 10% of disintegrant is required to facilitate dissolution.

Reference:

1. Asai Y, Nohara M, Fujioka S, Isaji K, Nagira S, Application of Neusilin UFL2 on manufacturing of tablets using direct compression method, Development of core tablets containing the function of small degree of decrease of hardness at the humid conditions. Pharm Tech Japan. 2009; 25: 67-70.

Neusilin®:

Chemical formula : $Al_2O_3 \cdot MgO \cdot 1.7SiO_2 \cdot xH_2O$

Chemical Abstract Service (CAS) Number: 12511-31-8

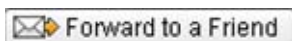
U.S. Drug Master File (DMF) filed, Conforms to USP/NF, JPC

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