The Specialty Excipient

Neusilin®

A totally synthetic Magnesium Aluminometasilicate (MAS) with exceptional excipient properties to improve API delivery and the quality of pharmaceutical preparations

Solving Puzzles since 1946

Creativity and Contribution

Fuji Chemical Industries Co., Ltd.

Blank

The Specialty Excipient

Neusilin®

A totally synthetic Magnesium Aluminometasilicate (MAS) with exceptional excipient properties to improve API delivery and the quality of pharmaceutical preparations

INTRODUCTION

Neusilin® is a synthetic, amorphous form of Magnesium Aluminometasilicate. It is a multifunctional excipient that can be used in both direct compression and wet granulation of solid dosage forms. Neusilin® is widely used for improvement of the quality of tablets, powder, granules and capsules.

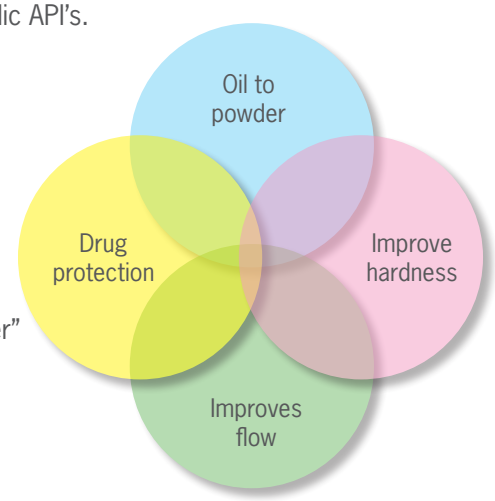
Neusilin® does not develop gels with aqueous solutions unlike other Magnesium Aluminum Silicates.

The different grades of Neusilin® have been highly evaluated at home and abroad. It has a market presence of over 60 years in Japan.

CHARACTERISTICS

1. Neusilin® occurs as a fine powder or as granules of Magnesium Aluminometasilicate.
2. Neusilin® is represented by an empirical formula $Al_2O_3 \cdot MgO \cdot 1.7SiO_2 \cdot xH_2O$.
3. Neusilin® is amorphous, possesses very large specific surface area and has high oil and water adsorption capacity.
4. Neusilin® is superior in compressibility. Neusilin® makes hard tablets at low compression force and in addition, at low concentrations can improve the hardness of other filler and binder excipients.
5. Compounding with Neusilin® helps stabilize moisture sensitive as well as lipophilic API's.
6. Neusilin® is stable against heat and has a long shelf life.
7. Neusilin® is available in various grades. The grades differ in their bulk density, water content, particle size and pH.
8. Neusilin® is an excellent carrier for solid dispersion via Self Micro-Emulsifying Drug Delivery System (SMEDDS) and Hot-Melt Extrusion.

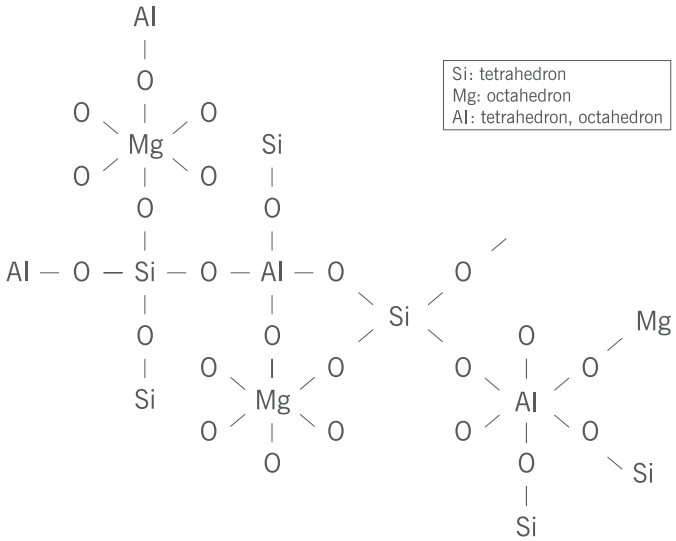
"Multi-problem solver"



STRUCTURE

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

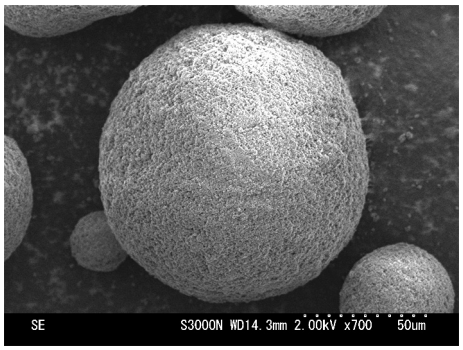
Neusilin® is amorphous and contains either tetrahedron or octahedron of Al, octahedron of Mg and tetrahedron of Si which are randomly attached to form a complex three dimensional structure. Neusilin® does not possess repeating units of a defined monomer.



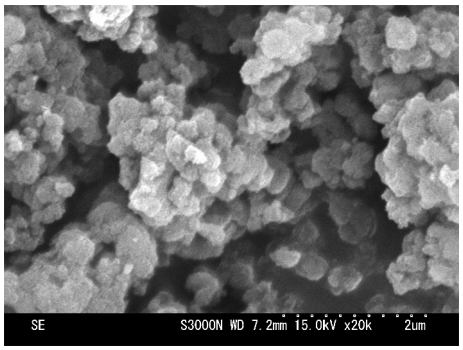
GENERAL PROPERTIES OF NEUSILIN®

Appearance	White powder or granules
Physical Form	Amorphous
True Specific Gravity	2.0-2.2
Solubility	Practically insoluble in water and in ethanol
Composition (%) on Dried Basis	Al_2O_3 – 29.1 – 35.5 MgO - 11.4 – 14.0 SiO_2 - 29.2 - 35.6
Loss on Drying	Less than 20 to 5% depending on grades
CAS Number	12511-31-8
EINECS Number	235-682-0

Photomicrographs of Neusilin®

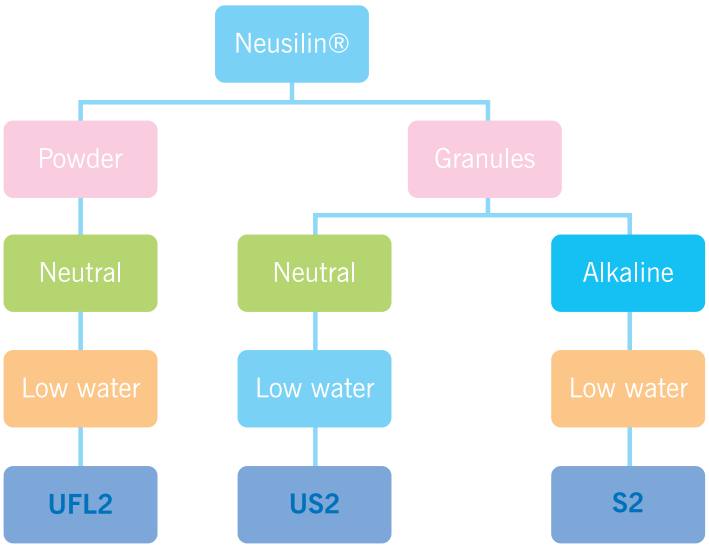


Neusilin® US2 Granules (x700)



Neusilin® UFL2 Powder (X20,000)

NEUSILIN® GRADES



TYPICAL PROPERTIES

GRADE		S2	US2	UFL2
Physical appearance		Granule	Granule	Powder
Degree of whiteness (%)		>95	>95	>95
Loss on drying (%) 110°C, 7hours		< 5	<7	<7
Bulk density	Loose (g/ml)	0.29-0.37	0.13-0.18	0.06-0.11
	Tapped (g/ml)	0.34-0.42	0.16-0.22	0.10-0.17
True specific gravity		2.2	2.2	2.2
Specific surface area (m^2/g)*1		110	300	300
Particle size distribution (µm)		44-250	44-177	–
Residue on 330 mesh sieve (%)		–	–	<0.5
Residue on 100 mesh sieve (%)		–	–	–
Angle of repose (°)		30	30	45
Oil adsorbing capacity (ml/g)*2		1.4	2.7-3.4	2.7-3.4
Water adsorbing capacity (ml/g)		1.2	2.4-3.1	2.4-3.1
Acid consuming capacity (ml/g)*3		>210	>210	>210
pH (4% slurry)*4		8.5-10.0	6.0-8.0	6.0-8.0

*1) BET surface area, nitrogen adsorption method
*2) Japanese Industrial Standard pigment test method (JIS K5101)
*3) Amount of 0.1N hydrochloric acid neutralized by 1g dried product (110°C. 7 hours)
*4) Weigh 2 g of sample, add water to make 50 ml. After stirring, allow to stand for 2 minutes, Measure pH using pH meter

TYPICAL APPLICATIONS AND QUANTITY NEEDED IN PHARMACEUTICAL PREPARATIONS

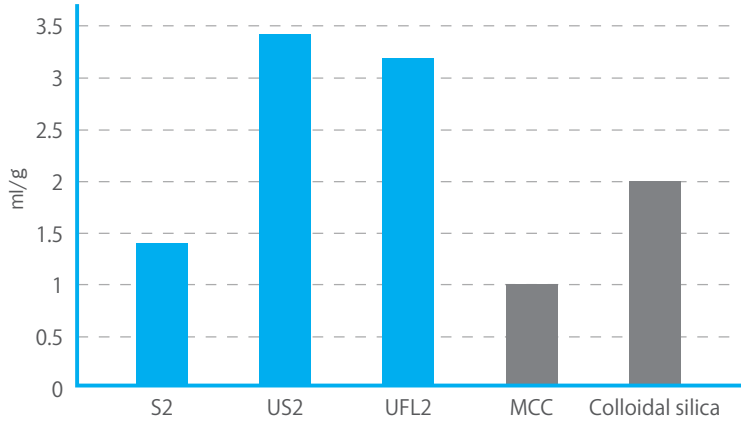
APPLICATION / FUNCTION	QUANTITY (%)		
	S2	US2	UFL2
Diluent in solid dosage forms	30-90	30-90	30-90
Binder, increasing hardness, Disintegration aid in tablets	5-20	1-10	1-10
Increase flowability	–	–	0.5-5
Anti-caking agent	–	–	0.5-5
Solidification of liquid API (eg: oil to powder)	–	30-50	30-50
For suspensions	–	–	1-5
Stabilization of deliquescent drugs	–	5-15	5-15
Solid dispersion, SMEDDS	–	20-50	20-50

PHARMACEUTICAL APPLICATIONS

I. Oils and extracts to powder

Schematic flow

Oil adsorption capacity



Neusilin® US2 and UFL2 grades show higher oil adsorption capacity* when compared to MCC or colloidal silica.

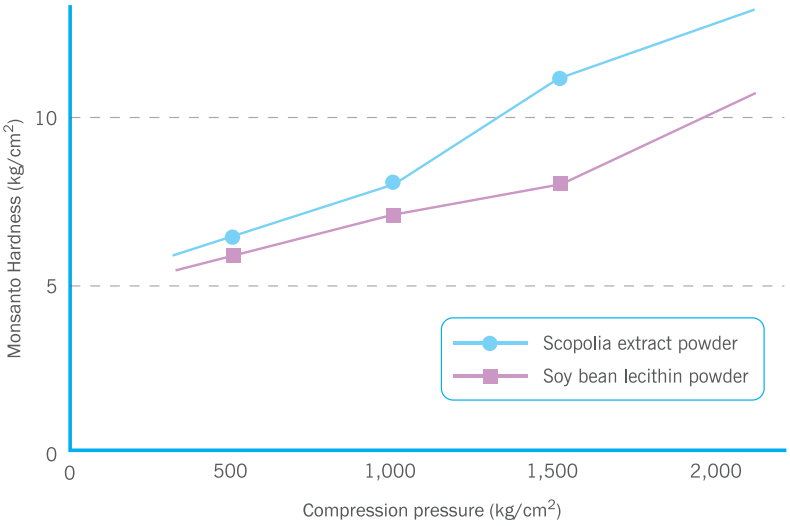
*Linseed oil direct adsorption

Free flowing powder of linseed oil

Neusilin® US2 +30% linseed oil, Dry at 50°C

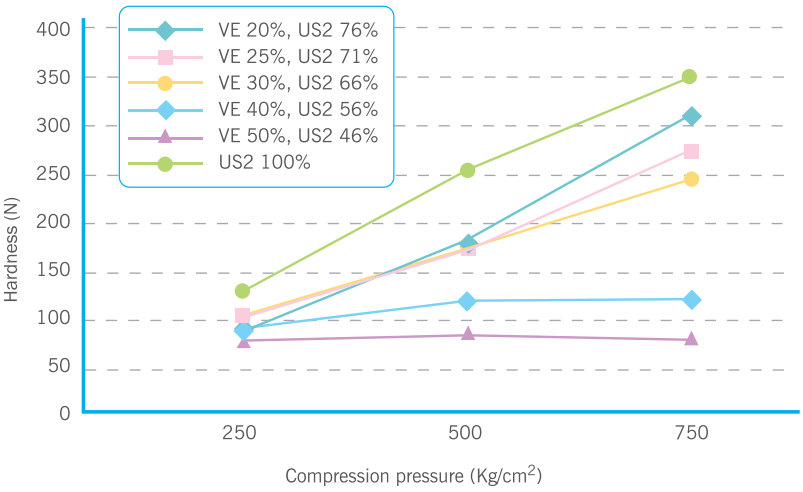
Linseed oil tablet, Ø11.3mm, 125N at 500kg/cm^2

Tablets of Scopolia extract and soybean oil (with Neusilin® UFL2)



A mixture containing 25% Scopolia extract or soybean oil and 25% UFL2 was compounded with equal amount of lactose. This mixture was subjected to static compression and tabletting. We found no adhesion to pestle and mortar and the compressibility was good. The tablet did not exude the extract or oil on storage.

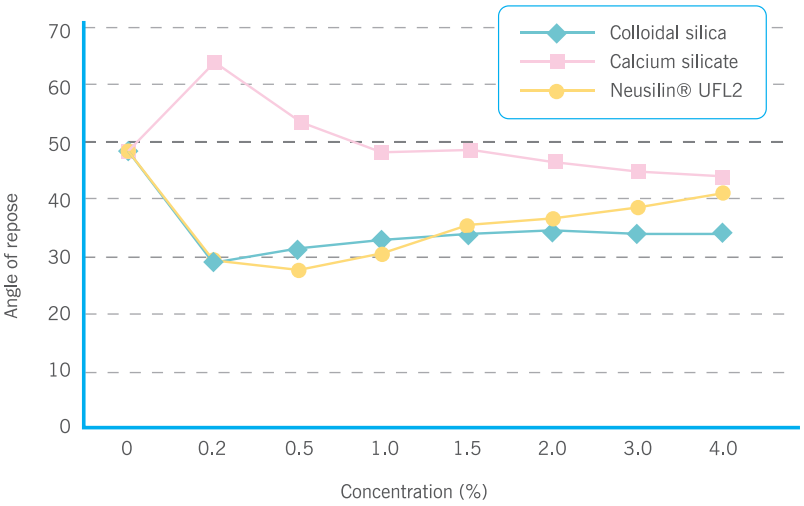
Tablets of Vitamin E (with Neusilin® US2)



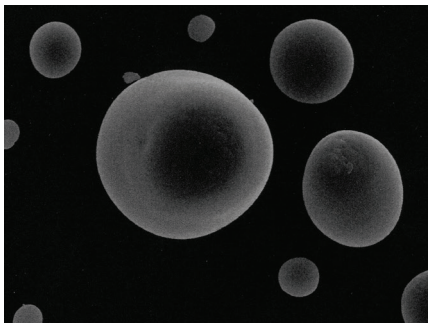
An ethanol solution of tocopherol acetate (VE) 20-50% was compounded with proportional amount of Neusilin® and mixed well. To this mixture, 3% croscarmellose sodium and 1% magnesium stearate were added before tabletting. High quality tablets with a load of up to 30% vitamin E can be prepared with Neusilin® US2.

II. Flowability Improvement

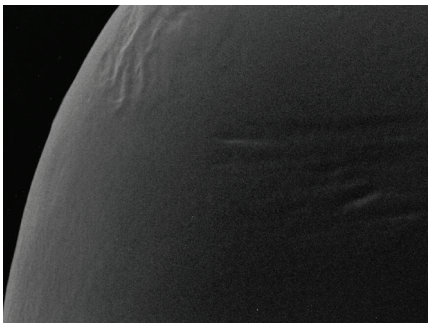
Angle of repose after adding Neusilin® UFL2 and other excipients to potato starch



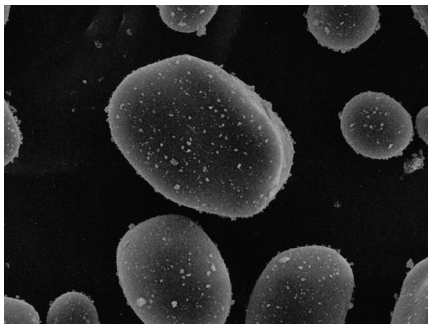
Neusilin® UFL2 particles stick to the surface and aid flow



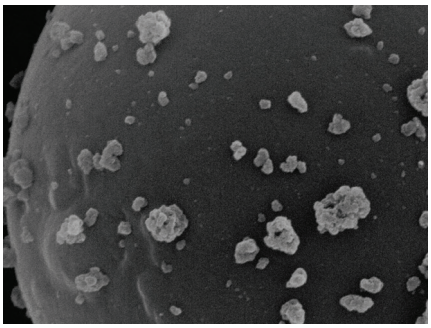
Potato starch
x 1,000



Potato starch
x 10,000



Neusilin® + Potato starch
x 1,000

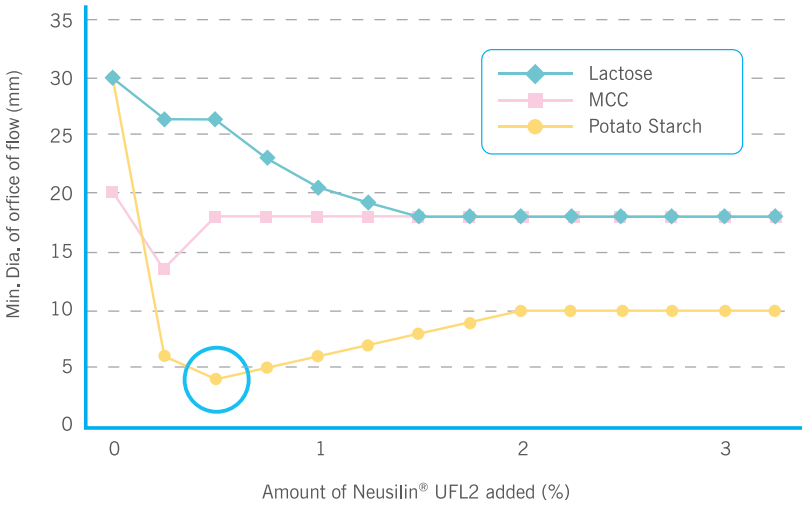


Neusilin® + Potato starch
x 10,000

Electron micrograph showing Neusilin® UFL2 particles sticking to the starch surface. On addition to starch, the UFL2 particles stick to the surface and facilitate flow as in a 'roller blade' model. A 0.5% addition of UFL2 to potato starch vastly improves flowability.

III. Anti caking

Addition of 0.5% Neusilin® UFL2 prevents caking



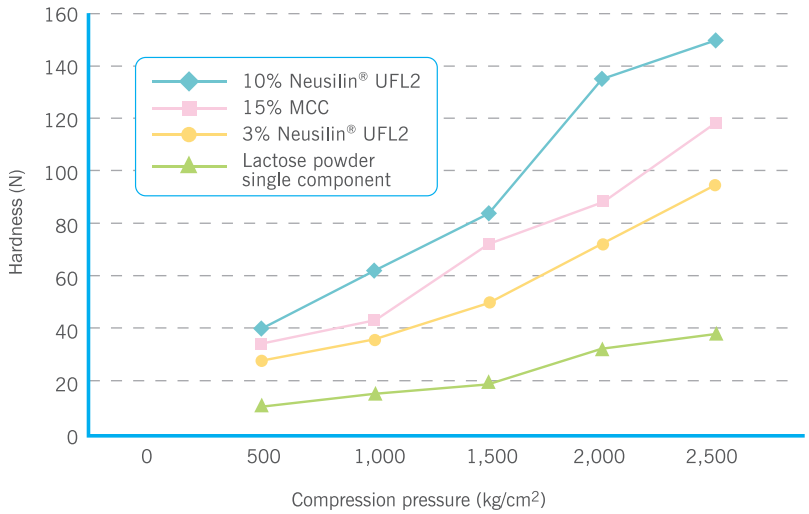
Neusilin® UFL2 prevents caking at high humidity conditions

Sodium L-aspartate at 45°C, 75% RH, 2 days

Sodium L-aspartate with 0.5% UFL2 at 45°C, 75% RH, 2 days

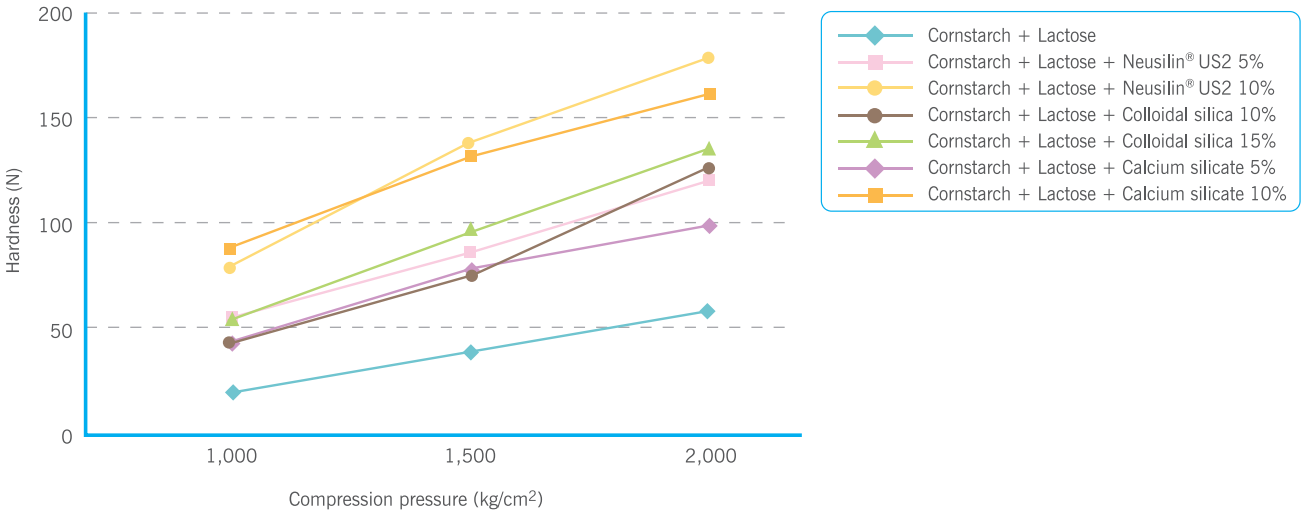
IV. Compressibility

Neusilin® UFL2 increases hardness of lactose tablet



Compounding lactose with 10% Neusilin® UFL2 results in higher hardness when compared to 15% microcrystalline cellulose

High quality tablets at low compression pressure



Tablet hardness of cornstarch/lactose based tablets compounded with either using Neusilin® US2, colloidal silica or calcium silicate. Corn starch, lactose and excipient were mixed thoroughly. Magnesium stearate as lubricant was added prior to tabletting. Compression with Neusilin® US2 generally gives harder tablets compared to that with colloidal silica.

V. Solid dispersion

Formulating poorly water soluble drugs by solid dispersion leads to a remarkable improvement in dissolution and bioavailability. Neusilin® can potentially resolve problems associated with tabletting and improve efficiency of solid dispersion.

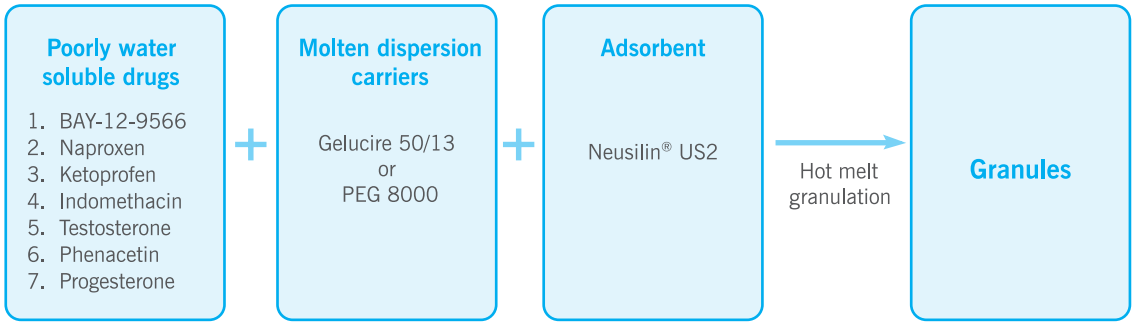
Key advantages of Neusilin® as an adsorbent

- Flowability improvement
- High quality tablets at low compression forces
- High specific surface area
- High adsorption capacity
- Higher API load
- Restriction on reversion of amorphous form to crystalline state
- Inert core material

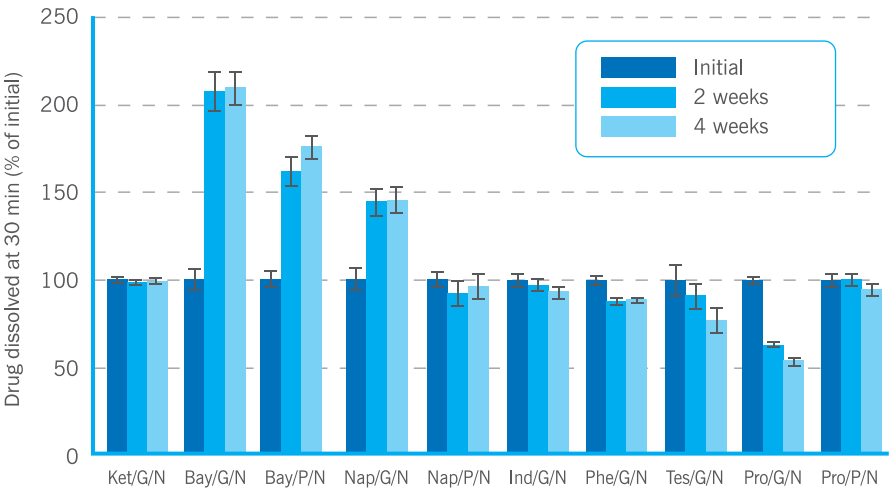
Published Examples

1) Solid dispersion granules

Gupta MK, *et al.* Hydrogen bonding with adsorbent during storage governs drug dissolution from solid-dispersion granules. Pharm Res. 2002; 19:1663-72.



Dissolution profile of solid dispersion granules



Ket: Ketoprofen
Bay: BAY-12-9566
Nap: Naproxen
Ind: Indomethacin
Phe: Phenacetin
Tes: Testosterone
Pro: Progesterone
N: Neusilin®
G: Gelucire
P: PEG 8000

Comparison of drug dissolution (after 30 min) from initial and stored solid-dispersion granules using USP Type II apparatus at 50 rpm. Data are shown for drug dissolution (% of initial) from solid-dispersion granules after storage at 40°c/75% RH (Gupta *et al*, 2002)

2) Solid SEDDS (Self Emulsifying Drug Delivery Systems) formulation

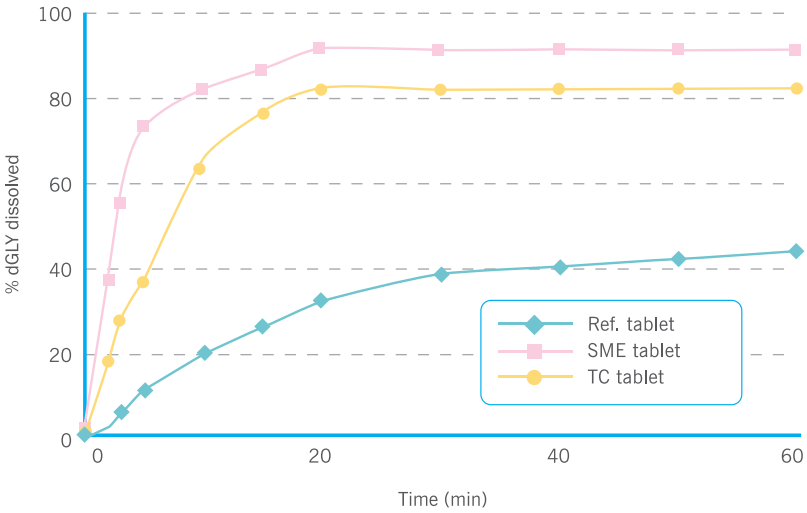
Use of Neusilin® as adsorbent carrier to convert liquid SEDDS to solid SEDDS

2)-1. Glyburide SEDDS tablets

Ref: Mura P, Valleri M, Cirri M, Mennini N. New solid self-microemulsifying systems to enhance dissolution rate of poorly water soluble drugs. Pharm Dev Technol. 2012; 17:277-84

Self Micro Emulsifying formulation was prepared by adding under continuous stirring Tween 20 and Labrafac Hydro® WL (oil phase) and then distilled water to glyburide solubilized in Transcutol®. Glyburide tablets were prepared by direct compression. The preparation with Neusilin® US2 resulted in improved flow, compact tablets and improved dissolution profile.

Dissolution profile of glyburide preparation



Glyburide (GLY) dissolution profile from the different tablet formulations (Ref. Tablet – commercial GLY formulation; SME tablet – glyburide SME formulation consisting of Labrafac Hydro® as oil phase, Tween 20 as surfactant and Transcutol® as co-surfactant; TC tablet – glyburide formulation consisting of Transcutol® (TC) paliperidone.

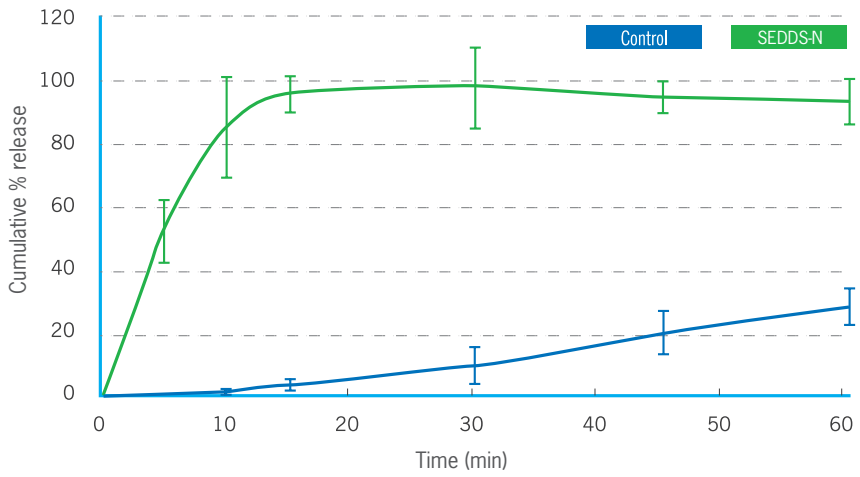
2)-2. Solid SEDDS of paliperidone

Ref: Kallakunta VR, Bandari S, Jukanti R, Veerareddy PR. Oral self emulsifying powder of lercanidipine hydrochloride: Formulation and evaluation. Powder Technology. 2012; 221:375–82.

Optimized SEDDS formulation containing oleic acid, Tween 80 and Capmul® MCM L8 was adsorbed onto Neusilin® to produce solid SEDDS (SEDDS-N). To understand the release behaviour of paliperidone from solid SEDDS and pure drug, in-vitro dissolution test was performed.

Dissolution profile of paliperidone powder

The drug release was faster and the dissolution efficiency was higher for the solid SEDDS compared to that of crystalline form.



3) Hot Melt Extrusion

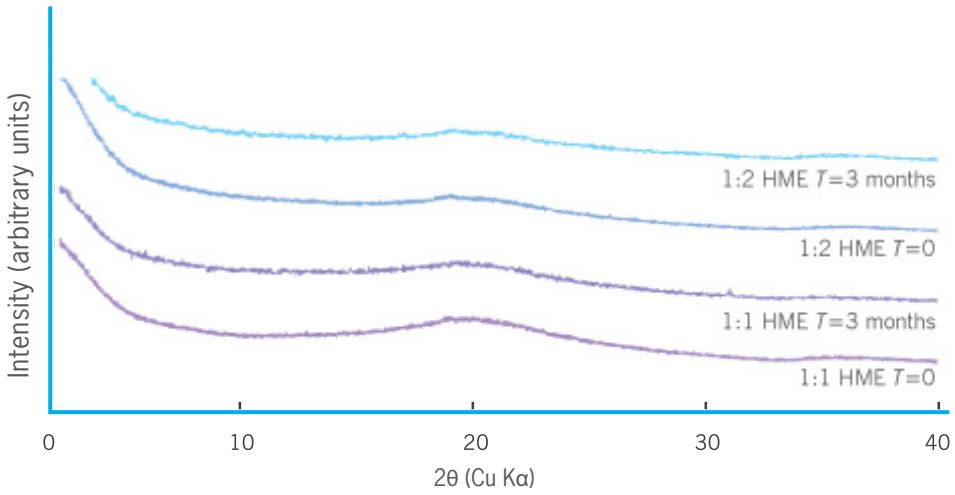
Ref: Maclean et al. Manufacturing and performance evaluation of a stable amorphous complex of an acidic drug molecule and Neusilin. J Pharm Sci. 2011; 100:3332-44.

Hot Melt Extrusion (HME) of Sulindac-Neusilin® Drug Complex

Blends of Sulindac-Neusilin® in 1:1 and 1:2 (w/w ratio) were prepared by HME at 200°C.

Physical / Chemical Stability of Sulindac-Neusilin® HME Complex

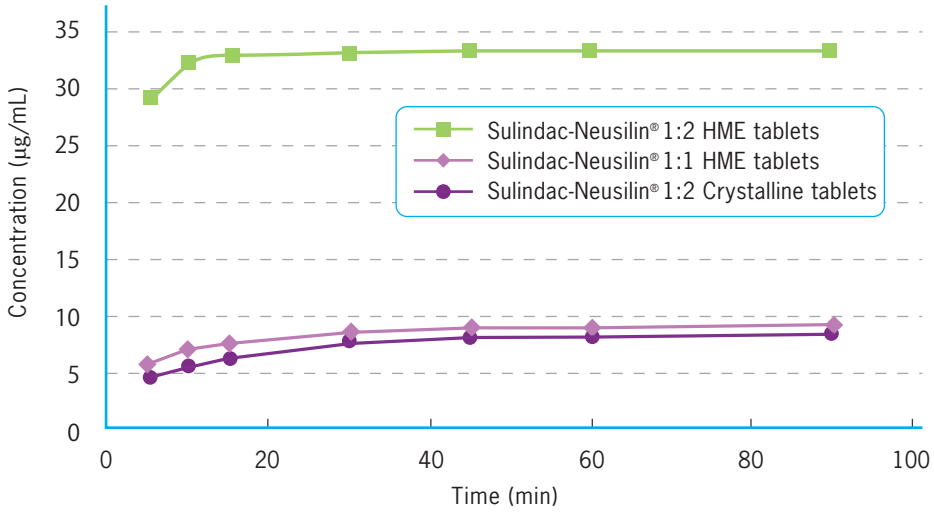
The HME samples remained amorphous after 3 months of storage at 40°C/75% RH. The samples were found to remain amorphous for more than one year at ambient conditions.



Sulindac-Neusilin® HME tablets

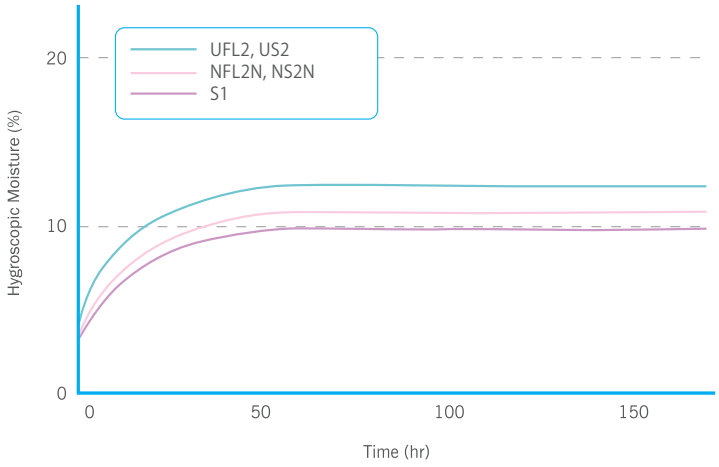
Sulindac-Neusilin® 1:2 HME tablets showed 100% release in 90 minutes as against 9% release of Sulindac-Neusilin® crystalline tablets.

Dissolution profiles of HME Sulindac-Neusilin® tablets

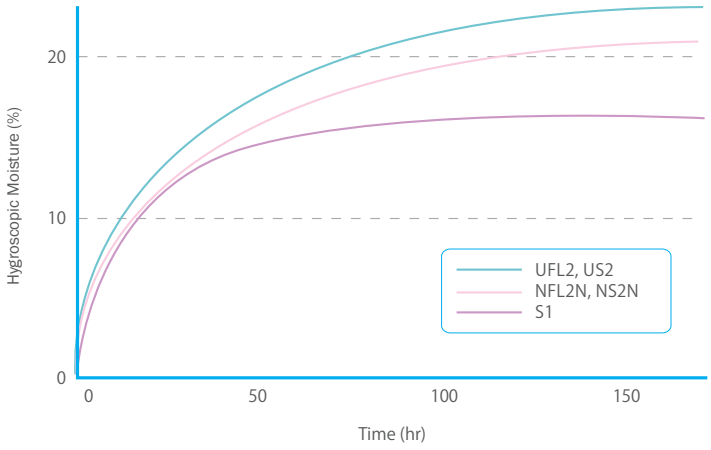


VI. Hygroscopic velocity curve of Neusilin®

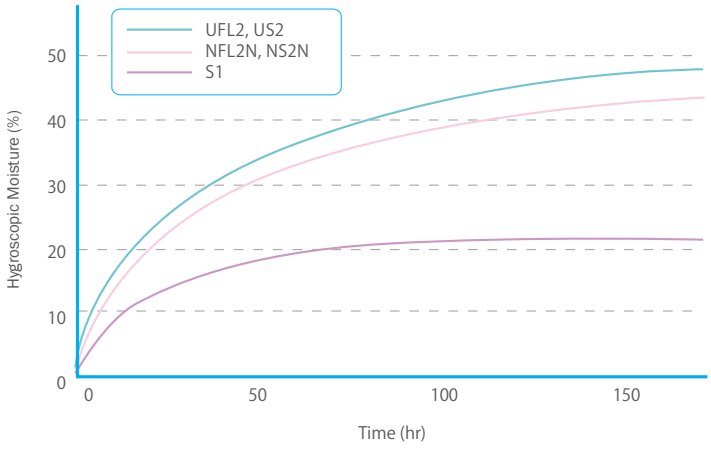
1) at 37°C, RH 53%



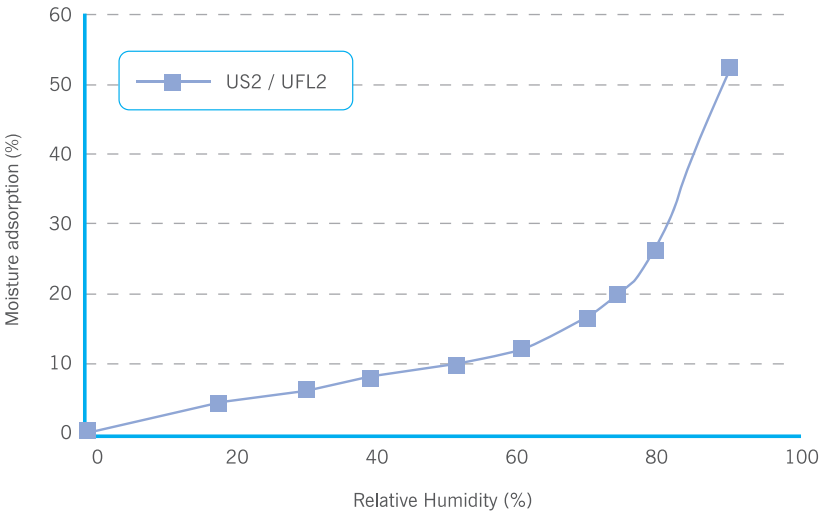
2) at 37°C, RH 75%



3) at 37°C, RH 92%

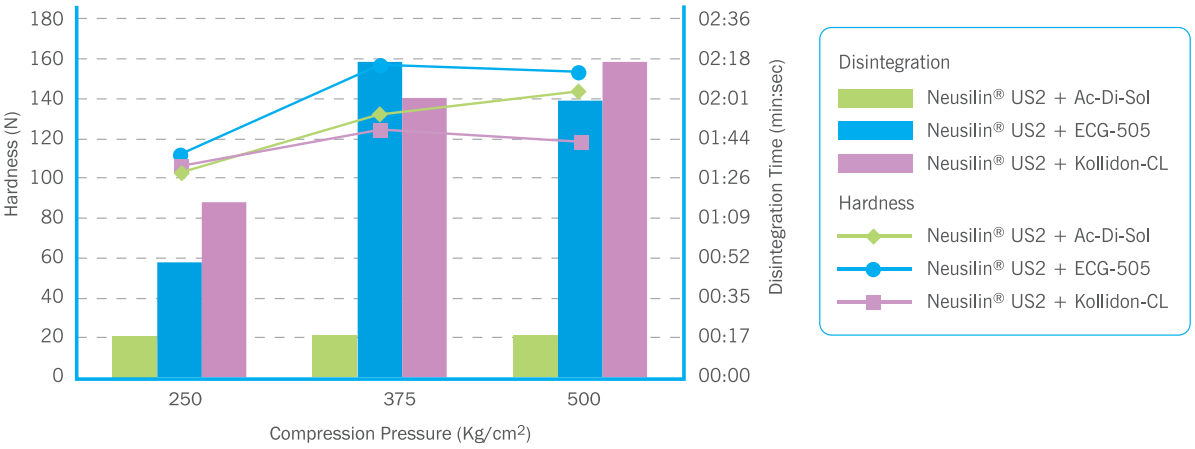


VII. Hygroscopic equilibrium curve of Neusilin®



The hygroscopic equilibrium curve of different grades of Neusilin® indicate that Neusilin® absorbs very low amout of moisture up to 70% RH.

VIII. Most compatible disintegrants



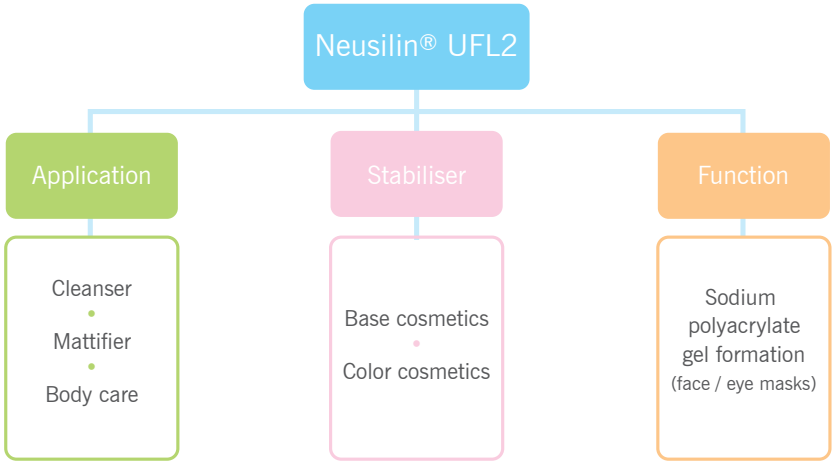
The most compatible disintegrant with Neusilin® US2 was found to be croscarmellose sodium (Ac-Di-Sol) followed by cross-linked polyvinylpyrrolidone (Kollidon-CL) and carmellose calcium (ECG-505). The characteristics (large surface area and porus nature) of US2 and the cross linking of croscarmellose sodium act synergestically allowing the tablet to swell and absorb many times of its weight in water leading to quick disintegration. Neusilin® US2 improves flowability and makes sufficiently hard tablets at low compression forces. Increase in hardness and compression pressure did not affect the disintegration time or tablet conformity when croscarmellose sodium was used as a disintegrant.
As most of the starch-type disintegrants do not go well with Neusilin® US2, croscarmellose sodium is your best choice when you choose Neusilin® US2 in your formulations.

COSMETIC APPLICATION

Unique properties of Neusilin® grade, UFL2 makes it an ideal component for cosmetic preparations. UFL2 adsorbs both oil and water up to 300% and remains flowable. It functions as an efficient carrier of volatile compounds such as fragrances and liquids giving long shelf life and lasting effect. The water activity of Neusilin® UFL2 is 0.22.

UFL2 is formulated in facial care products including lotions, eye shadow, cleansers, powders, acne and oily skin treatments and deodorants.

Neusilin® UFL2 Applications and categorized



Neusilin® UFL2: Odor adsorption

Foul Odor	Concentration / Amount Used	% Odor Eliminated
Ammonia	1,000 ppm / 100 mg 1,000 ppm / 200 mg	79.5 96.2
Trimethylamine	435 ppm / 100 mg	81.6
Hydrogen Sulfide	697 ppm / 100 mg	31.4
Isovaleric Acid	262 ppm / 20 mg	100
Acetic Acid	849.8 ppm / 100 mg	99.6

PACKAGE SIZE

	Grade	Package size
Alkaline Grades	S2	20 kg
Neutral Grades	UFL2	5 kg
	US2	10 kg

Samples are available upon request. Please contact your local distributor or sales person.

PHARMACOPOEIA AND REGULATORY INFORMATION

Neusilin® meets all the requirements of the current USP/NF and JPC. An US DMF type IV filed in 1998.

DOSAGE AND SAFETY

Neusilin® is safe with no reports of adverse reactions and is an accepted ingredient by the US Pharmacopoeia/National Formulary and Japanese Pharmaceutical Codex. Based on the usage as an excipient in various formulations in Japan, Neusilin® up to 1.05 g can be used for oral uptake per day.*[1] There are no established maximum oral intake limits specified by US-FDA.

*1) Encyclopedia of Pharmaceutical Additives, Japan, 2005

STABILITY

Neusilin® is a stable inorganic compound and meets JPC and NF specifications. The shelf life of Neusilin® is 3 years from the date of manufacture.

CONCLUSIONS

Neusilin® is a totally synthetic magnesium aluminometasilicate with exceptional excipient properties to improve API delivery and quality of oral solid-dosage form pharmaceuticals. Neusilin® is available in various grades and the two different pH options make it a versatile excipient for a wide-variety of applications.
With over 500 pharmaceutical preparations and a market presence of over 60 years in Japan, Neusilin® is well accepted by the formulators world-wide as an aid for formulations containing antibiotics, oily actives, poorly water soluble APIs, herbal mixtures, vitamins, etc. Neusilin® is also used as carrier for preparation of solid dispersion and self-micro emulsifying drug development systems.

Neusilin® has been demonstrated as an excellent adsorbent carrier for solid dispersion preparation via hot melt granulation, Self Micro-Emulsifying Drug Delivery Systems (SMEDDS) for BCS class II drugs such as meloxicam, naproxen, ketoprofen, glyburide and other highly permeable but poorly water soluble drugs. The most exciting use of Neusilin® is in Hot Melt Extrusion (HME). Neusilin® allows preparation of stable amorphous drug complex without any addition of polymers, waxes or plasticizers normally associated with HME. The samples can be recovered as amorphous powder and converted to highly stable tablets through direct compression.

REFERENCES

1. Gumaste S, Pawlak S, Dalrymple D, Nider C, Trombetta L, Serajuddin A. Development of Solid SEDDS, IV: Effect of Adsorbed Lipid and Surfactant on Tableting Properties and Surface Structures of Different Silicates. Pharma Res. 2013; 1-16.
2. Gumaste S, Dalrymple D, Serajuddin A. Development of Solid SEDDS, V: Compaction and Drug Release Properties of Tablets Prepared by Adsorbing Lipid-Based Formulations onto Neusilin® US2. Pharma Res. 2013; 1-14.
3. Lou H, Liu M, Wang L, Mishra S, Qu W, Johnson J, Brunson E and Almoazen H. Development of a Mini-Tablet of Co-Grinded Prednisone–Neusilin Complex for Pediatric Use. AAPS PharmSciTech. 2013; 1-9.
4. Khanfar M, Fares M, Salem M and Qandil A. Mesoporous silica based macromolecules for dissolution enhancement of Irbesartan drug using pre-adjusted pH method. Microporous and Mesoporous Materials. 2013; 173: 22-28.
5. Qian K, Bogner R. Application of Mesoporous Silicon Dioxide and Silicate in Oral Amorphous Drug Delivery Systems. J Pharma Sci. 2012; 101: 444-463
6. Sohn Y, Lee SY, Lee GH, Na YJ, Kim SY, Seong I, Lee BJ, Kuh HJ, Lee J. Development of self-microemulsifying bilayer tablets for pH-independent fast release of candesartan cilexetil. Pharmazie. 2012; 67:917-24.
7. Cha KH, Cho KJ, Kim MS, Kim JS, Park HJ, Park J, Cho W, Park JS, Hwang SJ. Enhancement of the dissolution rate and bioavailability of fenofibrate by a melt-adsorption method using supercritical carbon dioxide. Int J Nanomedicine. 2012; 7:5565-75.
8. Beg S, Swain S, Singh HP, Patra ChN, Rao MB. Development, optimization, and characterization of solid self-nanoemulsifying drug delivery systems of valsartan using porous carriers. AAPS PharmSciTech. 2012; 13:1416-27.
9. Alam MA, Ali R, Al-Jenoobi FI, Al-Mohizea AM. Solid dispersions: a strategy for poorly aqueous soluble drugs and technology updates. Expert Opin Drug Deliv. 2012; 9:1419-40.
10. Janga KY, Jukanti R, Sunkavalli S, Velpula A, Bandari S, Kandadi P, Veerareddy PR. In situ absorption and relative bioavailability studies of zaleplon loaded self-nanoemulsifying powders. J Microencapsul. 2012.
11. Kallakunta VR, Bandari S, Jukanti R, Veerareddy PR. Oral self emulsifying powder of lercanidipine hydrochloride: Formulation and evaluation. Powder Technology. 2012; 221:375–82.
12. Kanuganti S, Jukanti R, Veerareddy PR, Bandari S. Paliperidone-Loaded Self-Emulsifying Drug Delivery Systems (SEDDS) for Improved Oral Delivery. J Disp Sci Tech. 2012; 33:506-15.
13. Hentzschel CM, Alnaief M, Smirnova I, Sakmann A, Leopold CS. Enhancement of griseofulvin release from liquisolid compacts. Eur J Pharm Biopharm. 2012; 80:130-5.
14. Mura P, Valleri M, Cirri M, Mennini N. New solid self-microemulsifying systems to enhance dissolution rate of poorly water soluble drugs. Pharm Dev Technol. 2012; 17:277-84.
15. Hentzschel CM, Sakmann A, Leopold CS. Suitability of various excipients as carrier and coating materials for liquisolid compacts. Drug Dev Ind Pharm. 2011; 37:1200-7.
16. Maclean J, Medina C, Daurio D, Alvarez-Nunez F, Jona J, Munson E, Nagapudi K. Manufacturing and performance evaluation of a stable amorphous complex of an acidic drug molecule and Neusilin. J Pharm Sci. 2011; 100:3332-44.
17. Boldhane SP, Kuchekar BS. Development and optimization of metoprolol succinate gastroretentive drug delivery system. Acta Pharm. 2010; 60:415-25.
18. Chakraborty S, Shukla D, Vuddanda PR, Mishra B, Singh S. Utilization of adsorption technique in the development of oral delivery system of lipid based nanoparticles. Colloids Surf B Biointerfaces. 2010; 81:563-9.
19. Hailu SA, Bogner RH. Complex effects of drug/silicate ratio, solid-state equivalent pH, and moisture on chemical stability of amorphous quinapril hydrochloride coground with silicates. J Pharm Sci. 2010.
20. Hailu SA, Bogner RH. Solid-state surface acidity and pH-stability profiles of amorphous quinapril hydrochloride and silicate formulations. J Pharm Sci. 2010; 99:2786-99.
21. Krupa A, Majda D, Jachowicz R, Mozgawa W. Solid-state interaction of ibuprofen and Neusilin US2. Thermochim Acta. 2010; 509:12-7.
22. Sander C, Holm P. Porous magnesium aluminometasilicate tablets as carrier of a cyclosporine self-emulsifying formulation. AAPS PharmSciTech. 2009; 10:1388-95.
23. Vadher AH, Parikh JR, Parikh RH, Solanki AB. Preparation and characterization of co-grinded mixtures of aceclofenac and Neusilin US2 for dissolution enhancement of aceclofenac. AAPS PharmSciTech. 2009; 10:606-14.
24. Hailu SA, Bogner RH. Effect of the pH grade of silicates on chemical stability of coground amorphous quinapril hydrochloride and its stabilization using pH-modifiers. J Pharm Sci. 2009; 98:3358-72.
25. 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.
26. Asai Y, Nagira S, Owaki T. Application of Isomalt on manufacturing of tablets using direct compression method. Pharm Tech Japan. 2009; 25:79-83.
27. Agarwal V, Siddiqui A, Ali H, Nazzal S. Dissolution and powder flow characterization of solid self-emulsified drug delivery system (SEDDS). Int J Pharm. 2009; 366:44-52.
28. Ruhland T, Nielsen SD, Holm P, Christensen CH. Nanoporous magnesium aluminometasilicate tablets for precise, controlled, and continuous dosing of chemical reagents and catalysts: applications in parallel solution-phase synthesis. J Comb Chem. 2007; 9:301-5.
29. Bahl D, Bogner RH. Amorphization of indomethacin by co-grinding with Neusilin US2: amorphization kinetics, physical stability and mechanism. Pharm Res. 2006; 23:2317-25.
30. Ito Y, Arai H, Uchino K, Iwasaki K, Shibata N, Takada K. Effect of adsorbents on the adsorption of lansoprazole with surfactant. Int J Pharm. 2005; 289:69-77.
31. Gupta MK, Vanwert A, Bogner RH. Formation of physically stable amorphous drugs by milling with Neusilin. J Pharm Sci. 2003; 92:536-51.
32. Gupta MK, Tseng YC, Goldman D, Bogner RH. Hydrogen bonding with adsorbent during storage governs drug dissolution from solid-dispersion granules. Pharm Res. 2002; 19:1663-72.
33. Gupta MK, Bogner RH, Goldman D, Tseng YC. Mechanism for further enhancement in drug dissolution from solid-dispersion granules upon storage. Pharm Dev Technol. 2002; 7:103-12.
34. Gupta MK, Goldman D, Bogner RH, Tseng YC. Enhanced drug dissolution and bulk properties of solid-dispersions granulated with a surface adsorbent. Pharm Dev Technol. 2001; 6:563-72.
35. Konno T, Kinuno K, Physical and chemical changes of medicinal in mixtures with adsorbents in the solid state. II. Application of reduced pressure treatment for the improvement of dissolution of flufenamic acid. Chem Pharm Bull (Tokyo). 1989; 37:2481-4.
36. Konno T, Kinuno K, Kataoka K. Physical and chemical changes of medicinal in mixtures with adsorbents in the solid state. I. Effect of vapor pressure of the medicinal on changes in crystalline properties. Chem Pharm Bull (Tokyo). 1986; 34:301-7.

Neusilin®

www.neusilin.com

Fuji Chemical Industries Co., Ltd.

International Business Department: The Front Tower Shiba Koen 12th Floor, 2-6-3 Shiba Koen, Minato-ku, Tokyo 105-0011 JAPAN
Tel: +81-3-3437-2353 Fax: +81-3-3437-2348

Headquarters and Plant: 55 Yokohoonji, Kamiichi-machi, Nakaniikawa-gun, Toyama 930-0397JAPAN
Tel: +81-76-472-5549 Fax: +81-76-472-5417

www.fujichemical.co.jp **pharma@fujichemical.co.jp**

05.2013