Productgroup overview.

Disintegrants.

DMV International
The ingredients of success

DMV International is a leading manufacturer and supplier of excipients for a wide range of pharmaceutical applications. Our commitment is to supply highest quality products, which comply with the latest cGMP requirements and exceed all regional pharmacopoeias. Our technical sales support ensures that customers receive full advantage of the latest excipient technologies.

Superdisintegrants

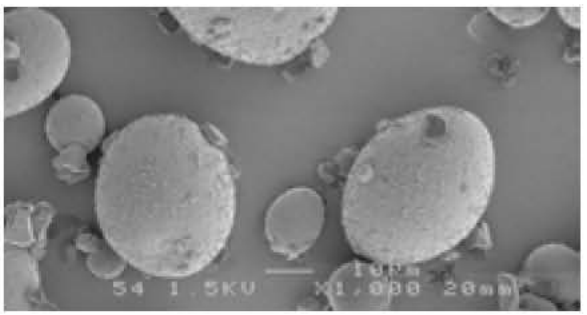
For tablets and capsules which need rapid disintegration, the inclusion of the right disintegrant is a prerequisite for optimal bioavailability. Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieved by decreasing the disintegration time which results in an increase in the drug dissolution rate. Super-disintegrants are widely used in direct compression and wet granulation applications. In order to closely match the functionality requirements, DMV produces two superdisintegrants, sodium starch glycolate (Primojel®) and crosscarmellose sodium (Primellose®), which show outstanding disintegration characteristics for tablets and capsules prepared by direct compression and wet granulation.

Your choice of disintegrants

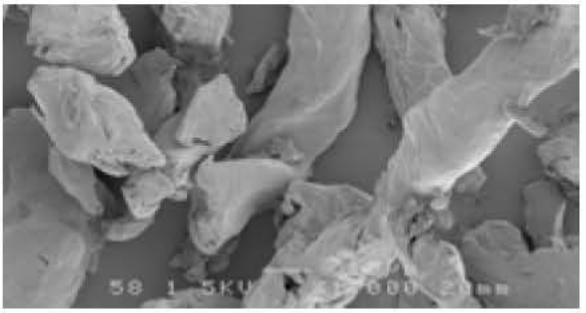
Why should you use Primojel® or Primellose®? Both products are hydrophilic and practically insoluble, which allows increased disintegration of solid dosage forms. Only superdisintegrants are effective with such as small concentration as 2-6%, while disintegrants such as starches require dosage of about 20%. Growing attention for the need of cost control in pharmaceutical industry makes the use of superdisintegrants such as Primojel® and Primellose® even more attractive. The comparatively low concentrations of the superdisintegrants can help to reduce overall tablet size, or allow for inclusion of higher levels of compressible fillers (see DMV range of DC lactose).

Technical support

DMV International supports you with your technical problems. Whether it is wet granulation or direct compression, our global net work of sales and distributorship enables us to be there for your problems.



SEM of Primojel®



SEM of Primellose®

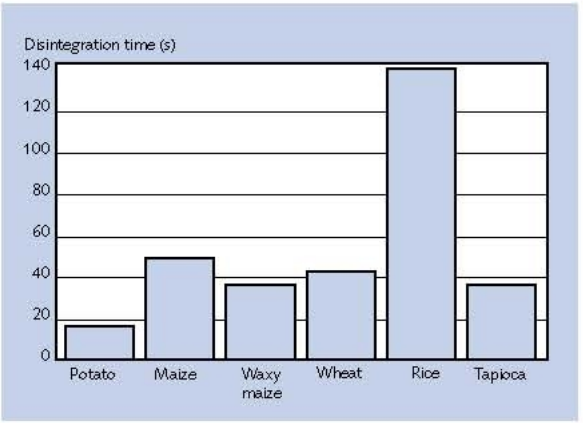


Chart 1. Disintegration time of a-lactose monohydrate tablets, containing 4% of different experimental sodium starch glycolates, respectively, as a disintegrant

Primojel® Ph. Eur., USP/NF, JPE

Primojel® is sodium starch glycolate, Ph. Eur., USP/NF, JPE, produced by cross-linking and carboxy-methylation of potato starch. The starch source, degree of cross-linking and degree of substitution are optimized in order to maintain maximum disintegration efficiency. Chart 1 shows that potato starch, the source material for Primojel, is the preferred type of starch for sodium starch glycolate.[1]

Disintegration mechanism
Primojel® takes up more than 20 times its own weight of water. The resulting high swelling capacity combined with high water penetration account for its high disintegration rate and efficiency.[2] The product is suitable for a variety of tablet and capsule formulations.

Reduction of negative effect of lubricants
The lubricant film around tablet ingredient particles, which is formed when mixing tablet ingredients with magnesium stearate is known to retard water penetration into tablet pores. When the tablet contains Primojel®, water is absorbed by Primojel® particles on the outside of the tablet, which is hardly affected by the presence of lubricant film. The outer shell of the tablet will be disrupted by the swelling of Primojel® and water can reach the underlying disintegrant particles. The tablet will thus progressively be disrupted from the outside of the tablet, resulting in a fast and complete disintegration.

Drug dissolution rate
After the fast disintegration of tablets or capsules containing Primojel®, the active ingredient will dissolve rapidly and enhance in vivo drug absorption rate as a result of the hydrophilic nature of Primojel® and of its counteracting effect on lubricants.[5]

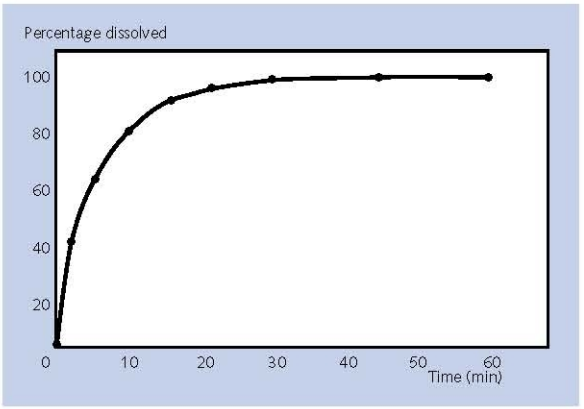
References

1. Bolhuis G.K., Van Kamp H.V., Lerk C.F., Gielen J.W., Arends A.W. and Stuut G.J. Effect of variation of degree of substitution, crosslinking and purity on the disintegration efficiency of sodium starch glycolate, Acta Pharm. Technol. 30, 24 (1984)
2. Van Kamp H.V., Bolhuis G.K., Lerk C.F. and Lie-A-Huen L. The role of water uptake on tablet disintegration. Design of an improved method for penetrationmeasurements. Phar. Acta Helv. 61, 22 (1986)
3. Bolhuis G.K., Smallenbroek A.J. and Lerk C.F. Interaction of tablet disintegrants and magnesium stearate during mixing I: Effect on tablet disintegration. J.Pharm.Sci. 70, 1328 (1981)
4. Bolhuis G.K., Van Kamp H.V., Lerk C.F. and Sessink G.M. On the mechanism of action of modern disintegrants. Acta Pharm. Technol. 28, 111 (1982)
5. Lerk C.F., Bolhuis G.K., Smallenbroek A.J. and Zuurman K. Interaction of tablet disintegrants and magnesium stearate during mixing II. Effect on dissolution rate. Pharm. Acta Helv. 57, 282 (1982)

Tablet formulation example with Primojel® for direct compression

Phenobarbitone tablets 50mg	
Phenobarbitone	25.0%
Microcrystalline cellulose	22.5%
Pharmatose® 100M	49.3%
Primojel®	2.5%
Colloidal silica	0.2%
Magnesium stearate	0.5%
Variation coefficient of tablet weight	0.6%
Friability	0.1%
Crushing strength	78N
Disintegration time (no disk)	20S

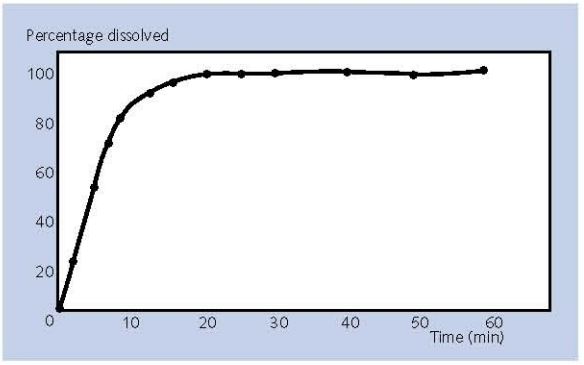
9mm, 200mg tablets



Tablet formulation example with Primojel® for wet granulation

Hydrochlorothiazide tablets 100mg	
Hydrochlorothiazide	20%
Pharmatose® 200M	75%
Primojel®	4%
PVP	0.5%
Magnesium stearate	0.5%
Crushing strength	65N
Disintegration time (no disk)	32S

13mm, 500mg tablets



Primellose® Ph. Eur., USP/NF, JPE

Primellose® is croscarmellose sodium, Ph. Eur., USP/NF, JPE, a cross-linked carboxymethyl cellulose sodium. Cross-linking reduces its water solubility and permits the material to swell and take up many times its weight in water without losing its fibrous integrity.

Disintegration mechanism
The combination of a rapid water penetration into tablets via the hydrophilic, fibrous disintegrant particles, and the subsequent development of a disintegration force are responsible for the excellent disintegration efficiency of croscarmellose sodium Primellose®.

Reduction of negative effect of lubricants
The high swelling capacity of Primellose® can counteract the deteriorating effect of hydrophobic lubricants on tablet disintegration, such as magnesium stearate. The water absorption of Primellose® destroys the magnesium stearate film around the particle and in tablet pores. When the swelling of Primellose® disrupts the outer shelf of the tablet, water can reach underlying disintegrant particles.

The tablet is then disrupted from the outside, resulting in a complete and fast disintegration.

Drug dissolution rate
Primellose® improves the drug dissolution rate from capsules and tablets prepared by both direct compression or by wet granulation. The hydrophilic nature of Primellose® helps the active ingredient dissolve quickly.

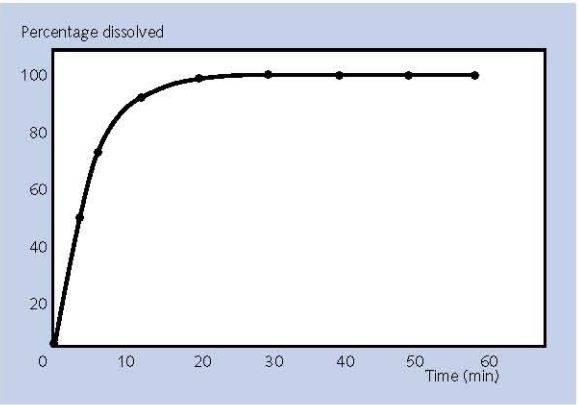
References

1. Carmella C., Colombo P., Conte U., Ferrari F., LaManna A., Van Kamp H.V. and Bolhuis G.K. Water uptake and disintegration force measurements: towards a general understanding of disintegration mechanisms. Drug Dev. Ind. Pharm. 12: 1749 (1986)
2. Proost J.H., Bolhuis G.K. and Lerk C.F. The effect of the swelling capacity of disintegrants on the invitro and in vivo availability of diazepam tablets containing magnesium stearate as a lubricant. Int. J. Pharm. 13, 287 (1983)
3. Van Kamp H.V., Bolhuis G.K. and Lerk C.F. Improvement by superdisintegrants of the properties of tablets containing lactose, prepared by wet granulation. Pharm. Weekblad Sci, 165 (1983)
4. F. Ferrari, S. Rossi, M.C. Bonferoni, S. Canevari, L. Dobetti and C. Carmella. The influence of product brand and batch-to-batch variability on super-disintegrant performance. S.T.P. Pharma Science 10. (6) 459-465 (2000)

Tablet formulation example with Primellose® for direct compression

Oxazepam tablets 10mg	
Oxazepam	4.0%
Pharmatose® DCL 11	45.4%
Pharmatose® 100M	45.4%
Primellose®	4.0%
Collodial silica	0.2%
Magnesium stearate	1.0%
Variation coefficient of tablet weight	0.95%
Crushing strength	70N
Disintegration time (no disk)	25S

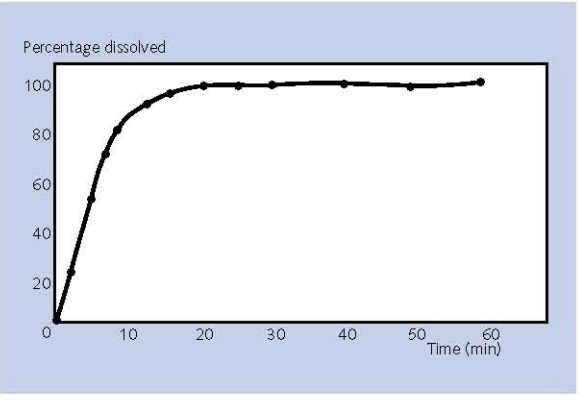
9mm, 200mg tablets



Tablet formulation example with Primellose® for wet granulation

Hydrochlorothiazide tablets 100mg	
Hydrochlorothiazide	20%
Pharmatose® 200M	77%
Primellose®	2.0%
PVP	0.5%
Magnesium stearate	0.5%
Crushing strength	60N
Disintegration time (no disk)	32S

13mm, 500mg tablets



Specifications

Primojel®		Primellose®	
Description	Sodium starch glycolate Ph.Eur, USP/NF, JPE (type A)	Description	Croscarmellose sodium Ph.Eur, USP/NF, JPE
Appearance	Fine, white powder	Appearance	Fine, white powder
Loss on drying	≤ 6.0%	Loss on drying	≤ 7.0%
pH	5.5-7.5	pH	5.0-7.0
Sieve Analysis	≤ 50mg/g on 63 micrometers	Sodium glycolate content and Sodium chloride content	≤ 0.5%
Sodium content (chemically linked)	2.8-4.2%	Water soluble material	1.0%-10.0%
Sodium glycolate content	≤ 2.0%	Settling volume	10-30ml
Sodium chloride content	≤ 5.5%	Degree of substitution	0.60-0.85
Alcohol soluble material	≤ 15.0%	Sulphated ash	14.0%-28.0%
Iron (Fe)	≤ 0.002%		
Heavy metals	≤ 0.002%	Heavy metals	≤ 0.001%
Organic volatile impurities as mentioned in USP/NF	absent	Organic volatile impurities as mentioned in USP/NF	absent
Total aerobic mesophilic count	≤ 100CFU/g	Total aerobic mesophilic count	≤ 100CFU/g
Yeasts	≤ 50CFU/g	Yeasts	≤ 20CFU/g
Moulds	≤ 50CFU/g	Moulds	≤ 20CFU/g
Candida albicans (1g)	negative	Candida albicans (1g)	negative
Pseudomonas aeruginosa (10g)	negative	Pseudomonas aeruginosa (10g)	negative
Staphylococcus aureus (10g)	negative	Staphylococcus aureus (10g)	negative
Escherichia coli (10g)	negative	Escherichia coli (10g)	negative
Salmonella (10g)	negative	Salmonella (10g)	negative

Pharmacopoeia
Primojel® and Primellose® comply with the latest editions of the Ph.Eur., USP/NF and JPE.

Drug Master File Number
Primojel®: No. 3015, submitted August 24, 1977.
Primellose®: No. 9662, submitted April 21, 1992.

Packaging
Primojel®: packed in a 50kg HDPE (high-density polyethylene) drum with a polyethylene inner bag.
Primellose®: packed in a 25kg fiber drum with a polyethylene inner bag.

Storage, stability and shelf life
The products should be stored under normal warehouse conditions, which are recommended temperature averaging between 5 and 25°C and a relative humidity of max. 70%. Under these conditions originally sealed packing can be stored for at least 5 years.

For further information please visit our website www.dmv-international-pharma.com or contact us on pharma@dmv-international.com

DMV International GmbH

NCB-laan 80
P.O. Box 13
5460 BA Veghel
The Netherlands

Phone: +31 413 372 222
Fax: +31 413 372 930
pharma@dmv-international.com
www.dmv-international-pharma.com

UK/Ireland Office
P.O. Box 11
Teddington Middlesex
TW 118YG
United Kingdom

Phone: + 44 20 8943 5220
Fax: + 44 20 8943 5231
nigel.roberts@dmv-international.com

Scandinavia Office
Hessvej 3
DK-7120 Vejle Ö
Denmark

Phone: + 45 7581 5533
Fax: + 45 7581 5677
henning.thomsen@dmv-international.com

Asia Pacific Office
1002, Bank of America Tower
12 Harcourt Road, Central
Hong Kong

Phone: + 852 2525 2145
Fax: + 852 2810 4543
desk@dmvfareast.com.hk

Japan Office
Kudan Vigas Bldg. 3F
1-10-9 Kudan-Kita, Chiyoda-ku
Tokyo 102-0073, Japan

Phone: + 81 3 5276 0441
Fax: + 81 3 5276 0445
sales@dmv-japan.com

North America Office
Customer Service
40196 State Highway 10 Delhi, NY 13753
USA

Phone: + 1 607 746 0109
Fax: + 1 607 746 7610
pharma@dmv-international.com

South America office
Av. Federico Lacroze 2201, Piso 18
C1426CPH
Buenos Aires
Argentina

Phone: + 54 11 4774 3782
Fax: + 54 11 4776 4408
baijens@dmvsamerica.com.ar

DMV International
The ingredients of success

Represented In India By :
Y. SAINATHAN,
3/20, Tardeo Air Conditioned Market,
5, Tardeo, Mumbai - 400 034.
Tel. : 91-22-2351 0937 / 2351 3014
Fax : 91-22-2352 0939
E-mail : ysnth@vsnl.com

Warranty