

Matrix Effects on the Performance of Disintegrants (I) – Hydrophobic Tablets

Abstract

Superdisintegrants are categorized by their mechanism of action such as wicking, swelling or shape recovery. In this study, the performance of disintegrants from each of these groups was tested in an insoluble, hydrophobic tablet formulation. The matrix' hydrophobicity led to strong deviations from the expected behaviors for insoluble tablets without distinct hydrophobicity. It is noteworthy that the differences only became obvious at sub-optimal, low dosage of the superdisintegrants. At the recommended standard use level, all formulations showed rapid disintegration.

Introduction

Recommendations for the selection of disintegrants are usually based on the solubility of the tablet matrix and the active ingredient. Wicking disintegrants, such as croscarmellose sodium (CCS), are commonly recommended for soluble matrices. Wicking enables fast distribution of water throughout the tablet matrix, thus leading to rapid dissolution of the soluble matrix components. Sodium starch glycolate (SSG) and other swelling-type disintegrants are often selected for insoluble matrices. In this case, the swelling potential of the disintegrant is utilized to mechanically disrupt the structure of the tablet. Crospovidone (PVPP) is considered a universally suitable disintegrant, exhibiting a combination of the three mechanisms mentioned above. In addition to being insoluble, certain APIs may display a high degree of hydrophobicity, thus affecting the wettability of the entire tablet. The aim of this study was to investigate into the effect of matrix hydrophobicity on the performance of different types of superdisintegrants.

Materials and Methods

The composition of the test matrix is shown in Table 1. **LUBRITAB®** (hydrogenated cotton-seed oil) was used as a highly hydrophobic model compound. **VIVASOL® CCS**, **EXPLATAB® SSG**, and **VIVAPHARM® PVPP XL** were used as superdisintegrants. **PRUV®** sodium stearyl fumarate (SSF) served as a lubricant.

- Tablets were compressed at four different compaction forces and stored for 1,7,14, and 28 days at 40 °C/75 % r.h. prior to testing the disintegration time. Water as well as pH 1 and pH 6.8 buffers were used for disintegration testing.

VIVAPUR® MCC (Insoluble Binder)	17 or 20 %
EMCOMPRESS® DCP (Insoluble Filler)	68 %
LUBRITAB® , Hydrogenated Cottonseed Oil (Hydrophobic Model Compound)	10 %
PRUV® SSF (Lubricant)	1 %
Disintegrants VIVASOL® CCS EXPLATAB® SSG VIVAPHARM® PVPP XL	1 or 4 %

Tab. 1 Tablet Matrix

Results

As a first step, the disintegrants were incorporated at a commonly used level of 4 %. The resulting disintegration times were recorded in the format shown in Table 2.

		Disintegration Times in seconds			
		1	7	14	28
Compaction Force [kN]	20	21	46	55	68
	15	27	38	40	57
	10	19	32	53	40
	5	19	28	17	36
		Storage Duration [days]			

Tab. 2 Format for Data Collection

Figure 1 summarizes the findings of the 4 % trials for all disintegrants and media used. Irrespective of the type of superdisintegrant and test medium, all disintegration times remained under 120 seconds. In order to obtain a clearer picture of the potential differences, more discriminating conditions were created by reducing the superdisintegrant level to 1 %. Figure 2 displays the corresponding results. As opposed to the first set of experiments, clear trends now became apparent:

- Interestingly, **VIVASOL® CCS** remained almost unaffected by compaction force, storage duration and media pH.
- EXPLATAB® SSG**, by contrast, showed slightly increased disintegration times in pH 1 upon storage.
- VIVAPHARM® PVPP** at 1 % exhibited prolonged disintegration in all media.

Results & Discussion

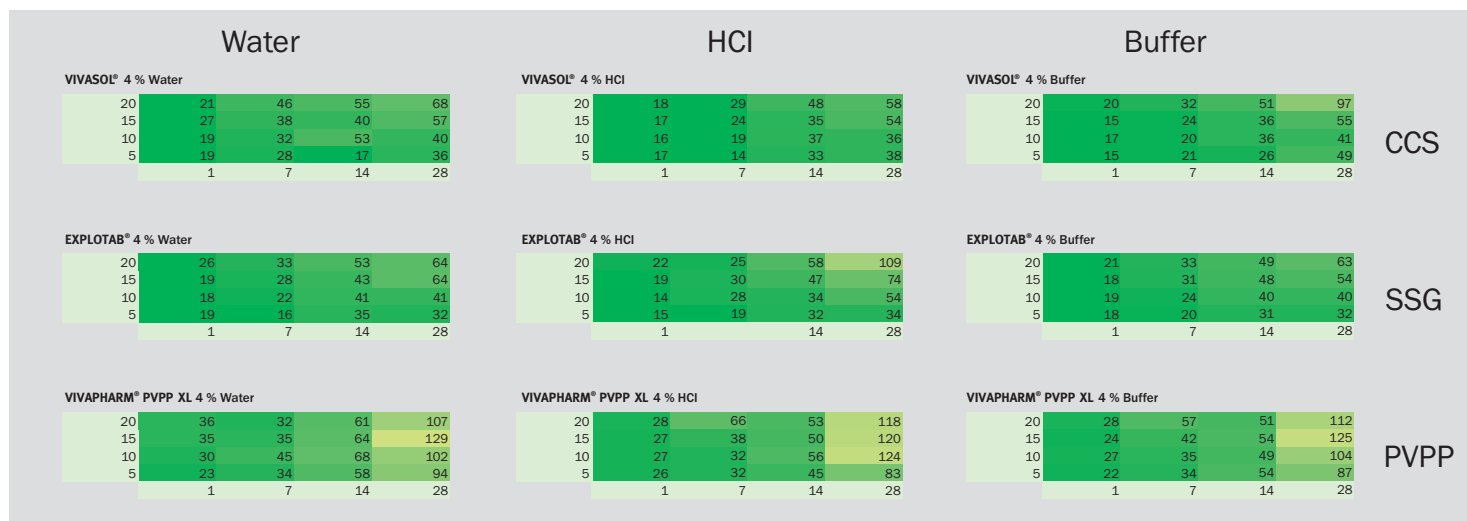


Fig. 1 Disintegration Times for 4 % Disintegrant Concentration

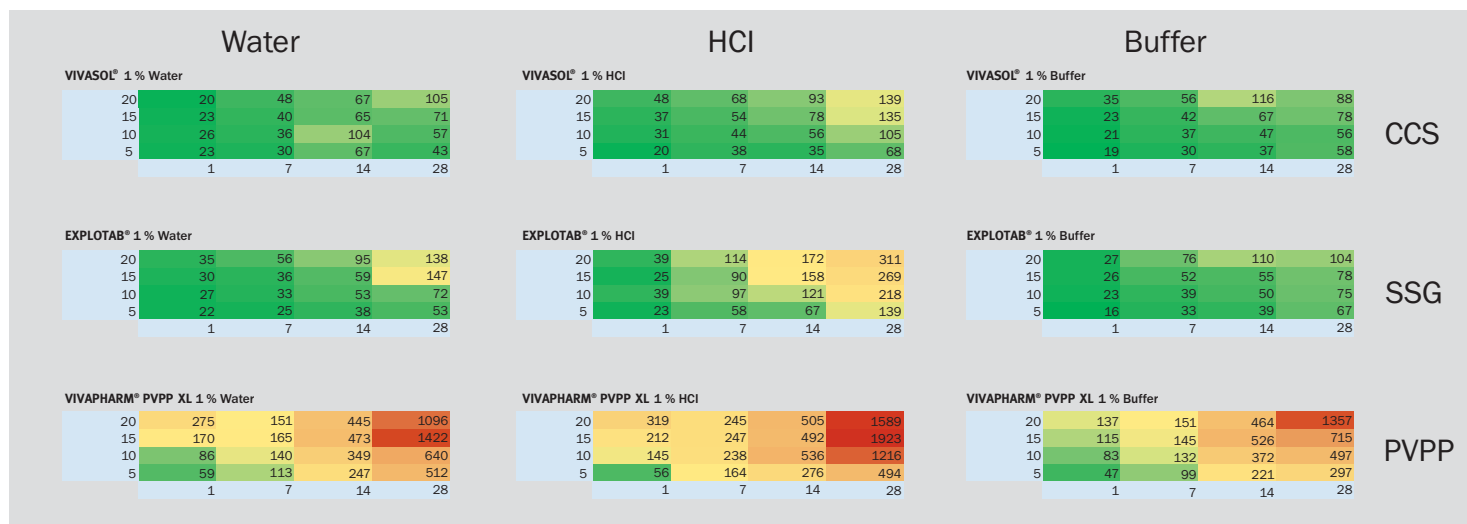
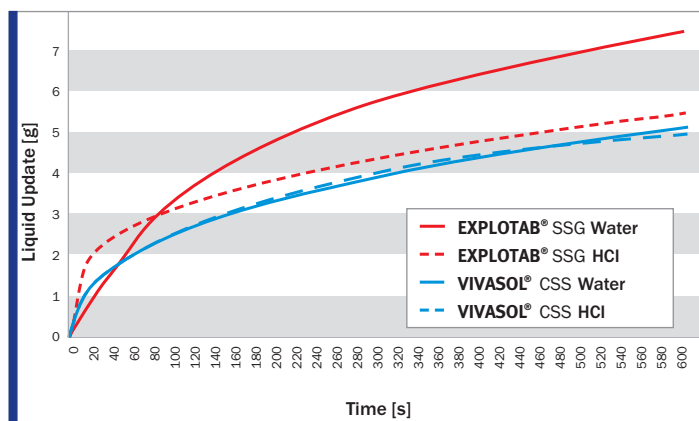


Fig. 2 Disintegration Times for 1 % Disintegrant Concentration



Discussion

Superdisintegrants do not follow a sole mechanism, but rather show a mix of the three main behaviors, namely wicking, swelling and shape recovery. Nonetheless, each type of super-disintegrant has its prevailing mechanism. For PVPP, the disintegration action is mainly based on a fast, but relatively short-ranged shape recovery. It exhibits only moderate swelling and wicking. In case of the hydrophobic, plastically deforming test matrix, 1 % of PVPP was apparently not sufficient for rapid disintegration because of low water ingress and because of the plastic matrix yielding to the short-range expansion of the superdisintegrant. CCS and SSG both possess carboxyl groups, which lose part of their water binding capacity at low pH. Reduced water binding leads to reduced swelling. Hence, SSG is less efficient at pH 1 than in water or at pH 6.8 respectively. Wicking, being CCS's predominant mechanism is less affected by pH, as shown in Graph 1.



Graph 1 Medium Uptake of Disintegrant Powder (100 %)

Summary

The expected behaviors of the three super-disintegrants in an insoluble matrix would have suggested the following ranking of suitability: SSG>PVPP>CCS.

In addition, a loss in efficiency was expected for SSG and CCS at low pH. The actually observed ranking, however, was CCS>SSG>PVPP. Only SSG lost some activity at pH 1, whereas CCS maintained its disintegration power.

Conclusion

At the recommended use level of 4 %, all superdisintegrants tested showed very fast disintegration in all test media.

The tablets' hydrophobicity presented an obstacle to fast water penetration of the tablets. The water-dependent swelling of SSG could therefore not be fully utilized.

The strong wicking effect of CCS helped to overcome the tablets' hydrophobicity and therefore enabled rapid and pH-independent disintegration.

The study demonstrated, that not only matrix solubility but also its affinity to water should be considered for disintegrant selection.

For very hydrophobic tablets, wicking disintegrants, such as **VIVASOL® CCS**, appear to be the best choice.

For further information on disintegration mechanism, please refer to our Technical Information "The Effect of Humidity on Tablet Surfaces Containing Different Types of Superdisintegrants".

To learn more, visit www.jrspharma.com

Disclaimer:

The information provided in this brochure is based on thorough research and is believed to be completely reliable. Application suggestions are given to assist our customers, but are for guidance only. Circumstances in which our material is used vary and are beyond our control. Therefore, we cannot assume any responsibility for risks or liabilities, which may result from the use of this technical advice.

The Global Excipient Maker

Global Network

GMP Manufacturing and Service Sites

- Excipients
- Coatings
- Biopharma Services
- JRS Sales Companies (Additionally, dedicated representatives in almost every country.)
- Technical Competence Centers
- Application Labs



HIGH FUNCTIONALITY EXCIPIENTS

- PROSOLV® SMCC**
Silicified Microcrystalline Cellulose
- PROSOLV® EASYtab SP**
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Sodium Starch Glycolate, Sodium Stearyl Fumarate
- PROSOLV® EASYtab NUTRA**
All-in-one Composite for Nutraceutical Applications
- PROSOLV® ODT G2**
Microcrystalline Cellulose, Colloidal Silicon Dioxide, Mannitol, Fructose, Crospovidone

DISINTEGRANTS

- VIVASTAR®, EXPLOTAB®**
Sodium Starch Glycolate, Sodium Carboxymethyl Starch
- VIVASOL®**
Croscarmellose Sodium
- EMCOSOY®**
Soy Polysaccharides
- VIVAPHARM® Crospovidone**
Polyvinylpyrrolidone, crosslinked

COATINGS

- VIVACOAT®**
Ready-to-Use Coating System
- VIVACOAT® protect**
Ready-to-Use High Functional Coating System
- VIVAPHARM® HPMC**
Hypromellose
- VIVAPHARM® PVA**
Polyvinyl Alcohol

BINDERS

- VIVAPUR®, EMCOCEL®**
Microcrystalline Cellulose
- EMDEX®**
Dextrates
- VIVAPHARM® Povidones**
Povidone and Copovidone

LUBRICANTS

- PRUV®**
Sodium Stearyl Fumarate
- LUBRITAB®**
Hydrogenated Vegetable Oil, Hydrogenated Oil
- LUBRI-PREZ™**
Magnesium Stearate

CARRIERS

- VIVAPUR® MCC SPHERES**
Microcrystalline Cellulose Pellets
- VIVAPHARM® Sugar Spheres**
Sugar Pellets, Non-GMO

FUNCTIONAL FILLERS

- ARBOCEL®**
Powdered Cellulose
- EMCOMPRESS®**
Calcium Phosphates
- COMPACTROL®**
Calcium Sulfate Dihydrate

THICKENERS • STABILIZERS • GELLING AGENTS

- VIVAPUR® MCG**
Microcrystalline Cellulose and Carboxymethylcellulose Sodium
- VIVAPHARM® Alginates**
Calcium Alginate
- VIVAPHARM® Alginates**
Sodium Alginate
- VIVAPHARM® Alginates**
Alginate Acid
- VIVAPHARM® Pectins**

BIOPHARMA SERVICES

