Matrix Effects on the Performance of Disintegrants in Hydrophobic Tablets

Sonja Bauhuber[1]; Maria Launer[1]: Andrea Geiß[1], Gernot Warnke[1]
[1] JRS PHARMA GmbH & Co KG, 73494 Rosenberg, Germany

Contact: gernot.warnke@jrspharma.de

Introduction

Recommendations for the selection of disintegrants are usually based on the solubility of the tablet matrix and the active ingredients. 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 superdisintegrants 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 suited disintegrant, exhibiting a combination of wicking, swelling and shape recovery.
In addition to being insoluble, certain actives may display a high degree of hydrophobicity, thus, affecting the wettability of the entire tablet. The aim of this study was to investigate the effect of matrix hydrophobicity on the performance of different types of superdisintegrants.

Material and Methods

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

VIVAPUR® MCC (insoluble binder)	17 or 20 %
EMCOMPRESS® DCP (insoluble filler)	68 %
LUBRITAB® hydrogenated vegetable oil (hydrophobic model compound)	10 %
PRUV® SSF (Lubricant)	1 %
Disintegrants	1 or 4 %
VIVASOL® CCS	
EXPLOTAB® SSG	
VIVAPHARM® PVPP XL	

Tab. 1 Composition Tablet Matrix.

Tablets were compressed at four different compression forces (5 kN, 10 kN, 15 kN and 20 kN) and stored for 1, 7, 14 and 28 days at 40 °C / 75 % r.h. prior to testing the disintegration time. Water, 0.1 N HCl (pH 1) and a phosphate buffer (pH 6.8) were used for disintegration testing.
Furthermore, the absorption capacity for different media of the different superdisintegrants was tested. For this purpose, 5 g of the respective superdisintegrant was placed into a frit which was immersed into either water or 0.1 N HCl. The liquid uptake was measured for 10 minutes and the liquid uptake per g superdisintegrant was calculated.

Results and Discussion

The superdisintegrants were incorporated in two different levels: a sub-optimal, low level (1 %) and a recommended level (4 %). The results for the disintegration testing in water is shown in Figure 1.

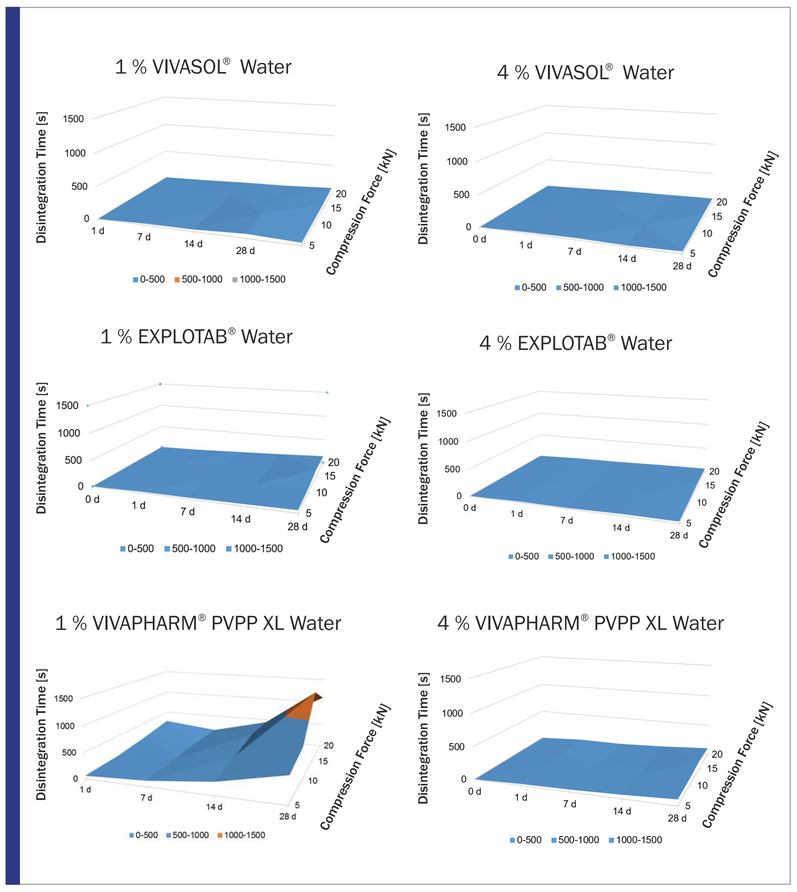

Fig. 1 Disintegration Times of VIVASOL® CCS, EXPLOTAB® SSG and VIVAPHARM® PVPP XL for Different Compression Forces and Different Storage Times.

At the recommended usage level of 4 %, all disintegration times were below two minutes. Furthermore, there was no difference between the different superdisintegrants. In order to check whether differences between the three superdisintegrants could be seen, their level was reduced to 1 %. At this level, it was possible to discriminate between the different superdisintegrants. While VIVASOL® CCS and EXPLOTAB® SSG were still exhibiting good disintegration times below 2.5 minutes, the disintegration time of VIVAPHARM® PVPP XL increased significantly.
In order to check possible differences between the two best performing superdisintegrants (i. e. VIVASOL® CCS and EXPLOTAB® SSG) in this hydrophobic tablet matrix the disintegration testing was also performed in a buffer and in 0.1 N HCl. Figure 2 displays the corresponding results.

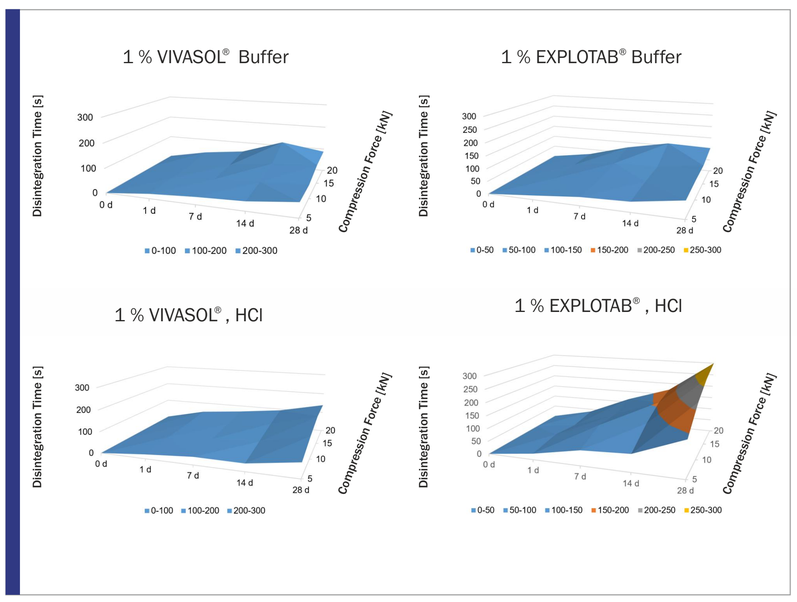

Fig. 2 Disintegration Times of VIVASOL® CCS and EXPLOTAB® in Buffer and 0.1 N HCl.

While the disintegration times for VIVASOL® CCS remained nearly unchanged, a significant prolongation of disintegration times in 0.1 N HCl could be seen for EXPLOTAB® SSG. This finding was also supported by the results of the medium uptake test (Figure 3).

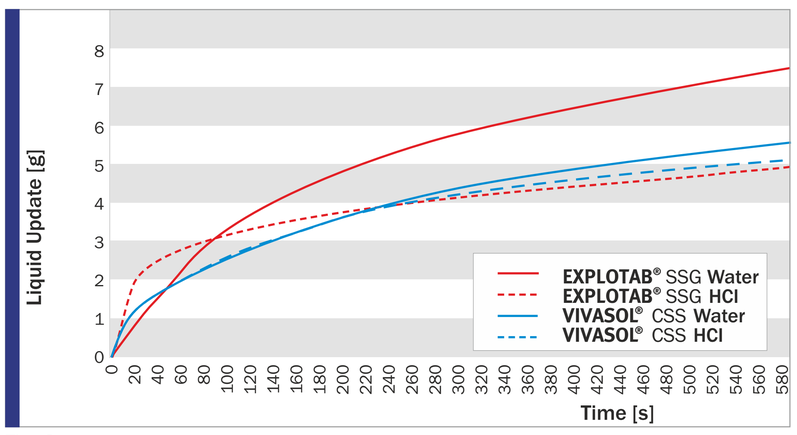

Fig. 3 Medium Uptake of Pure Disintegrant Powders.

EXPLOTAB® SSG showed enormous uptake of water and much less uptake of 0.1 N HCl. In contrast, the absorption capacity of VIVASOL® CCS remained the same - no matter which medium was used.

Superdisintegrants do not follow a sole mechanisms, but rather show a mix of the three main behaviors, namely wicking, swelling and shape recovery. Nonetheless, each type of superdisintegrant has its prevailing mechanism. For PVPP, the disintegration mechanism is mainly based on a fast, but short-ranged shape recovery. In case of the hydrophobic, plastically deforming test matrix, 1 % of PVPP was apparently not sufficient for rapid disintegration due to 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. Wicking, being CCS's predominant mechanism is less affected by pH.

Conclusion

At the recommended use levels of 4 %, all tested super-disintegrants showed very fast disintegration in all test media. The tablets' hydrophobicity presented an obstacle which was in case of low concentrations only mastered by CCS. This 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.

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WORLDWIDE HEADQUARTERS
JRS PHARMA GMBH & CO. KG
Business Unit Excipients
73494 Rosenberg (Germany)
Phone: +49 7967 152-312
ExcipientsService@JRSPharma.de
www.jrspharma.com