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# A Study of the Properties of Compacts from Silicified Microcrystalline Celluloses

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**ABSTRACT** The paper deals with a study of tensile strength and disintegration time of compacts made from silicified microcrystalline celluloses, Prosolv SMCC 90, and Prosolv HD 90, in dependence on compression force, addition of two types of lubricants, and two active ingredients. The lubricants were magnesium stearate and sodium stearyl fumarate in a concentration of 0.5%, the active ingredients being ascorbic acid and acetylsalicylic acid in a concentration of 50%.

Prosolv SMCC 90 proved to be better compatible than Prosolv HD 90; the compacts were of higher strength, which was markedly increased with increasing compression force. Prosolv HD 90 was more sensitive to additions of lubricants, and a greater decrease in strength was recorded due to the influence of sodium stearyl fumarate. The effect of lubricants on the strength of compacts in the presence of active ingredients was not identical. The disintegration time of compacts from Prosolv HD 90 without as well as with lubricants was shorter than from Prosolv SMCC 90 and was increasing with increasing compression force. Disintegration time was increased with added lubricants, and it was markedly shortened by addition of active ingredients. Compacts containing ascorbic acid possessed a shorter disintegration time than those containing acetylsalicylic acid, and it was not markedly influenced by the presence of lubricants.

**KEYWORDS** Prosolv SMCC 90, Prosolv HD 90, Lubricants, Ascorbic acid, Acetylsalicylic acid, Tensile strength of tablets, Disintegration time of tablets

## INTRODUCTION

Silicified microcrystalline cellulose is a coprocessed dry binder on the basis of microcrystalline cellulose enriched with 2% colloidal silicon dioxide. The substance was first introduced in 1996, by the firm Penwest Pharmaceuticals Co., under the name of Prosolv SMCC®. Silicified microcrystalline cellulose is manufactured by codrying a suspension of microcrystalline cellulose particles and colloidal silicon dioxide such that the dried finished product contains 2% colloidal silicon dioxide (Kibbe, 2000).

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This auxiliary substance is available in two size degrees, SMCC 50 and SMCC 90, and particle size distribution corresponds to two best known sorts of microcrystalline cellulose, Avicel PH-101 and Avicel PH-102. The flow properties of SMCC 90, however, are comparable with those of Avicel PH-200 (particle size about 180 μm) (Sherwood, Becker, 1998). Silicified microcrystalline cellulose (further on referred to as SMCC) also shows higher bulk density than the common types of microcrystalline cellulose (further on referred to as MCC), and better flow properties and compressibility associated with it (Luukkonen et al., 1999).

Silicification does not exert a marked influence on the primary chemical and polymorphic characteristics of MCC. SMCC and MCC are comparable cellulose polymers of similar molecular weights, polydispersity, particle size, porosity, and crystallinity, the principal difference being a changed (more rough) topography of the surface of MCC particles (Tobyn et al., 1998). The specific surface of SMCC is as much as five times larger with regard to the immense specific surface of colloidal silicon dioxide. No new covalent bonds develop; $SiO_2$ simply adheres to the surface of microcrystalline cellulose. Silicon dioxide occurs mainly on the surface of MCC particles, only a small amount was detected in the internal regions of the particles. Single particles or small agglomerates of silicon dioxide are uniformly distributed on the whole surface of MCC (particle size of silicon dioxide ranges about 15 nm). This high deagglomeration of silicon dioxide contrasts with a dry physical mixture of MCC with $SiO_2$, which contains large agglomerates of silicon dioxide. Only 20–30% of added $SiO_2$ was effectively used to improve the tableting properties of SMCC. A greater effect of silicification is observed in SMCC 90 with a larger particle size due to a larger available surface for covering with colloidal silicon dioxide. Silicon dioxide slightly facilitates the transport of particles in the initial stage of densification. Increased strength of tablets is most probably a consequence of intersurface interactions of $SiO_2$ and MCC (van Veen et al., 2005). Silicification improves flowability, lubricity, and compactibility (Hwang, Peck, 2001). The tensile strength of compacts of SMCC is greater than of the respective MCC, and more markedly for the larger 90 μm particle-sized grade (Edge et al., 2000).

Comparison of the compaction force versus tablet tensile strength profiles shows that Prosolv SMCC is approximately 20% more compactible than regular MCC. Typical values for tablet tensile strength at 12 kN compaction force were 10 MPa for regular MCC and over 13 MPa for Prosolv SMCC. Stronger tablets manufactured from Prosolv are easier to coat further and the size and weight of individual tablets are decreased, which increases patients' compliance (Allen, 1996). Prosolv possesses further advantages, decreasing the hygroscopicity of the active ingredient (increased stability of tablets). Due to a decreased size, higher compressibility, and better flow properties (lower sensitivity to the rate of tableting); a larger number of tablets in one batch can be achieved, which makes their manufacture substantially cheaper (Schaible, Montalto, 2005).

Prosolv is less sensitive to the content of lubricants (magnesium stearate). Silicon dioxide markedly suppresses the negative effect of stearate on the binding properties of MCC. This is explained by the interaction of silicon dioxide and magnesium stearate in the sense of competitive inhibition of stearate in the sites of adhesion, which are blocked by $SiO_2$ (Bolhuis, Lerk, 1981). Only 20–30% of the 2% colloidal silicon dioxide in SMCC is working effectively in relation to the negative effect of magnesium stearate on tablet strength. Higher tablet strengths were found for lubricated physical binary mixtures in comparison to lubricated SMCC (Van Veen et al., 2005).

A new degree of silicified microcrystalline cellulose Prosolv HD® 90 of high density develops by silicification of Avicel® PH-302. In contrast to this substance, it includes a lower share of powders and its particles possess a more spherical shape. The strength of compacts of HD SMCC is significantly greater than that of compacts of MCC. Additionally, the toughness and ductility of compacts of HD SMCC are greater than those for HD MCC: the toughness is approximately 60% greater in compacts of HD SMCC than HD MCC, which represents a considerable increase in the binding capability of HD SMCC and which may be reflected by a larger "carrying capacity" for this material. In contrast to routinely used Prosolv, the high-density degree shows further improvement in flow properties and lesser sensitivity to the rate of tableting. One disadvantage is observed regarding the higher sensitivity to lubricants, which is due to larger particle size of Prosolv HD. High density grades of MCC are produced from hardwood rather softwood sources. These HD materials exhibit subtle differences

in physicochemical characteristics such as crystallinity, surface area, and porosity compared to regular grades of MCC (Steele et al., 2004). Prosolv HD 90 possesses higher bulk and tapped densities than Prosolv SMCC 90. This is most probably due to slightly different particle size distribution. The manufacturer declares the following characteristics for Prosolv SMCC 90: bulk density–0.25–0.37 g/mL; tapped density–0.37–0.50 g/mL; particle size by Malvern®–$d_{10}$ 25–46 μm, $d_{50}$ 98–146 μm, $d_{90}$ 195–276 μm. Characteristics for Prosolv HD 90 are: bulk density–0.35–0.50 g/mL; tapped density–0.45–0.68 g/mL; particle size by Malvern®–$d_{10}$ 20–70 μm, $d_{50}$ 90–160 μm, $d_{90}$ 160–320 μm (JRS Pharma, 2006).

The paper aimed to evaluate and compare the tensile strength and disintegration time of compacts from two types of silicified microcrystalline cellulose, Prosolv SMCC 90, and Proslov HD 90. The examined factors influencing the above-mentioned properties included compression force, type of lubricant, and type of active ingredient.

## EXPERIMENTAL

### Material

Prosolv SMCC ®90–silicified microcrystalline cellulose (JRS Pharma LP, Patterson New York), bulk density–0.33 g/mL, tapped density–0.46 g/mL; particle size by Malvern: $d_{10}$ 37 μm, $d_{50}$ 122 μm, $d_{90}$ 242 μm;

Prosolv HD ®90–silicified high-density microcrystalline cellulose (JRS Pharma LP, Patterson New York), bulk density–0.40 g/mL, tapped density–0.53 g/mL; particle size by Malvern: $d_{10}$ 49 μm, $d_{50}$ 137 μm, $d_{90}$ 248 μm; magnesium stearate (Acros Organics, New Jersey); sodium stearyl fumarate–Pruv® (JRS Pharma LP, Patterson New York); ascorbic acid (Northeast General Pharmaceutical Factory, Shenyang, China); and acetylsalicylic acid (Merck KgaA, Darmstadt, SRN).

### Preparation of Tableting Materials and Tablets

A list of tableting materials evaluated in the study:

- Prosolv SMCC 90, Prosolv HD 90
- Prosolv SMCC 90 with 0.5% magnesium stearate, Prosolv HD 90 with 0.5% magnesium stearate
- Prosolv SMCC 90 with 0.5% sodium stearyl fumarate, Prosolv HD 90 with 0.5% sodium stearyl fumarate
- Prosolv SMCC 90 with 50% ascorbic acid, Prosolv HD 90 with 50% ascorbic acid
- Prosolv SMCC 90 with 50% acetylsalicylic acid, Prosolv HD 90 with 50% acetylsalicylic acid
- Prosolv SMCC 90 with 50% ascorbic acid and 0.5% magnesium stearate, Prosolv HD 90 with 50% ascorbic acid and 0.5% magnesium stearate
- Prosolv SMCC 90 with 50% ascorbic acid and 0.5% sodium stearyl fumarate, Prosolv HD 90 with 50% ascorbic acid and 0.5% sodium stearyl fumarate
- Prosolv SMCC 90 with 50% acetylsalicylic acid and 0.5% magnesium stearate, Prosolv HD 90 with 50% acetylsalicylic acid and 0.5% magnesium stearate
- Prosolv SMCC 90 with 50% acetylsalicylic acid and 0.5% sodium stearyl fumarate, Prosolv HD 90 with 50% acetylsalicylic acid and 0.5% sodium stearyl fumarate

The mixtures were prepared by mixing in a stainless mixing cube KB 15S (Erweka GmbH, Hausenstamm, Germany). Dry binders were mixed with lubricants for 5 min. If a mixture with an active ingredient was made, then the dry binder was first mixed with the active ingredient for 5 min and finally the lubricant was added for another period of 5 min. The mixing rate was 17 revolutions per min, the total amount always being 30 g.

Of all tableting materials, 16 tablets were compacted on a material-testing machine T1-FRO 50 TH.A1K Zwick/Roell (Zwick GmbH&Co, Ulm, Germany). A special matrix with an upper and a lower punch was employed for tablet compacting using this apparatus. Proper compaction took place by applying the pressure on the upper punch. The tablets were of cylindrical shape without facets, diameter 13 mm and weight 0.5 g ± 0,0010 g. Compaction rate was 30 mm/min and compaction forces 3; 3.5; and 4 kN. Mixtures with active ingredients were pressed only by a compression force of 4 kN.

### Measurement of Tensile Strength of Tablets and Evaluation of the Lubricant Sensitivity of Tableting Materials

Tensile strength was always evaluated in 10 tablets, first no sooner than 24 hr after compaction.

Measurements were performed on a Schleuniger apparatus (Dr. Schleuniger Pharmatron AG, Solothurn, Switzerland), which measured tablet sizes accurate to 0.01 mm and destruction force in N. Tensile strength of tablets was calculated according to Eq. (1):

$$P = \frac{2F}{\pi.d.h} \tag{1}$$

where $P$ is tensile strength of tablets [MPa], $F$ is destruction force [N], $d$ is tablet diameter [mm], and $h$ is thickness of the tablet [mm] (Fell, Newton, 1970).

LSR (lubricant sensitivity ratio) values, which make it possible to quantify and mutually compare the lubricant sensitivity of tableting materials, were calculated according to Eq. (2):

$$\mathrm{LSR} = \frac{(Csu - Csl)}{Csu}, \tag{2}$$

where *Csu* is the crushing strength of tablets without an added lubricant and *Csl* is the crushing strength with a lubricant. The more this value approaches 1, the more the dry binder is sensitive to an added lubricant from the viewpoint of decreased strength of compacts (Bos, et al., 1987). In the present paper, the values of tensile strength, not those of crushing strength, are used in the equation.

## Measurement of Disintegration Time of Tablets

Disintegration times were determined 24 hr after compaction in water of 37 ± 1°C using the Ph. Eur. apparatus. The test was carried out without discs using the procedure described in the chapter *Pharmaceutical Technical Procedures* in the Ph. Eur. 2005. The tablet was considered disintegrated at the moment when there was no residue on the net.

The results of strengths and disintegration times were statistically processed by means of the computer programmes Excel and Qcexpert. Elementary data analysis yielded the mean values with standard deviations, which were plotted into dependences on compression force. In the cases of unclear significance of differences in the values, unpaired *t*-test at a level of significance of 0.05 was employed.

## RESULTS AND DISCUSSION

The paper deals with the evaluation and comparison of the properties from two types of silicified microcrystalline celluloses, Prosolv SMCC90 and Prosolv HD90, the latter differing in higher density. The process of silicification improves both flow and compression characteristics of microcrystalline cellulose. The action of colloidal magnesium oxide, which uniformly adheres to the surface of the particles of microcrystalline cellulose and competitively inhibits the binding sites for the lubricant, produces a decrease in the effect of the presence of the lubricant on the strength of tablets (Bolhuis, Lerk, 1981).

The examined properties of tablets were tensile strength and disintegration time. The influential factors included compression force, type of lubricant, and type of active ingredient. Compression forces were set with the aim that the tensile strength of compacts would oscillate in the optimal range, i.e., 0.56–1.11 MPa as much as possible (Belousov, 1976). Compression forces were 3, 3.5, and 4 kN. In the mixtures containing the active ingredient only a compression force of 4 kN was employed. The tested substances included a 0.5% addition of the lubricants magnesium stearate and sodium stearyl fumarate, and 50% concentration of the active ingredients ascorbic acid and acetylsalicylic acid (i.e., 250 mg in one tablet). These active ingredients were selected because of the suitability of their processing into tablets by means of direct compression, because due to stability reasons, they cannot be processed by moist granulation. In addition, their mechanism of compression is different; acetylsalicylic acid is compressed prevalently by plastic deformation, ascorbic acid by particle fragmentation.

Figure 1 shows the dependence of tensile strength of tablets on compression force for Prosolv SMCC 90 and HD 90. It presents the strength of compacts from pure substances and the mixtures with an addition of 0.5% magnesium stearate and sodium stearyl fumarate. Prosolv SMCC 90 can be compressed in a better way as compared to that of Prosolv HD 90, whose compact strengths are lower. This is due to a larger particle size of Prosolv HD 90 and thus a smaller number of intersurface interactions in the course of plastic deformation of the substance on compresssion. The data clearly show a greater effect of added lubricant on decreased strength of tablets in

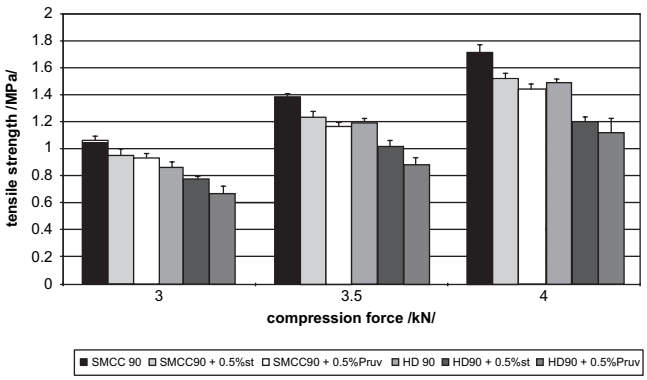


**FIGURE 1** **Tensile strength of tablets in function of compression force: Prosolvs without nad with lubricants.**

the substance Prosolv HD 90. High density MCCs exhibit poorer binding properties and greater sensitivity to lubricants (Steele et al., 2004). Again, this is due to a larger particle size and a smaller surface, as well as better flowability of the substance, which is important for the formation of the film of the lubricant on the particles of the dry binder during mixing. Sodium stearyl fumarate decreases the strength of compacts more; a more marked difference is seen again in the substance Prosolv HD 90. The strength increases with compression force and is always lower in Prosolv HD 90.

Figure 2 shows the mean values of tensile strengths of tablets from both types of dry binders with active ingredients. Tablets with Prosolv SMCC 90 are more compact than those with Prosolv HD 90 excepting the mixtures with 0 and 0.5% stearate and 50% acetylsalicylic acid, where there is no statistically significant difference between the values. The found sensitivity to lubricants was also different. In a mixture of Prosolv SMCC 90 with acetylsalicylic acid it produces a greater decrease in the strength of 0.5% stearate, in the case of Prosolv HD 90 it produces a greater decrease in 0.5% sodium stearyl fumarate. In the cases of mixtures with ascorbic acid it is the reverse, compacts containing ascorbic acid possess a lower strength than those with acetylsalicylic acid. Addition of active ingredients decreased the strength of compacts below the low limit of the optimal strength (0.56 MPa), excepting pure Prosolvs with acetylsalicylic acid. The lower strength of compacts containing ascorbic acid is due to different compressibility of the active ingredients. Acetylsalicylic acid densifies principally by plastic deformation as Prosolvs. Ascorbic acid is a brittle material, which fragments during compaction, and the interparticular bonds are weak (Bolhuis, Chowhan, 1996).

Sensitivity of dry binders to added lubricants was quantified by means of LSR values; the more the value approaches 1, the more the dry binder is sensitive to the lubricant added. The values are graphically represented in Figures 3–4. Figure 3 represents the LSR values for Prosolvs with lubricants. The highest LSR value is found in Prosolv HD 90 with 0.5% Pruv. Pruv produces a greater decrease in strength than stearate in the cases of both Prosolvs. The reason is most probably more perfect formation of the lubrication film during mixing on the particles of silicified microcrystalline celluloses than in the case of the stearate, or lower strength of the bonds Pruv–microcrystalline cellulose. Figure 4 presents the LSR values for mixtures of Prosolvs with active ingredients. Higher values are found in the case of mixtures with ascorbic acid. In the case of acetylsalicylic acid, Prosolv SMCC 90 is more sensitive.

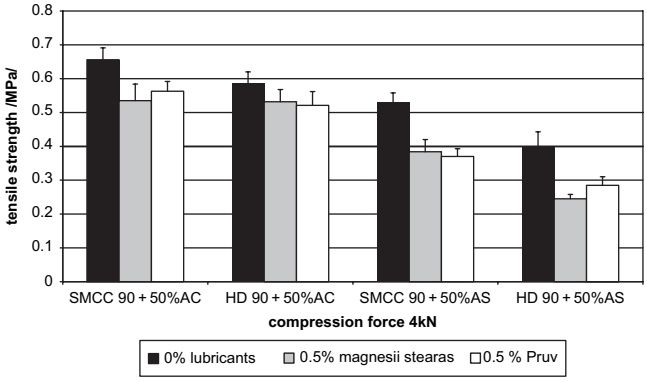


**FIGURE 2** **Tensile strength of tablets Prosolvs with the active ingredients.**

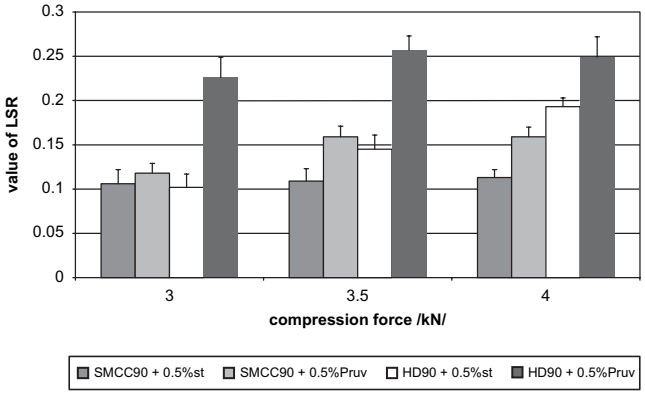


**FIGURE 3** **Values of LSR for Prosolvs.**

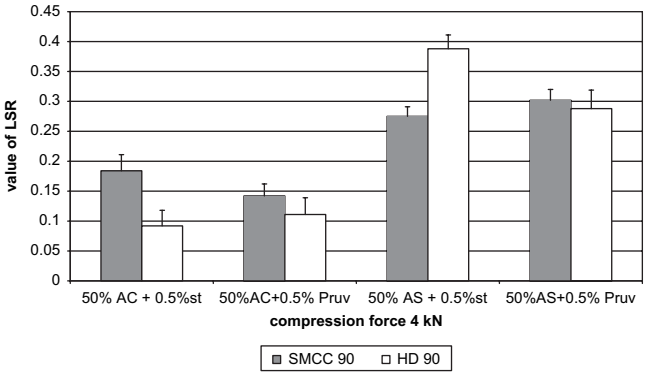


**FIGURE 4** **Values of LSR Prosolvs with the active ingredients.**

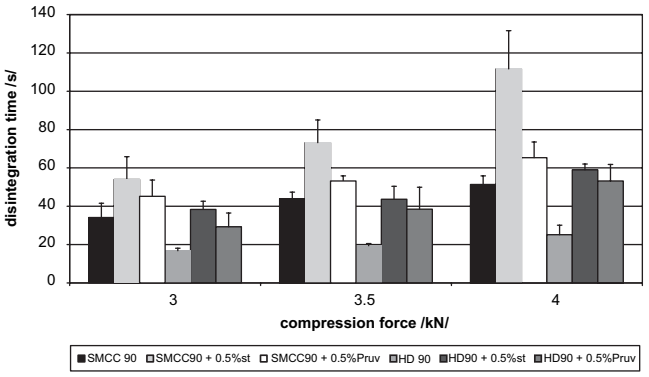


**FIGURE 5** **Disintegration time in function of compression force: Prosolvs without and with lubricants.**

Figure 5 presents the dependence of disintegration time on compression force for Prosolvs with varying content of lubricants. Addition of lubricants prolongs the length of disintegration time of compacts in both Prosolvs. The longest disintegration time was observed in tablets from Prosolv SMCC 90 with 0.5% stearate compressed under 4 kN. In the case of Prosolv HD 90, sodium stearyl fumarate intervenes into disintegration time more markedly than in the case of Prosolv SMCC 90. Disintegration times of compacts from Prosolv HD 90 both without and with lubricants are always shorter, which corresponds with lesser strength of bonds in this substance. No statistically significant difference was demonstrated between the values of disintegration time of tablets from Prosolv HD 90 with lubricants on the basis of *t*-test; the same holds true for a compression force of 3 kN in Prosolv SMCC 90. Disintegration time increases with compression force.

Figure 6 shows the dependence of disintegration time on compression force for both dry binders with

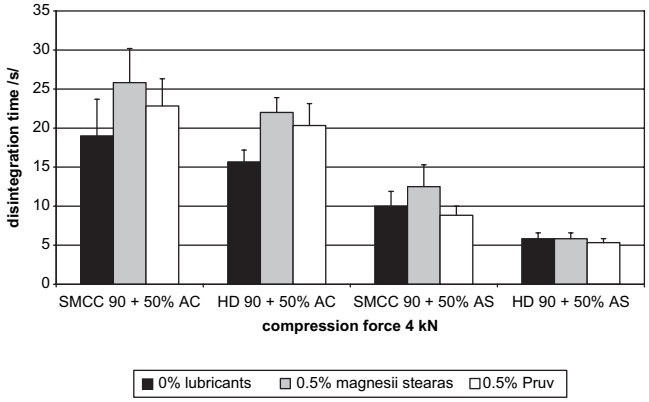


**FIGURE 6** **Disintegration time of tablets Prosolvs with the active ingredients.**

active ingredients. The presence of an active ingredient in tablets markedly decreased their disintegration time. The longest disintegration time was found in compacts with acetylsalicylic acid from Prosolv SMCC 90. In compacts with this active ingredient, lubricants again prolong disintegration time and stearate does this more than Pruv. Due to a great dispersion of values around the mean and thus a high standard deviation, indeed there is no statistically significant difference between the values within the framework of the type of the lubricant except for a mixture of Prosolv SMCC 90 and 50% ascorbic acid. Compacts containing ascorbic acid possess a shorter disintegration time and lubricants do not intervene into it in a statistically significant manner. A statistically significant difference occurs only between the values of Prosolv SMCC 90 with stearate and Pruv, with which the compacts show a shorter disintegration time. A much shorter disintegration time of compacts containing ascorbic acid is due not only to lower strength of compacts, but primarily due to easy solubility of ascorbic acid in water, in contrast to sparingly soluble acetylsalicylic acid (Goto et al., 1999).

## CONCLUSION

The paper evaluated the properties of compacts, particularly the tensile strength and disintegration time of compacts from two types of the silicified microcrystalline celluloses Prosolv SMCC 90 and high-density Prosolv HD 90 within the employed compression forces of 3, 3.5, and 4 kN. Both substances show excellent compressibility, but Prosolv

SMCC 90 provides stronger compacts and shows lesser lubricant sensitivity. The strength of tablets grows with increasing compression force. The lubricant sodium stearyl fumarate produces a greater decrease in the strength of compacts than magnesium stearate in the case of both Proslovs. Disintegration time of compacts from Prosolv HD 90 both without and with lubricants is shorter than that of those from Prosolv SMCC 90. The lubricants prolong disintegration time, in Prosolv HD 90 there is no statistically significant difference within the framework of the employed type of the lubricant, in Prosolv SMCC 90 magnesium stearate prolongs disintegration time in a more marked way. Disintegration time increases with compression force.

Compacts containing active ingredients possess lower strength and a shorter disintegration time. Tablets containing acetylsalicylic acid possess higher strength than those containing ascorbic acid thanks to better compaction properties of the substance. Active ingredients in the tableting material change the interventions of lubricants into the properties of compacts. In the mixture of Prosolv SMCC 90 and acetylsalicylic acid, a greater decrease in strength is caused by magnesium stearate, in the case of Prosolv HD 90 it is Pruv. In the mixtures with ascorbic acid it is the reverse. The disintegration time of compacts containing acetylsalicylic acid is longer because of bad solubility of acetylsalicylic acid in water, prolonged by the presence of lubricants. Compacts containing ascorbic acid possess a shorter disintegration time and it is not markedly influenced by the presence of a lubricant.

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