HUNGARIAN JOURNAL
OF INDUSTRIAL CHEMISTRY
VESZPRÉM
Vol. 30. pp. 73 - 76 (2002)

MEASUREMENT OF THE SWELLING FORCE OF SOME SODIUM STARCH GLYCOLATE PRODUCTS WITH NEW SOFTWARE

A. KELEMEN[1], A. SZÖLLŐSI, A. ZSÓTÉR, K. PINTYE-HÓDI, C. TÖRÖK[2] and I. ERŐS

(Department of Pharmaceutical Technology, Univertity of Szeged, Eötvös str. 6, H-6720 Szeged, HUNGARY
[1]Department of Medical Informatics, University of Szeged, Korányi fasor 9, H-6720 Szeged, HUNGARY
[2] Agrokémia Sellye Ltd, Malom str. 1 H-7960 Sellye, HUNGARY)

Received: October 12, 2001

The swelling properties of several experimental sodium starch glycolates (SSG) were investigated with new equipment and software. The characteristic swelling time ($t_{63.2\%}$) was calculated. The effects of the molecular structure (degree of substitution) on the swelling ability were also studied. It was found that the degree of cross-linking influenced the swelling ability of SSG products. The described equipment and the developed software are suitable for study of the swelling process and characterization of the different disintegrants.

Keywords: disintegrant, swelling force, force-time curve, characteristic swelling time

Introduction

Disintegrants are always added to conventional tablets in order to promote the break-up of the tablets when they are placed in an aqueous environment.

The first step in the process of dissolution of the drug is disintegration. The disintegrant causes rapid disintegration of the tablet, the increase in the surface area of the tablet promoting rapid release of the drug.

The mechanism of disintegration is influenced by different factors, among which the water uptake and swelling play very important roles [1-3]. The uptake of water by disintegrants is thought to initiate the process of disintegration [4, 5].

The swelling force is responsible for the breaking-up of the tablet. List and Muazzam [5] drew attention to the importance of the swelling force, and Caramella et al. [6, 9] also dealt with measurement of the swelling force.

The most common disintegrant employed in tablet formulation is starch. There are many types of modified starches (sodium starch glycolate = SSG) on the market. This material can be regarded as a super-disintegrant. It is official in the USP, BP and Ph.Eur. While the quantity of starch required is about 20%, 4-5% of SSG is sufficient.

Many reports have been published on Primojel and Explotab [8-16], the most widely used types.

The effectiveness of SSG is influenced by various factors. The degree of substitution, the degree of crosslinking and the sodium chloride content play important roles in the disintegration of the tablets [12, 16].

The present article reports an examination of the influence of the above-mentioned parameters on the swelling process. The most informative factor, the characteristic swelling time ($t_{63.2\%}$), was calculated from the modified Weibull equation (Rosin-Rammler-Sperling-Benett-Weibull = RRSBW) by nonlinear regression, $t_{63.2\%}$ being the time needed to attain 63.2% of the maximum swelling force. This factor could be utilized to compare the different disintegrants.

Experimental

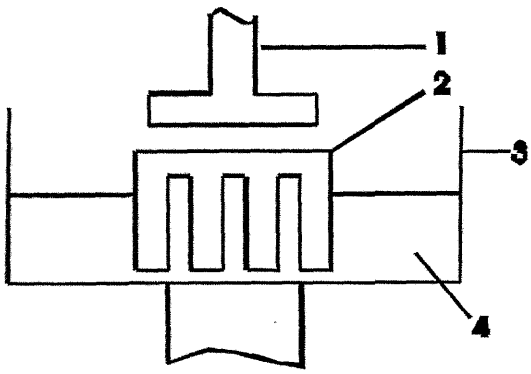
Materials

The present experimental SSG samples (from Agrochemia Co., Sellye, Hungary) are based on a sodium salt of a partially substituted carboxymethyl ether of potato starch. They have a moisture content that is lower than that of starches (<10%). The sodium chloride content is less than 1%. Different types are produced as regards the degree of crosslinking. The degree of substitution is the same (*Table 1*).

Indifferent tablets were prepared from the SSG products with the aim of a study of the swelling (*Table 2*). Dicalcium phosphate dihydrate (Parmcompress®, Parmentier AG, Germany) was used as binder. It was

Table 1 Parameters of SSG products

Product	NaCl content (%)	Na-glycolate (%)	Sedimentation (ml/100 ml)	Degree of substitution (mol -COOH/ mol starch)
SSG 1	0.65	0.80	82	0.24
SSG 2	0.62	0.80	57	0.24
SSG 3	0.72	1.00	48	0.25
SSG 4	0.74	1.00	36	0.25
SSG 5	0.81	1.05	28	0.24
SSG 6	0.94	1.10	17	0.24



1. punch, 2. holder, 3. water container, 4. water

Fig.1 Measuring part of swelling force equipment

necessary to apply a lubricant as well (magnesium stearate, Ph.Eur. 3rd). These materials do not swell in aqueous medium.

Methods

Sedimentation: A 2.00 g sample was suspended in 200 ml boiled distilled water. 100 ml of this suspension was poured into a cylinder. The volume of the sediment was read off after 24 hours.

Mixture: After sieving (0.8 mm wire distance), the components were blended at 50 rpm for 10 min in a Turbula mixer (Willy A. Bachofen Maschinenfabrik, Switzerland).

The moisture content of powder mixtures was determined gravimetrically, through water removal with an IR lamp mounted on a quick dryer (Organic Chemistry Co., Budapest, Hungary). The moisture content was in every case 0.3-0.4%.

Compression: Pressing was carried out with a Korsch EKO eccentric tablet machine (E. Korsch Maschinenfabrik, Germany) mounted with strain gauges and a displacement transducer was applied:

punches:	simple, 10 mm in diameter
pressure force:	5, 10 and 15 ± 1 kN
mass of tablet:	40%
air temperature:	23 °C
rate of pressing:	36 tablets/min

Table 2 Compositions of tablets

Materials	Mass (g)	(%)
SSG (1-6)	4.8	4
Parmcompress	114.6	95.5
Magnesium stearate	0.6	0.5
Total mass	120.0	100.0

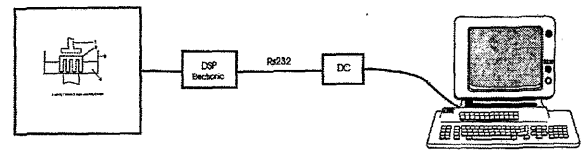


Fig.2 Scheme of measurement

Swelling force measurement

The equipment used to measure the swelling force (SF) was prepared on the basis of the principle of the List apparatus [5].

The measurement is performed with a balance (Sartorius microbalance) with electronic compensation, which is built in the equipment. The tablet-holder is a copper cylinder 10 mm in diameter with slits in the side. In this cylinder, a copper punch with the same diameter is fitted. The tablet-holder is in a copper cup. The tablet is placed in the holder and 5 ml distilled water is injected at the start of the measurement. The water penetrates into the tablet through the slits. The force that builds up inside the comprimate as it absorbs the water is transmitted vertically and is detected by the balance (*Fig.1*).

The equipment is linked with a PC by a RS232 cable (*Fig.2*). Software has been developed for data acquisition, evaluation and demonstration of the swelling process. The monitor displays the SF vs. time curve with the important parameters (SF, time characteristic swelling time ($t_{63.2\%}$)).

Mirroring the close logical or functional relationship between them, the SF functions are arrayed in separate groups (**Acquisition**, **Settings**, **Analysis**). Under the **Acquisition** menu point, it is possible to receive data from the serial port. During acquisition, the monitor shows the current SF and baseline values. At the end of the acquisition, the software saves the data on disk. With the **Settings** menu point, it is possible to configure the system (e.g. serial communication, acquisition file name, etc.). With the **Analysis** menu point, it is possible to evaluate the saved data. The screen depicts the SF vs. time curves (a maximum of 5) with the important parameters (time, SF, baseline, $t_{63.2\%}$) and dF/dt). The user can evaluate curves manually with the cursor, create reports, or print screen shots to the bitmap or to the printer.

The characteristic swelling time and shape parameter were calculated from the following form:

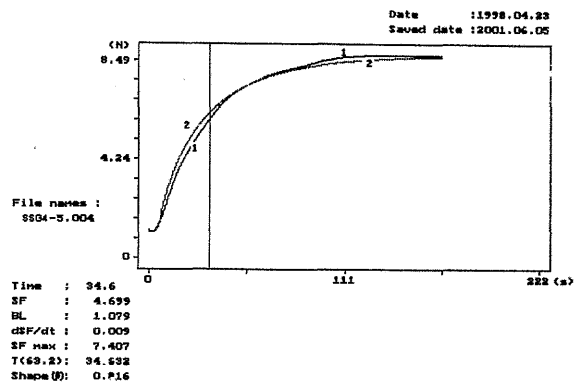
Table 3 Results of the swelling test

	Pressure force (kN)	Swelling force (N)	β	$t_{63.2\%}$ (s)
	5	8.56	0.830	119.13
		RSD=5.57		
SSG1	10	10.09	0.836	108.82
		RSD=9.95		
	15	12.49	0.858	125.87
		RSD=5.46		
	5	5.45	0.858	66.35
		RSD=11.56		
SSG2	10	7.16	0.832	61.67
		RSD=8.74		
	15	14.23	0.830	78.99
		RSD=11.09		
	5	6.96	0.816	48.55
		RSD=6.44		
SSG3	10	8.18	0.814	47.48
		RSD=7.62		
	15	18.33	0.830	95.03
		RSD=3.80		
	5	6.92	0.864	53.36
		RSD=6.21		
SSG4	10	8.14	0.808	30.10
		RSD=9.74		
	15	9.59	0.832	33.10
		RSD=11.09		
	5	9.94	0.832	89.24
		RSD=7.36		
SSG5	10	13.81	0.819	82.33
		RSD=8.58		
	15	13.49	0.831	40.71
		RSD=3.11		
	5	8.59	0.825	40.38
		RSD=0.37		
SSG6	10	11.25	0.813	48.88
		RSD=4.22		
	15	11.87	0.816	38.74
		RSD=2.85		

$$M(t) = M_{max}\left\{1-\exp\left(-\left[\frac{t-t_0}{\tau}\right]^{\beta}\right)\right\}$$

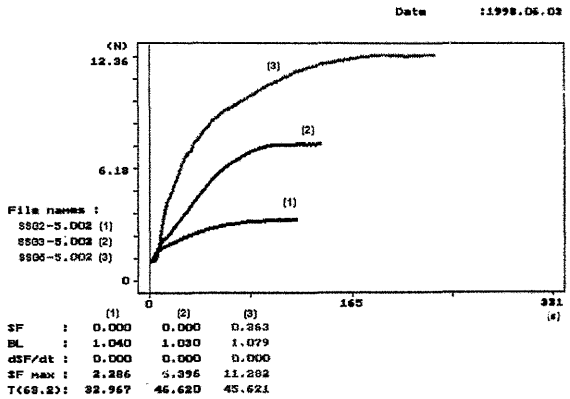
where τ is the time parameter, β is the shape parameter, M_{max} is the maximum value of the swelling, M is the swelling at time t, and t_0 is the start time. It is possible to calculate the characteristic swelling time. β=1 implies first-order kinetics in the swelling process; β<1 impliest fast swelling at the beginning of the process, followed by a slower swelling; β>1 implies a sigmoid curve: slow swelling is followed by a faster swelling process.

In the literature, these parameters are generally calculated by means of the Weibull distribution equation rearranged in linearized form [8]. Another way to solve this equation is nonlinear fitting. In the present paper, this method was used with GLOBAL software (http://www.jate.u-szeged.hu#csendes.htm) (*Fig.3*).



SF = swelling force (where the vertical measuring line is); **BL** = basic line; **SFmax** = maximum value in swelling force; **T(63.2)** = characteristic swelling time; **dsF/dt** = the speed of changing of force (where the vertical measuring line is)

Fig.3 Swelling force profile (1) and nonlinear fitting according to RRSBW equation (Pressure force: 5 kN)



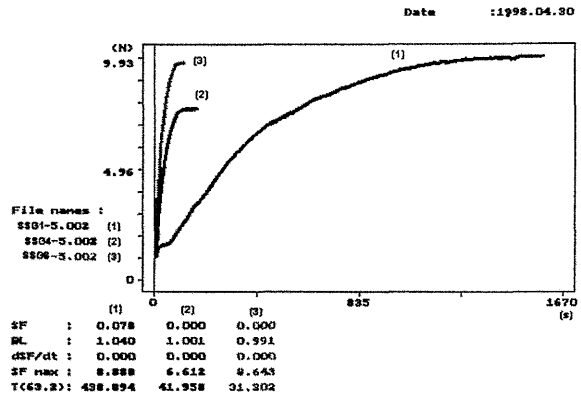
SF = swelling force (where the vertical measuring line is); **BL** = basic line; **SFmax** = maximum value in swelling force; **T(63.2)** = characteristic swelling time; **dsF/dt** = the speed of changing of force (where the vertical measuring line is)

Fig.4a Swelling process of SSG2, SSG3 and SSG5 comprimates (Pressure force: 5 kN)

Results and Discussion

Results are shown in *Table 3*. It can be seen that at 5 kN the SSG5 comprimates exhibited the highest, and the SSG2 comprimates the smallest SF (*Table 3*, *Figs.4/a* and *4/b*). The SSG1 and SSG6 comprimates (5 kN) had almost the same SF maximum, but there was a considerable difference in the $t_{63.2\%}$ values.

The SF increased at higher pressure force, but to different degrees. The reason lies in the texture of the comprimates and in the properties of the materials. Increase of the pressure force generally resulted in a decrease in the porosity. The texture of the comprimates is more compact. This has an important role in the disintegration. If the character of the composition is



SF = swelling force (where the vertical measuring line is); **BL** = basic line; **SFmax** = maximum value in swelling force; **T(63.2)** = characteristic swelling time; **dsF/dt** = the speed of changing of force (where the vertical measuring line is)

Fig.4b Swelling process of SSG1, SSG4 and SSG6 comprimates (Pressure force: 5 kN)

hydrophilic, the SF (disintegration force) can be better mediated by the water and the disintegration process will be rapid. The degree of the increase in the SF depends on the properties and the swelling ability of the disintegrants. By changing the disintegrant at the same composition, it is possible to study the influence of the pressure force on the SF.

The data allow the samples to be arranged in sequence.

For the SF:

5 kN: SSG 5 > SSG 6 = SSG 1 > SSG 4 = SSG 3 > SSG 2
10 kN: SSG 5 > SSG 6 > SSG 1 > SSG 4 = SSG 3 > SSG 2
15 kN: SSG 3 > SSG 2 > SSG 5 > SSG 1 > SSG 6 > SSG 4

For $t_{63.2\%}$:

5 kN: SSG 6 < SSG 3 < SSG 4 < SSG 2 < SSG 5 < SSG 1
10 kN: SSG 4 > SSG 6 = SSG 3 < SSG 2 < SSG 5 < SSG 1
15 kN: SSG 4 < SSG 6 = SSG 5 < SSG 2 < SSG 3 < SSG 1

It can be stated that increase of the degree of crosslinking and of the sodium chloride content led to a higher SF. However, this effect was observed only at pressure forces of 5 and 10 kN. The degree of crosslinking influenced the swelling ability of the SSG products. It was seen that, for the samples with a smaller degree of cross-linking (SSG1-SSG3), the SF increased in a stepwise manner with increase of the pressure force. The samples with a higher degree of crosslinking (SSG4-SSG6) demonstrated an increase in swelling only between 5 and 10 kN, but not when the pressure force was increased from 10 to 15 kN. The reason is the inflexible skeleton with a compact texture.

It can further be seen that the characteristic water-uptake time ($t_{63.2\%}$) is influenced primarily by the deformability of the particles and by the texture of the comprimates.

Conclusion

The results of these experiments suggest that the maximum SF and the factor $t_{63.2\%}$ may be used to compare the intrinsic capability of a disintegrant. Study of the swelling process is also important with respect to the pressure force. The porosity of the tablets depends on the deformability of the particles and the porosity has an important role in water transport into the interior of the tablets and hence in the swelling process, too.

On the basis of such results, it is possible to choose the pressure force suitable for tableting. If increase of the pressure force causes no change or only a very small change in the SF, it is unnecessary to use a high pressure force during tableting. The described equipment and the developed software are suitable for study of the swelling process and for comparison and characterization of the different disintegrants.

REFERENCES

1. LOWENTHAL W.: J. Pharm. Sci. *1972*, 61, 1695-1711
2. KANIG J. L. and RUDNIC E. M.: Pharm. Technol. *1984*, 8, 50-58, 61-63
3. BOLHUIS G. K., VAN KAMP H. V., LERK C. F. and SESSINK F. G. M.: Acta Pharm. Technol. *1982*, 28, 111-114
4. VAN KAMP H. V., BOLHUIS G. K., DE BOER A. H., LERK C. F. and LIE-A-HUEN L.: Pharm. Acta Helv. *1986*, 61, 22-29
5. LIST P. H., MUAZZAM U. A.: Pharm. Ind. *1979*, 41, 459-464
6. CARAMELLA C., COLOMBO P., CONTE U. and LA MANNA A.: Drug Dev. Ind. Pharm. *1986*, 12, 1749-1766
7. COLOMBO P., CONTE U., CARAMELLA C. and GEDDO M.: J. Pharm. Sci. *1984*, 73, 701-705
8. FERRARI F., GEDDO M., GAZZANIGA A., CARAMELLA C. and CONTE U.: S.T.P. Pharma, *1988*, 4, 481-484
9. CARAMELLA C.: Pharm Technol. Int. *1990*, Sept. 30-40, Oct. 30-37
10. BOLHUIS G. K., KAMP H. V., LERK C. F., GIELEN J. W., ARENDS A. W. and STUNT G. K.: Acta Pharm. Technol. *1984*, 30, 24-32
11. RUDNIC E. M., KANIG J. L. and RHODES C. T.: J. Pharm. Sci. *1985*, 74, 647-650
12. GRAF E., GHANEM A. H. and MAHMOUD H.: Pharm. Ind. *1985*, 47, 773-776
13. SAKR A., RIVERA D. and JIMENEZ W.: Pharm. Ind. *1986*, 48, 522-525
14. WAN L. S. C. and PRASAD P. P.: Acta Pharm Technol. *1988*, 34, 200-203
15. JOHNSON J. R., WANG L-H., GORDON M. S. and CHOWLAN Z. T.: J. Pharm. Sci. *1991*, 80, 469-471
16. MISETA M., PINTYE-HÓDI K., SZABÓ-RÉVÉSZ P., SZALAY L. and SÁGHI P.: Pharm. Ind. *1993*, 55, 515-518