Department of Pharmaceutical Technology[1], University of Szeged, Hungary; Institute of Pharmaceutics and Biopharmaceutics[2], Heinrich-Heine University, Düsseldorf, Germany

Pretreatment of pigments to prepare liquids for enteric coating

É. Bölcskei[1], J. Bajdik[1], J. Müller[2], K. Knop[2], P. Kleinebudde[2], K. Pintye-Hódi[1]

Received March 14, 2008, accepted March 30, 2008

Prof. Klára Pintye-Hódi, Department of Pharmaceutical Technology, H-6720 Szeged, Eötvös u. 6, Hungary klara.hodi@pharm.u-szeged.hu

Pharmazie 63: 514–515 (2008) *doi: 10.1691/ph.2008.8074*

Film coating fluids commonly contain different pigments. The objective of this work was a study of the distribution of these particles in the coating film. Different pretreatment forms (pigment suspension, pigment paste and untreated pigments) were applied. They were incorporated into a Eudragit® L 30 D-55 dispersion. The surface roughness and the mechanical properties of the free films indicated, that the most homogeneous film was obtained with the pigment paste. The homogeneity of the film was investigated by mechanical testing. The protective effect of the coating did not vary with the application of pigments in different forms, but the appearance of the coated tablets underwent a considerable change.

1. Introduction

Film-forming polymers in aqueous dispersions are increasingly utilized during the production of coated solid dosage forms (Cole et al. 1995). Various types of polymers can be used to form aqueous dispersions, and numerous water-soluble and insoluble additives are applied in the coating liquids (Bauer et al. 1988; Lehmann 1999; Nimkulrat et al. 2004). The mixing sequence for the preparation of a coating liquid containing insoluble particles is important. The insoluble materials can modify the properties of the film formed (Felton and McGinity 1999, 2002; Petereit and Weisbrod 1999; Plumb et al. 2002) and thus their homogeneous distribution is indispensable. The first step is the preparation of the pigment suspension (Eudragit Brochure 2005). Conventionally, the materials (glidants, pigments, plasticizers and other excipients) must be intensively homogenized in water with a high-speed mixing apparatus. Next, the homogeneous pigment suspension must be gently mixed with the polymer dispersion to prevent coagulation. Efforts are currently under way to make this process simpler and more effective. The application of ready-to-use preparations is currently spreading. One new possibility is a pigment paste which contains all the insoluble components with other additives as stabilizers of the paste.

2. Investigations, results and discussion

The aim of the present study was the evaluation of a conventionally prepared suspension and comparable suspensions prepared from a paste. These were incorporated into Eudragit® L 30 D-55 dispersions and were compared with a coating dispersion prepared without pretreatment of the pigments. Smoothness and mechanical properties of the free films were determined, the protective effect of the coating and the smoothness of the coated tablets.

It was observed that all of the parameters describing the surface roughness of the free films was best for the sample prepared with the paste (Table). The means of all parameters and also the deviations were the highest for the sample which did not undergo pretreatment. This can be explained by the insufficient distribution of the insoluble particles.

The surface roughness of the uncoated tablets (Ra: 2.46 ± 0.46 μm; Rq: 3.11 ± 0.63 μm; Rz: 14.49 ± 3.23 μm) was lowered by application of a coating fluid containing a pigment paste. The values were significantly ($p < 0.05$) lower for sample S2. Sample S3 once again exhibited the highest values and deviations for every parameter.

The mechanical properties of the poured films were different. Not only the deformation force, but also the characteristics of the curve changed (Fig). A sharp break was detected for S2 and a less sharp one for S3. A sharp deformation point indicates a very rapid modification of the film structure. Inhomogeneity in the structure leads to the formation of small film areas without solid particles or with more solid particles with different mechanical properties. The break points for such samples are therefore less sharp. The difference between S1 and S3 may well be due to the more homogeneous distribution of the different components in S1.

The lowest deformation force was detected for S2, possibly because of the paste-stabilizing component (e.g. preservative). The relative deviation of this parameter was also the highest for S3. This may be explained by the lower degree of homogeneity.

Table: Surface roughness of the product (n = 10)

Sample	Ra (μm)	Rq (μm)	Rz (μm)
S1 (film)	4.21 ± 0.98	5.47 ± 1.46	28.24 ± 6.52
S1 (tablet)	2.60 ± 0.38	3.32 ± 0.54	12.89 ± 2.72
S2 (film)	3.60 ± 0.24	4.44 ± 0.29	22.40 ± 3.02
S2 (tablet)	1.43 ± 0.34	1.73 ± 0.36	6.39 ± 1.44
S3 (film)	5.36 ± 5.68	7.70 ± 8.37	37.06 ± 30.64
S3 (tablet)	3.71 ± 1.17	4.54 ± 1.26	14.88 ± 3.61

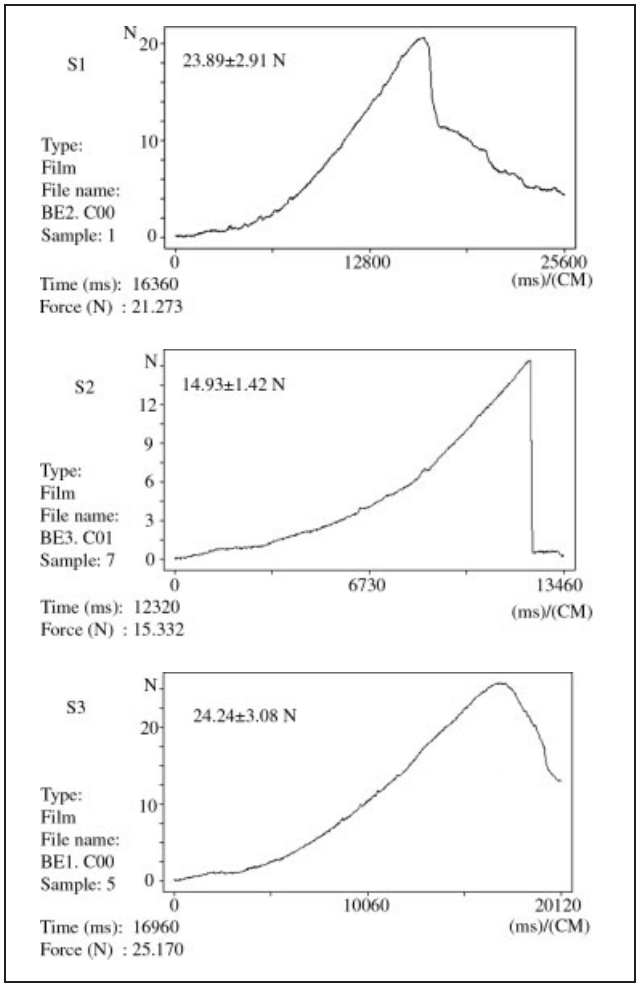

Fig.: Deformation curves of free films

The protective effect of the film (dry polymer content: 4 mg/cm^2) on the surface of the tablets was appropriate for all of the samples, independently of the surface roughness, since disintegration of the tablets in gastric juice was not detected.

It may be concluded that pretreatment of the pigments is important because surface roughness can differ significantly on change of the preparation method. Neglect of this step can result in a changed appearance of the product. A more homogeneous film can be achieved by the application of a pigment paste. The characteristics of the deformation curve are informative in the evaluation of the homogeneity of the film. The application of new ready-to-use pastes is a suitable method because the preparation is rapid and the film formed is smooth and homogeneous. However, the paste-stabilizing components change the properties of the film. Optimization of the preparation of pigments without additives is therefore also necessary.

3. Experimental

3.1. Materials

The aqueous polymer dispersion was the methacrylic acid copolymer Eudragit® L 30 D-55 (Degussa Pharma Polymers, Darmstadt, Germany). A pigment paste (W.A.S.-L – White, Rofarma Italia S.r.l., Milano, Italy) containing talc, titanium dioxide, triethyl citrate, propane-1,2-diol, alginate and potassium sorbate, with a solid content of 77.45%, was applied. The conventionally prepared pigment suspension contained titanium dioxide, talc, triethyl citrate (suggested ratio for Eudragit® L (Eudragit Brochure 2005)) 0.3% dimeticone (type E1049 a gift from EGIS Pharmaceuticals PLC) as antifoaming agent and 0.05% iron oxide (Sicovit Red, BASF GmbH, Ludwigshafen, Germany) as colouring pigment.

3.2. Preparation of products

The solid content of each of the coating dispersions was 20% (10% pigment + 10% polymer). Each sample contained colouring pigment for evaluation of the effect of iron oxide.

S1: The pigment suspension was prepared by mixing with an Ultra-Turrax (IKA-Werke GmbH & Co. KG, Staufen, Germany) at 20,000 rpm for 10 min. After this, the pigment suspension was poured into the polymer dispersion and mixed with an overhead stirrer (IKA-Werke GmbH & Co. KG).

S2: Sicovit Red was dispersed in water with Ultra-Turrax mixing (20,000 rpm) for only 1 min. The Ultra-Turrax was not used further. The W.A.S.-L paste was then added to the dye suspension, which was next poured into the polymer dispersion and mixed with an overhead stirrer.

S3: For comparison, a "base sample" was also prepared, where the S1 components were mixed with an overhead stirrer. The Ultra Turrax was not used.

The coated tablets were prepared in a pan coater (Bohle BFC, LBBohle, Ennigerloh, Germany). The process parameters were kept constant for all batches.

3.3. Evaluation of products

The surface roughness of the tablets and films was determined with a Mitutoyo SJ-201P tester (Mitutoyo Co., Kawasaki, Japan). An evaluation length of 0.8 mm was applied for tablets, and of 2.5 mm for films. For this test, free films were prepared. The liquid was atomized onto a glass surface (Ra: 0.10 ± 0.03 μm; Rq: 0.13 ± 0.03 μm; Rz: 1.23 ± 0.38 μm). The arithmetic mean deviation (Ra), root-mean-square deviation (Rq), and maximum height of the profile (Rz) were determined. 10 parallel tests were performed.

The breaking hardness of poured films prepared on a teflon surface was tested. The strength tester and the software were developed in our institute (Bajdik and Pintye-Hódi 2006; Bajdik et al. 2007). Ten tests were performed in parallel.

The enteric resistance was evaluated via the time of tablet disintegration, measured with an Erweka ZT 71 (Erweka GmbH, Heusenstamm, Germany) apparatus, in HCl solution at pH 1.2.

Acknowledgements: This work was supported by Hungarian Scientific Research Fund (OTKA) grant F-049310 and the DAAD/MÖB project (15/2007).

References

Bajdik J, Fehér M, Pintye-Hódi K (2007) Effect of plasticizer on surface of free films prepared from aqueous solutions of salts of cationic polymers with different plasticizers. Appl Surf Sci 253: 7303–7308.

Bajdik J, Pintye-Hódi K (2006) Study of deformation process of stored polymethacrylate free films. Pharmazie 61: 887–888.

Bauer KH, Lehmann K, Osterwald HP, Rothang G (1988) Coated Pharmaceutical Dosage Forms, Medpharm GmbH Scientific Publishers, Stuttgart.

Cole G, Hogan J, Aulton M, (1995) Pharmaceutical Coating Technology. Taylor & Francis Ltd., London.

Eudragit® brochure (2005) Röhm GmbH & Co. KG, Pharma Polymers, Darmstadt.

Felton LA, McGinity JW (1999) Adhesion of polymeric films to pharmaceutical solids. Eur J Pharm Biopharm 47: 3–14.

Felton LA, McGinity JW (2002) Influence of insoluble excipients on film coating systems Dev Ind Pharm 28: 225–243.

Lehmann K (1999) Practical Course in Film Coating of Pharmaceutical Dosage Forms with Eudragit®, Pharma Polymers, Darmstadt

Nimkulrat S, Suchiva K, Phinyocheep P, Puttipipatkhachorn S (2004) Influence of selected surfactants on the tackiness of acrylic polymer films. Int J Pharm 287: 27–37.

Petereit HU, Weisbrod W (1999) Formulation and process considerations affecting the stability of solid dosage forms formulated with methacrylate copolymers Eur J Pharm Biopharm 47: 15–25.

Plumb AP, Rowe RC, York P, Doherty C (2002) The effect of experimental design on the modeling of a tablet coating formulation using artificial neural networks. Eur J Pharm Sci 16: 281–288.