Influence of Formulation Parameters on Tablet Surface Properties and Film Coating Adhesion

Martin Wewers[1,2], Gernot Warnke[3], Jan Henrik Finke[1,2]

[1]Institute for Particle Technology, Technische Universität Braunschweig, Braunschweig; [2]Centre of Pharmaceutical Engineering (PVZ), Technische Universität Braunschweig, Braunschweig; [3]JRS Pharma GmbH & Co. KG, Rosenberg

Correspondence: Dr. Gernot Warnke, JRS Pharma GmbH & Co. KG, Holzmühle 1, 73494 Rosenberg, Germany; e-mail: gernot.warnke@jrspharma.de

Correspondence: Dr. Jan Henrik Finke, Institute for Particle Technology, Technische Universität Braunschweig, Volkmaroder Str. 5, 38104 Braunschweig, Germany; e-mail: jan.finke@tu-braunschweig.de

ABSTRACT

Tablets can be covered with film coatings to obtain special properties e.g. to achieve specific drug release profiles. During the coating process, the surface properties of the tablet cores directly influence the application of the coating dispersion and finally the quality attributes of the film. Aim of this study was to investigate the influence of different functional excipients in tablet cores on the apparent film coating adhesion. Commonly applied lubricants (magnesium stearate and sodium stearyl fumarate) and disintegrants (croscarmellose sodium, crospovidone, and sodium starch glycolate) were combined with microcrystalline cellulose and compressed to tablet cores. Additionally, a commercially available co-processed excipient for direct compression was part of the study. An HPMC-based (hydroxypropyl methylcellulose) tablet coating was applied to the tablet cores in a drum coater and the adhesion of the coating was evaluated. Generally, the tensile strength of the tablet cores showed to be the dominant factor influencing apparent film coating adhesion. However, the application of functional excipients in the tablet cores reduced the adhesion of film coatings in comparison to pure microcrystalline cellulose. The addition of lubricants had a much more adverse effect than disintegrants. Finally, the measured film coating adhesion was found to be the result of fundamental adhesion between the film coating and tablet surface and cohesive failure within the tablet core.

KEY WORDS

- Film coating
- Lubricants
- Disintegrants
- Film Coating Adhesion
- Cohesive and adhesive failure

Pharm. Ind. 82, Nr. 8, 1072–1077 (2020)

ZUSAMMENFASSUNG

Einfluss von Formulierungsparametern auf die Eigenschaften von Tablettenoberflächen und die Adhäsion von Film-Coatings

Tabletten können mit Film-Coatings überzogen werden, um spezielle Eigenschaften, wie z. B. spezifische Profile der Wirkstofffreisetzung, zu erhalten. Die Oberflächeneigenschaften der Tabletten beeinflussen hierbei direkt die Applikation der Coatingdispersion während des Coatingprozesses und die entsprechenden Qualitätsattribute des finalen Films. Das Ziel dieser Studie ist die Untersuchung des Einflusses verschiedener funktionaler Hilfsstoffe in Tablettenkernen auf die apparente Film-Coating-Adhäsion. Dazu wurden gängige Schmier- (Magnesiumstearat, Natriumstearylfumarat) und Sprengmittel (Natrium Croscarmellose, Crospovidon und Natriumstärkeglykolat) mit mikrokristalliner Cellulose zu Tabletten verarbeitet. Zusätzlich wurde ein kommerziell erhältlicher, coprozessierter Füllstoff zur Direkttablettierung betrachtet. Die Tablettenkerne wurden in einem Trommelcoater mit einem HPMC-basierten (Hydroxypropylmethylcellulose) Coating beschichtet. Anschließend wurde die apparente Adhäsion der Filme auf den Tablettenkernen evaluiert. Es wurde gezeigt, dass die Zugfestigkeit der Tablettenkerne einen entscheidenden Einflussfaktor für die apparente Haftung des Film-Coatings auf den Tabletten darstellt. Dennoch wurde eine Abschwächung der Adhäsion durch die Verarbeitung funktioneller Hilfsstoffe in den Tabletten im Vergleich zu reinen MCC-Tabletten beobachtet, wobei der Effekt der Schmiermittel den der Sprengmittel

Pharm. Ind. 82, Nr. 8, 1072–1077 (2020)

deutlich überwog. Insgesamt konnten beobachtete Unterschiede der apparanten Film-Coating-Adhäsion in unterschiedliche Anteile an Versagen der Kohäsion im Tablettenkern und der fundamentalen Adhäsion zwischen Kern und Coating am Gesamtversagen differenziert werden.

Introduction

Tablets are the most common dosage form in pharmaceutical industry. However, they are often further processed to coated tablets by application of one or more layers of mixtures consisting of a film-forming material and several functional excipients. The intention of this can be as versatile as the formulation itself. The film-coating can, for instance, fulfil protective functions. These can be related to the protection of the original dosage form against harmful influences, or the patient by increasing the pharmaceutical drug safety of the final product. Furthermore, the compliance of the patients can be enhanced by coatings covering unpleasant characteristics of the tablets, like appearance, odour or taste. Additionally, the drug release-profile or site of release can be altered significantly by application of appropriate film formers [1,2].

Although the process of film-coating has become a routine operation in pharmaceutical industry, it still bears an intrinsic complexity. This demands for intensive research for enabling a full comprehension of relationships between numerous variables, all affecting product performance. In this regard, the most important factor is the interaction between the film-coating and tablet core. Good adhesion between both is the major prerequisite, irrespective of the intended function of the coating [2,3]. A systematic investigation of this interaction in dependence of the most important formulation and process parameters offers numerous advantages concerning economics, product performance and sustainability.

The present study provides a systematic investigation of the influence of functional excipients in MCC-based tablet cores on the quality of an applied HPMC-based coating. The influence of the compaction pressure during tabletting and the resulting tablet core properties were studied concerning their influence on apparent film coating adhesion.

Materials and Methods

Materials

Microcrystalline cellulose (MCC; VIVAPUR 12), croscarmellose sodium (CCS, VIVASOL), crospovidone (PVPP, VIVAPHARM PVPP XL), sodium starch glycolate (SSG, EXPLOTAB), sodium stearyl fumarate (SSF, PRUV; all from JRS Pharma GmbH & Co KG, Germany) and magnesium stearate (MgSt, Ligamed MF-2-V, Peter Greven GmbH & Co. KG) were used as tablet core excipients. Additionally, a commercially available co-processed excipient for direct compression (EASYtab, PROSOLV EASYtab SP, JRS Pharma GmbH & Co. KG, Germany) consisting of SSF, SSG and silicified MCC (SMCC) was used for tablet core production. The tablet cores were coated with a ready-to-use HPMC coating (VIVACOAT A, JRS Pharma GmbH & Co. KG, Germany).

Tablet Core Production and Coating

Tablet cores were produced using a compaction simulator (STYL-One Evolution, MEDEL'Pharm, France) equipped with round bi-planar punches with a diameter of 11.28 mm. Investigated tablet core formulations can be found in table 1.

Tablet cores were produced applying compaction pressure of 75, 125, and 200 MPa. As the formulation containing MgSt showed capping above a pressure of 125 MPa, this formulation was compressed at 75, 100, and 125 MPa. Consequently, tablets consisting solely of MCC were additionally compressed at 100 MPa for a better comparability.

The coating of the tablet cores was conducted in a perforated drum coater (Solidlab2, Bosch Hüttlin, Germany) with a maximum load of 8 L operated at a rotation speed of 10 min^{-1}. 50 of each biplane tablet cores were coated by using oblong and convex EASYtab tablets for volume/mass-replenishment (total mass: 3 kg) and were manually re-assorted afterwards. The coating suspension, consisting of 15 wt% coating powder in bidistilled water, was applied with a mean spray rate of 20 $g \cdot min^{-1}$ and the temperature of the drying air (volume flow rate 200 $m^3 \cdot h^{-1}$) was adapted to achieve a tablet bed temperature of 38 ± 2 °C.

Characterization of Tablet Cores

The porosity of the tablet cores was calculated according to equation 1 by taking the true densities of the excipients ρ_s (data not shown), the mass m and the geometrical dimensions of the tablet cores (diameter d and height h) into account.

$$\varepsilon = 1 - \frac{m}{\pi \cdot \left(\frac{d}{2}\right)^2 \cdot h \cdot \rho_s} \quad (1)$$

Breaking force F of tablet cores was measured by means of a diametral compression test. The resulting tensile strength σ was calculated according to equation 2 with the geometrical dimensions of the tablet cores [4].

$$\sigma = \frac{2 \cdot F}{\pi \cdot d \cdot h} \quad (2)$$

Surface roughness of the tablet cores was measured profilometrically (DektakXT Stylus, Burker Corp. USA) with a stylus with a tip of 2 µm, a tracking speed of 5 µm/s and a tracking weight of 3 mg.

Measurement of Apparent Film Coating Adhesion

In this study, apparent adhesion between the tablet core and the film coating was determined according to an experimental setup (butt adhesion test) described by Fischer and Rowe [5]. Shortly, the coating at the edges of the coated tablets was carefully detached. Afterwards, the coated tablet was fixed with double sided adhesive tape to a flat punch of a material testing machine (Retroline BZ2, Zwick Roell AG, Germany). Double sided adhesive tape was also placed on the equivalent upper punch of the testing machine which was then pressed onto the tablet surface (film) with a fixed force of 100 N. After a defined contact time of 45 s, the upper punch was lifted with a constant speed of

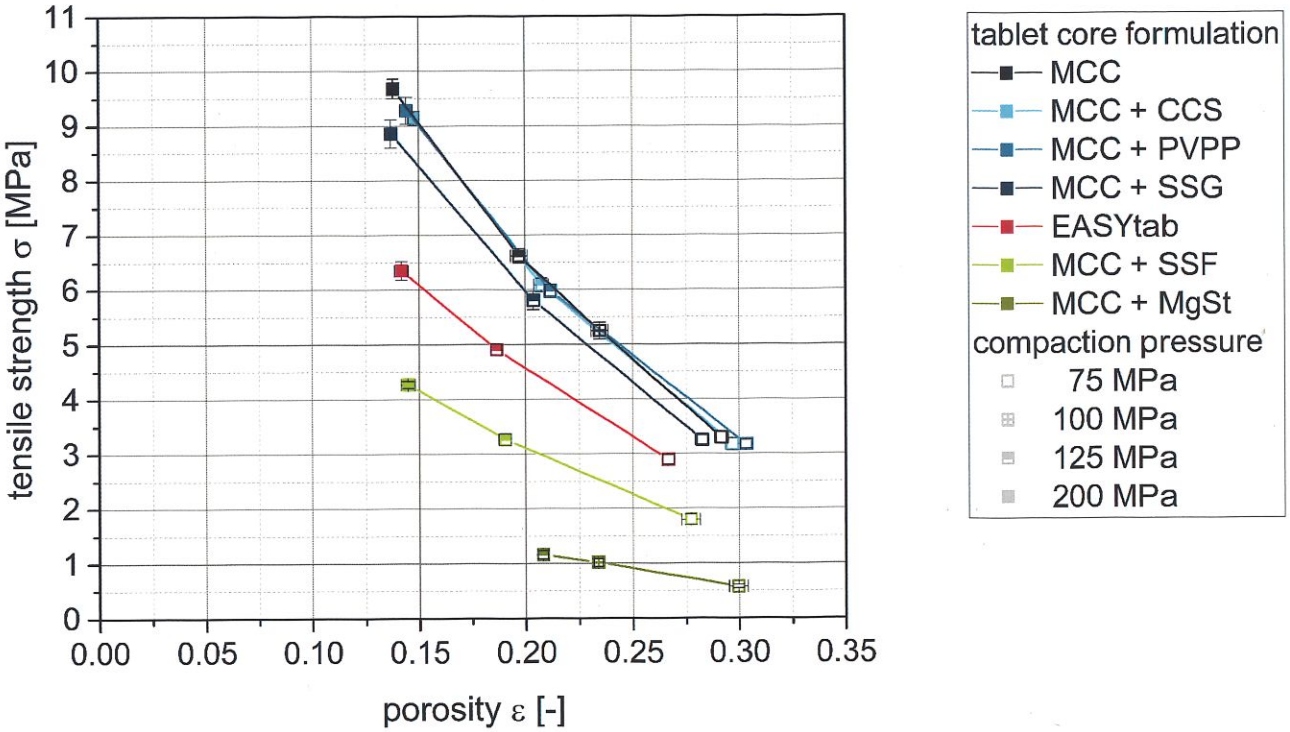

Figure 1: Bondability plots of the investigated tablet core formulations (n = 20); (source of all figures: the authors).

3 mm/s, detaching the film coating from the tablet core. The stress of failure was extracted and used as a measure for apparent film coating adhesion.

Results and Discussion

For the uncoated tablet cores, generally all formulations showed decreasing mechanical stability with increasing porosity or decreasing compaction pressure (fig. 1).

The formulation entirely consisting of the plastically deforming binder MCC showed the highest bondability (strength at given porosity) of all formulations whereby the addition of functional excipients decreases the binding capacity of MCC. However, the extent of the adverse effect is dependent on the excipients class. The addition of disintegrants decreased bondability only slightly. In fact, similar bondabilities to pure MCC were achieved when 5 % PVPP or CCS were applied. The addition of SSG caused a decrease in bondability, which may be attributed by a disturbance of interparticulate bonding forces between the MCC particles by the SSG particles. Addition of lubricants caused a more distinct decrease of bondability, which can be attributed to a profound disruption of interparticulate bonds by particles formation of hydrophobic layers around the MCC particles [6,7]. This effect was more pronounced for magnesium stearate, which decreased bondability to a higher extent than SSF, which is in accordance with the literature [8]. In contrast to formulations exclusively containing lubricants, EASYtab containing SSF among other excipients, exhibited an essentially increased bondability. This can either be caused by different amounts of lubricant in the commercial formulation and/or by a positive effect of the co-processing.

Results of adhesion measurements (i.e. stress of failure) of the HPMC-based coating on the tablet cores compressed with different compaction pressures can be found in fig. 2 as a function of the tensile strength (left) and porosity (right) of the tablet cores.

Results of adhesion measurements of the HPMC-based coating on the tablet cores show that the stress of failure increases with increasing tensile strength (fig. 2, left) or decreasing porosity (fig. 2, right) for all investigated tablet core formulations. Furthermore, it was observed that the amount of powder particles remaining on the detached films decreased with increasing compaction pressure. This indicates, that the portion of fundamental adhesion failure between the film coating and the tablet surface increases and the portion of cohesive failure between individual powder particles within the tablet core decreases with increasing tensile strength of the tablet cores. This observation highlights the importance of tensile strength for apparent film coating adhesion, as failure at lower tensile strength (and compaction pressures) are mainly caused by cohesive failure within the tablet core rather than by adhesive failure between the tablet core and the film coating. However, the influence of the tensile strength can be assumed to heterodyne with other properties of the tablet core, e.g. caused by incorporated functional excipients, which generally

Pharm. Ind. 82, Nr. 8, 1072–1077 (2020)

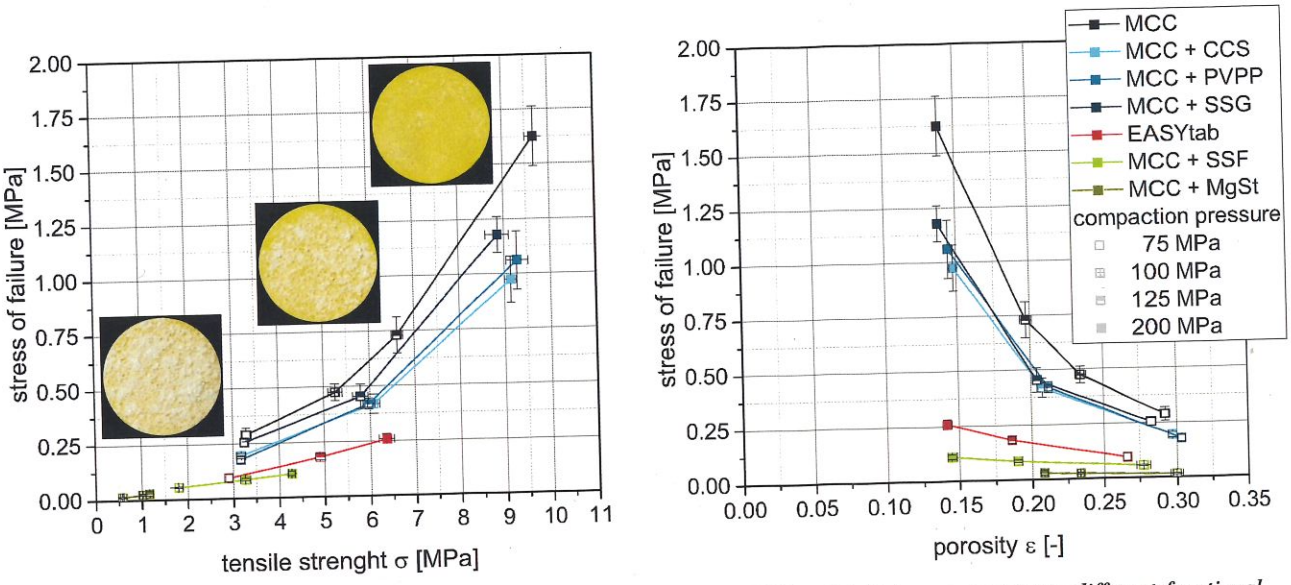

Figure 2: Stress necessary to detach the HPMC-based film coatings from MCC-based tablet cores containing different functional excipients as a function of the tensile strength (left) or porosity (right) (n = 10). Integrated pictures refer to typical appearance of the bottom side of detached films in the corresponding tensile strength region (white = remaining powder particles, yellow = film material).

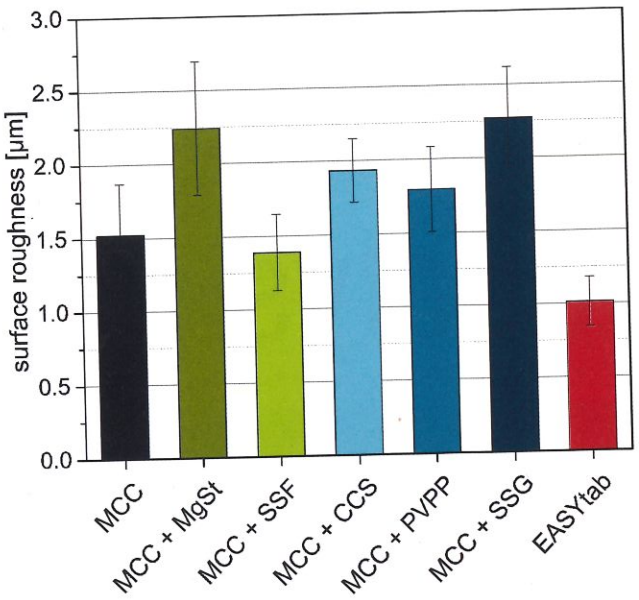

Figure 3: Mean surface roughness of the different tablet core formulations compressed at a compaction pressure of 125 MPa (n = 3).

had a negative effect on apparent film coating adhesiveness. This may be attributed to a decreasing fundamental adhesion between the tablet core and the film coating, as significantly different stresses of failure were observed for differently formulated tablet cores exhibiting similar tensile strengths. The addition of disintegrants (i.e. CCS, PVPP or SSG) decreased apparent adhesion to a lesser extent than lubricants (i.e. SSF, MgSt). The latter may decrease film coating adhesion by hydrophobization of the tablet core surface [9–11]. However, in the present study mainly cohesive failure within the tablet core was observed for the corresponding formulations indicating that fundamental film coating adhesion is not decisive for apparent film coating adhesion. Within the group of formulations containing lubricants (MCC + MgSt, MCC + SSF, EASYtab) film adhesion values showed the same ranking as for the corresponding tablet core's tensile strengths (fig. 1), i.e. highest for EASYtab and lowest for MCC + MgSt. This further indicates that the tensile strength is the superordinate factor influencing apparent film coating adhesion for the corresponding formulations. Disintegrants in the tablet core may take up water during the coating process and undergo a partial local disintegration of the tablet core at the surface, causing the apparent film coating adhesion to be reduced in comparison to pure MCC tablet cores. This hypothesis is assisted by the observation that a lower porosity is advantageous for the apparent film coating adhesion for the corresponding formulations, as a lower porosity is assumed to result in a lower water uptake by the tablet cores during the coating process.

Surface roughness of the tablet cores was increased by addition of functional excipients in comparison to pure MCC tablets (fig. 3) which can also influence film coating adhesion [3]. Exceptions of this are the formulation containing SSF as a lubricant and the ready-to-use formulation EASYtab. The latter provided the smoothest surface roughness of all formulations tested. These differences in surface roughness are in line with differences in porosity of the tablet cores (fig. 1) indicating that an increased surface roughness may be caused by an increased porosity of the corresponding tablet core.

Comparing data in fig. 2 and 3 clarifies, that no clear trend between film coating adhesion and surface roughness can be concluded. However, results for the formula-

Pharm. Ind. 82, Nr. 8, 1072–1077 (2020)

Table 1

Investigated tablet core formulations.

Formulation	Lubricant	Disintegrant	MCC
MCC	-	-	100 wt%
MCC + MgSt	1 wt% MgSt	-	99 wt%
MCC + SSF	1 wt% SSF	-	99 wt%
MCC + CCS	-	5 wt% CCS	95 wt%
MCC + PVPP	-	5 wt% PVPP	95 wt%
MCC + SSG	-	5 wt% SSG	95 wt%
EASYtab	SSF	SSG	SMCC

tion containing SSG exhibiting by trend the highest surface roughness and highest stresses of failure of all formulations containing disintegrants, may indicate that a higher surface roughness is advantageous for film coating adhesion e.g. by increasing the contact area between the tablet core and the film coating [3]. However, importance of tensile strength is assumed to be superordinate and should be controlled in order to achieve a sufficient apparent film coating adhesion.

Summary and Conclusion

The influence of functional excipients on the properties of MCC-based tablet cores compressed at different compaction pressures was investigated with special respect to the apparent adhesion of an applied HPMC-based film coating. It was found that different proportions of fundamental adhesion between the coating and the tablet surface and cohesion between the powder particles within the tablet core determined apparent, and by that process-relevant film coating adhesion. The proportion of fundamental adhesion failure (i.e. between coating and tablet core) was observed to increase with increasing tensile strength of tablet cores. At lower tensile strengths, cohesive failure within the tablet core was observed to be crucial for apparent film coating adhesion. Although functional excipients significantly influenced surface roughness of tablet cores, no clear correlation between the surface properties and the apparent adhesion of the film coating could be extracted, leading to the assumption that tensile strength of tablet core is the most dominant factor determining the apparent adhesion of an HPMC-based coating to MCC-tablet cores.

REFERENCES

[1] Warnke, G. Pharmaceutical Coatings. In: Ullmann's Encyclopedia of Industrial Chemistry; Wiley-VCH Verlag: 2000, ISBN 9783527303854.

[2] Felton LA. Porter SC. An update on pharmaceutical film coating for drug delivery. Expert. Opin. Drug. Deliv. 2013;10:421–435, doi:10.1517/17425247.2013.763792.

[3] Nadkarni PD, Kildsig DO, Kramer, PA, Banker GS. Effect of surface roughness and coating solvent on film adhesion to tablets. J. Pharm. Sci. 1975;64:1554–1557.

[4] Fell FT, Newton JM. Determination of tablet strength by the diametral-compression test. J. Pharm. Sci. 1970;59:688–691.

[5] Fischer D.G, Rowe RC. The adhesion of film coatings to tablet surfaces - instrumentation and preliminary evaluation. J. Pharm. Pharmacol. 1976;28:886–889.

[6] Strickland WA, Higuchi T, Busse LW. The physics of tablet compression X: Mechanism of action and evaluation of tablet lubricants. J. Am. Pharm. Assoc. 1960;49:35–40.

[7] Strickland WA, Nelson E, Busse, LW, Higuchi T. The physics of tablet compression IX: Fundamental aspects of tablet lubrication. J. Am. Pharm. Assoc. 1956;45:51–55.

[8] Louw, R. Evaluation and comparison of magnesium stearate and sodium stearyl fumarate (Pruv) as lubricants in directly compressible tablet formulations: Their effect on tablet properties and drug dissolution. Dissertation; Potchefstroomse Universiteit vir Christelike Hoer Onderwys, 2003.

[9] Kondo H, Toyota H, Kamiya T, et al. Effect of the external lubrication method for a rotary tablet press on the adhesion of the film coating layer 2017;65:848–853.

[10] Banovec M, Planinsek O, Vrecer F. The effect of cores and coating dispersion composition on the mechanical and adhesion properties of hydroxypropyl methylcellulose films. Pharmazie. 2014;69 (8):595–60

[11] Felton LA, McGinity JW. Influence of tablet hardness and hydrophobicity on the adhesive properties of an acrylic resin copolymer. Pharm. Dev. Technol. 1996;1:381–389, doi:10.3109/10837459609031433.