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Investigation of Ethylcellulose as a Matrix Former and a New Method to Regard and Evaluate the Compaction Data

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ABSTRACT

Three types of ethylcellulose—having different molecular weights, i.e., different viscosity grades (7, 22, 50 cP)—were used for our polymer compression tests for the production of matrix tablets. The production methods used were direct compression and wet granulation. We tested the compactability, the compressibility, and the energy involved in compaction by the use of F–D *curves and the controlled drug release from the ethylcellulose matrix tablets using the above-mentioned methods. A lower viscosity grade in ethylcellulose is more compressible than the higher grade. Wet-granulated ethylcellulose also shows a better compactibility than directly compressed ethylcellulose. Our investigation indicates also that the dissolution rates are indirectly proportional to the hardness of the tablets. Furthermore, wet-granulated tablets produce a more rapid drug release than those which are directly compressed.*

INTRODUCTION

Ethylcellulose is an inert, hydrophobic polymer (1,2) and has been extensively used as a pharmaceutical vehicle in a number of dosage forms. It has been used as a coating material for tablets and granules (3,4), as a tablet binder (5), in preparing microcapsules and microspheres (6,7), and also as film- and matrix-forming material for sustained-release dosage forms (8). It has also been used as a matrix for preparation of both water-soluble and water-insoluble drugs using the solid dispersion technique (9,10). Preparation of these forms

Presented at the 2nd European Congress for Pharmaceutical Science. This paper is dedicated to Prof. Dr. hc. Helmut Kala on the occasion of his 70th birthday.

required several unit operations. Especially noteworthy is that most of these processes require solubilization of all or part of the ethylcellulose using organic solvent. Environmental issues are making these processes less tolerable and more expensive.

Direct compression, then wet granulation with hydrophilic solution is the preferred method for the production of tablets.

The aim of this work is:

1. Investigation of the compressibility (11,12), the plasticity (13), and the compactability of ethylcellulose with different viscosity grades.
2. The examination of its mechanical properties during compaction by the use of *F–D* curves (14), the energy of the compaction (15), and the hardness of the tablets.
3. Testing whether the viscosity grade and the production method have an effect on the release from these matrix tablets.

EXPERIMENTAL METHOD

Material

Theophylline (anhydrous DAB 10) and magnesium stearate (DAB 10) were used. Three viscosity grades (7, 22, and 50 cP) of ethylcellulose were used. They were gifts (standard grade) from Hercules Aqualon company in Darmstadt, Germany, and have an ethoxyl content of 48.0–49.5%.

Experimental

Tablets were manufactured by direct compression and wet granulation with distilled water. The tablets were then dryed until they had the same humidity as before the wet granulation.

We used two recipes: in the first only ethylcellulose was used to examine its compressibility and compactibility; and in the second a 1:1 ratio of drug (theophylline) to polymer and 1% magnesium stearate was used.

1. The weight was fixed at 202 mg and the material was compressed using an eccentric tablet press EK-0 DMS (Korsch) connected to a measure-amplifier of the DMS-plus type from the HBM Company (Darmstadt Germany). The frequency carrier strengthening of 4.8 kHz of each channel was reinforced.
2. The material was compressed with flat circular punches of 9 mm diameter at a rate of 10 tablets/min.
3. Diametral crushing strength was tested using an Erweka strength tester (TBH-28, Erweka Gmbh; Germany).
4. Tablet height ($\pm$ 0.001) was measured using a micrometer calliper (Germany).
5. The disintegration time was determined for 6 tablets corresponding to DAB 10 in distilled water of 37°C.

Calculation

We used BEAM software (Ams–Flöha) to examine the measurements of mechanical and electrical quantities as well as to evaluate the measured data. We automated this program so that the compression and the evaluation (AUC, statistical evaluation, etc.) could be done simultaneously.

Discription of BEAM

The BEAM software offers unique possibilities when regarding measurements of mechanical and electrical quantities as well as the evaluation and presentation of measured data. It incorporates a versatile basis enabling the user to adjust the measuring parameters to specific requirements, being either a "high-end measurement" related to research and development, or a "one-key measurement" which has to always be repeated with the same settings.

Due to the visual and graphic advantages of the Macintosh system, BEAM also offers the possibility of presenting the process of tablet pressing in real time.

RESULTS AND DISCUSSION

The Compactibility and Compressibility

With an increase in viscosity grade, a decrease in compressibility and compactibility was observed in both production methods.

We also found that lower viscosity grade of ethylcellulose (EC) allows production of harder tablets when compressed under the same compression force (16) (Fig. 1).

Wet granulation also allows production of harder tablets than tablets directly compressed, which could occur through hydrogen bridging between the molecules (Fig. 2).

Numerous papers on the compression of powder discuss the compressibility, i.e., the ability of a powder to decrease in volume under compression stress (17). Figure 3 shows that ethylcellulose with a low viscosity

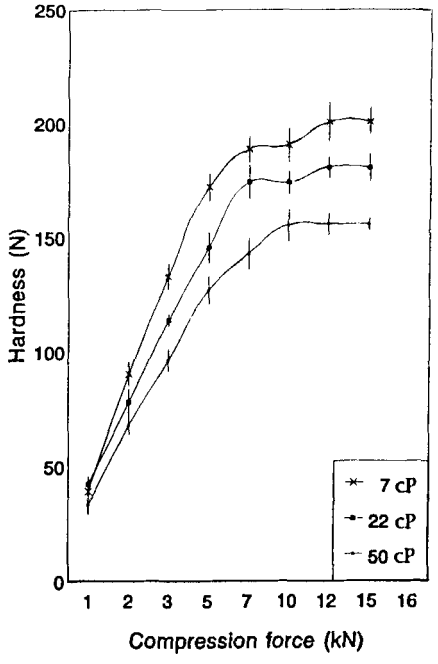

Figure 1. The compactibility of EC with different viscosity grades: directly compressed.

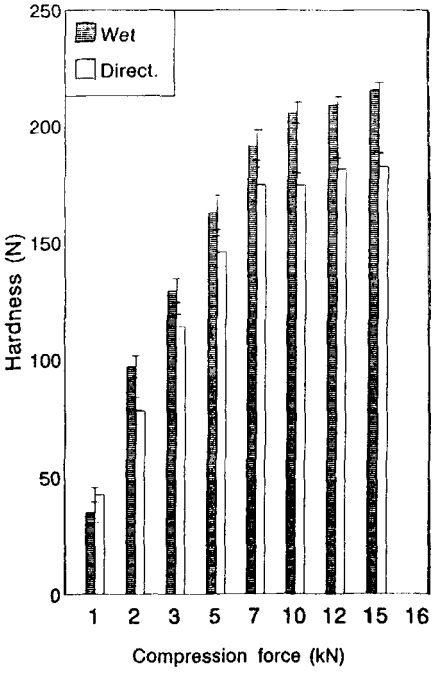

Figure 2. The compatibility of EC 22 cP, from two production methods: direct compression and wet granulation.

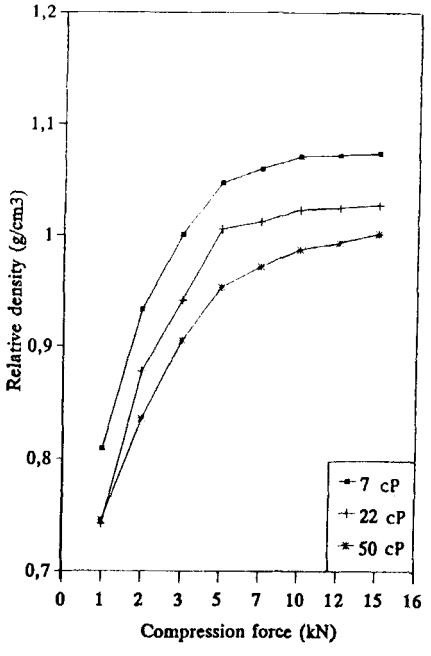

Figure 3. The compressibility of EC with different viscosity grades.

grade is more compressible than that with higher viscosity. The fragmentation rate (18) of EC with lower molecular weight is more effective than the rates of those with a higher molecular weight, which could be a reason for the better compressibility of this type of EC.

We have also examined the plasticity of Stamm and Mathis (14) and found that the plasticity is indirectly proportional to the molecular weight (Fig. 4). We could not find a significant difference in compressibility between the two production methods we used.

F–D Curves: Energy Involved in Compaction

A common method for assessment of the compaction behavior of materials is the use of compression force punch displacement profiles (*F–D* curves), from which the energy distribution can be calculated (Fig. 5).

We observed that the effective energy (formation energy) during compaction of different ethylcellulose viscosity grades and the hardness of their compacts were similar (Fig. 6).

The correlation coefficient found, 0.992, is evidence for the linearity between the hardness and the effective energy. Our conclusions support the work of Celik and Marshall (19). Fell and Newton (20) have the opinion that the total work done on the compaction ($E2 + E3$,

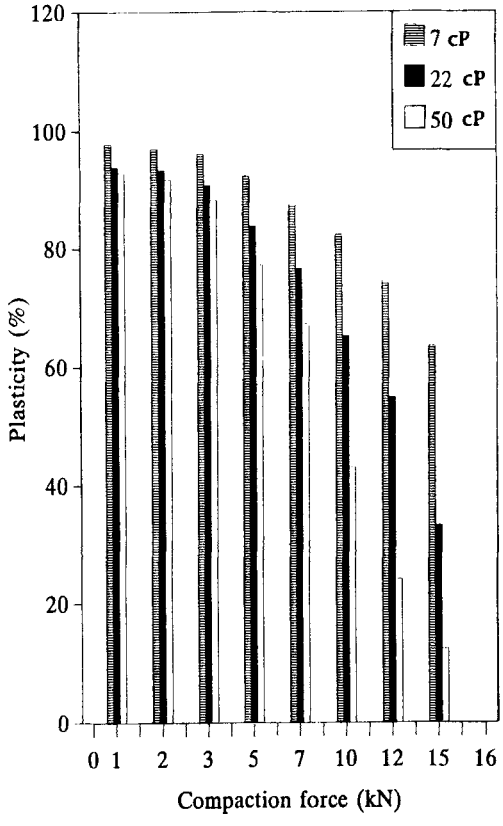

Figure 4. The plasticity (Stamm and Mathis, Ref. 14) of EC with different viscosity grades during compression.

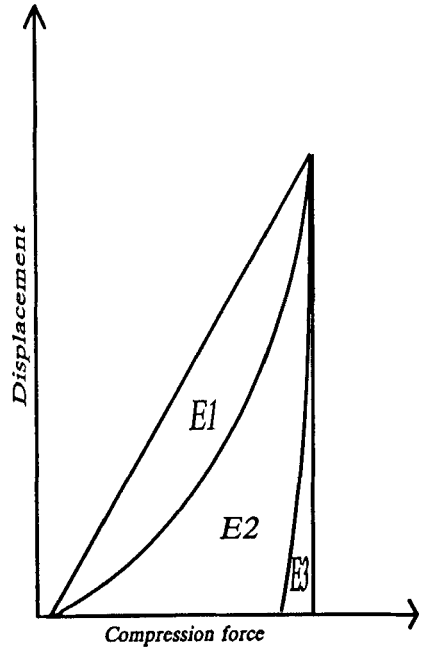

Figure 5. Force displacement curve.

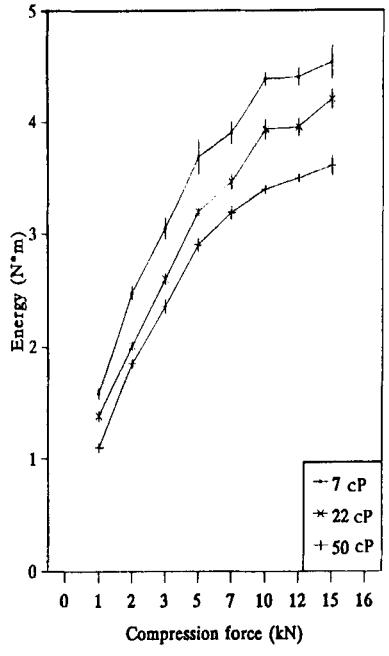

Figure 6. The formation energy of EC with different viscosity grades during compression.

Fig. 5) is not necessarily a criterion of the tablet strength.

The difference between the effective energy of wet-granulated tablets and directly compressed tablets was not significant.

During decompression some of this energy will be transfered back to the upper punch and this compact expansion is due to elastic recovery of the material, as Jones (21) pointed out; but this expansion may continue after the top punch has lost contact with the compact and, thus, the measured expansion may not truly represent the complete expansion of the compaction. For that reason, it was necessary to find another method to examine the ability and capacity of the compaction extension. That will be published soon.

Nevertheless, it was possible through *F–D* curves to point out that the higher the viscosity grade, the higher is the expansion of the compaction (Fig. 7).

The wet granulation method caused a decrease of the expansion (Fig. 8), which may be caused through a lowering of the ethylcellulose crystallinity and a increase in the amorphous part of EC (22).

We could measure a significant lowering in glass transition temperature of the wet-granulated ethylcellulose.

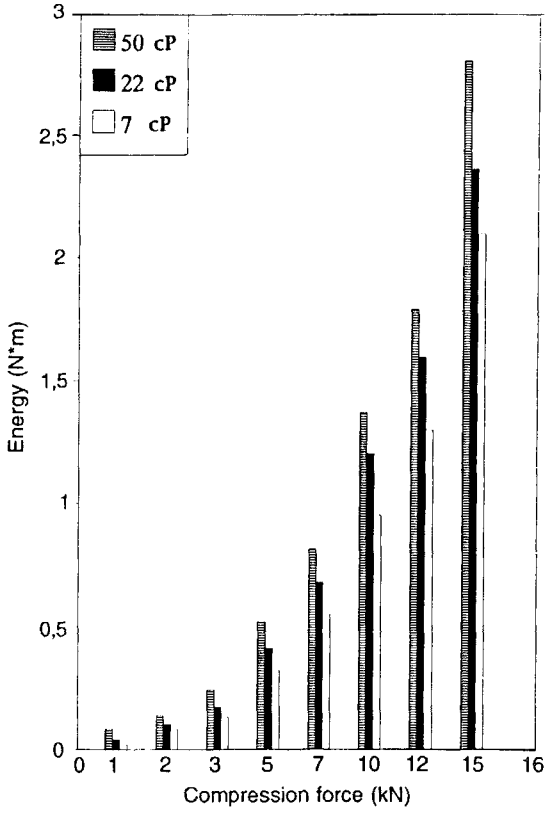

Figure 7. The elastic recovery energy (expansion) of EC with different viscosity grades.

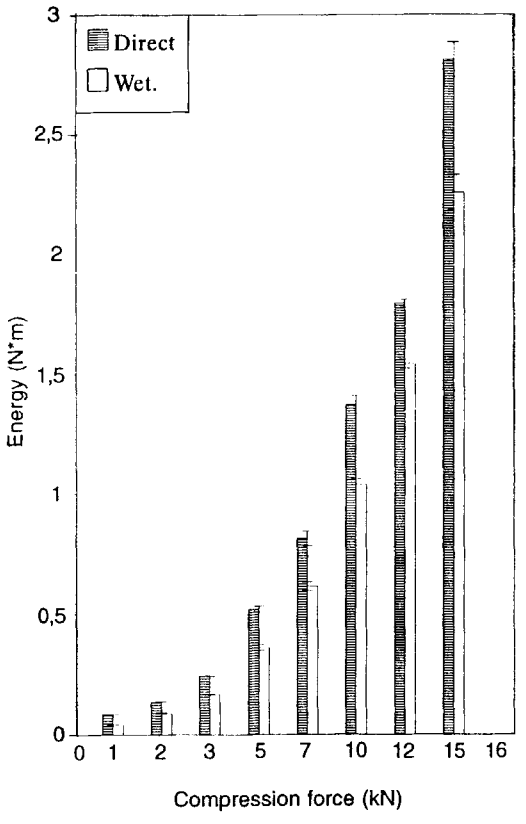

Figure 8. The elastic recovery energy (expansion) of EC, 50 cP, in different production methods.

Dissolution Profile of Directly Compressed Tablets

An increase in dissolution rates for the drug (theophylline) was also observed with a decrease in the hardness (16).

In order to separate the hardness effects from constituent effects, tablets incorporating each ethylcellulose viscosity grade were compressed to constant hardness (65 N) by varying the compression force.

Ethylcellulose with a lower viscosity grade produced the slowest dissolution rates, and that with a higher viscosity grade the fastest dissolution rates (Fig. 9). The drug release was determined through diffusion and erosion (23,24).

Tablets with a lower viscosity grade have a lower porosity (Fig. 10), causing slower diffusion rates than those which have a higher porosity.

We could influence the compressibility and the drug release through the addition of polyethylene glycol 6000 (25).

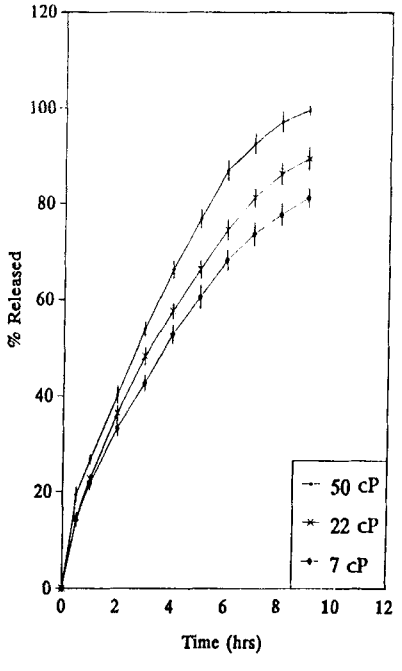

Figure 9. Dissolution profiles of tablets compressed directly to constant hardness with different viscosity grades of EC

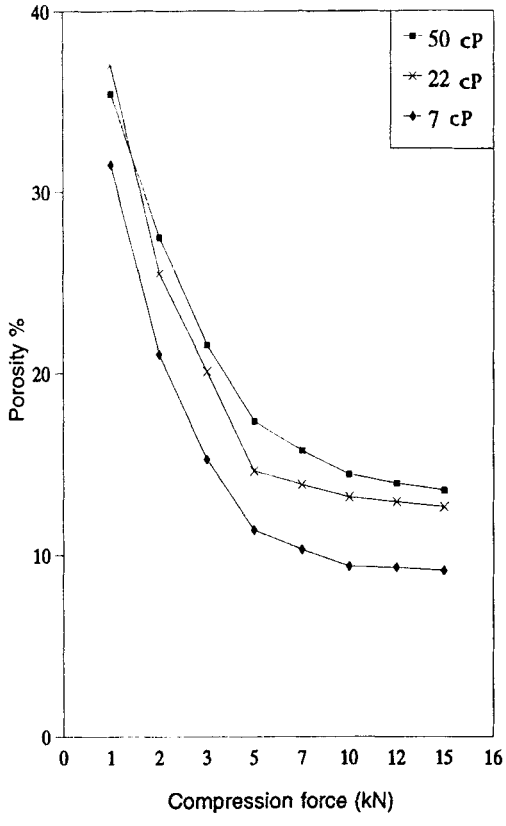

Figure 10. The porosity of EC tablets with different viscosity grades.

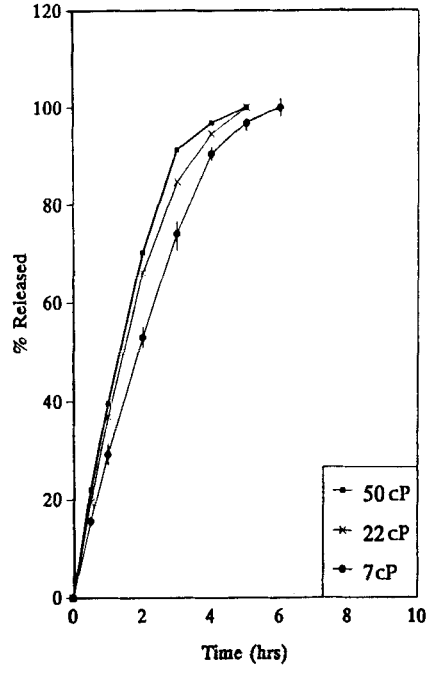

Figure 11. Dissolution profiles of tablets compressed after wet granulation to constant hardness with different viscosity grades of EC.

Dissolution Profile of Wet-Granulated Tablets

An increase in the dissolution rates for the drug was observed with wet granulation (Fig. 11). This could increase the erosion rates of the drug release from the tablets (26).

A part of the theophylline will be dissolved and after drying will be recrystallized on the surface of the EC particle, and then will be compressed. During the drug release examination water will be absorbed in the tablet; this will cause the solution of the theophylline, which will be a reason for the lowering in the binding force between the particles.

CONCLUSION

The results of the present investigation demonstrate that ethylcellulose is a good direct compression matrix former. The lower viscosity grades of ethylcellulose are more compressible and compactible than the higher viscosity grades.

The drug release can be controlled by altering different factors:

1. The hardness of the tablets
2. The viscosity grade of the ethylcellulose
3. The production method
4. Addition of polyethylenglycol 6000

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