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RESEARCH PAPERS

EFFECT OF SOME EXCIPIENTS AND COMPRESSION PRESSURE ON THE ADHESION OF AQUEOUS-BASED HYDROXYPROPYL METHYLCELLULOSE FILM COATINGS TO TABLET SURFACE

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ABSTRACT

The adhesion between aqueous-based hydroxypropyl methylcellulose (HPMC) films and tablet surface was evaluated using a Lloyd LRX materials testing machine. Special attention was paid to the effects of compression pressure and the excipients (microcrystalline cellulose, lactose and a commercial combination of lactose and cellulose (Cellactose^{R})) on the adhesion properties of the film.

The adhesion of HPMC films was the lowest for the tablets containing lactose as a diluent and the highest for the tablets containing microcrystalline cellulose. The adhesion to Cellactose^{R}-based tablets increased with increasing compression pressure. With microcrystalline cellulose (MCC) and lactose, the effect of compression pressure on film adhesion was not so clear. The increase in concentration of a hydrophopic lubricant, magnesium stearate, decreased the adhesion between the films and tablets cores. The greatest decrease was observed with the MCC tablets.

Furthermore the results showed that, the film coating increased clearly the mechanical strength of the tablets, depending on the excipient, the compression pressure and amount of magnesium stearate.

INTRODUCTION

The aqueous-based film coating of hydroxypropyl methylcellulose (HPMC) has been widely used in the pharmaceutical industry to protect tablets from physical enviromental stresses, such as air, moisture and light, to improve their mechanical strength and to mask unpleasant taste and odour. Thus uniform wetting of tablet cores with coating solution and good adhesion between a coating film and the tablet surface are desirable properties in a film coating process. The wettability of tablet cores can be predicted by using contact angle measurement (1, 2).

The adhesion of organic-solvent -based coatings to tablet core has been investigated in some previous studies (3, 4). Rowe (5) studied the effects of some direct compression excipients and lubricants on the adhesion of hydroxypropyl methylcellulose film. The adhesion was found to be influenced by the roughness of the tablet surface and its polarity. The addition of a hydrophopic lubricant, magnesium stearate, was found to decrease the adhesion. Fisher and Rowe (6) found adhesion to be dependent on the compression pressure used to prepare tablets. The adhesion decreased with increasing compression pressure. Nadkarni et al. (1) postulated that the solvent from which a polymer film is cast can significantly affect the film's adhesion to the tablet core.

The earlier studies (3, 4, 5) were based on organic solutions. At present, the use of aqueous-based HPMC solutions in film coating is increasing.

The objective of this work was to investigate the effects of excipients (microcrystalline cellulose, lactose and a commercial combination of lactose and cellulose (Cellactose^{R}) on the adhesion of aqueous-based hydroxypropyl methylcellulose (HPMC) film coatings. The mechanical strength of tablets was also examined.

MATERIALS AND METHODS

Tablet formulation and preparation

The tablets were compressed from microcrystalline cellulose (Emcocel 90 M, Edward Mendel, Finland), lactose (Lactose NF tablettose, Meggle, Germany) and a commercial combination of lactose and cellulose (Cellactose^{R}, Meggle, Germany). Magnesium stearate (Ph. Eur.) was used as an external lubricant at the concentrations of 0.5%, 1.0% and 1.5%. The tablet cores were compressed in an instrumented Korsch EK-O single-punch tablet machine (Korsch GmbH, Germany) using flat-faced 11 mm punches and compression pressures of 100, 150 and 200 MPa. The weight of the tablets was 300 mg. The mechanical strength of the tablets was measured using Pharmatest (Pharmatest, Sweden). The determination was repeated ten times for each tablet batch.

Surface morphology of tablets

The surface of the uncoated tablets was studied by scanning electron microscopy (JEOL JSM-820, Japanese Electron Optical Ltd., Tokyo, Japan).

Coating solution formulation and preparation

The aqueous film coating solution consisted of hydroxypropyl methylcellulose 10% (Methocel E5, Dow Chemical, U.S.A.), polyethylene glycol 20% of the polymer weight (Macrogol 400, Hoechst, Germany) as a plasticizer and purified water. For preparing coating solutions (10% of HPMC w/w), half of the calculated amount of water was heated and the polymer and polyethylene glycol were dissolved in this amount of water using magnetic mixing. The remaining cold water was added when all the polymer had dissolved, and the solution was allowed to complete solvation for at least 8 hours. The coating solutions were stored in a refrigerator ($+8 \pm 1°C$) until they were used.

Viscosity and surface tension measurements

The viscosity of the coating solution was determined by a Ubbelohde capillary viscosimeter (Schott Geräte, Germany). The surface tension was determined by a computer controlled and user programmable tensiometer (KSV, Sigma 70, Finland) at $20.0 \pm 1.0°C$ using the Wilhelmy plate method. The measurements were repeated ten times.

Coating procedure

The aqueous film coating of tablets was performed using a fluidized-bed coater (Aeromatic Strea-1, Aeromatic AG, Switzerland). The coating solution was continuously fed into a spraying nozzle by a peristaltic pump (Watson-Marlow, England) using a flow rate of 3.5 g/min. The atomizing air pressure was 2.0 bar and drying temperature was $55 \pm 5°C$. The batch size was 400 g. The total coating time was 30 minutes. The amount of coating solution used 125 g which led to a film thickness of 75 μm.

Contact angle measurement

The contact angles between the coating solution and tablets were determined by the sessile drop method (Lorenz & Wettre, Stockholm Sweden), placing small droplets (volume 10 μl) on the tablets.

The height of the droplet and the width of the base of the droplet were measured, and the contact angle was calculated (7). The measurements were repeated ten times for each tablet batch.

Adhesion measurement

A Lloyd LRX material testing machine (Lloyd Ltd., England) was used to measure the adhesion of film coatings to the tablet surface. In preparation for

testing, the film from around the edges of the tablets was removed using a sharp blade. The tablet was mounted into the lower grip of a material testing apparatus with a piece of double-sided adhesive tape. The upper grip with a piece of adhesive tape was then driven onto the tablet surface, and a fixed force of 3.0 N was used to get a firm contact of the tape to the film. The film was removed from tablet surface by lifting the upper grip. Adhesion strength measurements were performed using a 50 N load cell and a cross speed of 7.5 cm/min. The measurements were repeated six times.

RESULTS AND DISCUSSION

The evaluation of core tablet surfaces was based on SEM micrographs. As seen in Figure 1 a-b, the tablet cores were quite rough with low compression pressure, and they became smoother with increasing compression pressure. There is also a significant difference in microstructure of tablets based on different direct compression diluents.

Contact angle

The contact angles between HPMC solutions and the tablet cores are shown in Table 1. The contact angle between HPMC solutions and the tablet surface increased with increasing compression pressure.

According to Wenzel (8), polymer solution spreads more readily when the tablet surface is rough; the contact angle decreases with increasing roughness of tablets. Our results are in accordance with those presented by Wenzel (8). Even more clearly the contact angle increases with increasing concentration of magnesium stearate in the tablet formulation. The contact angles were the highest between polymer solution and microcrystalline cellulose tablets, ranging from 55.2 to 80.8°. The difference of contact angles between tablets is due to a difference in their composition.

Adhesion

The adhesion of the polymer film to tablet surface was measured as the force (N) required to remove the film from of the tablet surface. It is expected that the film adhesion to tablet surface increases with a decrease in the contact angle, i.e. solution spreads more readily on the tablet surface. Nadkarni et. al. (1) have studied adhesion between organic-based polymer films and tablets compressed at different compression pressures. They suggested that adhesion decreases as the compression pressure increases, because tablets produced at high compression pressure had smoother surfaces than those produced at lower compression pressure, resulting in a decrease in the effective area of contact between the film and the tablet surface. Fisher and Rowe (6) found that, after a certain critical

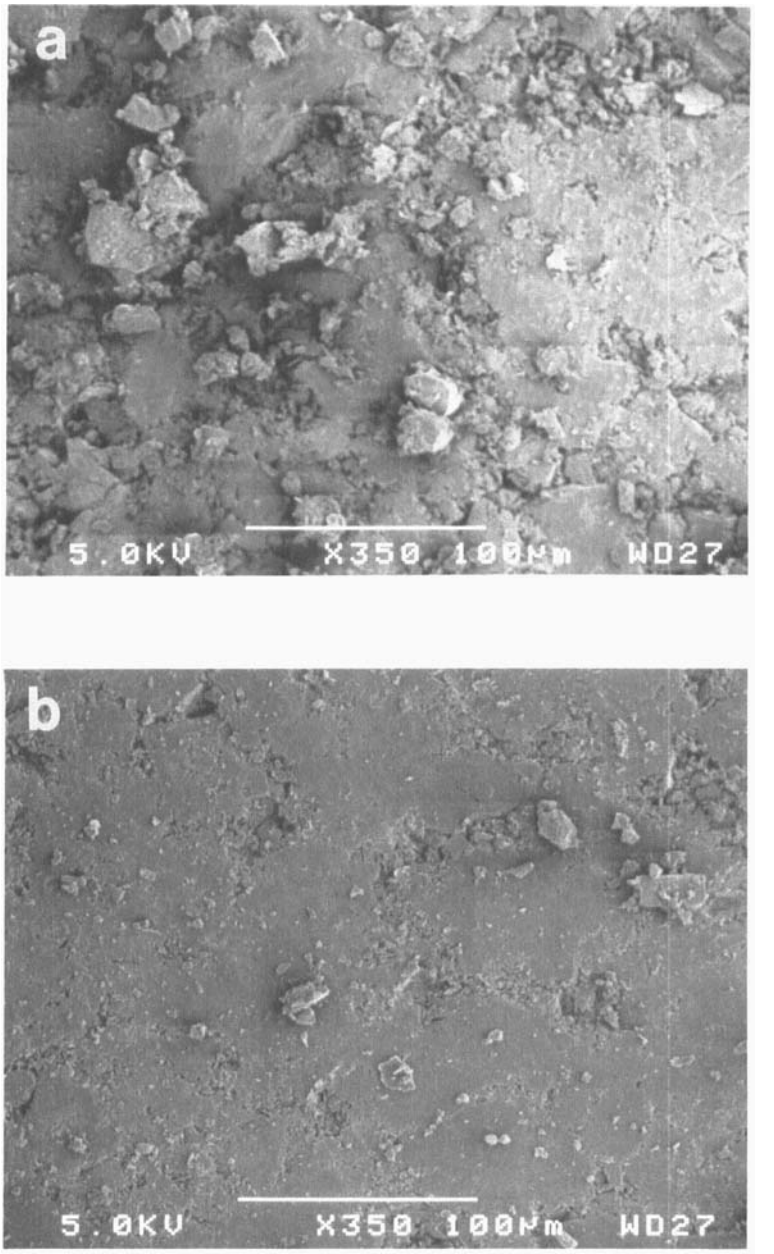

FIGURE 1 a-b
SEM micrographs of lactose tablet core surfaces. Compression pressures a) 100 MPa and b) 200 MPa. The bar in the figure is 100 μm.

TABLE 1
The contact angles between tablet cores and aqueous-based HPMC solutions (n = 10).

Tablet excipient	Compression pressure (MPa)	Amount of magn. stear. (%)	Contact angle (°) mean ± S.D.
MCC			
	100	0.5	56.5 ± 1.3
		1.0	63.6 ± 2.7
		1.5	68.9 ± 1.5
	150	0.5	55.2 ± 1.6
		1.0	66.6 ± 4.3
		1.5	69.8 ± 1.5
	200	0.5	62.2 ± 1.3
		1.0	72.1 ± 3.2
		1.5	80.8 ± 3.6
Lactose			
	100	0.5	40.2 ± 2.4
		1.0	58.3 ± 2.8
		1.5	68.0 ± 1.6
	150	0.5	46.2 ± 2.0
		1.0	64.2 ± 2.4
		1.5	71.9 ± 1.4
	200	0.5	50.8 ± 1.6
		1.0	66.4 ± 2.1
		1.5	78.4 ± 2.6
Cellactose^{R}			
	100	0.5	44.8 ± 1.5
		1.0	53.4 ± 1.3
		1.5	57.4 ± 2.2
	150	0.5	47.8 ± 2.1
		1.0	54.0 ± 1.8
		1.5	62.0 ± 2.9
	200	0.5	48.1 ± 1.4
		1.0	55.7 ± 1.2
		1.5	66.1 ± 2.1

compression pressure, the measured adhesion decreased as the compression pressure increased.

Fisher and Rowe (6) found that adhesion with low-viscosity organic-based film coating solution was higher than that with high-viscosity solution, because low-viscosity solution can easier penetrate into pores on the surface of tablets than high- viscosity solutions. With high-viscosity solutions the effective area of contact will be lower, resulting in lower adhesion values.

In our studies, aqueous-based HPMC solutions were used, and their viscosity (218 mPas) and surface tension (40.9 mN/m) were quite high compared to organic-based solutions. It can be supposed that high-viscosity solutions do not penetrate easily into small pores on the surface of tablets, resulting in a small effective contact area and low adhesion force between coating film and tablet core. When compression pressure increases with increasing smoothness of tablet surface, the contact area between polymer solution and tablet surface increases, resulting in higher adhesion values.

In our studies, adhesion between tablet cores and coating film increased with increasing compression pressure (Figures 2-4). The measured adhesion will be dependent on the area over which interaction occurs. The effect of compression pressure on adhesion was most obvious with Cellactose^{R}-based tablets. When compression pressure was increased from 100 MPa to 200 MPa, the adhesion increased from 106-107 kPa to 159-184 kPa, depending on the concentration of magnesium stearate.

The mechanical strength of microcrystalline cellulose tablets was quite high with the 100 MPa compression pressure, and increasing the compression pressure to 200 MPa had no significant effect on the mechanical strength and surface structure of the tablet (Table 2). For these reasons, the increase in adhesion with increasing compression pressure was not so clear between microcrystalline cellulose tablets as with Cellactose^{R} tablets.

The mechanical strength of lactose tablets was relatively low with a compression pressure of 100 MPa. In the adhesion test, traces of the lactose tablet substrate were observed on the detached films. This observation indicates that the failure was rather cohesive than adhesive. With higher compression pressures there were no traces of tablet substrate on the detached film, indicating that failure occurred strictly between film and tablet surface.

The increase in concentration of magnesium stearate decreased the film adhesion to tablets (Figures 2-4). According to Rowe (5), magnesium stearate interferes

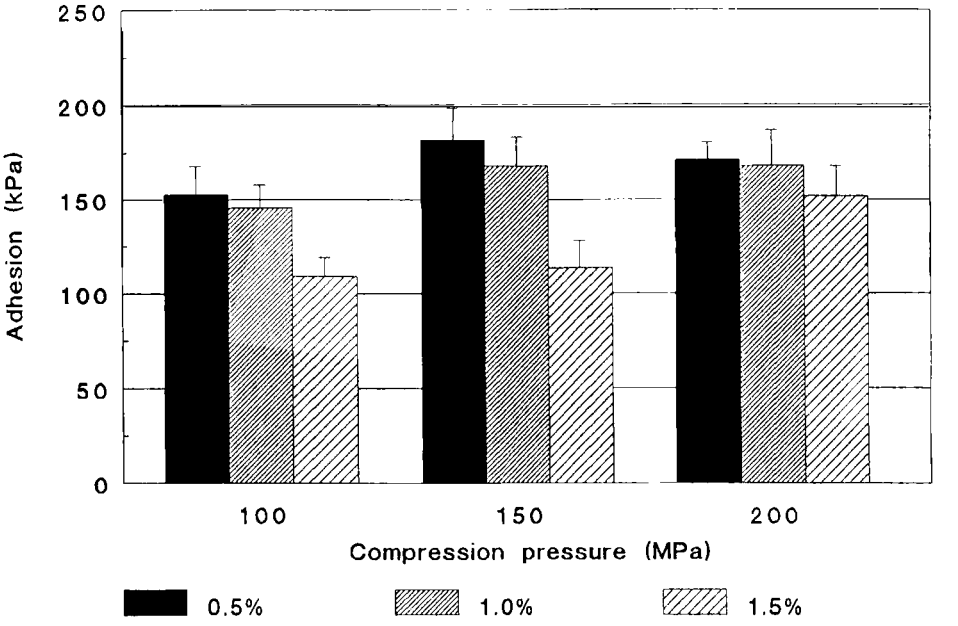

FIGURE 2
Effect of compression pressure and amount of magnesium stearate on adhesion between MCC tablets and HPMC film (n = 6).

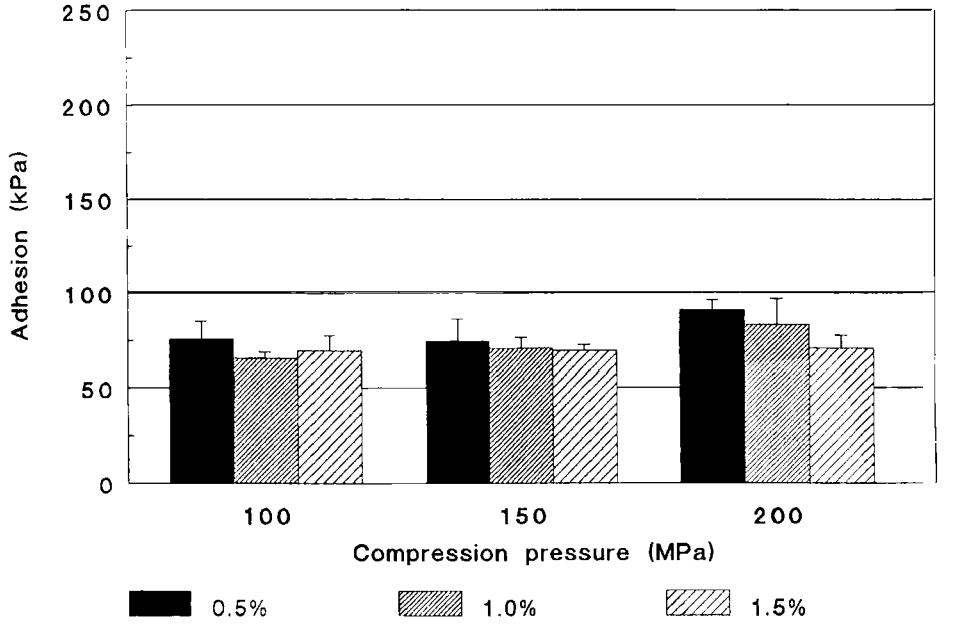

FIGURE 3
Effect of compression pressure and amount of magnesium stearate on adhesion between lactose tablets and HPMC film (n = 6).

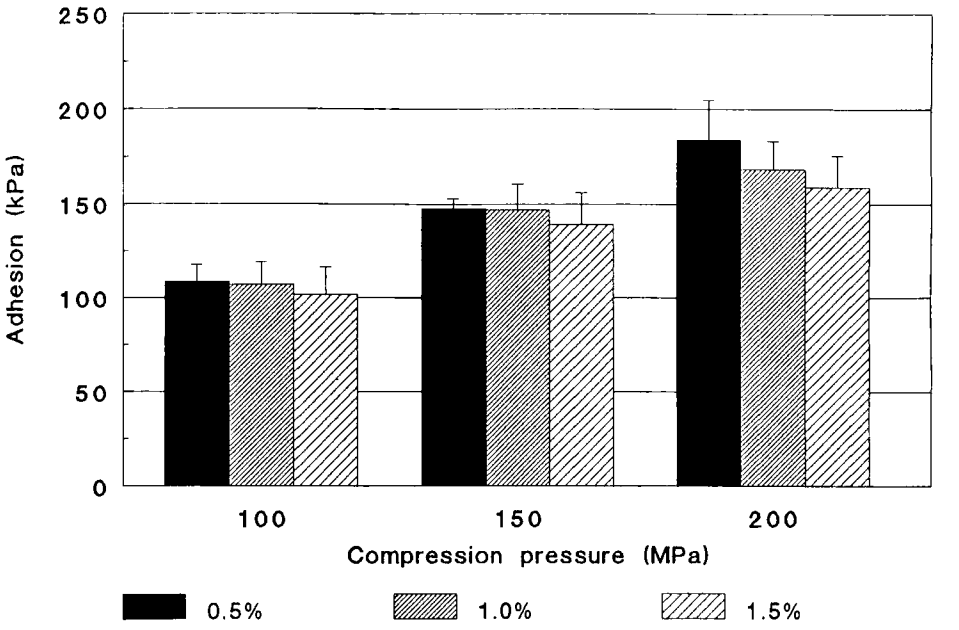

FIGURE 4
Effect of compression pressure and amount of magnesium stearate on adhesion between Cellactose[R] tablets and HPMC film (n = 6).

with the bond formation between tablet surface and coating polymer by presenting a surface consisting mainly of non-polar hydrocarbon groups, and thus the measured adhesion is lowered. Our results are in accordance with those presented by Rowe (5); with increasing concentration of magnesium stearate in the tablet the adhesion decreased.

It is generally accepted that adhesion of a film to tablet core is due to the formation of hydrogen bonds between the polar groups of the film former and the tablet core constituent (5). Both hydroxypropyl methylcellulose and microcrystalline cellulose contain hydroxyl group. Consequently, and for the reason mentioned above, there is a strong adhesion between HPMC film and tablets containing microcrystalline cellulose. With lactose tablets adhesion was the lowest. The results are in accordance with those presented by Rowe (5).

Mechanical strength

One reason for film coating tablets is to increase their mechanical strength and resistance to attrition in high-speed packaging and transportation.

TABLE 2

The mechanical strength of tablet cores and coated tablets compressed with different compression pressures. The amount of magnesium stearate is 1% (n=10).

Tablet excipient	Compression pressure (MPa)	Tablet cores (N) mean ± S.D.	Coated tablets (N) mean ± S.D.
MCC			
	100	204 ± 4	253 ± 10
	150	222 ± 7	253 ± 17
	200	250 ± 16	270 ± 14
Lactose			
	100	31 ± 2	71 ± 6
	150	48 ± 2	87 ± 7
	200	66 ± 3	92 ± 6
Cellactose[R]			
	100	67 ± 5	103 ± 4
	150	103 ± 4	139 ± 8
	200	181 ± 7	206 ± 7

In our studies the film coating increased the tablets' mechanical strength (Table 2). Over the pressure range studied, the mechanical strength of tablet cores and film-coated tablets increased with increasing compression pressure.

The differences in mechanical strength among tablets made of different diluents are due to their different compression behaviour characteristics. With increasing amount of magnesium stearate the mechanical strength of the tablet core and the film-coated tablet decreased.

Fell et al. (9) suggested that a film coat may increase a tablets' mechanical strength by acting as a padding material and also by filling irregularities on the tablet surface. The film may also have an intrinsic strength and elasticity to hold the tablet core together once it has broken. All this increases the strength of film-coated tablets compared to tablet cores.

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