Department of Manufacturing Pharmacy[1], Faculty of Pharmacy, Mahidol University, Bangkok; Department of Pharmaceutical Technology[2], Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok; Department of Pharmaceutical Technology[3], Faculty of Pharmacy, Srinakharinwirot University, Nakhonnayok; Division of Pharmaceutical Sciences[4], Faculty of Pharmacy, Thammasart University, Pathumthani, Thailand

Mechanical and adhesive properties of cellulosic film coats containing polymeric additives

S. Pooponpun[1], A. Polnok[2], O. Paeratakul[3], P. Kraisit[4], N. Sarisuta[1]

Received August 29, 2014, accepted November 23, 2014

Narong Sarisuta, Department of Manufacturing Pharmacy, Faculty of Pharmacy, Mahidol University, 447 Sri-Ayudhya Road, Bangkok 10400, Thailand
narong.sar@mahidol.ac.th

Pharmazie 70: 300–305 (2015) *doi: 10.1691/ph.2015.4129*

The effects of some polymeric additives, i.e. corn starch (CS) and magnesium stearate (MS), on mechanical properties (tensile strength, modulus of elasticity, and elongation at break) and adhesive toughness of hydroxypropyl methylcellulose (HPMC) and ethylcellulose (EC) film coats were investigated. The free and *in situ* films containing 10 and 20% additives by weight of polymer were prepared by spray method. The mechanical properties of both HPMC and EC free films decreased as the concentration of additives was increased because of the lower stiffening effect brought about by hydrodynamic or reinforcing effect. However, adhesive toughness of *in situ* films was found to increase for HPMC whereas that of EC films decreased with the increasing concentration of polymeric additives. Such contradictory results between these two film forming polymers may be attributed to the net result of the opposite effects between interference of film-tablet interfacial bonds and the reduction of mechanical properties. The former seemed to be preferential in the case of EC films, while the latter predominated for HPMC films. Such conclusions were supported by the FTIR results, in which the polymer-additive interaction was found for EC. Increase in concentration of polymeric additives resulted in the decrease in mechanical properties of free films whereas the adhesive toughness of *in situ* films may be influenced by either the interference of film-tablet interfacial bonds or the significant reduction of mechanical properties.

1. Introduction

Film coating has several advantages such as protection of the tablets from light, air, and moisture; masking undesirable taste; improving tablet appearance; controlling drug release, etc. Good adhesion between the polymer and solid surface is a major prerequisite for the film coating of pharmaceutical dosage forms. Loss of adhesion will not only adversely affect the appearance of the film-coated tablets, but also reduce the ability of the film to retain its integrity in protecting the dosage form and drug release characteristics (Felton and McGinity 1997; Felton and McGinity 1999; Missaghi and Fassihi 2004). In addition, substantial quantity of moisture could accumulate at the interfacial void space between the film coating and the tablet surface, a situation that is likely to accelerate the degradation of moisture sensitive drugs (Okhamafe and York 1985, Sarisuta et al. 2006). Coating films generally contain additives such as plasticizers, pigments, and opacifiers to obtain appropriate end-use properties. The mechanical properties of free films such as elongation and tensile strength were found to reduce with the addition of polydextrose, indicating decreased deformation capacity of film and a risk of cracking. It was also found that increasing the concentration of hydrophobic lubricant such as magnesium stearate in the tablet formulations resulted in the decrease in adhesive force of the aqueous-based hydroxypropyl methylcellulose film (Lethola et al. 1995). In addition, Okhamafe and York (1985) found that increase in concentration of pigment resulted in a further slight reduction in the HPMC film, the proposed mechanism of which was the continuous reduction of the tensile strength of the film.

This study focused on the effects of polymeric additives (corn starch and magnesium stearate) on the mechanical (tensile strength, modulus of elasticity, and elongation at break) and adhesive toughness of cellulosic polymeric films. Additionally, interactions between polymer and additive were investigated.

2. Investigations, results and discussion

2.1. Free films

The thicknesses of hydroxypropyl methylcellulose (HPMC) and ethylcellulose (EC) free films were accurately measured at five different points with a micrometer and values were found to be within the same order of magnitude of 0.060 - 0.070 mm with no significant difference. The mechanical properties including tensile strength, modulus of elasticity (Young's modulus), and elongation at break of HPMC and EC free films were determined from stress-strain curves as illustrated in Fig. 1. Modulus of elasticity could be defined as the proportionality constant of stress to strain ratio, which is equal to the slope of straight-line

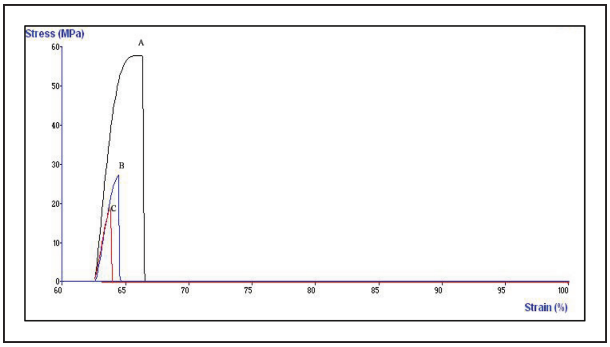

Fig. 1: Stress-strain curves of HPMC free films without additive (A), with 10% CS (B), and 20% CS (C).

portion of the elastic deformation curve of the film. The rest of the curve indicated plastic deformation of the film prior to failure (Aulton and Abdul-Razzak 1981).

In general, EC films possessed mechanical properties of tensile strength and modulus of elasticity far below those of HPMC films, but comparable values for elongation at break (Fig. 2). Such results may be explained on the basis of the degree of crystallinity of these two types of polymers, and hence molecular aggregates by hydrogen bonding between adjacent chains through polar groups (Gowariker et al. 1986). It has been reported that glass transition temperature (T_g) of HPMC films

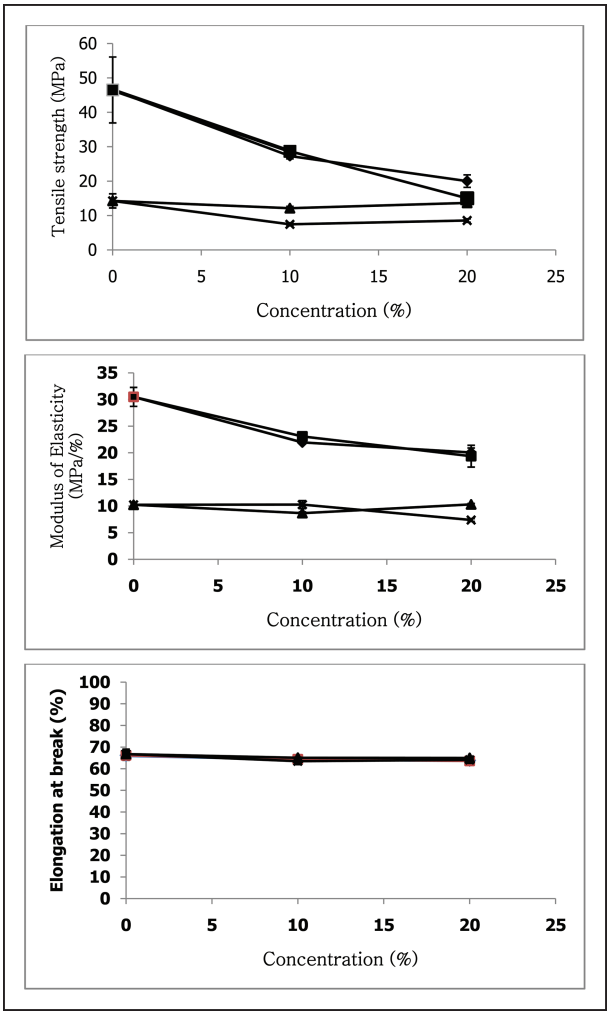

Fig. 2: Tensile strength (top), modulus of elasticity (middle), and elongation at break (bottom) of HPMC free films containing CS (♦) and MS (■), and EC free films containing CS (▲) and MS (×) at various concentrations. Each data representing mean ± SD of 5 determinations.

(180 °C) was considerably higher than that of EC films (125 °C) (Bauer et al. 1998). Regarding the more polar hydroxypropyl groups compared to nonpolar ethyl group within the film matrix, this certainly resulted in the stronger and tougher film for the former.

Addition of either corn starch (CS) or magnesium stearate (MS) was found to significantly reduce tensile strength and modulus of elasticity of HPMC free films whereas slightly affecting those of EC free films as shown in Fig. 2. Two main factors were thought to determine the influence of pigments on the tensile strength of film (Okhamafe and York 1985). There were the internal stress of the films and the degree of pigment-polymer interaction. Incorporation of the pigment particles in a film would cause discontinuities in the network of polymer matrix as hydrogen bonds between adjacent polymer segments were broken. Although pigment-polymer interaction probably occurred by a dipole-dipole mechanism (since both the polymers and pigments used were polar in character), this bonding interaction was weaker than the deteriorated hydrogen bonds. Thus, the pigment-polymer interface constituted a weak link in the structure of the film and may therefore be regarded as a stress concentration. Hence the internal stress of the film would increase as filler concentration rose, leading to a fall in tensile strength. On the other hand, an increase in filler-polymer interaction with the increasing filler content could oppositely enhance tensile strength. In HPMC films containing CS and MS, the polymer-additive interaction factor exhibited only a slight effect on the overall strength of the films while the internal stress factor played far more important role in films. However, the situation was contradictory in the case of EC films containing CS and MS, in which the polymer-additive interaction could substantially compensate the internal stress in the films and rendered minimal changes in tensile strength. Such behavior needs further evidences based on characterization of polymer-additive interaction in the next section.

Modulus of elasticity in general practice was found to increase when pigments were added to the polymer systems (Rowe 1983a; Okhamafe and York 1985a, b). Increased modulus is usually due to a rise in the stiffness or rigidity of the polymer matrix which may be brought about in two ways. First, the mobility of the polymer phase may be physically hindered by the presence of the hard filler particles. This is a hydrodynamic effect. Second, filler-polymer interaction (a reinforcing effect) could stiffen the molecular chains of portions of the polymer matrix at the filler-polymer interface thus reducing segmental mobility. The stiffening effect can be transmitted further through the network of the polymer phase.

According to previous reports (Croll 1979; Sato 1980; Okutgen 1995), Young's modulus is proportional to internal stress; the value of Young's modulus increased with increasing internal stress. Nevertheless, it has recently been reported that addition of polysaccharide such as polydextrose to HPMC films slightly decreased the values of Young's modulus (Lehtola et al. 1995). Obviously, polydextrose could thus decrease the internal stress in the film. In this study, both CS and MS could analogously reduce the modulus of elasticity of HPMC films. CS, a polysaccharide as polydextrose but higher molecular weight, and MS may be considered as very small spherical or ovoid granules with inert properties. When compared to other particulate fillers such as talcum or titanium dioxide, CS and MS would probably be expected to introduce lower stiffening effect brought about by hydrodynamic or reinforcing effect. In contrast, addition of either CS or MS did not apparently affect the modulus of elasticity of EC films. Such results may be attributed to the difference in degree of crystallinity of these two films in conjunction with the possible polymer-additive interaction in EC films as mentioned earlier.

Table 1: Physical properties (weight, hardness, thickness, and disintegration time) of SDRS tablets coated with HPMC films containing various concentrations of CS and MS

Formulation	Weight (g) Mean (SD)[a]	Hardness (kp) Mean (SD)[b]	Thickness (mm) Mean (SD)[b]	Disintegration time (min) Mean (SD)[c]
HPMC	0.309 (0.008)	11.0 (0.7)	3.5 (0.0)	4.1 (0.0)
HPMC + 10%CS	0.318 (0.013)	11.7 (0.3)	3.5 (0.1)	4.1 (0.0)
HPMC + 20%CS	0.320 (0.015)	12.1 (1.0)	3.5 (0.1)	4.1 (0.0)
HPMC + 10%MS	0.313 (0.013)	12.0 (0.6)	3.4 (0.0)	6.5 (0.0)
HPMC + 20%MS	0.322 (0.012)	12.0 (0.6)	3.4 (0.1)	7.0 (0.2)
EC	0.324 (0.013)	12.1 (0.8)	3.5 (0.0)	> 60
EC + 10%CS	0.326 (0.014)	12.1 (0.1)	3.4 (0.2)	> 60
EC + 20%CS	0.298 (0.013)	10.7 (0.5)	3.5 (0.1)	> 60
EC + 10%MS	0.329 (0.011)	12.0 (0.5)	3.3 (0.0)	> 60
EC + 20%MS	0.303 (0.017)	11.0 (0.8)	3.5 (0.0)	> 60

[a] Average of 20 tablets
[b] Average of 10 tablets
[c] Average of 6 tablets

In all cases of this study, there was a slight decline of elongation at the same order of magnitude with increasing CS and MS concentrations. It has been reported that pigment incorporation in films usually results in a decrease in film elongation even if the pigment does not interact with the polymer phase (Okhamafe and York 1985b). This would possibly be the case of inert CS and MS in HPMC and EC films. However, the greater the degree of filler polymer interaction, the more pronounced is the fall in elongation. In addition to the role played by filler polymer interaction, the particle shape and size (a hydrodynamic factor) would have a considerable influence on the magnitude of film elongation. As discussed earlier, the filler-polymer interface is recognized as a stress concentration; the stress associated with CS and MS would be lower than that found for talcum or titanium dioxide. Elongation has been considered as a measure of the deformation capacity, i.e. the ability to deform under stress, of a film. Stress concentrations, which precisely are flaws in the film, will enhance film failure and therefore decrease elongation.

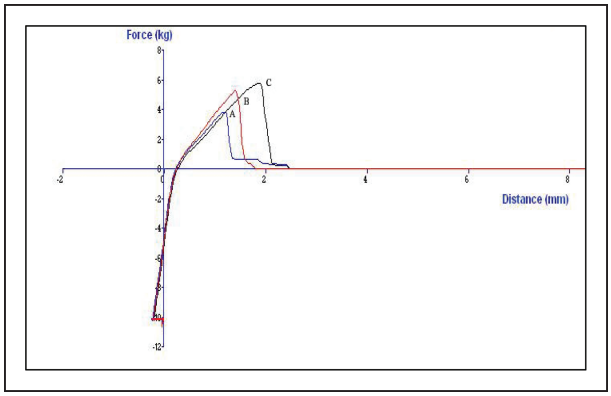

Fig. 3: Force-deflection profiles obtained from texture analyzer testing method of HPMC film coats without additive (A), with 10% CS (B), and 20% CS (C).

2.2. *In situ films*

The HPMC and EC film-coated tablets had average weights in the range of 0.295 - 0.325 g, average hardnesses in the range of 10 - 12 kp, and average thicknesses in the range of 3.3 - 3.5 mm (Table 1). In general, all physical properties except disintegration time of tablets coated with both types of film polymer with various additive concentrations were in the same order of magnitude. Tablets coated with EC films possessed the disintegration time of more than 60 min because of its hydrophobic properties in medium whereas those coated with HPMC films could completely disintegrate within 7 min. It was also shown that the disintegration time of HPMC film-coated tablets was not affected by CS, but was significantly prolonged with MS. MS has recently been used in the film-coated tablets in order to improve not only their mechanical properties of film coat, but also the drug release characteristics from tablets (Sungthongjeen et al 2004).

The adhesive toughness of HPMC and EC film coats on surface of the tablets were determined from the force-deflection profiles as illustrated in Fig. 3. The effect of concentrations of CS and MS added into HPMC and EC films on adhesive toughness are demonstrated in Fig. 4. It has previously been suggested that the work done in removing the film gives a much more accurate and quantitative measure of the adhesion than direct force measurement (Rowe 1977). Therefore, the adhesive toughness, which is defined as the area under the force-deflection profile and equal to the work required to remove the film from the sur-

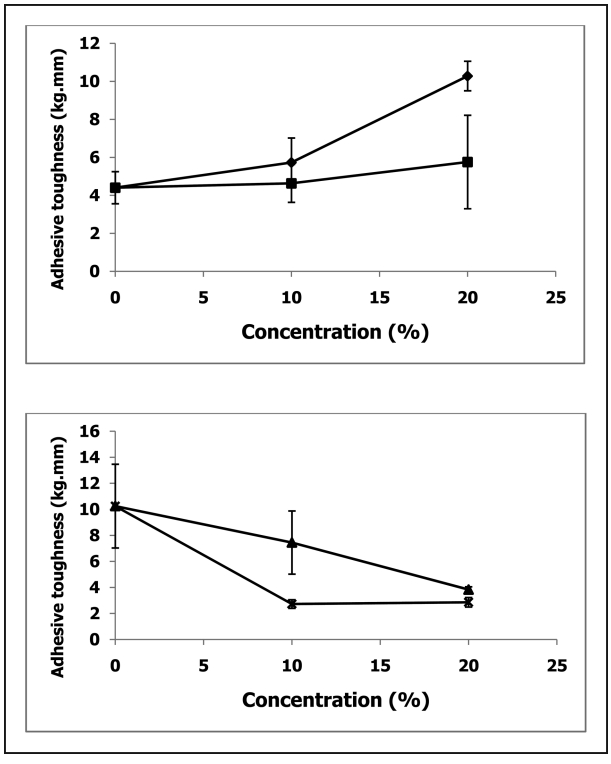

Fig. 4: Adhesive toughness of HPMC film coats (upper) containing CS (♦) and MS (■), and EC film coats (lower) containing CS (▲) and MS (×) at various concentrations. Each data representing mean ± SD of 5 determinations.

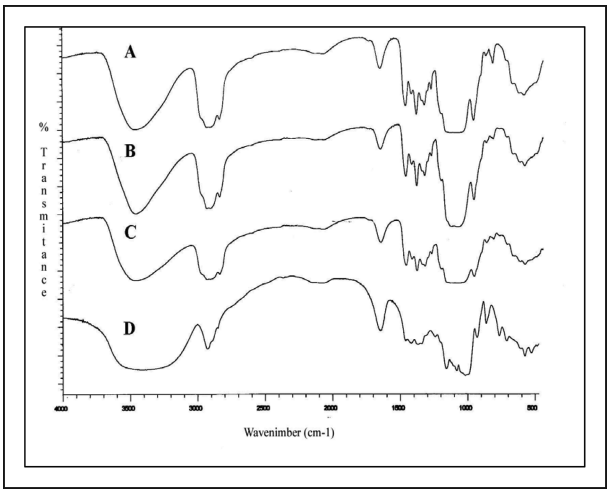

Fig. 5: FTIR spectra of HPMC films without additive (A), with 10% CS (B), 20% CS (C), and CS (D).

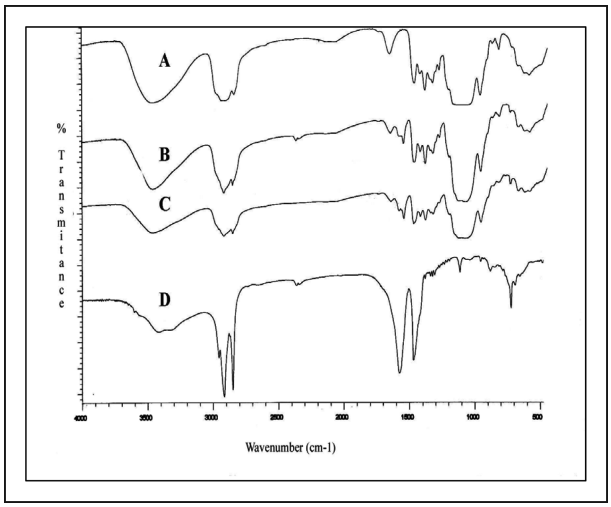

Fig. 6: FTIR spectra of HPMC films without additive (A), with 10% MS (B), 20% MS (C), and MS (D).

face of solid, was employed as the assessment parameter (Felton and McGinity 1996). It can clearly be seen that the adhesive toughness of HPMC film-coated tablets significantly rose when concentrations of both CS and MS reached 20%.

The two major forces that have been found to affect polymer-tablet adhesion include the strength of the interfacial bond and the internal stress within the film coating (Felton and McGinity 1999). For pharmaceutical products, hydrogen bond formation is the primary type of interfacial bonding mechanism between the tablet surface and polymer (Pritchard and Alner 1971). Dipole-dipole and dipole-induced dipole interactions also occur, however, to a lesser extent. Factors affecting the type or the number of bonds formed between the polymer and the solid surface will influence film adhesion. The second major factor influencing polymer adhesion is the internal stress within the film. When a polymeric solution or dispersion is applied to a substrate, an internal stress inevitably develops within the film (Rowe 1983b). The total stresses within a film is the sum of all the stresses acting on the polymer, including stress due to shrinkage of the film on evaporation of the solvent, thermal stress due to the difference in the thermal expansion of the film and the substrate, and volumetric stress due to the change in volume when a substrate swells during storage. Several researchers have developed equations to estimate the total stress within a film (Rowe 1983b). From these equations, the total stress within a film is directly proportional to the elasticity of the polymer. Factors that influence the elastic modulus of the polymer will, therefore, affect the internal stress within the film and hence adhesion. It has been demonstrated in the previous section that CS as well as MS could markedly reduce the elastic modulus of HPMC free films, and thus internal stress within the film. The net result would be the improvement in film adhesion on tablets. Such a conclusion was in accordance with previous reports, which revealed that addition of polydextrose (Lehtola et al. 1995) and maltodextrin (Felton and McGinity 1996) to the HPMC films decreased the values of Young's modulus and enhanced polymer adhesion to tablet compacts.

On the other hand, EC films exhibited different adhesive behavior from those of HPMC films with increasing concentration of either CS or MS, which caused a gradual decline in adhesive toughness. As already mentioned that the two major forces that influencing film-tablet adhesion include the film-tablet interfacial bond and the internal stress within the film coating. Balance between these two forces will determine the strength of adhesion of the film on tablet surface. For HPMC film coats, hydrogen bond formation is believed to be the primary type of interfacial bonding mechanism because of the abundance of polar hydroxypropyl functional group on the glucose units of cellulose polymer chains within the film and free hydroxy groups on the glucose units of starch grains in tablet substrate. However, this is not the case for EC film coats whose substituted groups are only nonpolar ethyl ether groups and dipole-induced dipole or Van der Waal interaction at the film-tablet interface would be assumed. It has been demonstrated in the previous section that CS as well as MS could readily reduce the elastic modulus of EC free films, and thus internal stress within the film. The net result would be the enhancement in film-tablet adhesion. Conversely, opposite results were obtained in this study. Therefore it could reasonably be presumed that these additives would possibly affect the or interfere with the type or the number of bonds formed between the polymer and the tablet surface at a preferential degree than the reduction of elastic modulus of the film. Such an assumption could be proven by further characterization of polymer-additive interaction.

2.3. Characterization of polymer-additive interaction

The FTIR results of HPMC films with various concentrations of CS and MS are shown in Figs. 5 and 6, respectively. There was neither a shift in peak nor a new peak in the spectrum, which indicated no direct interaction between the solid additive and the cellulose polymer chain. The FTIR spectra of EC films with various concentrations of CS and MS are shown in Figs. 7 and 8, respectively. There was neither a shift in peak nor a new peak in the spectrum of EC film containing 10% CS, while there was a new strong peak emerged at 1540 cm^{-1} in that containing 20% CS. Such a finding indicated a possible strong interaction between the free hydroxy groups of CS and the ether oxygen atoms in glucose units of EC, which became obvious at high concentration. This proposed interaction may be responsible for the increase in modulus of elasticity of EC free films at 20% CS as mentioned in the preceding section. Similarly, there were new strong and weak peaks emerged at 1540 cm^{-1} and 1420 cm^{-1}, respectively, in FTIR spectra of EC films containing 10% or 20% MS, which may be attributed to the interaction between magnesium ion of MS and ether oxygen atoms in glucose units of EC. This compelling exidence on polymer-additive interaction confirmed the possibility of hypothesis previously proposed that these additives would strongly perturb the bonds formed between the polymer and the tablet surface at a higher degree than the reduction of elastic modulus of the film. The

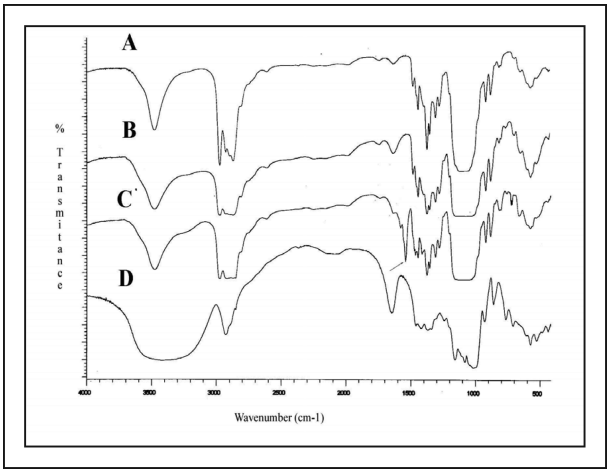

Fig. 7: FTIR spectra of EC films without additive (A), with 10% CS (B), 20% CS (C), and CS (D).

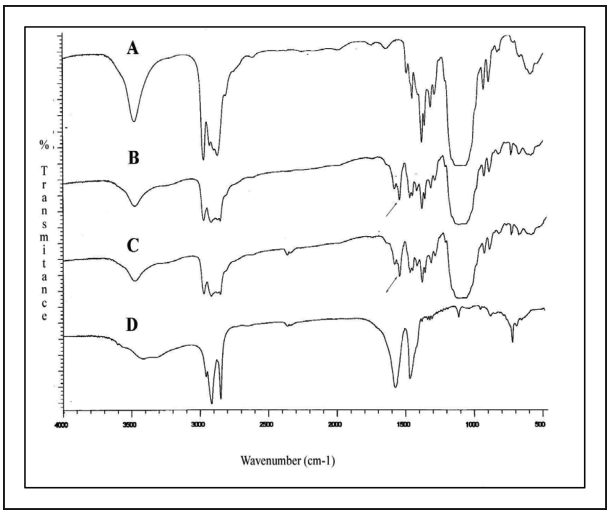

Fig. 8: FTIR spectra of EC films without additive (A), with 10% MS (B), 20% MS (C), and MS (D).

net result would lead to the reduction in film-tablet adhesion as concentration of additive (CS or MS) was increased.

2.4. Conclusion

The mechanical properties, i.e. tensile strength, modulus of elasticity, and elongation at break, of HPMC free films were found to decrease whereas the adhesive toughness increased as the concentration of solid additives (CS and MS) was increased. In the case of EC films it was found that both mechanical properties and adhesive toughness decreased as the concentration of solid additives (CS and MS) was increased. However, the modulus of elasticity of EC films containing 20% CS slightly increased, which could be attributed to the interaction between solid additives and EC films as evidenced by FTIR spectra. Thus the solid additives incorporated in polymeric film can exert two opposing effect on adhesion, that is, decreasing the adhesion properties by increasing the internal stress, and increasing the adhesion properties by strengthening the film-tablet interface.

3. Experimental

3.1. Materials

Hydroxypropyl methylcellulose (HPMC; Methocel® standard 15) and ethyl cellulose (EC; Ethocel® standard 10) were obtained from Dow Chemical, USA. Corn starch (CS) was from Wellington, New Zealand. Magnesium stearate (MS) was purchased from Siam Chemi Pharm, Thailand. Spray dried rice starch (SDRS; Era-tab®) was from Erawan Pharmaceuticals, Thailand. Methylene chloride was from Mallinkrodt, USA. Ethanol 95% v/v was from Ayudhaya Liquor Factory, Thailand.

3.2. Preparation of film coating dispersions

The 3% w/v HPMC and EC coating dispersions were prepared by dispersing the polymer in 1:1 – methylene chloride: 95% ethanol and 95% ethanol, respectively, with continuous stirring until homogeneous dispersions were obtained. CS or MS at 10 and 20% by weight of polymer were subsequently dispersed and mixed into the dispersions and stirred until homogeneous dispersions were obtained.

3.3. Free films

3.3.1. Preparation of free films

Free films in this study were prepared by using a spray box apparatus in order to mimic the coating processes typically used in the pharmaceutical industry and could produce more uniform film surfaces (Obara and McGinity 1994). The spray apparatus used in this study consisted of a spray gun with an atomizing-air supply system and a stainless steel drum of 15-cm diameter. The coating dispersion was pumped to the spray nozzle by a peristaltic pump (Watson Marlow, USA) at a rate of 1.5 g/min and atomized by pressurized air at 2.5 bar. The coating dispersion was sprayed onto the stainless steel drum rotating at 2 rpm. Heated dry air was supplied to the cylinder surface to maintain the temperature of the drum surface at 35 °C. The distance between the spray nozzle and the cylinder surface was 15 cm. The amount of coating dispersion to be sprayed was predetermined so that the resulting film possessed the same thickness as that of the cast film. After spraying, the film overlaid on the drum was removed and kept in a desiccated chamber until the mechanical tests were performed.

3.3.2. Determination of mechanical properties

A texture analyser testing machine (Stable Micro Systems Texture Analyser®, Model TA-XT plus, UK) was used to determine the mechanical and stress-strain properties of free films under ambient condition at 25 °C and 45% RH. The thickness of each film was measured at five different points and the films with thicknesses of 60-70 μm were cut into 8 x 1 cm strip. The measurements were carried out in five replicates using a 50 N load cell. Tensile strength, elongation (strain) at break, modulus of elasticity (Young's modulus) and toughness (work done) were subsequently calculated from the stress-strain curve.

3.4. In situ films

3.4.1. Preparation of film-coated tablets

The SDRS core tablets with 0.5% MS as lubricant were prepared by direct compression method with a 4-punch rotary tablet machine (Colton Model 204-3, Vector Corp., Marion, Iowa, USA) using a 3/8" flat-faced punch-and-die set to obtain the hardness of 8-10 kg. Batches of 1/2-kg core tablets were coated in a 15" perforated pan coater (Thai Coater® 15", Pharmaceutical and Medical Supply, Bangkok, Thailand). The inlet air temperature was 30-40 °C, the spray rate was 15 mL/min, and the atomizing air pressure was 2.5 kg/cm^2. The rotational speed of the coating pan was 10 rpm and the total coating time was 1 h. The film-coated tablets were kept in a desiccated chamber until the mechanical tests were performed.

3.4.2. Determination of physical properties of film-coated tablets

Twenty film-coated tablets were individually weighed and the average weight, standard deviation, and percent relative standard deviation (%RSD) were calculated. Ten film-coated tablets were individually measured for their thicknesses, and diameters and hardnesses employing a multipurpose measuring device (Pharmatest® PTB311, Sartorius, Germany). Disintegration time of the core and film-coated tablets were determined in distilled water at 37 °C using the USP disintegration test apparatus (QC21, Hanson Research, USA) and were reported as the mean of six tablets.

3.4.3. Determination of adhesive toughness

The adhesion of film coating to the tablet surface in terms of the force-deflection profile was measured with a texture analyser testing machine (Stable Micro Systems Texture Analyser®, Model TA-XT plus, UK). The tablet was mounted onto the lower grip of a material testing apparatus using double-side adhesive tape. The upper grip was then driven onto the tablet surface with a piece of adhesive tape on it at a fixed force of 100.0 N for a period of 50 s to ensure firm adhesion of the tape to the film surface. The

adhesion measurements were performed in ten replicates using a 50 N load cell. The adhesive toughness, which is defined as the area under the force-deflection profile and equal to the work required to remove the film from the surface of solid, was then calculated.

3.5. Characterization of polymer-additive interaction

The physical structures of solid additives in polymeric films as well as the interaction between additives and polymers were characterized by the use of Fourier transform infrared spectroscopy (FTIR) (Model Magna-IR550, Nicolet, USA). The free film samples prepared by spray method were used directly for running FTIR spectra, whereas the KBr method was used for powder samples. The powder samples were mixed with micronized KBr powder gently using the weight ratio of 1:100 in mortar, which were subsequently spread uniformly in a die and compressed at a pressure of 5 kN for 1 min by a hydraulic press (Carver® laboratory press model C, Freds, Carver, USA). The film and disc samples were placed in a sample holder and scanned from 4000 to 400 cm^{-1} with a number of sample scan of 32 and resolution of 4.000 cm^{-1}.

Conflict of interests: All the authors hereby declare that there is no conflict of interests regarding the publication of this paper.

References

Aulton EM, Abdul-Razzak HM (1981) The mechanical properties of hydroxypropyl methylcellulose films derived from aqueous systems. Drug Dev Ind Pharm 7: 649–668.

Bauer KH, Lehmann K, Osterwald HP, Rothgang G (1998) Coated pharmaceutical dosage forms. Stuttgart, Medpharm GmbH Scientific Publisher.

Croll AG (1979) The origin of residual internal stress in solvent-cast thermoplastic coatings. J Appl Polym Sci 23: 847–858.

Felton LA, McGinity JW (1996) Influence of tablet hardness and hydrophobicity on the adhesive properties of an acrylic resin copolymer. Pharm Dev Tech 1: 381–389.

Felton LA, McGinity JW (1997). Influence of plasticizers on the adhesive properties of an acrylic resin copolymer to hydrophilic and hydrophobic tablet compacts. Int J Pharm 154: 167–178.

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

Gowariker VR, Viswanathan NV, Sreedhar J. (1986) Polymer science. New Delhi: Wiley Eastern Limited.

Lehtola VM, Heinamaki JT, Nikuppavo P, Yliruusi JK (1995) The mechanical and adhesion properties of aqueous-based hydroxypropyl methylcellulose coating systems containing polydextrose and titanium dioxide. Drug Dev Ind Pharm 21: 675–685.

Missaghi S, Fassihi R (2004) A novel approach in the assessment of polymeric film formation and film adhesion on different pharmaceutical solid substrates. AAPS PharmSciTech 5: e29.

Obara S, McGinity JW (1994). Properties of free films prepared from aqueous polymers by a spraying techniques. Pharm Res 11: 1562–1567.

Okhamafe AO, York P (1985a) The adhesion characteristics of some pigmented and unpigmented aqueous-based film coatings applied to aspirin tablets. J Pharm Pharmacol 37: 849–853.

Okhamafe AO, York P (1985b) Relationship between stress, interaction and the mechanical properties of some pigmented tablet coating films. Drug Dev Ind Pharm 11: 131–146.

Okutgen E, Hogen JE, Auton ME (1995) Quantitative estimation of internal stress development in aqueous HPMC tablet film coats. Int J Pharm 119: 193–202.

Porter SC, Felton LA (2010) Techniques to assess film coatings and evaluate film-coated products. Drug Dev Ind Pharm 36: 128–142.

Pritchard HW, Alner DJ (1971) Aspects of Adhesion. London, University of London.

Rowe RC (1977) The adhesion of film coatings to tablet surfaces-measurement on biconvex tablets. J Pharm Pharmacol 29: 28–29.

Rowe RC (1983a) Modulus enhancement in pigmented tablet film coating formulation. Int J Pharm 14: 353–359.

Rowe RC (1983b) A reappraisal of the equations used to predict the internal stress in film coatings applied to tablet substrates. J Pharm Pharmacol 35: 112–113.

Sarisuta N, Srikummoon K, Lawanprasert P, Puttipipatkhachorn S (2006) The influence of drug-excipient and drug-polymer interactions on butt adhesive strength of ranitidine hydrochloride film-coated tablets. Drug Dev Ind Pharm 32: 463–471.

Sato K (1980) The internal stress of coating films. Prog Org Coat 8: 143–160.

Sungthongjeen S, Puttipiputkhachorn S, Paeratalul O, Dashevsky A, Bodmeier R (2004) Development of pulsatile release tablets with swelling and rupturable layers. J Control Release 95: 147–159.