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Relationship between aggregation of HPMC coated spheroids and tackiness/viscosity/additives of the coating formulations

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Abstract

This study reports the relationship between the percentage of aggregates formed during film coating of pellets in the Wurster process and the tack force, viscosity, and cloud point of hydroxypropyl methylcellulose (HPMC) coating formulations; mechanical strength of the HPMC cast films; and the release rate constant and dissolution $T_{50\%}$ values of the HPMC coated spheroids. From the results, it is shown that the percentage of aggregates is associated linearly with the tack force and correlated in a nonlinear manner with the viscosity of the coating formulations. However, there is no strong indication that percentage of aggregates is correlated with cloud point, mechanical strength, dissolution $T_{50\%}$ value and release rate constant. Dissolution $T_{50\%}$ values demonstrated a negative correlation with mechanical strength, cloud point and release rate constant. The incorporation of the plasticizers, polyethylene glycol 400, triacetin and triethyl citrate, and film formers, vinylpyrrolidone/vinyl acetate copolymers and polyvinylpyrrolidone in the HPMC solution reduced the values of percentage aggregates, tack force and viscosity. The addition of thickener, methyl vinyl ether/maleic anhydride decadiene crosspolymer had the opposite effect.

Keywords: Coated spheroids; Hydroxypropyl methylcellulose; Aggregation; Effect of additives; Tack force; Coating solution viscosity

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1. Introduction

The importance of pellets in drug dosage form design and development is indisputable. Pellets have been successfully used to provide flexibility in dose strength, maximization of drug absorption, minimization of local irritation of the gastrointestinal tract and control of the bioavailability of the active drug (Ghebre-Sellassie and Knock, 1995). In addition, pellets have a low surface area-to-volume ratio, thus this provides an ideal shape for the application of film coating.

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Film coatings are applied to pellets to mask the undesirable tastes, odours and colours, to control the release of active ingredient, to provide stability during storage and transportation and to impart protection against air, moisture and light (Seitz, 1988).

Hydropropyl methylcellulose (HPMC) is an aqueous, soluble polymer commonly used for film coating. It is stable in the presence of heat, light, air and moisture. Films of this polymer are flexible, able to tolerate the presence of additives and are resistant to abrasion (Seitz, 1988). Different additives such as plasticizers (Entwistle and Rowe, 1979; Okhamafe and York, 1983, 1984; Sakellariou et al., 1986; Johnson et al., 1991) and film formers (Okhamafe and York, 1983; Wan et al., 1994, 1995) have been added to HPMC in order to modify or improve its properties. Substantial attention has been given to the influence of additives on cloud point, disintegration and dissolution of HPMC dosage forms (Ford et al., 1985; Mitchell et al., 1990), mechanical properties of HPMC films (Aulton and Abdul-Razzak, 1981; Okhamafe and York, 1983, 1984; Gibson et al., 1988; Johnson et al., 1991; Heinamaki et al., 1994; Lehtola et al., 1995), glass transition temperatures of HPMC formulation using torsional braid pendulum (Sakellariou et al., 1986), permeation characteristics of HPMC film (Okhamafe and York, 1983; Heinamaki et al., 1994) and the intrinsic viscosities of HPMC solutions (Entwistle and Rowe, 1979). However, data on how the efficiency of plasticizers and film formers correlate with the performance of HPMC during film coating process and its relationship to undesirable aggregation formation are limited, except that given in two reports (Wan and Lai, 1992a,b) on the relationship between tackiness of methylcellulose with various additives and its performance during the fluidized bed coating and the accounts of Fukumori et al. (1991a,b, 1992, 1993) on the agglomeration problem of pulverized powders with a size range of less than 75 μm in aqueous coating by the Wurster process.

A major problem encountered during film coating of pellets using the fluidization technique is the liability to pellet aggregation. Aggregates are usually clusters of a few pellets stuck together. Not only do aggregates inhibit the formation of uniform and complete film coating around the individual pellets, the resultant oversized clusters may become too heavy to be fluidized evenly. As the proportion of aggregates increases, defluidization may occur bringing the coating process to an unexpected end.

In view of the importance of avoiding pellet aggregation during film coating in a fluidized bed, a study was carried out to assess the various polymer-related properties, for their potential as a predictor of the tendency of a coating solution to cause pellet aggregation. This present work reports how the tackiness, viscosity, and cloud point of the HPMC coating formulation, the mechanical strength of the HPMC cast films, the release rate constant and the dissolution $T_{50\%}$ value of the HPMC coated spheroids are correlated with the percentage of aggregates formed during the coating process. Several coating formulations were evaluated. They consisted of HPMC with and without additives. The additives are primarily divided into three groups i.e. plasticizers — polyethylene glycol 400, triethyl citrate and triacetin; film formers — vinylpyrrolidone/vinyl acetate co-polymers and polyvinylpyrrolidone, and thickeners — methyl vinyl ether/maleic anhydride decadiene crosspolymer.

2. Materials and methods

2.1. Materials

Chlorpheniramine maleate (BP grade) was used as a model drug with lactose monohydrate (Pharmatose 200M, DMV, The Netherlands) and microcrystalline cellulose (Emcocel 50M, Mendell, USA) as excipients. Hydroxypropyl methylcellulose (HPMC; Metolose 60-SH, 400 mPas, Shin-Etsu, Japan) was used as the hydrophilic polymer. Polyethylene glycol 400 (PEG; BHD Chemicals, Poole, UK), triethyl citrate (TEC; Merck, Germany) and triacetin (TA; Merck, Germany) were used as the plasticizers. Vinylpyrrolidone/vinyl acetate copolymers (PVP/VA; ISP, USA) and polyvinylpyrrolidone (PVP; Plasdone C-15, ISP, USA) were soluble film formers and methyl vinyl

Table 1
The various formulations for HPMC polymeric solutions

Formulation code	HPMC (% w/w)	Film former (% w/w)	Plasticizer (% w/w)	Thickener (% w/w)
HPMC	1.2 (2.4)	—	—	—
HPVP/VA	1.0 (2.0)	PVP/VA 0.2 (0.4)	—	—
HPVP	1.0 (2.0)	PVP 0.2 (0.4)	—	—
HPEG	1.0 (2.0)	—	PEG 0.2 (0.4)	—
HTEC	1.0 (2.0)	—	TEC 0.2 (0.4)	—
HTA	1.0 (2.0)	—	TA 0.2 (0.4)	—
HPVM/MA/DC	1.0 (2.0)	—	—	PVM/MA/DC 0.2 (0.4)

Values shown are concentrations used for the normal coating process and the aggregation test; values in parentheses are the concentrations used for the viscosity, tack force, and cloud point determinations and for the casting of films.

ether/maleic anhydride decadiene crosspolymer (PVM/MA/DC; Gantrez XL, ISP, USA) was the thickener used.

2.2. Methods

2.2.1. Preparation of drug spheroids and coating process

Core spheroids composed of microcrystalline cellulose, lactose and drug in the ratio by weight of 12:37:1 respectively, were prepared by rotary processor (Niro-Aeromatic, MP-1 with rotoprocessor, Switzerland). Chlorpheniramine maleate was dissolved in distilled water and sprayed radially under pressure onto the rotating powder mixture of microcrystalline cellulose and lactose. The spheroids formed were sieved and 200-g batches of size fractions of 0.85-1.18 mm were coated in a bottom-spray fluidized bed (Niro-Aeromatic, Strea-1, Switzerland). Process parameters were as previously reported (Wan et al., 1995). The coating solutions of HPMC with and without additives are shown in Table 1. The coating level is the quotient of the dry weight of polymer and the weight of the uncoated spheroids, expressed as a percentage.

2.2.2. Dissolution studies

Dissolution studies were carried out in 1 litre deaerated distilled water, using the paddle method (Method II, USP XXII; Hanson Research, 72-RL, USA) at a stirring speed of 50 rev./min. At preselected intervals, samples were collected using an automated sampler (Hanson Research, Dissoette 27-6A, USA). The amount of chlorpheniramine maleate was determined spectrophotometrically at 262 nm (Hewlett Packard, 8451A, USA).

2.2.3. Aggregation test

Polymeric solutions of HPMC with and without additives were sprayed onto 200 g of chlorpheniramine spheroids with size range of 0.85-1.18 mm. The parameters of coating procedure were similar to the previous study (Wan et al., 1995), except that a faster spray rate of 10 ± 1 ml/min was used.

The resultant spheroids and aggregates were sieved mechanically (Endecotts Sieve Shaker, Model EVS1, UK), vibrating at an amplitude of 1 mm for 15 min. The size distribution was evaluated and the percentage of spheroids or aggregates greater than 1.18 mm was recorded. At least triplicates were carried out and the results averaged.

2.2.4. Tack measurement

Tack measurements of the various polymeric solutions (Table 1) were carried out at ambient temperature of 28 ± 1°C, according to the technique reported by Wan and Lai (1992a,b). A 2-ml sample of the test solution was used each time and the separating rate was maintained at 182 mm/min. Ten replicates were taken and averaged.

2.2.5. Viscosity measurement

Viscosity measurements of the test solutions were determined using a synchrolectric viscometer

Table 2
Bi-exponential first-order parameters for spheroids coated with various formulations

Formulation code	A	B	k_1 (min^{-1})	k_2 (min^{-1})	$T_{50\%}$ (min)
HPMC	57.5	42.3	0.1513	0.0138	9.80
HPVP/VA	75.1	26.9	0.0934	0.0127	10.65
HPVP	74.6	27.4	0.0877	0.0120	11.80
HPEG	75.8	27.5	0.0721	0.0123	14.51
HTEC	74.6	27.1	0.0718	0.0146	14.00
HTA	74.5	27.9	0.0782	0.0135	13.40
HPVM/MA/DC	59.9	42.0	0.0531	0.0040	19.41

(Brookfield LVT, USA) with spindle # 1 at 6 rev./min at ambient temperature of 28 ± 1°C.

2.2.6. Cloud point measurement

Cloud point determinations were obtained using a suspended-level viscometer BP, size # 2, in a thermostatically controlled water bath. The flow times at different temperatures were recorded. The cloud point was taken as the inflection point of a plot of flow time against temperature. Triplicates were carried out and results averaged.

2.2.7. Preparation of polymeric films

The films were cast from various polymeric solutions with or without additives. The formulations are shown in Table 1. Twenty millilitres of each solution were poured into a levelled plastic Petri dish (diameter 9 cm) and allowed to dry in an air convection oven at 60°C for 18 h. Upon drying, the films were peeled and conditioned by storing at 28 ± 1°C in a desiccator until constant weight, before being used for the mechanical strength evaluation. Dry film thicknesses were measured and only those that ranged from 50–70 μm were used.

2.2.8. Mechanical strength evaluation

Films cut into bow-shaped sections, length 4 cm, ends 1.3 cm and mid-width 1 cm, were used for the mechanical strength tests using a tensile tester (Autograph AGS 500D, Shimadzu, Japan). In order to avoid orientation effects (particle orientation at the edges of the film would differ from that in the central portion of the film) (Gibson et al., 1988), almost the whole of the circular films was used. The rate of pull is 25 mm/min and gauge length was 20 mm. The maximum load force (N) to break the film was recorded. Four replicates were taken and load force averaged.

3. Results and discussion

3.1. Effect of additives on drug release from HPMC coated spheroids

The chlorpheniramine spheroids were coated with HPMC both in the presence and absence of additives. The coating level achieved was 10% for all the formulations. From Table 2, it can be seen that the additives have all reduced the drug release to a certain extent. Dissolution $T_{50\%}$ value for spheroids coated with HPMC alone was 9.80 min. Film formers PVP/VA and PVP only increased the dissolution $T_{50\%}$ values slightly to 10.65 and 11.80 min respectively, while all the three plasticizers PEG, TEC and TA decreased the drug release and dissolution $T_{50\%}$ values were in the range of 13.40–14.50 min. Spheroids coated with HPVM/MA/DC had the longest dissolution $T_{50\%}$ value, twice that of spheroids coated with only HPMC. It was reported in a previous study (Heng et al., 1995), that the thickener PVM/MA/DC, an anionic crosspolymer, prolonged the drug release by interacting with the cationic chlorpheniramine maleate, forming a less soluble complex and subsequently reducing the drug release.

The drug release data of the formulations were analysed and found to follow a biphasic profile exhibiting a bi-exponential first-order kinetic model:

Table 3
The effects of additives on the percentage of aggregates, tack force, viscosity, cloud point of HPMC solutions and the mechanical strength of the HPMC cast films

Formulation code	Aggregates (%)	Tack force (N/cm^2)	Viscosity (mPa s)	Cloud point (°C)	Mechanical strength (N)
HPMC	45.24 ± 6.08	1.87 ± 0.14	445	60.2	38.61 ± 6.82
HPVP/VA	28.86 ± 2.70	1.32 ± 0.20	232	60.2	41.69 ± 0.71
HPVP	2.25 ± 0.98	1.10 ± 0.11	155	60.0	33.63 ± 1.57
HPEG	31.24 ± 9.40	1.54 ± 0.08	225	60.3	22.03 ± 2.14
HTEC	15.57 ± 8.67	1.17 ± 0.11	195	60.3	21.71 ± 0.97
HTA	25.89 ± 3.32	1.32 ± 0.17	223	58.5	24.97 ± 4.69
HPVM/MA/DC	51.40 ± 4.60	1.96 ± 0.14	1050	55.2	18.15 ± 1.72

Values are mean ± S.D.

$$W = A exp(-k_1 t) + B exp(-k_2 t)$$

where W is amount (%) of drug remaining at time t, k_1 and k_2 are corresponding release rate constants and A and B are constants. The drug release process consists of $[A/(A + B)] \times 100\%$, the initial phase and $[B/(A + B)] \times 100\%$, the terminal phase.

3.2. Effect of additives on aggregation of pellets during film coating process

During film coating in a fluidized bed coater, when the concentration of the coating polymer is high, the likelihood of aggregation of the pellets is increased, since the amount and concentration of the coating material can affect the strength of liquid bridge between the contact point of the pellets (Gutierrez-Rocca and McGinity, 1993). In order to avoid the problem of aggregation, diluted coating solution is frequently applied. However, this increases the total volume to be sprayed, which will translate to a longer process time and impart a greater drug-solvent migration related problem. Organic solvents, such as methanol and ethanol, can be an alternative to aqueous medium to enable a higher concentration of coating polymer to be sprayed but, in general, the use of organic solvents is best avoided as it is more expensive, less environmentally friendly and has associated explosion risks. The preferred approach is the incorporation of adjuvants which modify the unwanted characteristics of the coating polymer. Adjuvants such as antitack agent, plasticizer, film former and surfactant, are useful additives.

Under the accelerated spraying condition studied, solution of HPMC alone resulted in 45.24% of aggregates (Table 3). The three plasticizers reduced the percentage of aggregates to less than 32%. Film formers have also decreased the percentage of aggregates by more than 36%. Interestingly, the addition of PVP, an additive usually incorporated as a binder, has greatly reduced aggregation. Coating of HPVP solution only produced 2.25% of aggregates. Throughout the coating process, the pellets were well fluidized and aggregates were almost non-existent. PVM/MA/DC did not alleviate the aggregate formation, on the contrary, HPVM/MA/DC has increased the percentage of aggregates to 51.4% (Table 3).

3.3. Effect of additives on tack measurement of HPMC solution

Tack is defined as the force or impulse per unit area required to separate two parallel surfaces initially in contact through an intervening liquid film (Bikerman, 1947).

In this study, the tack force determined is taken as a measurement of the apparent tack force, which is a representation of the summation of all intermolecular interactions or cohesion of the liquid film, interfacial interactions between the test liquid and the probe surface and other factors related to the method of measurement (Wan and Lai, 1992a). The contact time of the test probe with the polymeric liquid film was kept constant at 30 s before separation of the probe was initiated. The standardized contact time was to ensure the probe was sufficiently wetted and a more uniform stress pattern was established (Wan and Lai, 1992a).

As seen in Table 3, the tack force for HPMC solution without additives was 1.87 N/cm^2. The incorporation of plasticizers and film formers have reduced the tack force to values ranging from 1.10 to 1.54 N/cm^2. On the other hand, PVM/MA/DC increased the maximum tack force to 1.96 N/cm^2. This may be due to its viscosity inducing effect.

3.4. Effect of additives on viscosity of HPMC solution

The viscosity of a 2.4% w/w HPMC solution was 445 mPa s at 28°C. The addition of the three plasticizers and the two film formers all reduced the viscosity to values ranging from 155 to 232 mPa s. Thickener PVM/MA/DC showed the reverse effect, with the viscosity greatly enhanced to a value of 1050 mPa s (Table 3).

3.5. Effect of additives on cloud point of HPMC solution

At 28°C, the ambient temperature, HPMC solution exists as a clear viscous liquid. As the temperature was gradually increased, the viscosity, as measured by flow time of the solution, decreased. With further increase in temperature, HPMC was precipitated, turbidity was observed and the corresponding flow time was also decreased substantially.

Table 3 shows the effect of additives on the cloud point of HPMC solution. The cloud point values were determined from the inflection point obtained by determining the intersecting point of two linear regression lines from a plot of flow time against temperature. The coefficients of determination, r^2 for the regression lines are all above 0.9. A 2.4% w/w of HPMC solution has a cloud point value of 60.2°C. This value is lower than the reported values of HPMC gels prepared using higher viscosity grade HPMC. However, it has also been ascertained by both Mitchell et al. (1990) and Sarkar (1979) that there were some differences between the cloud points of HPMC of different viscosity grades. The cloud point of HPMC K15M gel was reported to be 2°C lower than HPMC K100 gel and the cloud point of HPMC K4M was 6°C lower than HPMC K100.

Plasticizers, PEG and TEC, and film formers, PVP/VA and PVP, have little influence on the cloud point, while plasticizer TA and thickener PVM/MA/DC both reduced the cloud point to values of 58.5 and 55.2°C, respectively.

3.6. Cast films

Free films are normally prepared by the casting (Bodmeier and Paeratakul, 1990; Lin et al., 1991; Guo et al., 1992; Gutierrez-Rocca and McGinity, 1993; Lim and Wan, 1994) or spraying technique (Obara and McGinity, 1994; Lehtola et al., 1995). The casting method may be deemed less suitable if some components in the test formulations are insoluble. The suspended particles may sediment during the drying process, resulting in the formation of uneven and inhomogeneous films (Seitz, 1988).

In this study, the additives were hydrophilic and soluble in water. All the formulations also produced films with satisfactory appearances except for the HPVM/MA/DC film. The transparent and flexible films can be peeled off easily from the Petri dishes. HPVM/MA/DC film, though flexible and easily detachable from the Petri dishes, had rough and uneven surfaces.

3.7. Effect of additives on mechanical strength of the HPMC cast films

Incorporation of additives into the HPMC films brought about considerable changes in the physicomechanical behaviour of the polymer. The mean maximum load forces required to break the various types of films are shown in Table 3. The breaking force for HPMC film was 38.61 N. As expected, the addition of plasticizers to the HPMC films resulted in a decrease in the mechanical strength of the film. The mean maximum break force for the three types of plasticized films

Table 4
Pearson correlation coefficients for the various experimental determinations

	AGGR.	TACK	VISC.	CL.PT.	M.ST.	$T_{50\%}$	K_1
AGGR.	1.0000	0.9515**	0.7746*	−0.5507	−0.1283	0.3563	0.1472
TACK	0.9515**	1.0000	0.8241*	−0.5617	−0.1501	0.3752	0.2015
VISC.	0.7746*	0.8241*	1.0000	−0.8837**	−0.3724	0.7039	−0.2213
CL.PT.	−0.5507	−0.5617	−0.8837**	1.0000	0.5406	−0.8217*	0.5071
M.ST.	−0.1283	−0.1501	−0.3724	0.5406	1.0000	−0.8765**	0.7641*
$T_{50\%}$	0.3563	0.3752	0.7039	−0.8217*	−0.8765**	1.0000	−0.8042*
K_1	0.1472	0.2015	−0.2213	0.5071	0.7641*	−0.8042*	1.0000

AGGR., percentage of aggregate; TACK, tack force; VISC., viscosity; CL.PT., cloud point; M.ST., mechanical strength; $T_{50\%}$, dissolution $T_{50\%}$ value; K_1, initial release rate constant.
*At 0.05 level of significance.
**At 0.01 level of significance.

was less than 25 N and reduction of mechanical strength followed the order HTEC > HPEG > HTA. This is in agreement with the findings of Johnson et al. (1991) who found that both PEG 400 and triacetin reduced the tensile modulus at break-up of the HPMC films, but PEG 400 reduced the mechanical strength of the film to a greater extent than triacetin. Film former PVP reduced the mechanical strength of the film slightly but PVP/VA increased the mechanical strength of the film due to its good binding and film forming properties.

HPVM/MA/DC films exhibited the lowest mechanical strength among all the formulations studied. This may be attributed to the unevenness of the cast film formed. Sediments were observed on the cast film which disrupted the continuity of the film and subsequently weakened the mechanical strength of the film.

3.8. Correlation between the percentage of aggregates and the various tests

The results of the various experimental determinations were subjected to the bivariate correlation statistical treatment using the PC-based SPSS Software (Release 6.0).

The Pearson correlation coefficients are shown in Table 4. It can be seen that the percentage aggregate is best associated with tack force (correlation coefficient = 0.9515, at 0.01 level of significance), followed by viscosity (correlation coefficient = 0.7746, at 0.05 level of significance). However, there is no strong indication showing that the percentage aggregate is correlated with cloud point, mechanical strength, dissolution $T_{50\%}$ value and initial release rate constant. The respective scatterplots with regression lines are found in Figs. 1 and 2. Nevertheless, it should be pointed out that the dissolution $T_{50\%}$ value showed a negative correlation with mechanical strength, cloud point and initial release rate constant (Table 4, Fig. 3).

Aggregation occurs through interparticulate bridging. The strength of the bridge is largely dependent on the concentration and nature of the coating solution applied to the interparticulate contact point. Initially, the coating solution is adsorbed onto the surface of the pellets as liquid films. These films act by smoothing out surface imperfections and subsequently decreasing the contact area between pellets. When the liquid bridges dry up, solid bridges are formed which bind the pellets together in clusters. As the aggregates grow in size, they reach a stage when the clusters of pellets may be too heavy to be fluidized evenly. If the larger and heavier aggregates are accumulated within the central partition tube of the fluidized bed coater, they may even result in fluidization failure.

From the statistical treatment, it is observed that tack force and viscosity determinations are better correlated with the percentage aggregates. Tack force and the viscosity of the coating solution all are directly related to the binding strength of the liquid bridge at the interparticulate contact point. As a result, these determinations also provide a reasonable reflection of the degree of the aggregation problem.

Viscosity of the coating solution is often regarded as a causative factor of agglomeration and coalescence during film coating of powder, granules and pellets. In general, the higher the viscosity of the coating solution, the bigger will be the yield of agglomerates and aggregates. Among all the coating formulations tested, HPVM/MA/DC was the solution that has the highest viscosity value of 1050 mPa s. This value was more than twice the viscosity value of a 2.4% w/w HPMC solution. However, its corresponding percentage of aggregates was only 14% more than the per-

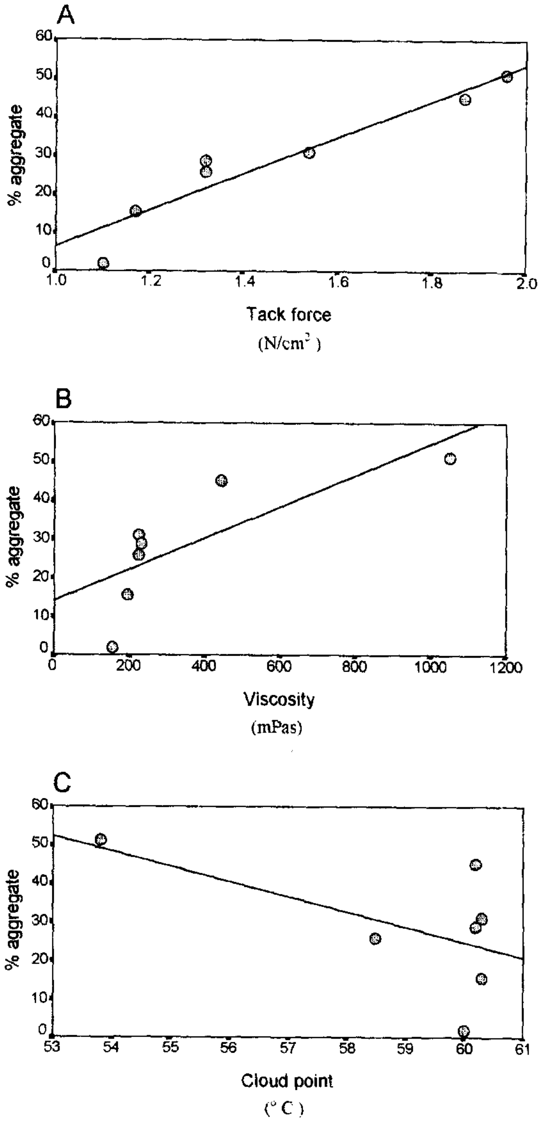

Fig. 1. Scatterplots with regressions lines showing the correlation between percentage of aggregate and (A) tack force, (B) viscosity and (C) cloud point.

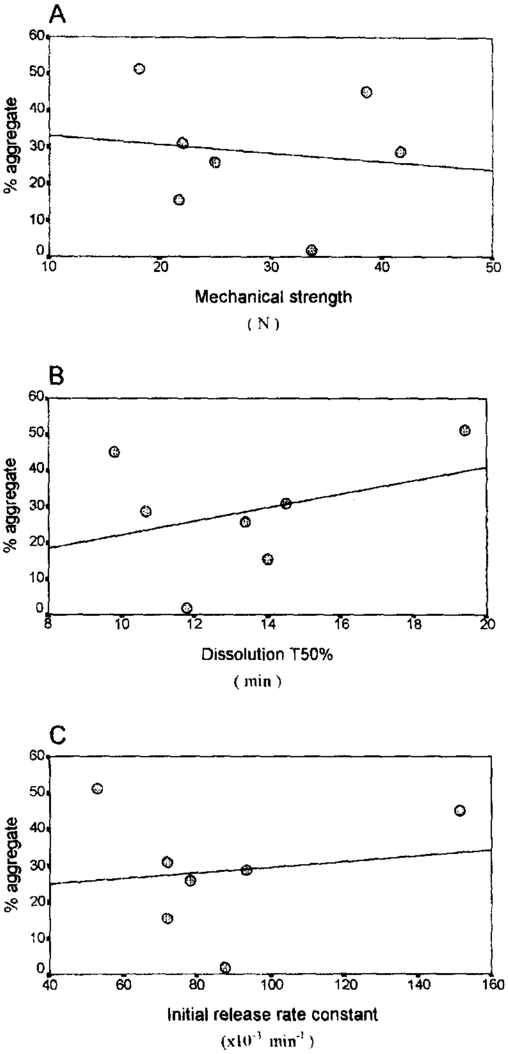

Fig. 2. Scatterplots with regressions lines showing the correlation between percentage of aggregate and (A) mechanical strength, (B) dissolution $T_{50\%}$ and (C) initial release rate constant.

centage aggregates caused by the HPMC solution. This indicates a possible nonlinear relationship between percentage aggregates and viscosity (Fig. 1B). Whereas tack force measurement indicated a linear correlation with percentage aggregates (Fig. 1A).

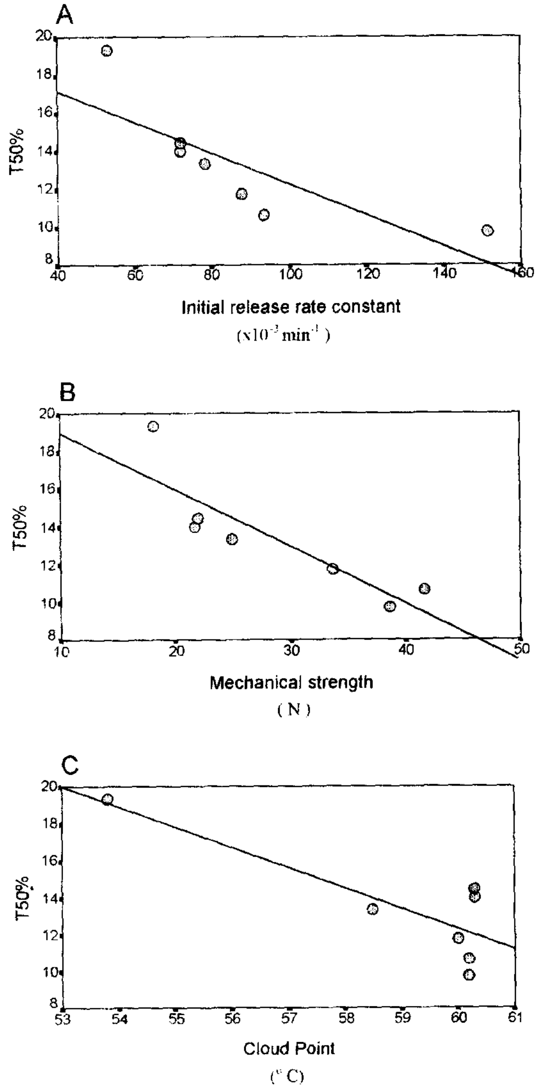

Fig. 3. Scatterplots with regressions lines showing the correlation between dissolution $T_{50\%}$ and (A) initial release rate constant, (B) mechanical strength and (C) cloud point.

4. Conclusion

From this study, the percentage of aggregates formed during film coating of pellets in the Wurster process is well associated linearly with the tack force of the various coating formulations. Percentage of aggregates is also correlated to the viscosity of the coating formulations but in a nonlinear manner. However, there is no strong indication showing that the percentage of aggregates is correlated with cloud point, mechanical strength, dissolution $T_{50\%}$ value and initial release rate constant. Dissolution $T_{50\%}$ values showed a negative correlation with mechanical strength, cloud point and initial release rate constant. The incorporation of the plasticizers polyethylene glycol 400, triacetin and triethyl citrate, and film formers vinylpyrrolidone/ vinyl acetate copolymers and polyvinylpyrrolidone in the HPMC solution have all reduced the percentage of aggregates, tack force and viscosity values. The resultant reductions all followed the order of HTEC > HTA > HPEG and HPVP > HPVP/VA. Methyl vinyl ether/maleic anhydride decadiene crosspolymer increased the percentage aggregate, the tack force and viscosity values.

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