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EVALUATING THE EFFECTS OF PLASTICIZER INTERACTIONS WITH HPMC ON THE TACK-BEHAVIOR OF POLYMER FILM-FORMING COATING SOLUTIONS

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ABSTRACT

Tack is a concept that is widely used to describe the forces or energies involved in the separation of two parallel surfaces initially in contact through an intervening thin liquid film. The tackiness may cause tablets to stick with each other or to the walls of the coating apparatus. In this study, the HPMC coating solutions were evaluated for their tackiness and the effects of interactions between the polymer and plasticizers on the tack behavior of HPMC film-forming coating solutions were investigated, using type TA-XT2 texture analyzer. It was found that experimental factors such as the contact time, rate of separation and volume of the film-forming test solution could effectively influence the magnitude of tack behavior. Moreover, up to certain levels, the addition of plasticizers such as PEG 400 & 1000 and of triacetin caused a reduction in the tack value of the polymer solutions. It was concluded that in general, the tackiness depended upon the molecular weight and/or type and concentration of a plasticizer. The efficiency of plasticizers used to reduce the tackiness of HPMC solutions ranked as PEG1000 > triacetin > PEG400.

INTRODUCTION

Utilization of a coating process to modify the characteristics of dosage forms, especially tablets has been practiced for over 150 years (Lieberman and Lachman, 1990). Tablet coating is perhaps one of the oldest pharmaceutical processes still in existence. Film coatings are an integral part of the dosage form development process. The process of film coating involves the application of a thin polymeric film onto the surface of a solid substrate. In film coating formulations, polymers are the major ingredients and consequently these materials will have the greatest impact on final properties of the coating.

Hydroxypropyl-methylcellulose (HPMC) is a polymer commonly used in conventional film coating formulations. It has an advantage of being soluble in both organic solvents as well as water over the entire biological pH range. However, coating formulations consisting of soluble polymeric film-formers, particularly the water-soluble cellulose ethers (Lindberg, and Johnson, 1972; Al-Dujaili *et al*., 1986) are known to be tacky in nature. Tack is a concept that is widely used to describe the forces or energies involved in the separation of two parallel surfaces initially in contact through an intervening thin liquid film (Chopra and Tawashi, 1982; 1984 and 1985). The tackiness may cause tablets to stick with each other or to the walls of the coating apparatus.

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Until the late 1970s, the typical approach to formulating new coating was to evaluate only its end-use properties on the substrate. Parameters such as moisture/air permeability, drug release profile, abrasion resistance, and stability were tested. However, it is also important to evaluate the film or film forming materials prior to their end-use. A fundamental understanding of the physical and mechanical properties of the components of film-coating formulation and their interaction is essential to enable the formulators to predict end-use properties, thereby saving time and money. The most useful methods of evaluation include the characterization of the moisture permeability, mechanical, and thermal properties of the film coating.

In this study, the HPMC coating solutions were evaluated for their tackiness and the effects of interactions between the polymer and plasticizers on the tack behavior of HPMC film-forming coating solutions were investigated.

EXPERIMENTAL

Materials

The materials used were hydroxypropyl methylcellulose (HPMC – Pharmacoat 606, Shin-Etsu Chemical Co., Tokyo, Japan), polyvinyl alcohol (PVA) 86.5 – 89% degree of hydrolysis (BDH, UK), polyethylene glycols (PEG) with nominal molecular weights 400 and 1000 g/mole (BDH UK), triacetin (TA) (Sigma, Germany).

Equipments

The equipments used in this study were: analytical balance model AA-160 (Denver Instrument, USA), torsion balance (White electric), Vacuum pump (Buchi B169, Switzerland), Ubbelohde Viscometer (Cannon instrument, USA), glass plates, hot air ovens, micrometer (Mitutoyo, Japan), Hygrometer type: 814 (Gebrauchsanleitung fur, Germany), texture analyzer type TA-XT2 (TA, England).

METHODS

Viscosity measurement

Apparent viscosities ranging between 2% and 10% w/v Pharmacoat-606 aqueous solutions were measured by McGinity Method (1989), using 3 C K610 Ubbelohde type viscometer. The viscosity required for aqueous film coating is commonly less than 100 cP (McGinity, 1989). Five measurements were performed for each system and all viscosity measurements were performed at constant temperature (25± 2ºC). It was found that a solution with a Pharmacoat-606 concentration of 7% w/v could produce viscosities lower than 100 cP, so the 7% w/v Pharmacoat-606 concentration was chosen for all preparations.

Preparation of coating solution

7 gm of the Pharmacoat-606 was put in about 40 ml distilled water, previously heated to more than 80ºC, with constant stirring. Uniformly wet dispersion was obtained and then cold distilled water was added to make 100 ml, while stirring well. Pharmacoat-606 dissolved completely when the temperature of the coating solution cooled down to less than 30ºC. Polymers blends were also prepared by mixing solutions of 7%w/v HPMC and 7% PVA at the ratios of 9:1, 8:2, 7:3, 6:4 and 5:5. These blends (HPMC: PVA) were prepared by adding 10, 20, 30, 40 and 50 ml of 7% PVA solution to 90, 80, 70, 60 and 50 ml of 7% HPMC solutions, respectively.

Coating solutions were then plasticized with 0, 10, 20, 30 and 40% W/W of polyethylene glycol (PEG400 and 1000) as well as triacetin (TA). The percent plasticizer in the system is

expressed as the %w/w against the weight of polymer in case of HPMC solutions and against the weight of total solid contents of the blend (weight of HPMC plus weight of PVA in the blend). The coating solutions were then filtered under vacuum and allowed to stand for 24 hours before performing any test to ensure that the solution was free from bubbles.

Tack measurement of coating solution

Influence of experimental conditions on the apparent tack force of splitting liquid film was investigated to achieve the optimum experimental parameters for tack measurements. These factors are duration of contact time, volume of test solution and rate of separation of liquid film.

The method reported by Wan and Lai (1992a) was used that utilized the translation and load measuring facilities of a texture analyzer (TA, England). A schematic diagram of the setup of the apparatus used is shown in Fig.1. Acrylic plastic probe of a cylindrical shape with a round and flat contact surface area (r = 0.5 cm) was used. 2 ml of the sample to be tested was placed in a glass Petri dish with an internal diameter of 9 cm, which were kept in a horizontal position with a metallic clamp. The probe was mounted vertically on the load test shaft of the tensile tester and the surface of the Petri dish was checked to be parallel to this by using a spirit level. During the operation of the test, the probe was lowered vertically and brought into contact with the liquid film in the Petri dish and allowed to rest against the film for 30 seconds. The probe was then raised at 5mm min^{-1} rate of separation. The maximum force generated during separation was recorded. Six replicate determinations were carried out. The liquid film was bubble free. All the tack measurements were carried out at ambient temperature (25±2ºC) and the volume of the test solution was the same for all measurements.

RESULT AND DISCUSSION

Viscosity and Concentration Studies

The rheology of the coating solution will influence pumping and spray characteristics, as well as interactions with core material (as related to wetting, spreading and coalescence) which will ultimately affect the final quality of the coated product. The viscosity of polymeric solution is directly related to the concentration of solution.

With aqueous film-coating process, the concentration of ingredients used in the coating formulation is usually higher than that seen when using organic solvents. This is a direct result of a desire to counteract the effect of the higher latent heat of vaporization of water. Fig.2 illustrates the relationships between the concentrations of HPMC (pharmacoat 606) and the viscosities of their solutions. It was found that as the solids content of the solution increased, the viscosity increased exponentially. Regardless of the delivery system, the coating solution must be formulated to have a viscosity of sprayable solution. McGinity (1989) reported that for aqueous film coating, concentrations reaching 80 – 100 m Poise are optimum. In this work, the HPMC concentration at 7% w/v level fulfilled this requirement, thus this concentration was selected for all studies conducted in this work.

Tack Studies

Tack is a concept that is widely used to describe the forces or energies involved in the separation of two parallel surfaces initially in contact through an intervening thin liquid film (Bikerman, 1947). The basic expression for the separation of two flat circular plates in a viscous Newtonian liquid was given by Bikerman (1968).

$$F = \frac{3\pi\eta r^4}{4t}\left[\frac{1}{h^2_1} - \frac{1}{h^2_2}\right]$$

Where F is the force of separation (dynes), η is the viscosity (poise) of the liquid, r is the radius (cm) of the plates, h_1 and h_2 are the initial and final thickness (cm) of the liquid film and t is the time required for separation (seconds). The force of separation per square centimeter (f) is equal to $F/\pi r^2$ where, πr^2 is the surface area of the plates. Therefore tack can be expressed as

$$f\,t = \frac{3\eta r^2}{4}\left[\frac{1}{h^2_1} - \frac{1}{h^2_2}\right]$$

At any given moment during the process of pan coating, a thin film of coating solution is present between two tablets, or between a tablet and the wall of coating pan (Chopra and Tawashi, 1982). The force exerted by moving tablets splits the liquid film before the complete evaporation of the solvent occurs. If the force that splits the liquid film (tack force) is greater than the forces of adhesion between the polymer film and the tablets, then picking may occur (Patrik, 1969).

Experimental factors influencing tack measurements

Effect of length of contact time

When the liquid came into contact with the probe surface, it deformed and began to penetrate the microscopic surface imperfections in order to wet the probe surface completely. There could be also a possibility of air entrapment at the probe-liquid interface and the necessity for diffusion of this entrapped air before wetting can become complete. Therefore, the wetting process was not instantaneous and the tack force measured was dependent on the contact time of the probe on the liquid film prior to separation. The relationship between the maximum tack force and the contact time is shown in Table-1a. These results show that the tack force increased as the contact time increased up to 30 seconds. Beyond this time the tack force decreased. It could be concluded that the tack force reached its maximum at time 30 seconds and it decreased on further extension of time. Therefore the contact time is an important factor in tack measurement and in this study a contact time of 30 second was selected for further tack measurements.

Effect of the rate of separation on tack

Table-1b shows the relationship between the maximum tack forces obtained for 7% w/v solution of hydroxypropyl methylcellulose at various rate of separation of the probe from the liquid film. The results show that the maximum tack force increased with an increase in the rate of separation up to 5 mm/sec, beyond that the tack force was decreased. The reason for obtaining low tack values at higher rates of separation may be due to visco-elastic response of liquid film. When the probe is pulled away from the plate the liquid flows towards the axis of the plates at rates governed by thickness (h), time (t) and viscosity (η) of the liquid. When stress is applied slowly (when t is long), the liquid responds by flow. If t is too short, the liquid film gets no chance to flow and the elastic force become more important for the breakdown of the liquid film. Under such circumstances the measured tack value decreased (Patrik, 1969; Voet and Gefftken, 1951). Hence, the results indicate that 5 mm/s was the optimum rate of separation for 7% w/v HPMC solution and this rate was selected for further tack measurements.

Effect of volume of test solution

The thickness of the liquid film in the Petri dish altered with varying the volume of test solution. Values in Table-1c show that as the volume of test solution was increased, the maximum

tack force decreased. Therefore, a thinner film imparts a greater resistance to separation, leading to a stronger tack force. These results are in agreement with the work of (Wan and Lai, 1992b; Sarwar, 1999). The minimum possible volume of test solution to be spread in 9 mm internal diameter Petri dish was found to be 2ml. Therefore the optimum volume of the test solution used for further test was 2ml.

Tables 1a, b, c: Evaluation of experimental factors affecting tack force measurement, using 7% w/v solution of HPMC (pharmacoat 606).

Table-1a
Effect of length of contact time on tack

Contact time (second)	Mean maximum tack force at 25 ± 2ºC, 75% RH (mN/cm²)
10	69.86 ± 8.62
20	90.20 ± 2.75
30	113.91 ± 3.89
40	60.22 ± 2.77

Table-1b
Effect of withdrawal rate on tack time

Rate of withdrawal of test probe (mm/second)	Mean maximum tack force at 25 ± 2ºC, 75% RH (mN/cm²)
1	21.50 ± 1.13
2	31.28 ± 1.05
3	37.16 ± 1.04
4	57.07 ± 6.29
5	113.91 ± 3.89
6	98.04 ± 1.04

Table-1c
Effect of solution volume on tack time

Volume of test solution (ml)	Mean maximum tack force at 25 ± 2ºC, 75% RH (mN/cm²)
2	113.91 ± 3.89
3	94.34 ± 4.03
4	92.51 ± 4.76

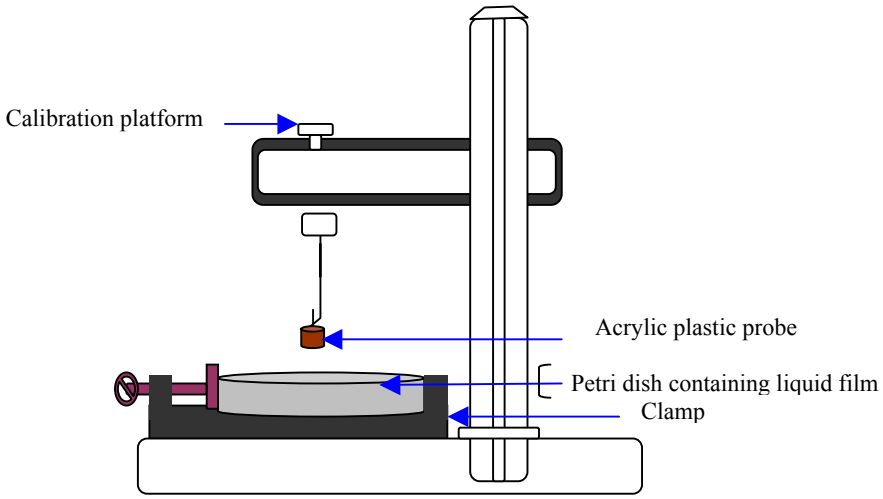

Fig. 1: Schematic diagram of the set up of TA-XT2 Texture analyzer for tack measurements.

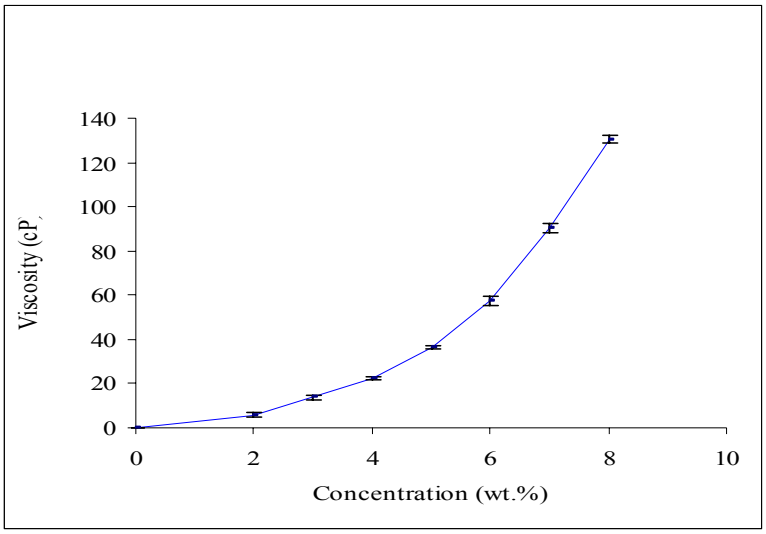

Fig. 2: Viscosity- concentration relationship of HPMC (pharmacoat 606)

Effect of additives on tack behavior of HPMC solutions

Additives can profoundly affect the tackiness of solutions of polymer (Sakellariou *et al*., 1993a). The effects of additives on tack behavior of HPMC solutions are presented in Tables-2, 3 and 4 and Figs. 3a, 3b, 4 and 5. The probe method used in this study provided a simple, quick, quantitative and reproducible evaluation system for comparing the tackiness of the coating material. The plasticizers used with HPMC which optimize the end-use of tablet coating also reduced the HPMC tackiness. Both PEG 400 and 1000 reduced the tackiness of HPMC solutions (Table-3). In addition PEG1000 was found to exert more tack reduction effect compared to

PEG400. This indicates that increasing the molecular weight of PEG will reduce the tackiness of HPMC solutions. The addition of triacetin to HPMC solution was also found to decrease the tackiness of the solutions to a greater extent compared to PEG400. When present at concentration of 20% w/w the PEG400, PEG1000 and triacetin decreased the tack forces of HPMC solutions from 113.91 to 77.43, 66.9 and 61.28 respectively. When concentrations of PEG400 and triacetin were increased above these limits the tack force started to increase. But in case of PEG1000, a further decrease in the tack force was observed at concentration of 30%.

Table-2
Comparison of tack forces for 7% w/v HPMC solutions blended with PVA at 9:1 & 8:2 blend ratio

%w/w additives	Mean maximum tack force at 25 ± 2ºC, 75% RH (mN/cm²)
HPMC 606 alone (0%)	113.91 ± 3.89
HPMC : PVA 9:1	86.04 ± 9.80
HPMC : PVA 8:2	48.76 ± 7.44

Table-3
Comparison of tack forces for 7% w/v HPMC solutions plasticized with PEG400, PEG1000 and triacetin

%w/w additives		Mean maximum tack force at 25±2 ºC, 75% RH (mN/cm²)
HPMC 606 alone (0%)		113.91 ± 3.89
PEG400	10%	93.65 ± 3.11
20%		77.43 ± 3.04
30%		79.26 ± 7.16
40%		86.34 ± 4.58
PEG1000	10%	76.13 ± 1.40
20%		61.28 ± 8.30
30%		51.70 ± 1.88
40%		65.06 ± 17.16
Triacetin	10%	81.36 ± 1.08
20%		66.90 ± 2.04
30%		72.63 ± 5.6
40%		80.37 ± 5.04

It was concluded that in general, the tackiness depended upon the molecular weight and concentration of PEG and on the type and concentration of a plasticizer. Efficiency of the plasticizers to reduce the tackiness of the HPMC solution ranked as PEG1000 > triacetin > PEG400.

Table-4
Comparison of tack forces for7%w/v (9:1 & 8:2 HPMC:PVA blends) solutions containing different concentration of polyethylene glycol 400 (PEG400), polyethylene glycol 1000 (PEG1000) and triacetin.

%w/w additives against HPMC		Mean maximum tack force at 25±2 ºC, 75% RH (mN/cm²) for 9:1	Mean maximum tack force at 25±2 ºC, 75% RH (mN/cm²) for 8:2
	(0%)	113.91 ± 3.89	113.91 ±3.89
HPMC:PVA		86.04 ± 9.8	48.76 ± 7.4
PEG400	10%	85.91 ± 4.1	94.97 ± 5.14
20%		67.28 ± 3.69	90.54 ± 2.32
30%		84.25 ± 2.38	59.73 ± 7.2
40%		78.61 ± 3.61	71.54 ± 5.53
PEG1000	10%	72.15 ± 4.19	52.81 ± 1.21
20%		58.32 ± 1.24	56.68 ± 12.20
30%		75.01 ± 1.12	40.77 ± 1.22
40%		62.04 ± 4.50	37.08 ± 4.2
Triacetin	10%	76.50 ± 7.8	54.75 ± 8.9
20%		61.36 ± 2.86	60.25 ± 1.94
30%		78.79 ± 3.40	40.28 ± 1.23
40%		63.04 ± 2.75	38.32 ± 2.14

Incorporation of PVA in HPMC solutions was also found to reduce the tackiness of the solutions in a PVA concentration dependent manner (Table-3). The tack forces of plasticized HPMC: PVA blends were significantly lower than that of control film (HPMC 606) (Table-4). For 9:1 HPMC: PVA blends the lowest tack forces recorded for all three plasticizers were at the concentration of 20% and the trend of change in tack force with the concentration of plasticizers was similar for all plasticizers used. In case of 8:2 blends, the lowest tack forces were recorded at the concentration of 30% level of PEG400 but at 40% level in case of PEG1000 and triacetin. Moreover, the trend of change in the tack forces with plasticizer concentration was not consistent as in 9:1 blend ratio.

Tackiness may be due to interaction between polymer molecules in solution working against the elongation of the solution between two separating surfaces. Reduction in such interactions would lead to lower tackiness. All PEGs, triacetin and PVA are believed to interfere in this interaction and therefore decrease the tackiness of HPMC solution (Sakellariou *et al*., 1993a; 1993b; 1994).

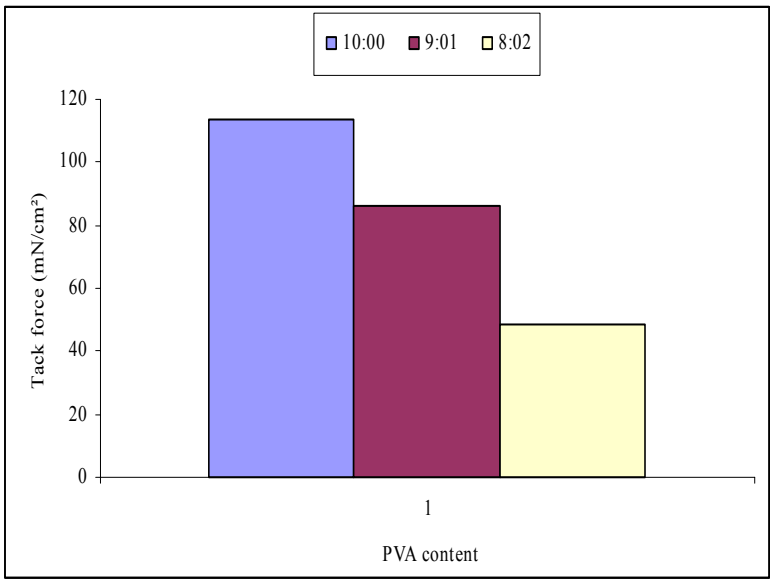

Fig. 3a: Tack force of 7% w/v HPMC (PHARMACOAT 606) solutions containing PVA at HPMC: PVA ratios of 9:1 and 8:2.

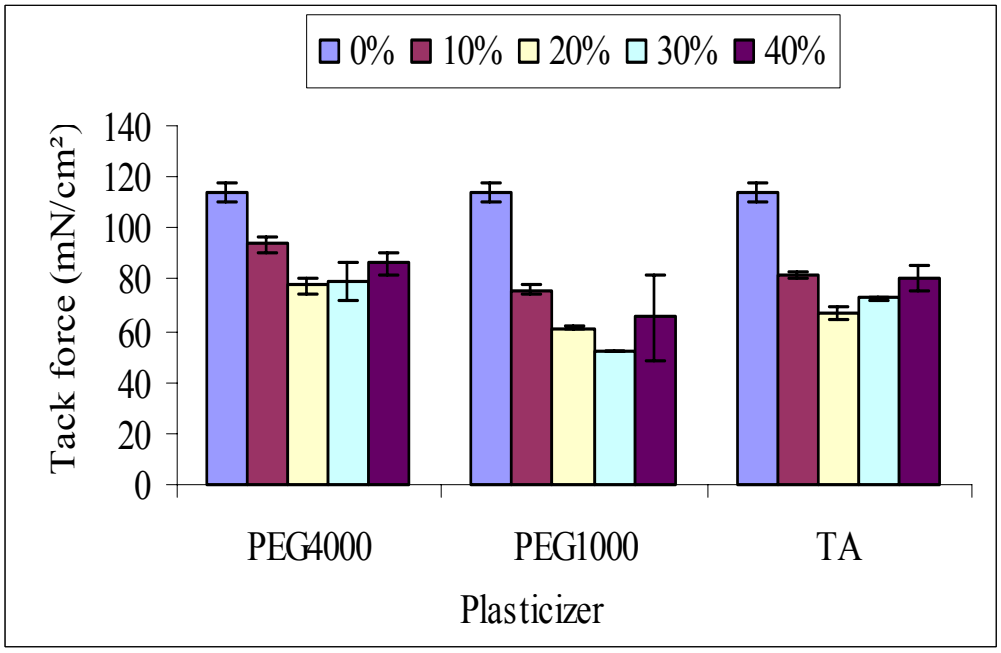

Fig 3b: Tack force of 7% w/v HPMC (PHARMACOAT 606) solutions containing 0-40% w/w plasticizers (PEG400, PEG1000 and triacetin).

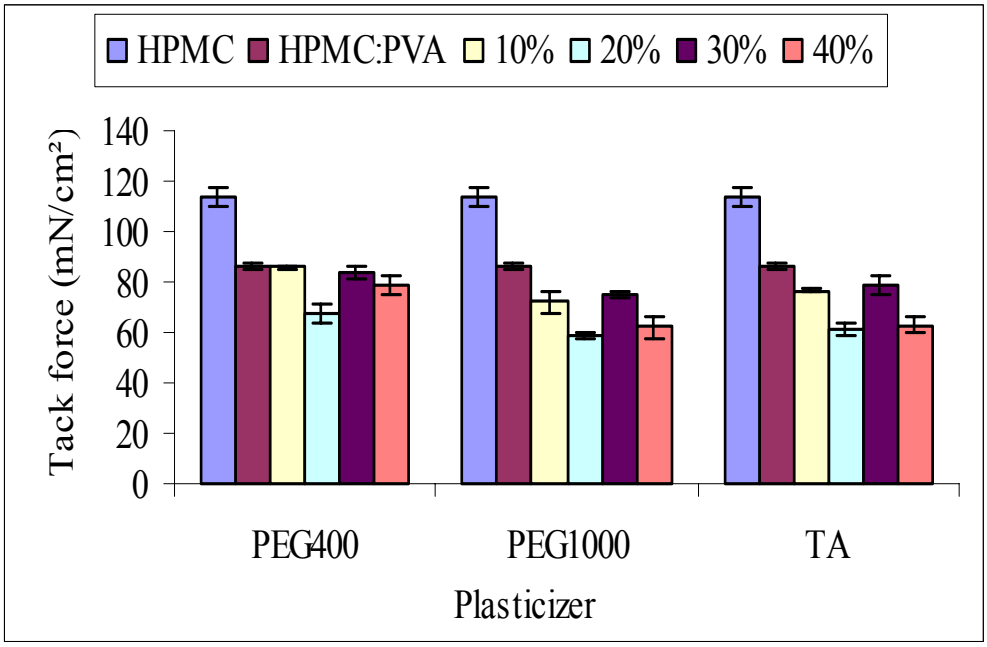

Fig. 4: Tack force of 7% w/v (9:1 HPMC/PVA) solutions containing 0-40% w/w plasticizers (PEG400, PEG1000 and triacetin) compared with control solution (7% w/v HPMC 606).

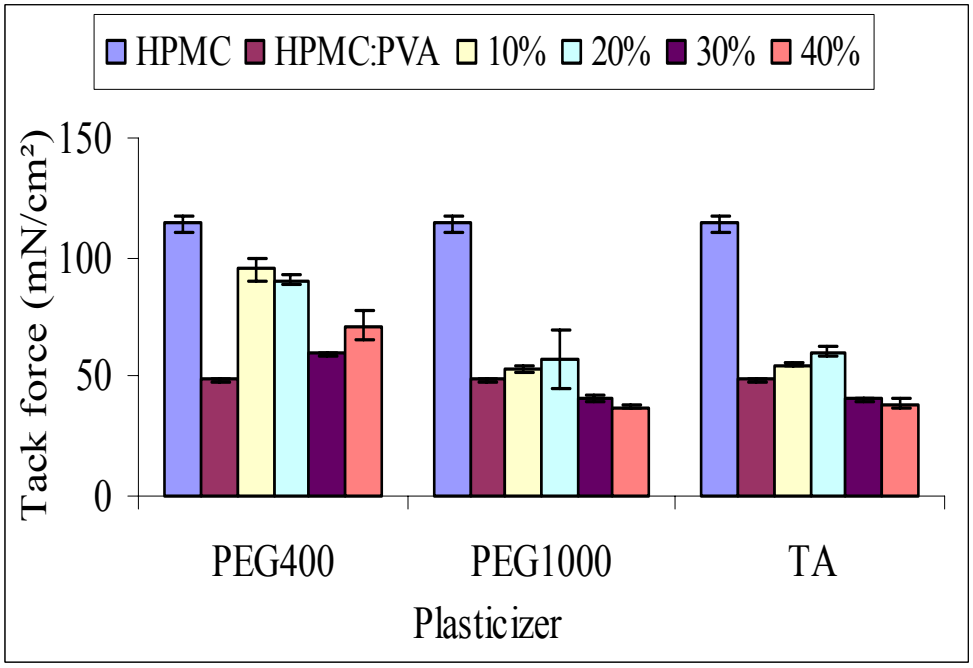

Fig. 5: Tack force of 7% w/v (8:2 HPMC/PVA) solutions containing 0 - 40% w/w plasticizers (PEG400, PEG1000 and triacetin) compared with control solution (7% w/v HPMC 606).

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