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THE EFFECTS OF INCLUSIONS ON THE PROPERTIES OF POLYMER FILMS, GRANULES AND COMPACTS.

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ABSTRACT

Polymer films have been prepared using four tablet binders, lactose, sodium lauryl sulphate and polyethylene glycol 600 have been used as inclusions in the films. The films have been tested to failure in tension and stress/strain diagrams have been prepared for each system examined. Granules and compacts have been prepared using the polymers as binders with, and without, the inclusions. The substrate for the granules was sand to eliminate the effects of solubility. Granules have been examined for size, friability and strength; compacts have been made when possible and tested for strength. The strength of bonds, between glass plates, has been measured using a butt-joint test.

The inclusions resulted in a reduction of the ultimate tensile strength of all the binder films. PEG 600 had little plasticising effect, sodium lauryl sulphate and lactose both made some films of PVP and Starch too brittle to test. Effects on bond strengths varied with film/inclusion combination.

The inclusions weakened the granules but had little effect on friability. Compact strengths were reduced by the inclusions except for lactose combined with either gelatin or starch.

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INTRODUCTION

In granules prepared by the wet-massing method the binder forms solid bonds between individual particles. Under stress these bonds can fail either adhesively, by pulling away from the substrate, or cohesively by fracture. When the granules are compressed such failures occur as the particles are forced together to form a compact. In the compact the binder may flow due to plastic deformation with new regions of adhesive bonding being formed. In the compressed tablet the binder is distributed as a fine matrix[1]. Healey et al[2] reported studies on the mechanical properties of films prepared from tablet binders and Reading et al[3] have extended similar studies to examine the effects of humidity and rate of strain on the properties of films and to examine also granules and compacts prepared using sand as an inert substrate. Highest compact strengths were found with binders having a high tensile strength and a low Brinell Hardness.

In practice, binder films will contain components of the compact due to dissolution during wet massing and therefore, the properties of binder films, granules and compacts have been studied using sand as substrate and lactose, sodium lauryl sulphate and polyethylene glycol 600 as additives with gelatin Byco C, methylcellulose, hydrolysed maize starch and polyvinylpyrrolidone as binders.

MATERIALS AND METHODS

Films were prepared using gelatin Byco C (Croda Gelatin Ltd., Widnes, U.K.), maize starch (BDH Chemicals Ltd., Poole, U.K.) methylcellulose (Methocel A15, Colorcon Ltd., Orpington, U.K.) and polyvinylpyrrolidone, PVP, mol. wt. 40,000 (BDH Chemicals Ltd.,)

Inclusions were lactose B.P. (BDH), sodium lauryl sulphate, SLS, (BDH) and polyethyleneglycol 600, PEG, (BDH).

Preparation of Films. Films were prepared on glass plates, using a chromotography spreader, from solutions of the binder containing the required concentration of inclusion. The basic binder solutions were those described previously[3] as were the methods of drying, peeling, cutting and conditioning of the films.

Testing of Films. The apparatus used has been described elsewhere[3] and depended for its operation on the measured deflection of a metal beam fitted with strain guages. Strips, 6 cm x 0.5 cm and 50 - 80 μm thick, were tested to failure in tension, following equilibration at a fixed relative humidity. From each test measurement values were calculated for Ultimate Tensile Strength (UTS, σ), Young's Modulus (ε), elongation at fracture, Proportional limit, Toughness, elastic resilience[4] and the σ/ε ratio as proposed by Rowe[5].

Preparation of Granules. Granules were prepared in 500 g batches using a Z-blade mixer (Winkworth, Staines, U.K.) from sand (Grade HPF3, 22μm, British Industrial Sand, Oakamoor, Staffs U.K.) and solutions of the binders, with and without inclusions. Gelatin, gelatinised maize starch and PVP were added as 18.75% $^{w}/_{w}$ solutions, the methylcellulose was added as dry powder followed by 80 cm^{-3} distilled water. The inclusions were dissolved or dispersed in the aqueous phases to give the required concentration, in each case the binder concentration was 3% $^{w}/_{w}$. The damp masses were screened through a 2mm screen using an oscillating granulator, the granules were dried in an hot air oven at 60^{o} to a moisture content of less than 0.5%.

Preparation of Compacts. Compacts were made from the 355 - 500 μm size fraction of each batch of granules, after conditioning at the required humidity, using an hydraulic press (Instron Ltd., High Wycombe, U.K.) at 0.033 mm s^{-1}. Each compact was made using 550mg of granule (dry weight) in a circular, 12.7 mm die, with flat faced punches.

Testing of Granules and Compacts. Granule and compact strengths were measured using the Tensile Test equipment modified to operate as an apparatus that would record the force required to crush individual granules, from the 710 - 1000 μm size fraction, or to cause the compacts to fail in diametral compression. This was achieved by replacing the grips with flat blocks running on a horizontal table and by reversing the direction of movement of the loading jack.

Granule friability was assessed using a Roche friabilator with 5 g granule from the 710 - 1000µm size fraction, rotated at 30 rpm for 5 min, the percentage loss in weight was recorded.

Measurement of Bond Strengths. Glass chromotography plates were cut into 2 cm x 2 cm squares and were fixed to aluminium base plates using an adhesive. The glass was cleaned using a detergent, rinsed and dried at 120° for 60 min.; 1% solutions of the binders 5µl, with and without inclusions were placed onto the glass using a micropipette. The joint was made and the two plates were held at room temperature for 48 hrs while the film dried. Using the tensile test apparatus, modified to hold the plates in the vertical plane, the force required to separate the plates was measured.

RESULTS

Films. The results for Ultimate Tensile Strength (UTS) and elongation at fracture are given in Figures 1 - 4, the values for other physical properties measured are summarised in Table 1. The results given are the mean of nine replicate tests, the coefficients of variation were in the order of 20% for UTS, elongation at fracture, proportional limit and Young's Modulus; for the derived values of Toughness and Elastic Resilience the coefficients of variation were about 30%. Representitive stress/strain curves for the binders are given in Figures 5 - 8. These are based on reconstructions using the mean values obtained for UTS, Young's Modulus, proportional limit and elongation at fracture.

Granules. Results of measurements made on the granules from the 710 - 1000µm size fractions are given in Table 2. Thirty individual granules were tested for each mean value recorded in the table, granules were conditioned at 44% RH and at 25° for seven days before testing.

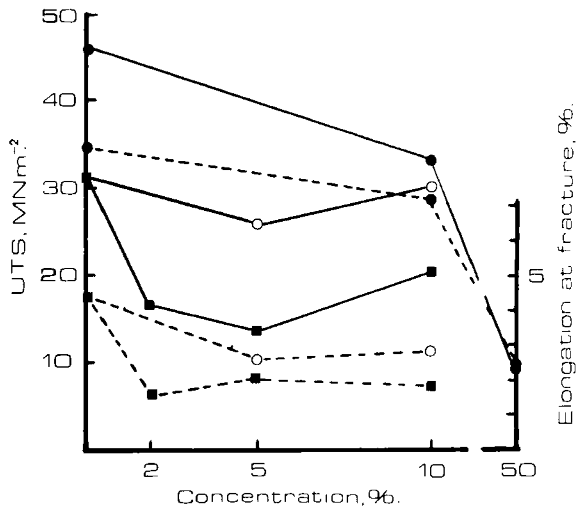

FIGURE 1

Effects of additives on the Ultimate Tensile Strength —— and Elongation at Fracture – – – of Gelatin Byco C films. Lactose ●, (81%RH); PEG 600 O, SLS ■, (44%RH). Additive concentration is expressed as percentage of binder present.

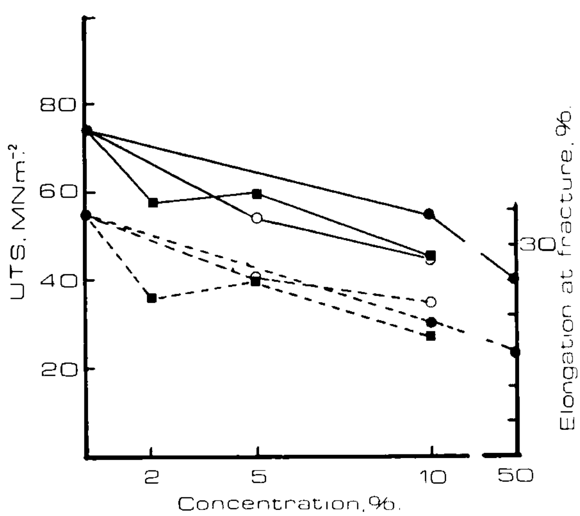

FIGURE 2

Effects of additives on the Ultimate Tensile Strength —— and Elongation at Fracture - - - of Methylcellulose films. Lactose ● ; PEG 600 O ; SLS ■ ; (44%RH). Additive concentration is expressed as percentage of binder present.

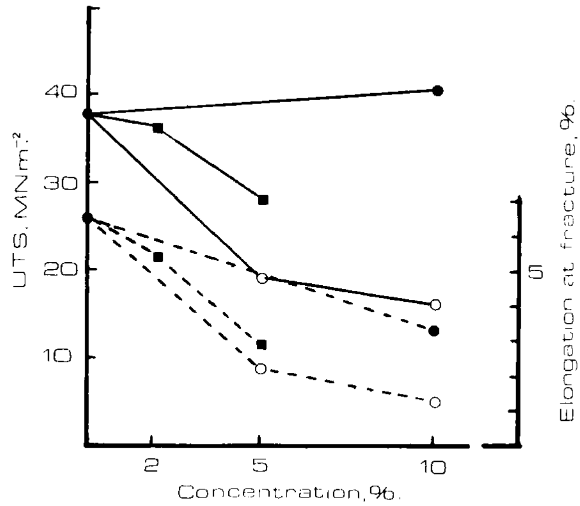

FIGURE 3

Effects of additives on the Ultimate Tensile Strength — and Elongation at Fracture - - - of Maize Starch filme. Lactose ● ; P.E.G.600 ○ ; S.L.S. ■ ; (44% RH). Additive concentration is expressed as percentage of binder present.

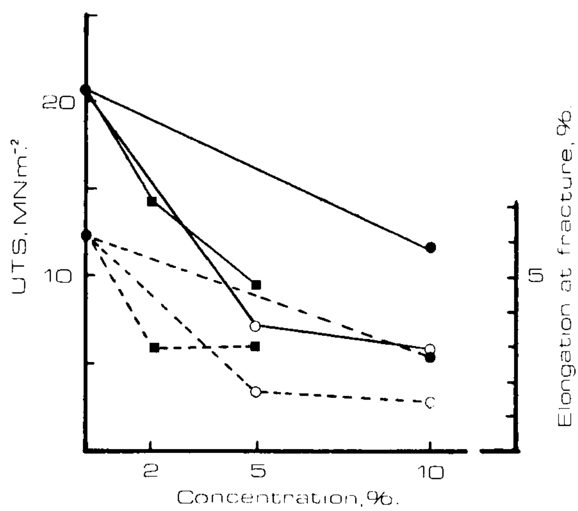

FIGURE 4

Effects of additives on the Ultimate Tensile Strength — and Elongation at Fracture --- of Polyvinylpyrrolidone films. Lactose ● ;PEG 600 ○ ; SLS ■ ;(44%RH). Additive concentration is expressed as percentage of binder present.

TABLE 1

Physical Properties of Films of Binders with Inclusions, means of 9 replicate measurements.

Binder	Additive as % of Binder	Young's Modulus (ε) (MNm^{-2})	Prop. Limit (%)	Elastic Resilience ($Jm^{-3}x10^5$)	Toughness ($Jm^{-3}x10^5$)	σ/ε $x10^{-2}$ Ratio
G	0	1058	88.6	5.3	13.8	3.0
G	2 SLS	1367	73.3	0.6	2.6	1.3
G	5 SLS	844	98.1	1.5	2.6	1.7
G	10 SLS	1222	78.5	1.4	3.6	1.7
G	5 PEG	1212	83.7	2.4	6.8	2.2
G	10 PEG	1352	62.5	1.6	7.2	2.2
G 81%RH	0	900	48.7	3.5	30.7	5.2
G	10 L	783	46.7	1.7	17.9	4.3
G	50 L	435	100	1.1	2.2	2.2
MC	0	1136	41.9	4.0	179.2	6.4
MC	2 SLS	1496	41.7	1.9	94.6	3.8
MC	5 SLS	1476	45.9	2.0	106.9	4.0
MC	10 SLS	1122	54.6	2.9	60.8	4.1
MC	5 PEG	1173	39.5	2.0	98.2	4.6
MC	10 PEG	1151	52.9	2.4	82.4	3.9
MC	10 L	977	54.1	5.1	85.9	5.7
MC	50 L	580	47.9	3.4	66.0	6.9
MS	0	867	86.5	7.4	25.2	4.4
MS	2 SLS	1463	48.8	1.0	15.6	2.5
MS	5 SLS	1603	62.3	1.0	6.7	1.8
MS	10 SLS	Film cracked and could not be tested.				
MS	5 PEG	1164	97.7	2.7	5.5	1.7
MS	10 PEG	1153	64.9	0.6	2.3	1.4
MS	10 L	1422	87.4	5.0	14.0	2.9
MS	50 L	Film too brittle to test.				
PVP	0	414	65.6	1.7	8.9	5.0
PVP	2 SLS	686	70.0	0.7	3.7	2.1
PVP	5 SLS	445	71.9	0.7	2.4	2.1
PVP	5 PEG	610	72.7	0.3	0.9	1.1
PVP	10 PEG	492	100	0.4	0.9	1.2
PVP	10 L	578	70.0	0.7	2.9	2.0
PVP	50 L	Film too brittle to test.				

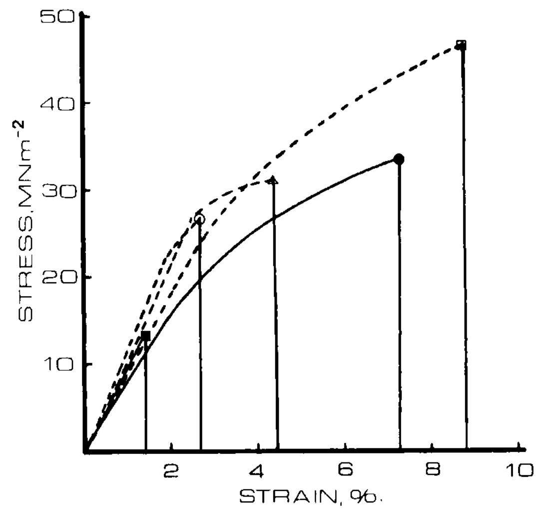

FIGURE 5

Reconstructed Stress/Strain curves for Gelatin Byco C films alone △ (44%RH), □ (81%RH) , and with lactose 10% ● , PEG 600 5% ○ , SLS 5% ■ .

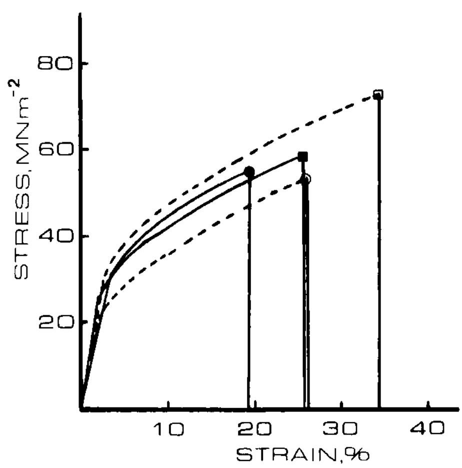

FIGURE 6

Reconstructed Stress/Strain curves for Methylcellulose films alone □ , and with lactose 10% ● , PEG 600 5% ○ , SLS 5% ■ .

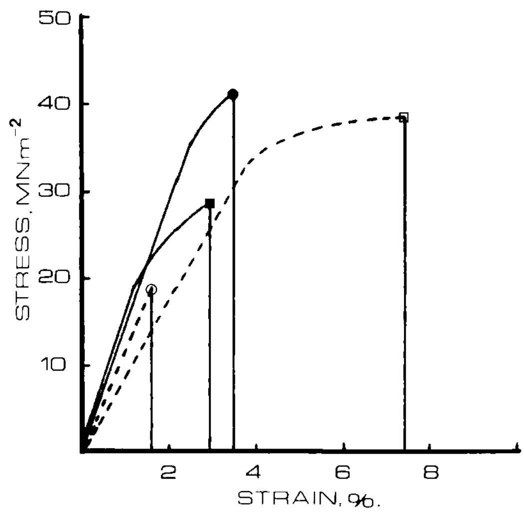

FIGURE 7

Reconstructed Stress/Strain curves for Maize Starch films alone □ , and with lactose 10% ● , PEG 600 5% ○ , SLS 5% ■ .

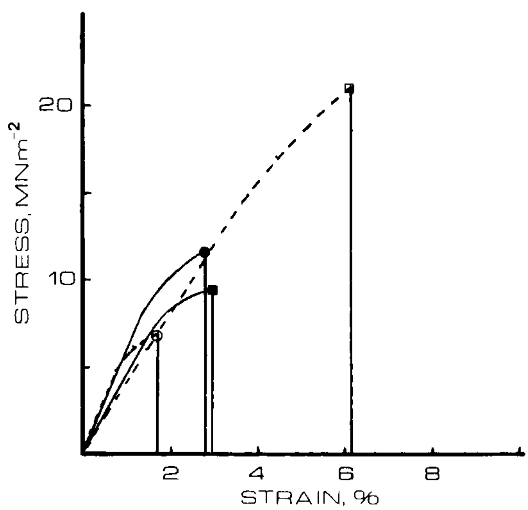

FIGURE 8

Reconstructed Stress/Strain curves for Polyvinylpyrrolidone films alone □ , and with lactose 10% ● , PEG 600 5% ○ , SLS 5% ■ .

TABLE 2

Properties of Granules, 710μm - 1000μm, with and without Inclusions.

Binder 3% w/w	Additive (%)	Size (μm)	Strength (g)	Work to Crush (mJ)	Friability (%)
G	0	365	347	1.43	14.6
G	0.3 L	485	337	1.03	13.6
G	0.9 L	730	417	1.24	4.1
G	0.3 PEG	800	146	0.32	17.4
G	0.3 SLS	1000	237	0.51	16.3
MC	0	680	324	1.39	5.0
MC	0.3 L	425	221	1.24	6.1
MC	0.9 L	500	215	1.37	7.7
MC	0.3 PEG	710	163	0.49	7.3
MC	0.3 SLS	950	83	0.32	10.5
MS	0	200	132	0.78	20.4
MS	0.3 L	130	125	0.68	24
MS	0.9 L	125	97	0.62	27.5
MS	0.3 PEG	210	95	0.31	27.6
MS	0.3 SLS	360	5.5	0.04	38.4
PVP	0	445	340	1.05	11
PVP	0.3 L	410	332	1.29	11.9
PVP	0.9 L	355	345	1.30	12
PVP	0.3 PEG	550	87	0.21	13.4
PVP	0.3 SLS	680	152	0.32	12.3

<u>Compacts</u>. The effects of compression pressure on the diametral crushing strength of compacts prepared from the 355-500 μm size fraction are shown in Figures 9 - 12.

<u>Bond Strengths</u>. The force required to separate two glass plates joined by dry binder films was measured with and without additives, the results are given in Table 3.

DISCUSSION

Films were equilibrated at 44% RH, however, with lactose in Gelatin Byco C films the films proved too brittle to remove from the plates. Therefore, Gelatin films containing lactose were

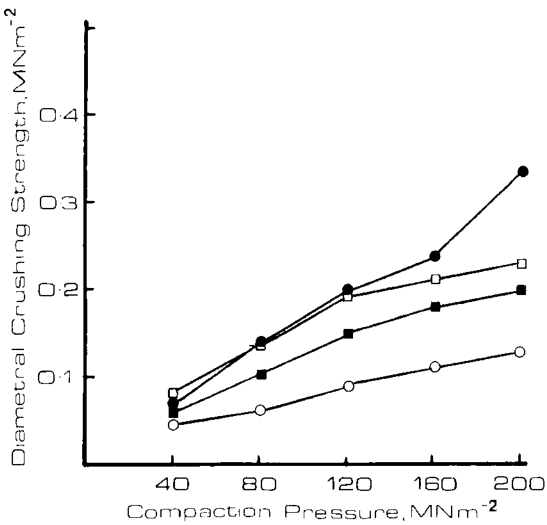

FIGURE 9

Effects of Compression Pressure on the Diametral Crushing Strength of Compacts made from the 355-500 μm size fraction of granules prepared using Gelatin Byco C alone □ , and plus lactose 10% ● , PEG 600 10% ○ , SLS 10% ■ .

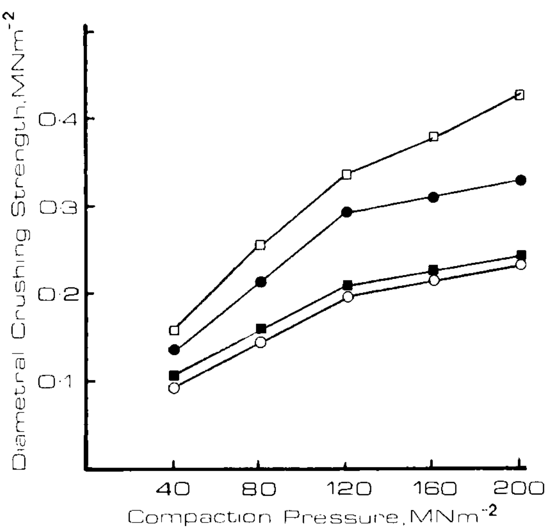

FIGURE 10

Effects of Compression Pressure on the Diametral Crushing strength of Compacts made from the 355-500 μm size fraction of granules prepared using Methylcellulose alone □ , and plus lactose 10% ● , PEG 600 10% ○ , SLS 10% ■ .

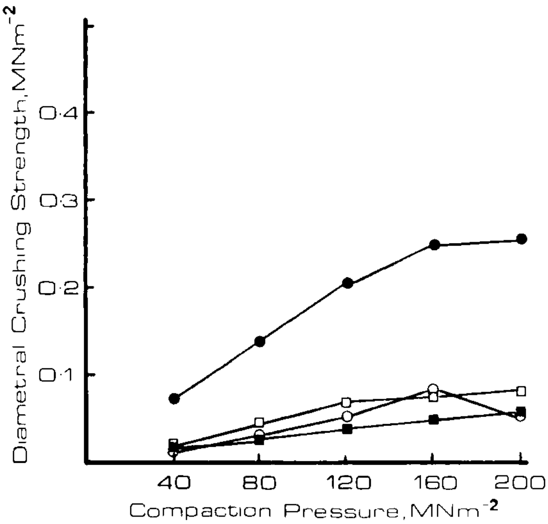

FIGURE 11

Effect of Compression Pressure on the Diametral Crushing Strength of Compacts made from the 355-500 μm size fraction of granules prepared using Maize Starch alone □ , and plus lactose 10% ● , PEG 600 10% ○ , SLS 10% ■ .

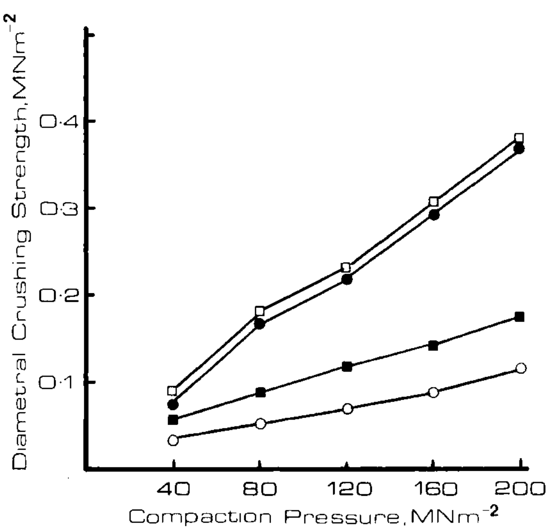

FIGURE 12

Effects of Compression Pressure on the Diametral Crushing Strength of Compacts made from the 355-500 μm size fraction of granules prepared using Polyvinylpyrrolidone alone □ , and plus lactose 10% ● , PEG 600 10% ○ , SLS 10% ■ .

TABLE 3

The strengths of Bonds formed between two glass plates using binder films with and without additives. Means of replicates.

Inclusion (10% of binder)	Gelatin Byco C	Methyl-cellulose	Maize Starch	PVP
	Force required to separate plates, kNm^{-2} (std dev)			
None	61.3(8.7)	2.2(0.6)	76.0(16.3)	46.9(7.4)
lactose	61.6(9.7)	14.7(7.7)	63.7(15.9)	67.6(14.2)
SLS	38.9(9.1)	2.0(0.4)	60.6(16.0)	32.7(9.0)
PEG 600	34.8(9.1)	2.5(1.7)	34.5(6.2)	44.4(14.1)

equilibrated at 81% RH and so direct comparison of the effects of different inclusions is not possible in this case.

Effects of Inclusions on Gelatin Byco C Films. Lactose at 44% RH produced films that were too brittle to test; at 81% RH (Figures 1 & 5, Table 1) the films were weakened and with 50% lactose weak films were produced. Sodium lauryl sulphate (SLS) weakened the film at 2% additive but further increase in concentration to 5% and 10% had little extra effect. Polyethyleneglycol 600 (PEG) produced only a small increase in Young's Modulus, the PEG had been added as possible plasticizer but no such effect could be demonstrated.

Effects of Inclusions on Methylcellulose (MC) Films. All three inclusions produced similar effects with methylcellulose films, which were stronger and more plastic than the other three films examined (Figures 2 & 6, Table 1). The films were weakened and their elongation at fracture reduced, SLS produced a significant increase in Young's Modulus.

Effects of Inclusions on Maize Starch (MS) Films. Both SLS at 10% and lactose at 50% addition produced films that could not be tested due to cracking of the film with SLS and excessive brittleness with lactose. Otherwise, all three inclusions reduced elongation at fracture but lactose at 10% produced a film of greater Ultimate

Tensile Strength (Figures 2 & 7). Young's Moduli were increased by the inclusions (Table 1) in keeping with the observed results of greater brittleness.

Effects of Inclusions on Polyvinylpyrrolidone (PVP) Films. The three inclusions all produced a significant weakening of the PVP films (Figures 4 & 8, Table 1). The films became more brittle, with greater Young's Moduli, and with 50% added lactose the film was too brittle to handle without breaking.

Granules were prepared containing 3% $^{w}/w$ binder plus an additional 0.3% inclusion, granules were also prepared with an additional 0.9% lactose because of the widespread use of lactose in tabletting when it will present in the binder film after drying the granules. The results are summarised in Table 2.

Effects of Inclusions on Granules and Compacts made with Gelatin Byco C as Binder. In comparison with granules made with binder alone the granules containing the inclusions had greater mean sizes but only those with 0.9% lactose were stronger. Lactose as an inclusion produced very brittle films at 44% RH but the granules containing 0.9% lactose in addition to the binder were stronger and less friable than the other gelatin based granules. The granule strength results are reflected in the strength of the compacts (Figure 9).

Effects of Inclusions on Granules and Compacts made with Methylcellulose as Binder. In this case lactose as an inclusion resulted in smaller granules and all three inclusions gave weaker and more friable granules than were seen with MC alone. The strongest granules gave the strongest compacts as with Gelatin films, however, the binders with PEG and SLS gave compacts of similar strength but the granules were different in strength by a factor of two.

Effects of Inclusions on Granules and Compacts made with Maize Starch as Binder. Granules were small when made using MS as binder and the inclusion of lactose produced even smaller granules. Compacts were weak, although those containing lactose were significantly stronger than those without inclusion or with PEG or SLS added (Figure 11).

Effects of Inclusions on Granules and Compacts made with PVP as Binder. Lactose, again, gave smaller granules but although those with PEG or SLS were larger than those without inclusions these two materials gave very weak granules. This weakness was reflected in the strengths of the compacts. (Figure 12).

Effects of Inclusions on Bond Strengths. These results are given in Table 3. Bond strengths without additive were in the order MS, G, PVP, MC with the MC bonds being very weak. The bond strengths are not reflected in compact or granule strengths. For example, MC forms a coherent film of high Ultimate Tensile Strength and relatively strong granules and compacts, however, the bond strength is very weak.

CONCLUSIONS

The presence of the selected inclusions in the binder film had, in general, a weakening effect on the films. Compacts were also weakened except with lactose as additive in Gelatin and Maize Starch films. PEG 600 showed no plasticizing effects in the films studied and tended to give weak granules and compacts when included with each of the four binders studied. Bond tensile strengths were not correlated with granule strengths.

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