Acta Poloniae Pharmaceutica – Drug Research, Vol. 61 No. 4 pp. 255–258, 2004

ISSN 0001-6837
Polish Pharmaceutical Society

BIOPHARMACY

EFFECT OF CATION CONTENT OF CERTAIN AMMONIOMETHACRYLATE COPOLYMERS TYPE A (RL) AND B (RS) ON THEIR BINDER PROPERTY IN TABLETING

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Abstract: Tablets of salicylic acid (drug model) have been formed using two analogous acrylatemethacrylate copolymers designated here as **A** and **B** as binders. **A** and **B** differ only in their content of quaternary ammonium (cationic) groups in the ratio 2:1 (**A**:**B**). The aim was to investigate the effect of the cationic groups on the tableting characteristics of the formed granules. In the procedure, aqueous dispersions of the polymers of concentrations 1 to 5% w/v were used in a separate experiment for granulation of the salicylic acid powder and then tableted. The final concentration of the binder in the tablets varied from 0.4 to 2% w/w. The parameters assessed were the tablet tensile strength (T) and their brittle fracture index (BFI) which are indicative of the plasto–elasticity of the granules; for instance, a high T value together with a low BFI value are indicative of a high plasto–elasticity. **A** and **B** generally displayed a strong binder property as they individually produced hard tablets even at the low concentration 0.4% w/w. As the binder concentration in the tablets increased to 2% w/w, tensile strength (MNm^{-2}) increased from 1.08 to 1.80 (tablets of polymer **A**), 1.08 to 2.02 (tablets of polymer **B**). BFI values decreased from 0.24 to 0.06 (tablets of polymer **A**) and 0.16 to 0.04 (tablets of polymer **B**). These results indicate that the presence of the cationic groups in the polymer structure promoted elastic rather than plastic compression.

Keywords: polymer structural effects, acrylatemethacrylates, plasto-elasticity, plastic/elastic compression, salicylic acid tablets

The acrylatemethacrylates are water–insoluble copolymers, which have been frequently exploited in film coating for sustained release applications (1, 2, 3). The type studied here contains in their molecular structure a certain amount of quaternary ammonium (cation) groups, which have been found to have profound effects on the porosity of resulting films (4). The analogue with a higher cation content gave more porous films, an effect attributed to the mutual repulsiveness of the cationic groups during film formation.

In the present study, the copolymers are being studied for the first time as binders in tableting by measuring the mechanical properties (tensile strength and brittle fracture index) of resulting tablets. Perhaps the presence of the cations may influence the plasto–elasticity of the granules; this aspect was investigated here.

Theoretical considerations. The parameters measured were the tablet tensile strength (T) and the brittle fracture index (BFI). The later was taken as a measure of the plasto–elasticity of the granules from which the tablets were made. Tablet tensile strength is the stress needed to fracture a tablet diametrally and it is given by the expression (5):

$$T = 2P/\pi Dt \qquad (1)$$

where P is the load (Kg) causing fracture of the tablet of diameter D (m) and thickness, t (m). It is a measure of the degree of interparticulate bonding in the tablet. On the other hand, the brittle fracture index (BFI) of a tablet is a measure of its tendency to laminate or cap during ejection from the machine die and it is given by the expression (6):

$$BFI = 0.5\ (T/To - 1) \qquad (2)$$

where To and T are the tensile strengths of tablets with and without a centre hole respectively. The centre hole is a built–in model defect, which simulates the voids (i.e. weak points) in actual tablets.

Thus a tablet may be hard and yet fracture easily if these weak points exist in its structure. Plastic deformation of particles during compression helps to eliminate these voids and hence polymeric binders, which promote plastic deformation increase, tablet tensile strength, but ameliorate their brittle fracture tendency (6, 7).

The term plasto–elasticity is defined by the ratio ER/PC, where ER is the tablet elastic recovery as measured by the percentage increase in tablet thickness after its ejection from the machine die as a result of elastic rebound, while PC is the tablet plastic compression as measured by the percentage decrease in tablet thickness while under a constant load in the die for thirty seconds, attributable to plastic deformation of the particles (7). Thus a plastic material will display a low plasto–elasticity, while an elastic material will display a high plasto–elasticity.

EXPERIMENTAL

Two acrylatemetharcylate copolymers, designated **A** and **B** (trade names: Eudragit RL100 and RS100, respectively), were received from Rhoma Pharma, Darmstadt, Germany. The polymer molecular structure (Figure 1) shows the quartenary ammonium (cationic) group. **A** and **B** differ only in their content of these cation groups in the ratio 2:1 (**A**:**B**). **A** contains 66 moles of the cation per one mole of the polymer chain, while **B** contains 33 moles of the cation per one mole of the polymer chain (4). Both polymers are water–insoluble. Their aqueous dispersions were used as binders during wet granulation. Salicylic acid (analar grade, BDH) was used as a drug model which requires preliminary granulation before it can be tableted. Ethanol (i.e. absolute alcohol BP) was used as solvent for the polymer in the preparation of the granulating fluid.

Preparation of the polymer dispersions and the granulation technique

Aqueous dispersions of the water – insoluble copolymers were prepared by a coacervation technique, details of which have been reported elsewhere (3). In the procedure, excess water (i.e. non–solvent for the polymer) was added to an ethanol solution of the polymer with vigorous shaking to form a latex dispersion. The ratio of water to ethanol in the dispersion was constant 95:5, but the polymer content was varied in different batches from 1 to 5% w/v.

To form the granules, a sample of the salicylic acid powder (20 g) was wet–massed with the polymer dispersion (8 ml). The wet mass was pressed through a sieve of an aperture size of 1.4 mm and then dried at 60°C for 1 h in a hot air oven. The half dried mass was pressed through the same sieve and dried finally at 60°C for 3 h to a moisture content of 2.1±0.3% w/w and then pressed through a sieve of an aperture size of 710 μm. Particle size

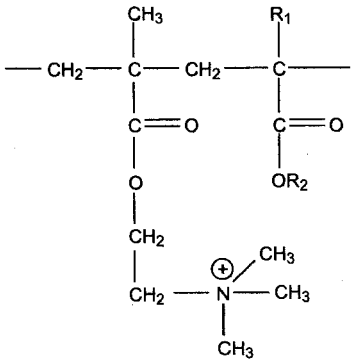

Figure 1. General structure oh the acrylatemethacrylate copolymers.

in the granules varied from 120–510 μm as determined by sieve analysis.

Preparation of tablets and their evaluation

In order to investigate the BFI values of tablets (eqn. 2), it was necessary to form tablets with and without a centre hole. A procedure for preparing tablets with this centre hole has been described previously (7, 8). It involves the use of a lower punch with a centre pin and an upper punch with a centre through hole for the compression of the granules. The resulting tablets were of diameter 12.5 mm, weight 550 mg, thickness 3.38 mm and diameter of centre hole 1.60 mm. Tablets without a centre hole were formed by using similar punches, but without a centre pin or a centre through hole. The tablets were compressed to a packing fraction of 0.91±0.03 (tablets of polymer **A**) or 0.92±0.02 (tablets of polymer **B**).

The resulting tablets were evaluated for tensile strength and brittle fracture index using eqs. 1 and 2, respectively. The tablet tensile strength was determined by the diametral compression method as described by Newton and Fell (5).

Determination of viscosity of the polymer dispersion

Viscosities of the liquids were measured using a U–tube (Ostward) capillary viscometer (model B/S/U445). Viscosity η is related to the time of flow by the expression (9).

$$\frac{V}{t} = \frac{\pi P r 4}{8\eta\rho} \qquad (3)$$

Where V is the volume of liquid flowing in time t through a fine capillary of radius r, and length ρ, P is the liquid pressure above the capillary. For a given viscometer, the terms v, P, ρ and

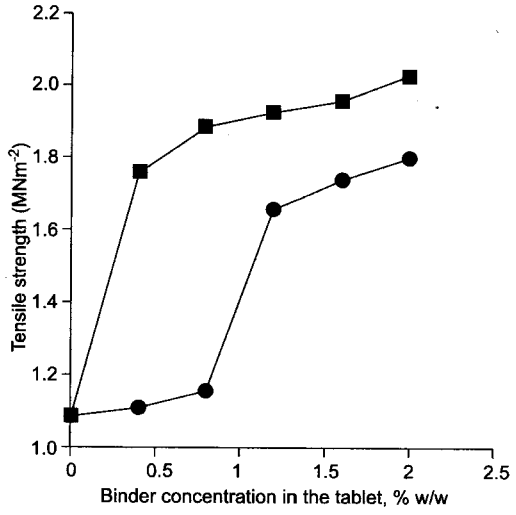

Figure 2. Effect of binder type on the tensile strength of salicylic acid tablet, polymer A (•) and B (■).

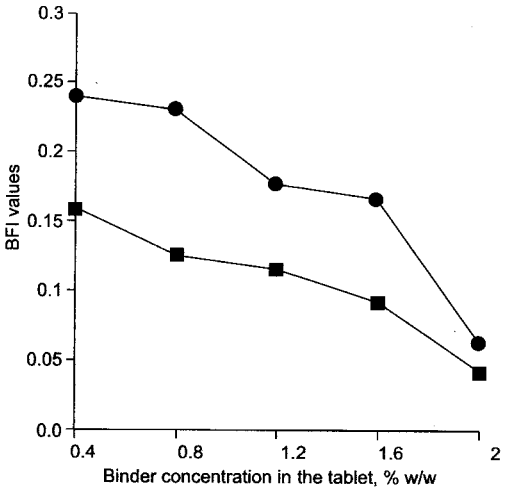

Figure 3. Effect of binder type on the brittle fracture index of salicylic acid tablets, polymer (•) and B (■).

r are constants and η varies directly with t. Since the present measurement was of a comparative value only, the time of flow (seconds) of a given volume of the liquid through the capillary was taken as index of viscosity. The determination was carried out in triplicates and the mean results are reported in Table 1.

RESULTS AND DISCUSSION

The acrylatemethacrylates proved to be strong and effective binders as they produced hard tablets at very low concentration such as 0.4% w/w (Figure 2). This is reflected by the high tensile strengths and the low BFI values of the tablets, generally.

Table 1. Viscosities of the polymer dispersions

Concentration of the polymer dispersions, % w/v	Viscosity index time of flow (S)	
	A	**B**
1	35	54
2	39	65
3	54	73
4	62	100
5	77	138

Polymer **A** with the higher cation content (compared with **B**) gave tablets of lower tensile strengths (Figure 2) but also produced tablets of higher BFI values (Figure 3). These difference can be explained as follows: plastic deformation of the particles during compression would increase the area of contact for interparticulate cohesion. The higher tensile strengths of polymer **B** thus suggest that polymer **B** (compared with **A**) imparted greater plasticity to the granules. This suggestion is further supported by the lower BFI values of tablets of polymer **B**. Previous studies (9, 11) have shown that a higher BFI value of tablets is invariably associated with the high plasto–elasticity of the granules from which the tablets were made; hence BFI values may be taken as measure of plasto–elasticity. Thus, the lower BFI values of polymer **B** (compared with **A**) are an additional evidence that polymer **B** imparted greater plasticity to the granules.

Another consideration is that viscous binder fluids (compared with less viscous fluids) are expected to give harder tablets. As can be seen in Table 1, **B** gave higher viscosities than **A**, which explains the higher plasticity of **B** and its stronger binder property. The lower viscosity of the dispersions of polymer **A** is, in turn, explained on the basis of lesser polymer – polymer cohesion due to the mutual repulsiveness of the charged cationic groups.

CONCLUSIONS

The results of this study indicate that the presence of the cationic groups in the polymer structure imparts some degree of elastic compression to the granules. It is also concluded that the

acrylatemethacrylates are strong and effective binders in tableting.

Acknowledgement

The authors wish to thank Rhom Pharma, Darmstadt, Germany, for their kind gift of the Eudragit polymers.

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Received: 24.09.2003