peel test by Nadkarni et al (1975) who showed that the adhesion was best when solvents with solubility parameters close to that of the polymer were used. In this case ϕ_s will be small since polymer solutions prepared using good solvents will solidify at lower dilutions than those prepared using poorer solvents resulting in the internal stress P being minimal.

Film thickness

The relationship between P and t, the thickness of the film coating and hence F, the measured adhesion, has already been studied (Rowe 1978) confirming the mechanism given above. An extension of the work into the study of bridging of the intagliations gave results also in agreement with this mechanism (Rowe & Forse 1980). This factor also offers the opportunity of obtaining a true value for A—the intrinsic adhesion at the interface—since by extrapolating measured adhesion values to zero thickness, P and hence R can be effectively eliminated.

Conditions of measurement

The value of keeping the conditions of measurement constant during testing can now be seen since any change in both the ambient temperature and the humidity will affect the value of P by affecting Δt and ϕ_r. The latter will, of course, be especially important for hygroscopic polymers since in this case ϕ_r will increase with increasing humidity resulting in a decrease in both P and R and hence an increase in the measured adhesion. Evidence for this can be obtained from the work of Fung & Parrott (1980) who showed an increase in the measured adhesions of a variety of film-coated tablets on increasing the relative humidity.

Conclusions

The model based on a modified stress distribution at the film/tablet interface which provides for the presence of internal stresses within the film is able to account for the trends in the results obtained from both adhesion testing and experiments on the bridging of intagliations. It should, therefore, be considered in parallel with the current models of simple intermolecular association when attempting to explain results from such studies. Unfortunately it is one further variable to be considered before fundamental studies into the strength of the adhesive bond at the film/tablet interface can be undertaken.

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Inability of degraded carrageenan fractions to induce inflammatory bowel ulceration in the guinea-pig

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Ulcerative disease of the large bowel has been induced readily in several animal species (viz. guinea-pigs, rabbits, rhesus monkeys) by the oral administration of degraded carrageenan, a sulphated polysaccharide derived from the red seaweed, *Eucheuma spinosum* (Marcus & Watt 1969; Benitz et al 1973; Abraham et al 1974). Since the degraded form of carrageenan is difficult and expensive to obtain, Watt et al (1979) described in this journal a method for the hydrolysis of a native form of *Eucheuma spinosum* carrageenan, leading to the more ulcerogenic degraded product.

Using the same method of degradation as these workers, we investigated the actions of a variety of carrageenan fractions on the guinea-pig bowel, with the purpose of developing a reliable model for the assessment of anticolitic drugs. The carrageenan fractions were obtained from Sigma Chemical Co. Ltd (London, U.K.), a source not des-

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cribed previously for this type of study and in a form which required degradation in order to produce a non-viscous, concentrated solution, suitable for oral administration. Those examined were: iota (ι)—(from *Eucheuma spinosum*); kappa (κ)—(from *Eucheuma cottonii*); lambda (λ)—(from *Gigartina aciculaire* and *pistillata*). The average molecular weights (obtained from Sigma Chemicals) for each fraction, before degradation, were: ι, 140 000; κ, 154 000; λ, 300 000. In a preliminary experiment using a 1% (w/v) solution of ι-carrageenan (a concentration which did not require degradation before drinking), we found no adverse effects on the appearance, behaviour or gastrointestinal tract of a group of 6 guinea-pigs after 4 months oral administration. Consequently, preparations containing 3% of each degraded carrageenan fraction were administered to different groups of guinea-pigs (male, Dunkin-Hartley; 350–400 g), as their only source of drinking water for 3 weeks, or until animals appeared moribund, at which point they were killed.

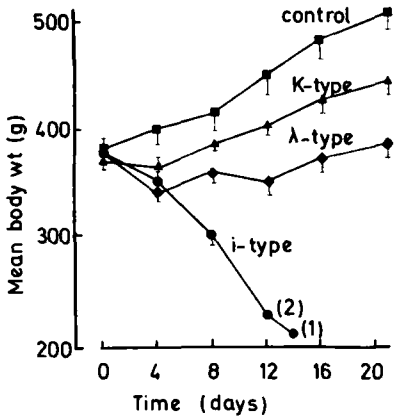

FIG. 1. Effect of oral administration of 3% degraded carrageenan fractions on body weight. Values are expressed as mean ± s.e.m. (N = 4, except where shown otherwise in parentheses.)

All three carrageenans caused a significant reduction in mean body weight gain ($P<0.05$) (Fig. 1), while the average food intake per animal was also reduced compared with controls. In both cases, the order of potency was ι > λ>κ, although the mean daily carrageenan consumption per group (ι:4 3, λ:7·1 and κ:7·7 g kg^{-1}) was the reverse of this order, indicating that potency was not related to intake concentration. Interestingly, this order of potency parallels their previously reported comparative activity as acute or chronic inflammatory agents in vivo (Winter et al 1962).

Animals given ι-carrageenan became moribund within 9 days, and although a frequent diarrhoea was observed after 7 days, neither ulceration of the caecum nor large bowel was evident on macroscopic examination, using a dissecting magnifying lens. Furthermore, microscopic studies failed to reveal histopathological changes in bowel sections. The precise cause of death was unknown, but may have resulted from excessive loss of body fluids, interference with nutrition, or the known toxic systemic effects of carrageenan (Di Rosa 1972).

A mild diarrhoea was occasionally observed in the λ-carrageenan group, while loose, watery stools appeared in the κ-carrageenan group, between 7 and 10 days. In both groups the appearance of caecum and colon was normal, both macroscopically and microscopically.

Earlier findings by Engster & Abraham (1976) also failed to demonstrate an ulcerogenic effect in guinea-pigs with κ- and λ-carrageenan fractions, while the ι-form appeared to show molecular weight-related ulcerogenicity. They found high (145 000) and low (5 000) weight ι-fractions to be without effect on the caecum, but showed marked histopathological changes with intermediate molecular weight fractions. Although the molecular weights of the degraded carrageenans used in the present study were not known, the lack of inflammatory activity of these products may also have been the result of a certain range obtained. The other possiblity is that the chemical degradation process may have interfered with their ulcerogenicity. However, the absence of bowel ulceration after chronic administration of non-degraded ι-carrageenan seen in our preliminary experiments would argue against this.

In conclusion, it is apparent that in order to develop a model of inflammatory bowel ulceration in guinea-pigs using carrageenan, it is necessary to obtain a specific source, type and molecular weight range of carrageenan. Degraded, whole extract (unfractionated) *Eucheuma spinosum* used by Watt et al (1979) appears to be highly ulcerogenic, while its degraded, fractionated ι-form investigated in the present study is not.

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