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Influence of probe shape on gel strength test

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Abstract

The mechanical resistance of gel systems was measured by means of a gel strength tester. Measurements were performed using a standard sample holder and probes of different geometry (conical, spherical and cylindrical). The systems tested were a κ-carrageenan aqueous gel and a semisolid hydrophilic colloidal solution of hydroxypropylmethylcellulose. Blank measurements were also carried out using distilled water in order to take into account the buoyancy effect of the probe. The conical probe exerts mainly shear stresses on the gel, whereas the spherical and, to a greater extent, the cylindrical probe mainly exert compression stresses. Analysis of the shapes of the force-displacement curves has led to isolation of the shear and compressive deformation occurring in the systems and this, in turn, has enabled the differentiation between the structure and performance of the two semisolids.

Keywords: Gel system; Gel strength test; Probe shape

1. Introduction

Gels are commonly used as vehicles for pharmaceutical and cosmetic preparations in many types of applications (dermatological, ophthalmic and intramuscular injectable).

Gel formation is also involved in drug release from hydrophilic swellable matrices, which are widely used in prolonged medication (Colombo et al., 1987; Conte et al., 1988). In such systems, polymer hydration results in the formation of an outer gel layer that controls drug diffusion and that eventually undergoes erosion. Therefore, drug release depends on the physical and mechanical properties of the gel layer (Van Aerde and Remon, 1988; Herman and Remon, 1989; Herman et al., 1989).

It is important, therefore, to evaluate and quantify the strength of pharmaceutical gels.

A new apparatus for gel strength measurements was described and validated in a previous work (Ferrari et al., 1994).

The apparatus basically consists of a sample holder placed on an electronic microbalance. A probe is lowered into the sample at a constant rate. The penetrating force is measured by the balance and recorded as a function of time. Such

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an increase is a function of the mechanical resistance (gel strength) with which the sample opposes the lowering of the probe. Gel strength is defined as the ratio between the penetrating force displayed on the balance at a certain time and the depth at which the probe has moved inside the sample at the same time.

Previous findings (Ferrari et al., 1994) described measurements performed with a cylindrical probe. These data indicated that, for a given material, gel strength measurements were influenced by the shape of the sample holder, hence the geometry of the sample under test. It was envisaged that the differences observed were due to the different stresses (compressive and shear forces) involved, but the use only of a cylindrical probe did not enable us, at that time, to distinguish the contributions of the two types of stresses.

In order to investigate further and possibly quantify these contributions, in the present work the mechanical resistance of the model gel systems was measured by means of the previously described apparatus equipped with probes of different shapes.

Three probes of different geometry (conical, spherical and cylindrical) were used.

Measurements were carried out using a standard sample holder, a fixed sample depth and a constant lowering speed of the probe.

A κ-carrageenan aqueous gel and a semisolid hydrophilic colloidal solution of hydroxypropylmethylcellulose were tested. Blank measurements were made on distilled water (as a Newtonian fluid) in order to take into account the buoyancy effect that the displaced medium has on the recorded force.

2. Materials and Methods

2.1. Materials

Hydroxypropylmethylcellulose (HPMC) (Methocel® K4M, kindly provided by Colorcon, Orpington, UK) and κ-carrageenan (Satiagel® HMR XZ, Sanofi Bio-Industries, Paris, France) were used.

2.2. Sample preparation

A 6% (w/w) HPMC K4M aqueous colloidal solution was obtained after complete cold hydration.

A 1.5% (w/w) gel of κ-carrageenan was prepared by dispersion, under magnetic stirring, in cold distilled water.

Samples were centrifuged at 1500 × g for 20 min (centrifuge model: AHT, Tecnofarma, Pavia, Italy) in order to exclude any possible effect from air entrapment, then poured into Petri dishes and the samples allowed to remain undisturbed overnight in a refrigerator (4° C). Prior to testing, samples were allowed to equilibrate to ambient temperature for at least 1 h.

2.3. Methods

The apparatus for gel strength measurements is illustrated schematically in Fig. 1 (Ferrari et al., 1994).

The gel sample had a fixed depth (15 mm) and was placed in a standard sample holder (a Petri dish, Ø = 90 mm).

The probe was lowered into the sample at a constant speed (8 mm/min). The probe details were as follows: a conical probe (conicity angle of 10°), a spherical probe (Ø = 15 mm) and a cylindrical probe (Ø = 15 mm).

Blank measurements were carried out on distilled water under the same conditions.

Three replicates were made for each sample examined.

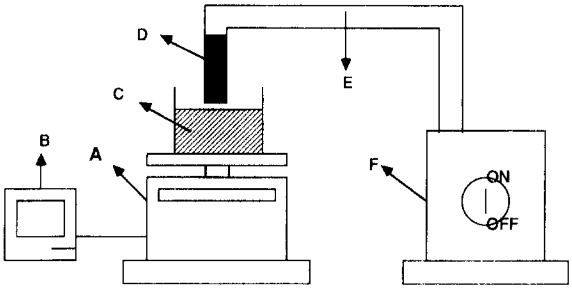

Fig. 1. Design of the apparatus for gel strength measurements. A, balance; B, computer; C, sample; D, probe; E, lateral arm; F, motor

3. Results and discussion

In Fig. 2a the force vs displacement profiles obtained for distilled water with different probes are presented. Each profile is the mean of three replicates (C.V. less than 3%).

The profile obtained with the conical probe shows that the increase in displacement is accompanied by an almost indiscernible increase in penetrating force.

The profiles obtained with the spherical and the cylindrical probes demonstrate an almost linear increase in penetrating force on increasing displacement after some initial deviation. This increase is due to a buoyancy effect.

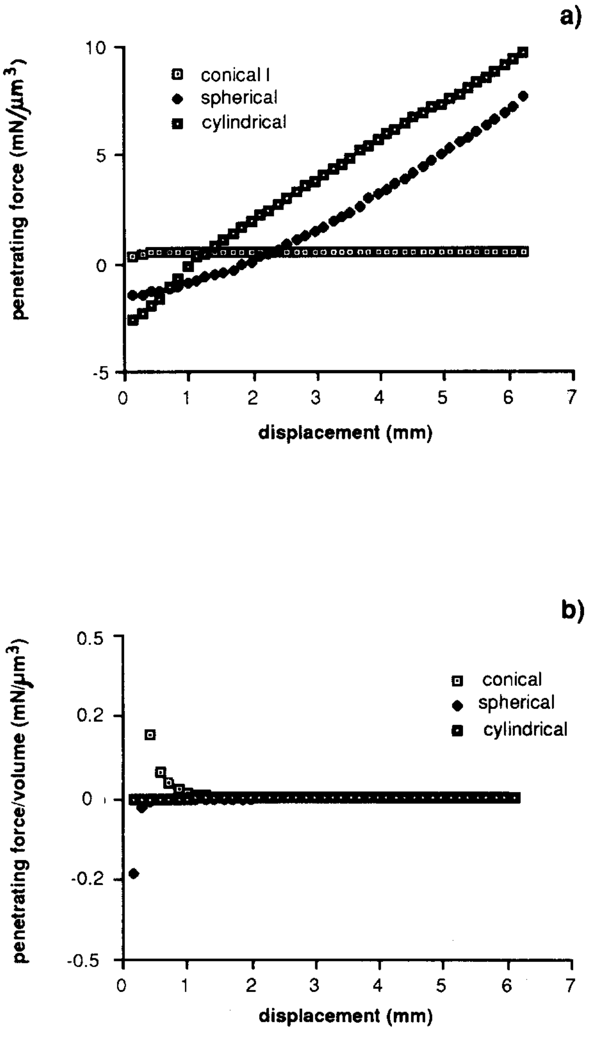

Fig. 2. Penetrating force vs displacement profiles for distilled water: (a) measured values; (b) normalised (per unit volume) values.

In both cases (spherical and cylindrical probes) negative force values are observed initially. These negative values presumably reflect the attractive forces as a consequence of water surface tension. The slight differences between the two probes are probably due to their different shapes.

The normalised force (force divided by the volume penetrated at each time point) vs displacement profiles, obtained for the three probes (Fig. 2b), are almost superimposable. This confirms that the force measured by the balance is, after buoyancy correction, consistent with Archimedes' law.

In Fig. 3–5 the penetrating force vs displacement profiles for the systems tested are presented. Each profile represents the mean of three replicates (C.V. less than 5%). The actual penetrating force values obtained with each tested material and each probe have been corrected for buoyancy effects by subtracting blank measurements, i.e., the penetrating force values obtained for distilled water with the same probe at the same depth of penetration.

When gel systems instead of water were tested, no initial negative values were observed, presumably due to the smaller influence of surface tension phenomena.

Fig. 3 (a and b) shows the profiles obtained for HPMC K4M (6% w/w) aqueous colloidal solution with different probes.

All the profiles display continuous patterns without any break point, as expected from the fact that HPMC K4M colloidal solution does not exhibit any yield point in rheological measurements (Ferrari et al., 1994).

The profiles in Fig. 3a show an almost linear increase in penetrating force on increasing displacement. The resistance offered by the conical probe is far less than that offered by either spherical or cylindrical probes; this could be attributable either to the different areas of contact between the probe and the sample or to the different stresses involved. To differentiate between these two possibilities, penetrating force values were normalised per unit penetrated area and plotted vs displacement (Fig. 3b). Since normalisation of force per unit area emphasises the contribution of applied stresses, the differences observed between probes after normalisation are to be attributed to the different contributions of shear and compressive stresses beneath or around the probes. The shear contribution is greater at any depth for conical than for spherical and cylindrical probe.

In Fig. 4 the profiles obtained for κ-carrageenan (1.5% w/w) aqueous gel are shown.

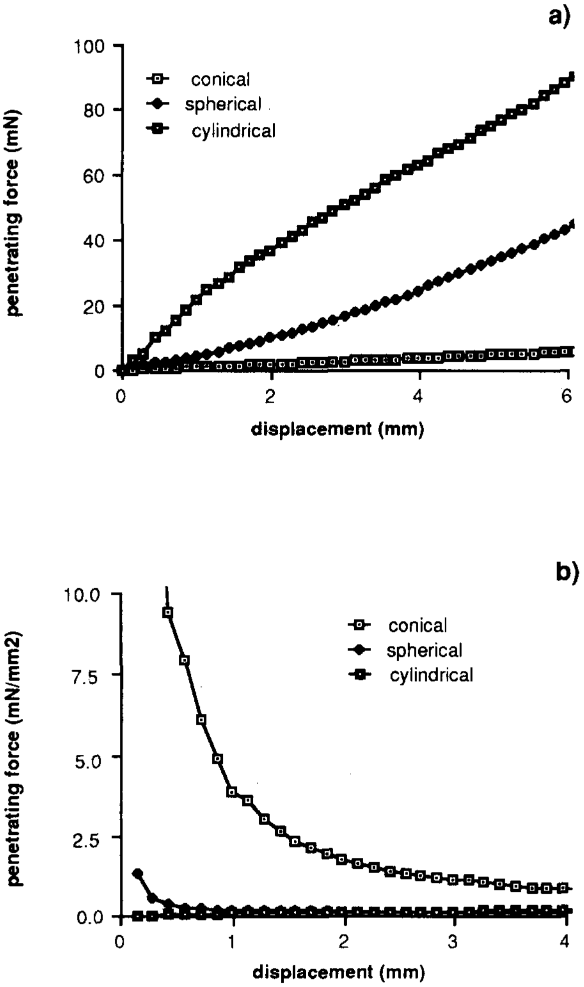

Fig. 3. Penetrating force vs displacement profiles for HPMC K4M 6% (w/w) colloidal solution: (a) measured values; (b) normalised (per unit area) values.

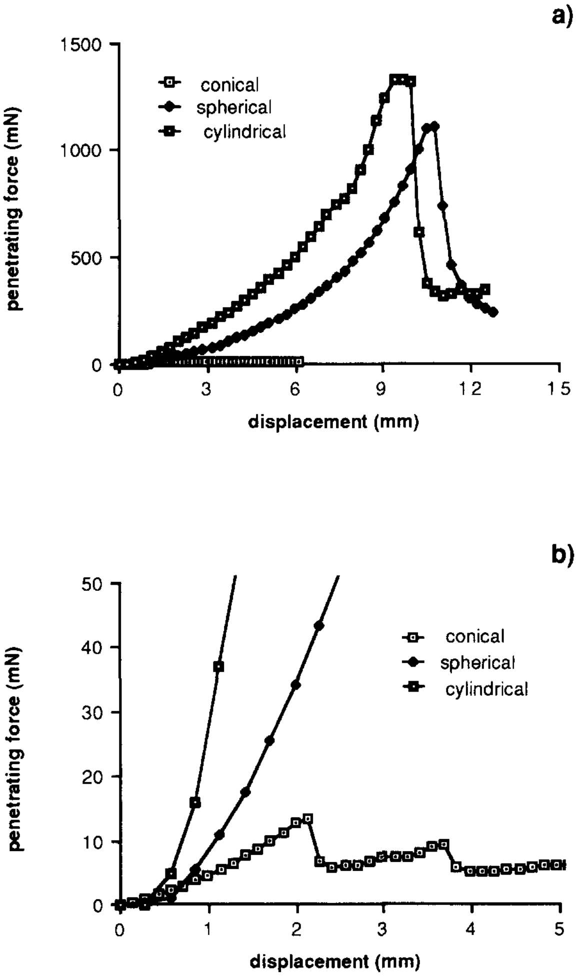

Fig. 4. Penetrating force vs displacement profiles for κ-carrageenan 1.5% (w/w) gel: (a) normal scale; (b) expanded scale.

The profiles are given on two different penetrating force scales (Fig. 4a,b) to allow a better resolution of the first experimental points.

All the profiles show break points, which indicates the loss of gel structure integrity upon penetration of the probe. More than one break point is observed, on the expanded scale, with the conical probe. This is probably due to the occurrence of many sequential rupture steps.

In Fig. 5a and b penetrating force values (normalised per unit penetrated area) obtained for κ-carrageenan (1.5% w/w) gel are plotted vs displacement, on two different scales.

For κ-carrageenan gel the normalisation per unit area also tends to emphasise the differences between the various probes due to the different contribution of shear stresses. Shear stresses are more pronounced with the conical probe. Moreover, break points in the normalised force vs displacement patterns are observable especially on the expanded scale; these are due to the loss of gel structure integrity at these points.

Fig. 6 shows plots of penetrating force vs displacement for the cylindrical probe into both HPMC K4M and κ-carrageenan systems (for κ-carrageenan the experimental points up to the break point are considered). A difference in shape of the curve is apparent; the relationship for HPMC K4M is linear while that for κ-carrageenan is curved (showing a good fit to a quadratic relationship, as is shown by a comparison of the x^2 term in the curve fit data recorded in Fig. 6).

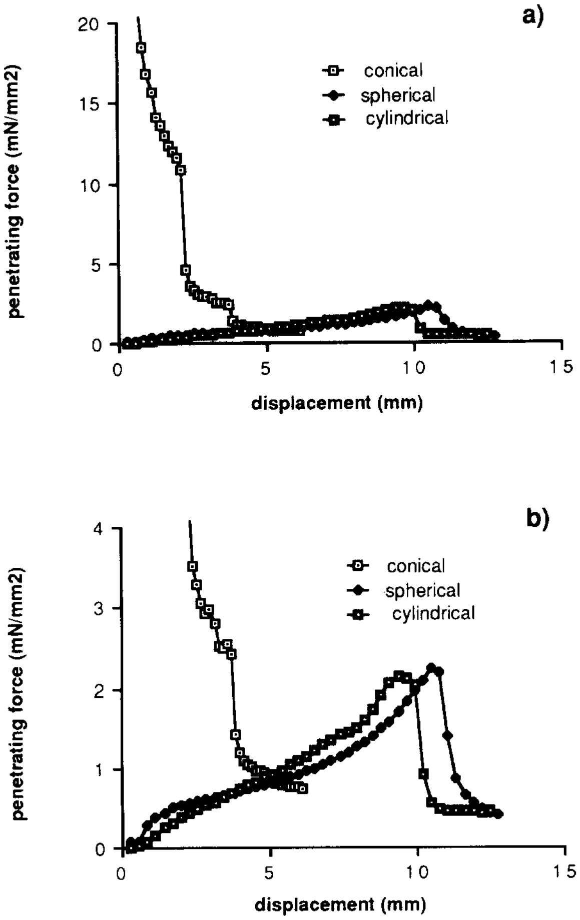

Fig. 5. Penetrating force (normalised per unit area) vs displacement profiles for κ-carrageenan 1.5% (w/w) gel: (a) normal scale; (b) expanded scale.

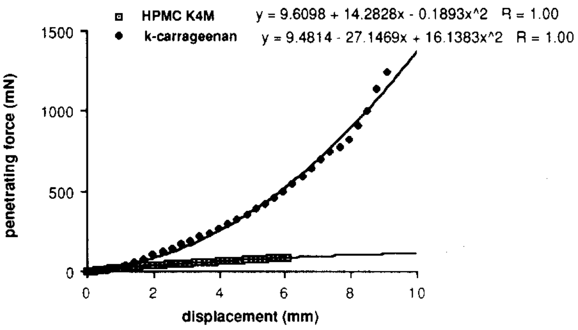

Fig. 6. Penetrating force vs displacement curves for the cylindrical probe into HPMC and κ-carrageenan semisolid systems. The equation of fit for each line is also given.

This difference in shape may be explained by differences in the structure of the two semisolids (Ferrari et al., 1994). The 6% (w/w) HPMC K4M colloidal solution is composed of entangled linear polymeric chains. As the probe penetrates the system, these chains flow, as a viscous solution, around the indented probe to produce the observed linear relationship. With the three-dimensional gel structure of κ-carrageenan, the elastic bonds between the polymers are compressed initially. As the intermolecular distance between the components of the gel is reduced, the force needed to deform these elastic bonds also increase resulting in the curve shown in Fig. 6. This continues until a break point in the gel structure occurs (see Fig. 4a). At this point some of the bonds within the structure fracture. This process is repeated resulting in the series of breaks shown in Fig. 4b.

With the cylindrical probe it is difficult to deduce any additional fundamental information due to the complex nature of the deformation beneath the probe, this being a mixture of shear (occurring at the edges of the flat face of the cylinder) and compression (at the centre of the flat face). It is not possible to quantify the individual contributions of each of these deformation mechanisms.

The deformation characteristics beneath a sphere and a narrow cone are, however, well documented and understood and these two may be pursued further. The deformation forces occurring beneath a sphere is mainly compressive, and that beneath a narrow cone is mainly shear.

The mechanical deformation beneath a spherical indenter has been studied over many years and is well documented. The mathematical solution to the changing stress pattern beneath a spherical probe penetrating into a flat substrate has been solved by Lee and Radok (1960). They derived the following equation:

$$J(t) = (16/3) \cdot R^{0.5} \cdot (1/F) \cdot h(t)^{1.5} \qquad (1)$$

where $J(t)$ is the overall creep compliance (strain/stress, Pa^{-1}) at time t, R denotes the radius of the indenting sphere (m), F is the applied force (N) and $h(t)$ represents the depth of penetration (m) at the same time t.

From this it is apparent for a material which has a constant compliance that the penetrating force at any time is directly proportional to the (depth of penetration of the probe)$^{1.5}$ at that time. Fig. 7 shows a plot of this relationship for both HPMC K4M and κ-carrageenan. There is an excellent fit for both systems (as is shown by the linear regression data accompanying the graphs). It is suggested that a coefficient (PV_1), equal to the slope of this plot, is a reflection of the comparative compressive rigidity of these two semisolids (PV_1 for HPMC K4M = 2.80 and PV_1 for κ-carrageenan = 19.8). These numbers conform with a qualitative assessment of the relative rigidity of these two systems.

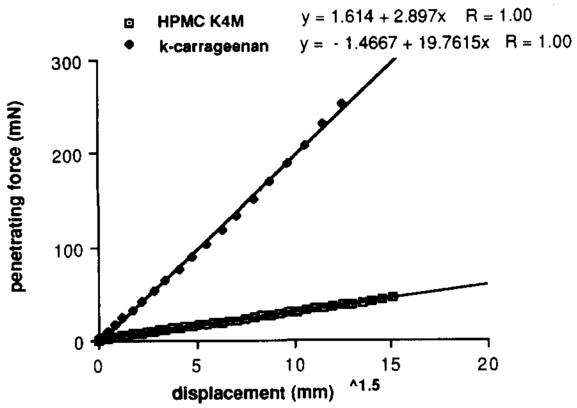

Fig. 7. Relationships for the spherical probe between penetrating force and displacement, modified according to the Lee and Radok equation.

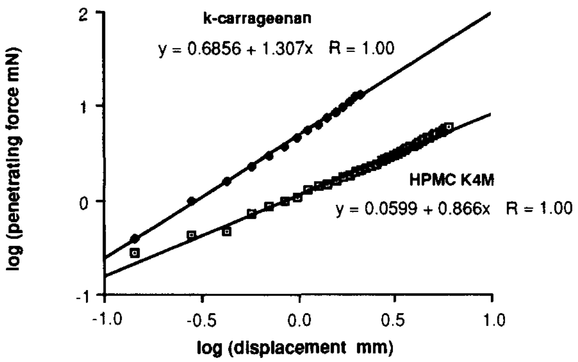

Fig. 8. Penetrating force vs displacement relationships for the needle probe (log-log transform of the Knight and Johnson equation).

A conical probe with a narrow cone angle will cause deformations in the semisolids which are mainly by shear. A relationship for the deformation beneath such a probe has been expressed by Knight and Johnson (1988) as follows:

$$f_c = k \cdot F/h^n \qquad (2)$$

where f_c is the unconfined compression strength of the material, k denotes a proportionality constant which is a function of both the interfacial friction coefficient and the internal friction angle, F is the penetrating force (N), h represents the depth of penetration at the same time, and n is a power function.

Rearranging Eq. 2 we obtain:

$$\log F = n \log h + \log(f_c/k) \qquad (3)$$

and thus a plot of log F vs log h should be linear. Such plots are shown in Fig. 8. A difference can be observed in the slope of the line, i.e., n in Eq. 3 is 1.307 for κ-carrageenan and 0.866 for HPMC K4M.

Fig. 9 replots these data as penetrating force vs (displacement)^n. The resulting graph gives linear plots and it is suggested that the slope of these lines can be used as a coefficient (PV_2) to quantify the differences in shear resistance of the

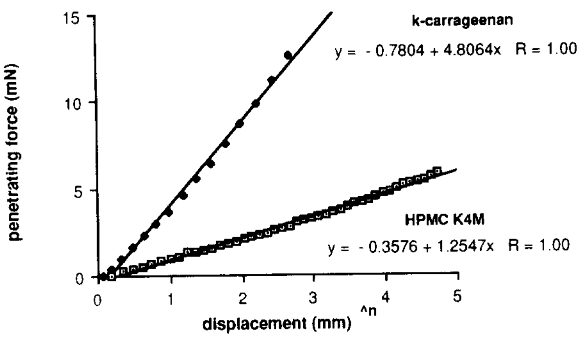

Fig. 9. Relationships for the needle probe between penetrating force and displacement raised by the n exponent of the Knight and Johnson equation: $n = 0.866$ for HPMC K4M; $n = 1.307$ for κ-carrageenan.

two systems tested here (PV_2 for κ-carrageenan is 4.806 and PV_2 for HPMC K4M is 1.255).

4. Conclusions

The two systems tested were differentiated, as far as their mechanical resistance (gel strength) is concerned, using the apparatus and probes described in this work. HPMC K4M colloidal solution did not show break points in the profiles, whereas κ-carrageenan gel did.

Marked differences in penetrating force profiles were observed with the different probes for both HPMC K4M and κ-carrageenan systems. These differences were observed even after allowance for probe buoyancy and normalisation per unit penetrated area. The differences are a reflection of the different mechanical properties of the two gels and also the different stress patterns produced by indenter geometry. The stress distribution between the cylindrical probe is complex and unsuitable for quantitative analysis. The conical probe exerts mainly shear deformation of the material and the spherical probe mainly compression. Analyses and coefficients are suggested which quantitatively differentiate between the two gels.

Acknowledgements

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