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Research paper

In-vitro comparative study of buccal mucoadhesive performance of different polymeric films

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Abstract

A comparison of the buccal mucoadhesive performance of different polymeric films was carried out using texture analyzer TA-XT2i. A large range of putative polymers differing in their chemical nature, molecular structure as well as hydration status was used. The used polymeric films were classified in rank order of buccal mucoadhesive performance, namely carbopol 971P > polycarbophil > Carrrageenan type λ > Sodium carboxymethylcellulose. Swelling state as well as tensile strength of the used polymeric films was used as measuring parameters of mucoadhesive interaction. These two approaches gave two opposite orders of performance between CMC and Carrrageenan type λ after a contact time of 15 min. However the measurement of the viscoelastic moduli of the hydrogels gave the same ranking order of mucoadhesive performance after the same contact time. In reference to the previous works, we noted the importance of the molecular weight, the density of charges, the composition of which the chains of molecules are capable to arrange themselves in a network like form, thus those which are characterized by a $\tan \delta < 1$ (i.e network formation), are those which develop the best synergism with the mucus because of the reinforcement of an established link. The goal of this study is to assess the buccal mucoadhesive performance aiming to optimize the design of drug delivery via buccal mucoadhesive polymeric films

Keywords: Polymeric films; Buccal mucoadhesive; Oscillatory rheology; Swelling status; TA-XT2i texture analyzer

1. Introduction

The buccal mucosa provides a readily accessible route for transmucosal delivery [1]. However, a number of factors limit the absorption of drugs from the oral mucosa, including environmental factors such as the exposure of oral mucosa to salivary flow and the production of shearing forces due to tongue movement and swallowing, thus displacing an adhering vehicle [2]. Mucoadhesive polymers have been extensively studied as a mean of prolonging the residence time of the dosage form on the adsorbing membrane as well as localizing drugs in a particular region [3], thereby improving and enhancing the bioavailability and that's why the concept of buccal mucoadhesion has received a considerable interest in formulation science [4]. Several approaches have been explored to obtain buccal mucoadhesive dosage forms as a platform for controlled delivery of drugs [5]. Previous studies have examined a range of putative mucoadhesive polymers in the form of gels, for the correlation of the rheological properties with the chemical structure of polymers [6,7].

Unfortunately, application of mucoadhesive gels creates considerable technical problems [8], however, other approaches have been reviewed recently for buccal mucoadhesive polymeric films formulations [9,10]. It has been proposed that the interaction between the mucus and mucoadhesive polymers is a result of physical entanglement and secondary bonding, mainly hydrogen bonding and Van der Waals attractions [11,12], these forces are related to the chemical structure of the polymers. The types of surface chemical groups that would contribute to this type of adhesion include hydroxyls, carboxyls, amines and amides [8,13]. Physical properties such as the rate of hydration and rheological properties of the polymeric formulations are likely to have a major impact on their bioadhesion and consequently their eventual duration of retention [14,15]. Previous studies suggested that hydration as well as rheological studies may give certain information on the behaviour of the polymer chain structures, thereby allows a much more complete analysis of bioadhesive properties particularly in term of the rigidity and deformability of the systems. The

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contribution of these properties to the retention on the mucosa might differ depending on their chemical structures [2].

In this study a large range of mucoadhesive polymers, differing in their cross-linking status were selected, namely carbopol 971P, polycarbophil, (synthetic), Sodium carboxymethylcellulose (semisynthetic), and Carrageenan type λ (natural). The buccal mucoadhesive performance of the polymeric films has been assessed using texture analyzer TA-XT2i, in order classify them in rank order of their mucoadhesion, aiming to optimize the designing of drug delivery via buccal mucoadhesive polymeric films.

2. Materials and methods

2.1. Materials

Polyvinylpyrrolidone (Plasdone® K-90): ISP Technologies, INC. France; carbopol 971P and polycarbophil (Noveon™ AA1): BF Goodrich chemical, USA; sodium carboxymethylcellulose (Blanose 7M31CF): Hercules UK; Carrageenan type λ (Satiagum UTC 10): Sanofi Bio-Industries, France; triethanolamine and propylene glycol: Cooper, France.

2.2. Equipment

Paddle-strirrer mixer: IKA Rw 20 DZM Camlab, Cambridge,UK; Oven Halvatia de Luxe, France; micrometer: Digimatic micrometer Mitutoyo Corporation, Japan; Scales, with an accuracy of 10^{-4} g, Sartorius, France; controlled shear rate rheometer (HAAKE-VT500); controlled stress rheometer (Rheostress-RS100) and TA-XT2-texture analyzer: RHEO, France

2.3. Methods

2.3.1. Preparation of the polymeric films

The procedure illustrated in Fig. 1 for the preparation of polymeric films was performed. PVP K-90 was used as a film-forming polymer. Mucoadhesive polymers namely, carbopol 971P, polycarbophil, CMC and Carrageenan were used in different concentrations according to the flow properties of their dispersions, Table 1. However, the obtained polymeric hydrogels were approximately isoviscous.

Ten percent PVP K-90 aqueous solution was mixed with mucoadhesive polymeric hydrogels that were prepared by dispersing carbopol 971P, polycarbophil, CMC, or Carrageenan in deionized water using a variable speed mixer, under constant stirring (600 rev/min), fitted with a four-bladed paddle at room temperature for 15 min. In case of poly(acrylic acid) polymers, the produced gels were neutralized to pH 6.9–7.2 using triethanolamine. The samples were kept in the dark in sealed vials at 4°C until use. The samples were stored for at least 24 h before experimentation, to ensure total hydration of the polymer and to exclude entrapped air.

Propylene glycol was used as plasticizer at a concentration of 50% w/w of polymer content, thus protecting the polymeric films from being brittle upon storage. Before pouring on Teflon molds (50 mm^2, 10 mm depth), the resulted polymeric gels were brought back to ambient temperature. The aqueous polymeric hydrogels were dried at 38 ± 0.3°C in an oven for 18 h and stored at room temperature in a desiccator. The obtained polymeric films were translucent and pliable with 0.4 ± 0.05 mm thickness measured by using a micrometer.

2.3.2. Rheological examination

The rheological behaviour of the formulated gels from which different polymeric films were prepared, was determined after 24 h of the formulation, using (HAAKE–VT500, RHEO) controlled shear rate rheometer, fitted with 1.1/3.2 cm radius/high parallel plate geometry and a gap setting of 900 μm between the plates. The hydrogel sample was kept in a parallel plate geometry for 15 min in order to homogenize its temperature, which was carefully controlled during testing at a temperature of 37°C. Flow curves were produced at a shear rate range from zero to 200 s^{-1} and that took a duration of 2 min to achieve maximum shear rate of 200 s^{-1}, followed by 1 min for establishment, and a further 2 min period during which the shear rate was reduced to zero. Up and down curves of shear stress as a function of shear rate were obtained.

2.3.3. Oscillatory examination

Oscillatory rheometry was performed using Rheostress RS 100- RHEO controlled stress rheometer, fitted with plane-cone geometry of 35 mm diameter and a gap setting angle of 2°. The rheological behaviour was measured using the dynamic moduli G' and G'' as a function of frequency and torque. Where G' is the storage (elastic) modulus and G'' is the loss (viscous) modulus. Analysis of this behaviour gives information on the structure of samples, particularly in term of the rigidity, elasticity and deformability of the systems.

The storage modulus G' is a measure of the energy stored and recovered per cycle of deformation and is taken as a representative viscoelastic parameter for dynamic oscillatory measurements, being a measure of sample resistance to elastic deformation (i.e. reflection of the polymer network connectivity and the solid-like component of a viscoelastic material). While the loss modulus G'' is a measure of the energy loss per cycle and quantifies the viscous component indicating a lack of structure, thus reflects the liquid-like component [6].

In addition to the dynamic moduli the viscoelastic nature of the test samples was described using the loss tangent,(tan δ). This is considered as another useful parameter summarizing the rheological properties of semisolids. Tan δ is an indicator of the overall viscoelasticity of samples being a

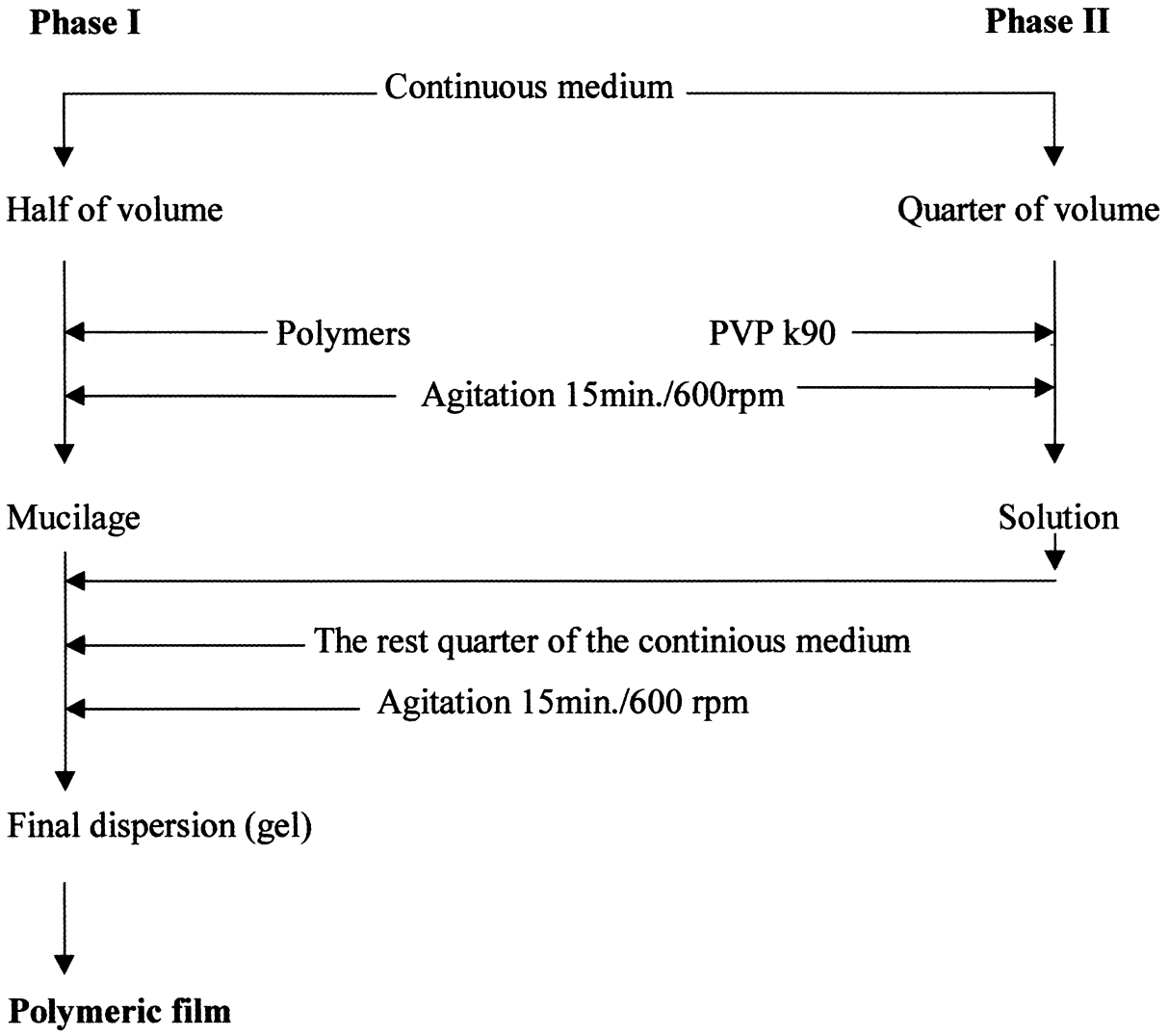

Fig. 1. Preparation scheme.

measure of the ratio (G''/G'), tan $\delta < 1$ indicates a solid-like response. Thus, as tan δ becomes smaller the elasticity of the material is increased, while the viscoelastic behaviour is reduced [6,15].

2.3.3.1. Torque sweep. Prior to carrying out oscillatory experiments the appropriate shear stress range for testing which would not damage an existing gel structure (linear viscoelastic region), was determined by carrying out a torque sweep experiment on the samples. A stress range of 0.4–50 Pa was applied and the values G' and G'' were determined at an intermediate frequency of 1 Hz. The equilibration time before starting the test was standardized at 1 min. and a temperature of 37°C.

2.3.3.2. Frequency sweep. The storage modulus (G') and loss modulus (G'') were measured in a frequency range of 0.1–10 Hz, with a constant stress of 1 Pa ensuring that all samples remained in the viscoelastic region. These moduli provide direct evidence regarding the physical nature of the formulations.

2.3.4. Swelling behaviour of the prepared polymeric films

This study examined the hydration of the different polymeric films used when placed in contact with artificial saliva. The swelling of polymeric films was evaluated by measurement of weight. All polymeric films were prepared

Table 1
Polymers ratio in each formula (%)

Polymers	I	II	III	IV
Polyvinylpyrrolidone	10	10	10	10
carbopol 971P	0.3	–	–	–
Polycarbophil AA1	–	0.3	–	–
Sodium CMC	–	–	2.0	–
Carrageenan	–	–	–	1.5
PH	7.1	7.1	6.9	7.2

at least 48 h before the test. Using a pastry cutter, samples (25 mm^2) of each polymeric film were cut and then weighed by one scale before and after wetting with artificial saliva [16]. The polymeric film sample was placed in a petrydish, artificial saliva (0.1 ml) was added onto the surface of the polymeric film using a micropipette, and then incubated in one dessicator at room temperature. The wetted film was removed at each observation point at time intervals of (0.5, 2, 15, and 30 min), where the surface was gently dried using blotting paper and reweighed again. For each observation point, the test was repeated five times. The hydration percentages of the wet polymeric films were calculated according to the following equation:

$$\text{Hydration}(\%) = (W_H - W_D)/W_D \times 100 \text{ [17]}$$

where W_H and W_D represent the weight of the dried and hydrated polymeric films respectively

2.3.5. Evaluation of mucoadhesive performance of the prepared polymeric films

Tensile test using TA-XT2i-texture analyzer is a useful technique that has been extensively employed as a valid means for mechanical characterization of pharmaceutical mucoadhesive solid and semisolid dosage form [18]. A software-controlled penetrometer, TA-XT2i-texture analyzer, with a 5 kg load cell, a force measurement accuracy of 0.0025% and a resolution distance of 0.0025 mm, was

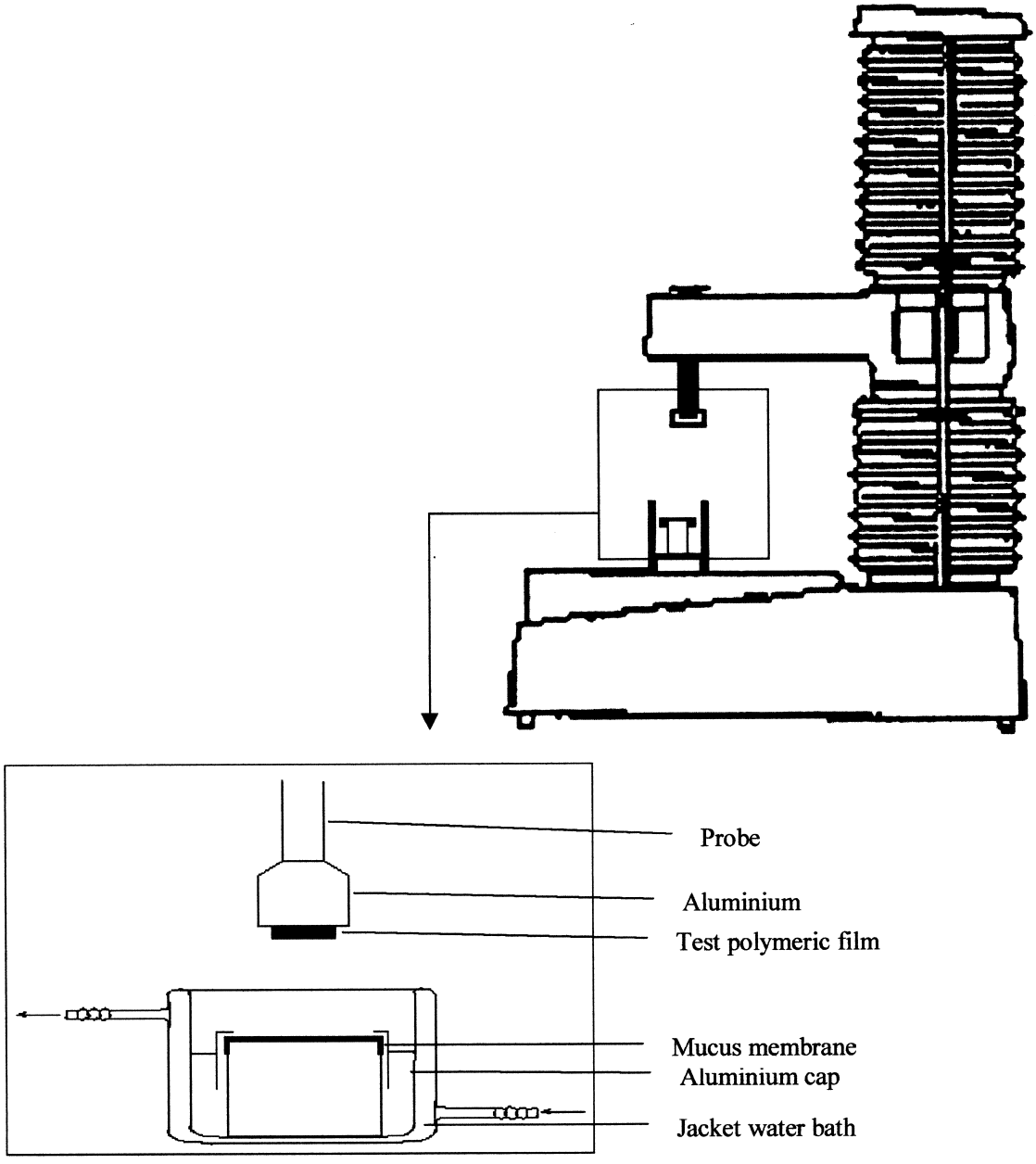

Fig. 2. Mucoadhesion performance measurement using texture analyzer (type TA-XT2).

used for tensile mucoadhesive experiments (Fig. 2). The pre-test speed, the test speed, and the withdrawal speed were set up at 1, 0.5, and 0.5 mm/s respectively, with an acquisition rate of 100 points. The probe used was an aluminium cylinder having a diameter of 28. ± 0.2 mm. The study was carried out at a temperature of 37°C.

For mucoadhesive measurements, a sample of the prepared polymeric films (25 mm_2) was attached (using Loctite superglue 3) to the base of aluminium probe, which is fixed to the mobile arm of the TA-XT2i. Sublingual mucosa of bovine origin were sampled at a slaughterhouse, just after slaughtering the animal (mucosa was obtained from three different cow tongues), rapidly frozen to −80°C, and thawed at the time of use by immersion in a bath of isotonic sodium chloride solution at ambient temperature. A piece of sublingual epithelium mucosa was then mounted securely in place (mucosa side upwards) on a platform within a jacketed water bath containing artificial saliva at a temperature of 37°C, which was then wetted by 0.1 ml of artificial saliva (introduced by a micropipette) onto the center of the mucosa and instantly spread over the whole surface. Upon making contact between the polymeric film sample and the mucus layer, a constant force of 0.5 N was imposed for 0.5, 2, 15, and 30 min, respectively. The mucoadhesive performance of the samples were determined by measuring the resistance to the withdrawal of the probe (maximum detachment force Fmax in Newton 'N') reflecting the mucoadhesion characterization of the polymeric films with mucus. The areas under the force/distance curves (AUC in mJ) were also determined to represent the work or energy required for detachment of the two systems (mucosa/polymeric film). The polymeric film of PVP K-90 was used as a blank for detachment measures. At least five repetitions were obtained for each measurement.

For intraday precision, the coefficient of variation was 4.5%, while day-to-day reproducibility of the measurement was determined on five consecutive days. The coefficient of variation turned out to be 6.2% revealing the validity of the technique.

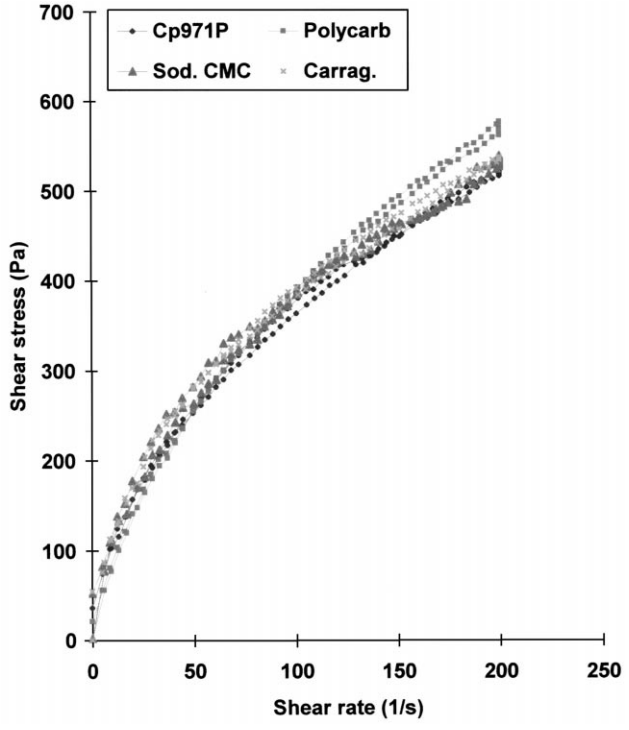

Fig. 3. Flow curves of the prepared isoviscous hydrogels.

3. Results and discussion

3.1. Neutralization effect on poly(acrylic acid) mucilage

It is known that the acidic poly(acrylic acid) hydrogels contain only coiled macromolecules, unable to form an elastic polymer network as a result of the repulsion forces of negative charges [19]. Due to the coiled conformation, many of the adhesively active groups are shielded inside the coils and are not active to participate in the adhesion process due to the intramolecular hydrogen bonds that rendered them ineffective. Thus, in the preparation of the poly(acrylic acid) hydrogels, we have to neutralize the produced anionic gels to form an expanded gel network [8], propylene glycol was added to the prepared gels to enhance the gel structures to produce rigid film

3.2. Rheological examination

Fig. 3 demonstrates the continuous shear flow curves for the gels formulations used for the preparation of polymeric films, showing shear stress plotted as a function of shear rate. Fig. 3 illustrates that the four gel formulations exhibited approximately the same flow behaviour at maximum shear rate (200 s^{-1}), with shear stress ranging between 500–600 Pa. The flow curves profile also revealed that, the used gels formulations showed no apparent yield values, indicating the limited resistance to flow at low stress values characteristic of pseudoplastique flow. This could be a useful property that indicates the displacement of the gels from tissue surfaces [2], a result that confirms with that previously reported [8]. This observation together with the present findings of minimal hysteresis (area between the up and down curves) suggest thixotropic behaviour where minimal breakdown occurs within the gel structure and the apparent viscosity of the gel is decreased with increasing shear stress, indicating that the recovery of structure is time-dependent, a property that does not help the retention of gels on the buccal mucosa [2].

3.3. Oscillatory examination

Although it is less clear which physical property or properties of the polymer will be important for the bioadhesion potential of the hydrogel but it is likely that the differences between the physical properties of the formulations might

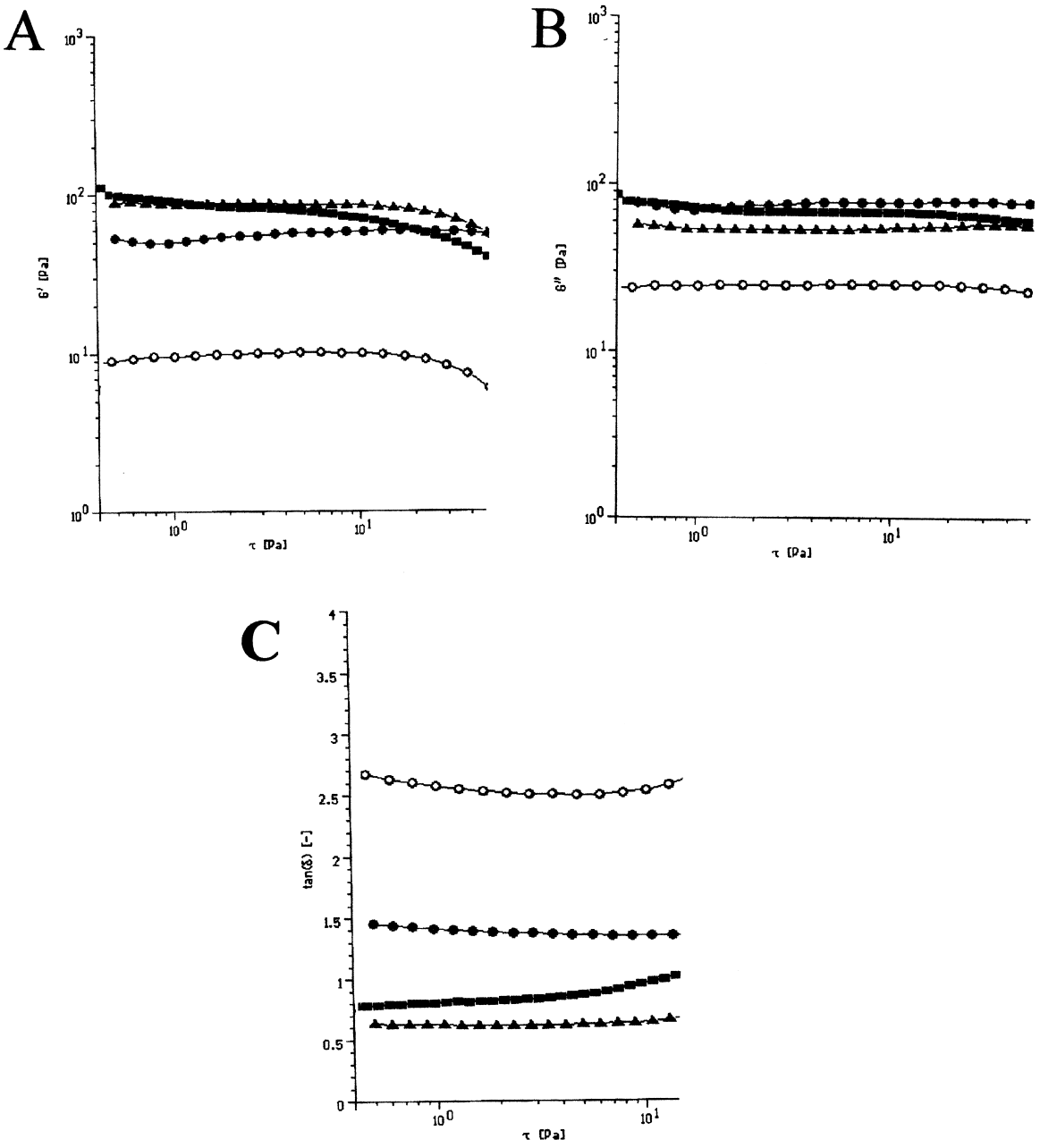

Fig. 4. Dynamic oscillation spectra of the prepared gels as a function of Torque sweep at 1 HZ showing storage moduli (A), loss moduli (B) and tan δ (C). (▲ CP 971P, ■ polycarb, ● Sod. C.M.C. and ○ Carrag.).

help to explain their bioadhesive behaviour range. Fig. 4a–c and Table 2 illustrate the parameters characterizing the rheological behaviour of the prepared gel systems at a representative low frequency 1 Hz. The torque sweep confirmed that the shear stress values applied in the frequency sweep experiments were within the viscoelastic range of the materials tested since the storage modulus (G') as well as loss modulus (G'') remained constant above this low range of frequency, therefore validating the conditions of the test. For both carbopol 971P and polycarbophil a predominance of G' over G'' was formed indicating energy storage within

Table 2
Viscoelastic parameters of the prepared polymeric gel systems at a representative frequency of 1 Hz

	G' SD (Pa)	G'' SD (Pa)	Tan δ SD
Cp 971P	86.9 ± 0.7	54.3 ± 0.3	0.63 ± 0.01
Polycarb.	98.9 ± 2.3	79.0 ± 2.0	0.80 ± 0.01
Sod. CMC	56.2 ± 3.0	76.9 ± 3.0	1.37 ± 0.02
Carrag.	9.96 ± 0.17	25.2 ± 0.24	2.53 ± 0.03

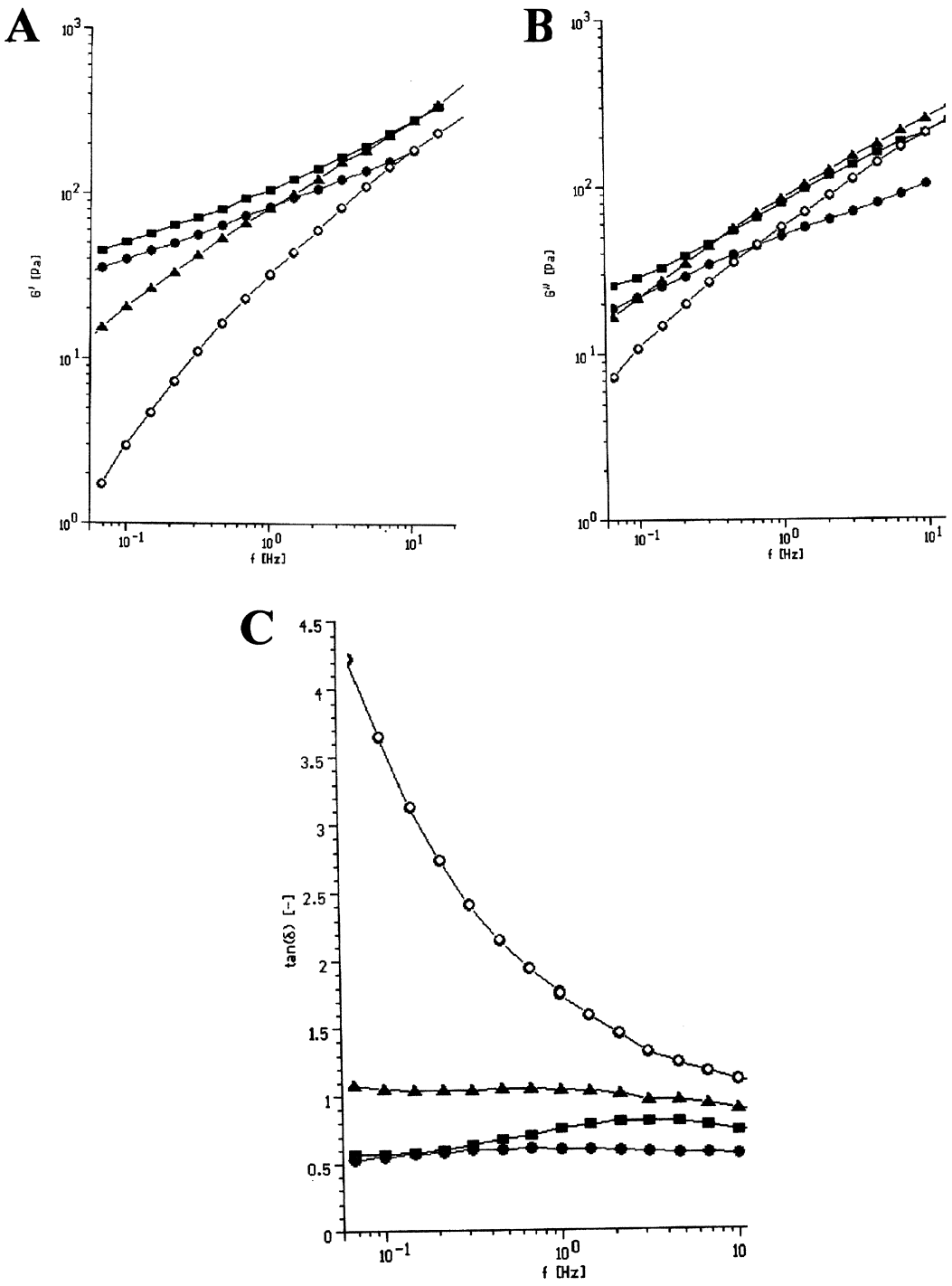

Fig. 5. Dynamic oscillation spectra of the prepared gels as a function of frequency sweep showing storage moduli (A), loss moduli (B) and tan δ (C). (● CP 971P., ■ polycarb., ▲ Sod. C.M.C. and ○ Carrag.).

the gel structure reflecting a high cross-linkage as well as a physically entangled system [2]. However, the level of cross-linking [20], helical structure as well as the high molecular weight of polymers [2], was previously shown to be prominent factors in the 'gel-strengthening' phenomenon. While, carbopol 971P being a bifunctional cross-linker, was considerably less cross-linked than polycarbophil which contains a tetrafunctional cross-linking agent, divinyl glycol [21]. Carbopol 971P achieved a more pronounced shift in terms of tan δ from a predominantly viscous state to a solid elastic behaviour than polycarbophil ($P > 0.05$). This can be explained on the fact of the swelling characterization of polycarbophil that is pH-dependent as its swelling increases with the pH (the pH of neutralized gel) resulting in an increment in hydration state of the polymer [22].

CMC showed a small increase in G'' relative to the other

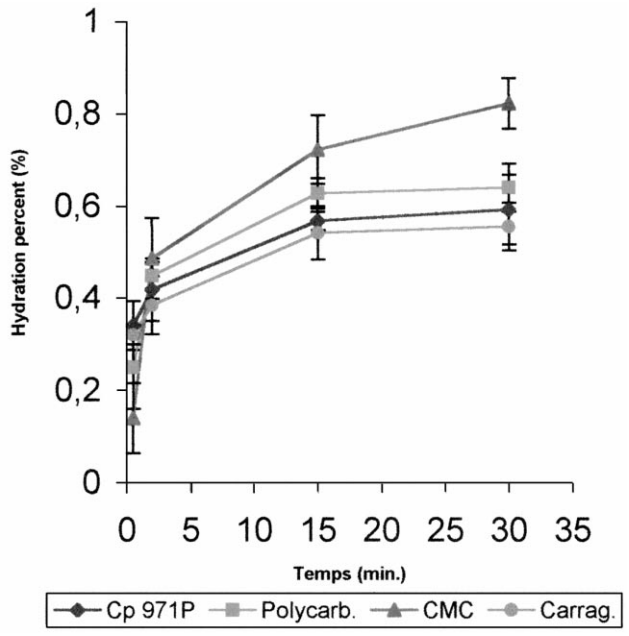

Fig. 6. Hydration percent of the prepared polymeric films at different contact times.

poly(acrylic acid) polymers, indicating an increase in the viscous properties of the system ($P > 0.05$). This result may be ascribed to the state of hydration of CMC [6]. Unfortunately, the rheological response of Carrageenan is the lowest as regard to both the storage and loss moduli of the gel, but it showed a highest tan δ value implying a proportionately greater viscous component for the gel ($P < 0.05$). This may be possibly explained by the fact that molecules adopt a less helical structure with less tendency to form intermolecular associations and entanglements [2].

Fig. 5a–c shows the dynamic oscillation spectra of prepared gels at a temperature of 37°C and a frequency range of 0.1–10 Hz. The figure illustrates that in all cases, as frequency increased the storage modulus G' (a) increased together with the loss modulus G'' (b). At high frequencies the gel systems may behave as elastic solids, whereby recovery is complete after the removal of the applied stress.

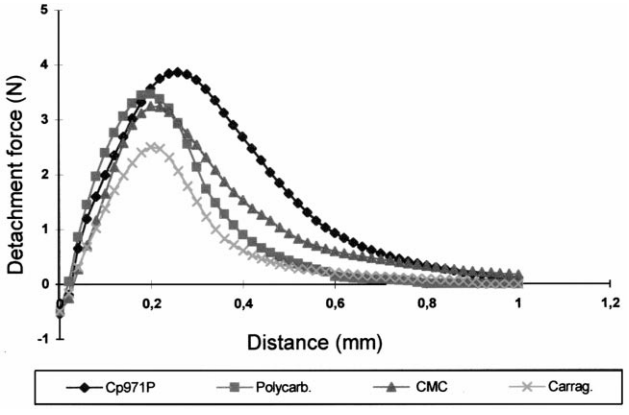

Fig. 7. Detachment profile of prepared polymeric films at 15 min.

However, at low frequencies the samples showed viscous behaviour, whereby irreversible deformation occurs on application of stress. At intermediate frequencies, the samples show components of both types of behaviour, in particular, the tan δ spectra of carbopol 971P, polycarbophil as well as CMC are comparatively flat, indicating that the systems may be in the plateau region of response over this frequency range. where, the cross-links and entanglements within the gels prevent any substantial rearrangement of the molecules, hence the ratio of both moduli remain largely unchanged. Unfortunately, for Carrageenan, the tanδ value decreased by increasing the frequency, indicating a large increase in the preponderance of viscous behaviour of the sample at low frequencies.

3.4. Swelling properties

Some degrees of hydration appear to be beneficial to bioadhesion [2]. An examination of the hydration rates;of polymeric films with different bioadhesive characteristics might be helpful to explore the mechanism underlying bioadhesion. Fig. 6 shows the swelling characterization of the used polymeric films. Accordingly, shortly after beginning the swelling test (2 min), the used polymeric films swelled in the following order, namely CMC>polycarbophil carbopol carbopol 971P> Carrageenan, indicating that CMC took the least time for swelling, followed by polycarbophil which has a high swelling characterization in the neutral and alkaline media [22]. This swelling time is an important factor for assessment of adhesiveness [8]. Previous studies have shown that shortly after the beginning of swelling, adhesion does occur, but the bond formed is not very strong [23]. Excessive hydration of CMC polymeric films, (contact time 15 min.) with artificial saliva resulted in a slippage of macromolecular chains of the formulation that results in a dramatic decrease in the formulation consistency [8]. However, polycarbophil, carbopol 971P as well as Carrageenan polymeric films have reached an equilibrium state of swelling after 15 min. This state of equilibrium was reached with carbopol 971P, polycarbophil and Carrageenan, but not with CMC as it's hydration was continuous.

Thus we conclude that excessive hydration can lead to a weakening of the bioadhesive bond, probably as a result of dilution of functional groups available for adhesive interactions at the interface between the bioadhesive film and the mucus.

3.5. Mucoadhesive performance evaluation

Fig. 7 shows the detachment profiles of the prepared different polymeric films at a contact time of 15 min., obtained from TA-XT2i-texture-analyzer. All measurements were analyzed statistically using the variance (ANOVA), comparison of arithmetic mean ± SD with 5% limit, the results are given in Table 3 which illustrates that, both the forces (Fmax) as well as the work of detachment (AUC) are ranged in rank orders depending on their contact

Table 3
Mucoadhesive performance of prepared polymeric films at different contact times[a]

Muc. Perf	Mucoadhesive force (N)				Mucoadhesive work (mJ)			
	Contact time (min)				Contact time (min)			
Poly.type	0.5	2	15	30	0.5	2	15	30
Cp971P	1.19 ± 0.23	1.22 ± 0.19	2.19 ± 0.25	4.47 ± 0.27	0.096 ± 0.066	0.224 ± 0.049	0.84 ± 0.08	1.1 ± 0.07
Polycarb.	0.24 ± 0.11	1.37 ± 0.27	2.03 ± 0.43	3.69 ± 0.39	0.038 ± 0.016	0.304 ± 0.026	0.75 ± 0.05	0.96 ± 0.042
CMC	0.19 ± 0.079	2.02 ± 0.28	1.87 ± 0.21	0.49 ± 0.25	0.014 ± 0.011	0.374 ± 0.079	0.51 ± 0.07	0.15 ± 0.056
Carrag.	0.51 ± 0.23	0.73 ± 0.21	1.56 ± 0.22	2.05 ± 0.27	0.074 ± 0.033	0.122 ± 0.08	0.227 ± 0.04	0.7 ± 0.047

[a] *Muc. Perf., mucoadhesion performance; poly, polymer.

times. No significant difference was found between the detachment forces of the tissues obtained from different tongues ($P > 0.05$, one-way analysis of variance).

Figs. 8 and 9 represent the maximum detachment forces as well as adhesion work of the used polymeric films as a function of contact time, respectively. The figures revealed that at 2 min CMC showed the greatest force and work of adhesion followed by polycarbophil, carbopol 971P and Carrageenan. However, the order was changed beyond a contact time of 15 min., notably a new order was observed namely carbopol 971P >polycarbophil > Carrageenan > CMC.

The initial mucoadhesive range of the used polymeric films could be explained as a result of swelling time characterization (Fig. 6). Accordingly, shortly after starting the tensile test (2 min.), the used polymeric films swelled according to the same order of their adhesiveness, namely, CMC > polycarbophil > carbopol 971P >Carrageenan. While, the order was reversed after a contact time of 15 min..Carrageenan showed the lowest force of adhesion (lowest detachment force) at 15 min that is significantly lower than that of poly(acrylic) polymers $P < 0.05$ (Table 3). Also we can deduce that from the four studied polymeric films, Carrageenan is the one that revealed dominance in the viscous properties due to the absence of structure on the molecular level. In regard to these results, we can conclude that such property allows the polymeric chains to spread easily while diffusing all along the mucus/polymeric film interface, once sufficiently hydrated and also allows an establishment of maximum hydrogen-bonding. The fact that one polymer is less adhesive than the other may be attributed to the presence of SO_3^- groups which forms less strong hydrogen-bonding than $-COO^-$ groups.

Previous studies have shown that the swelling state of the

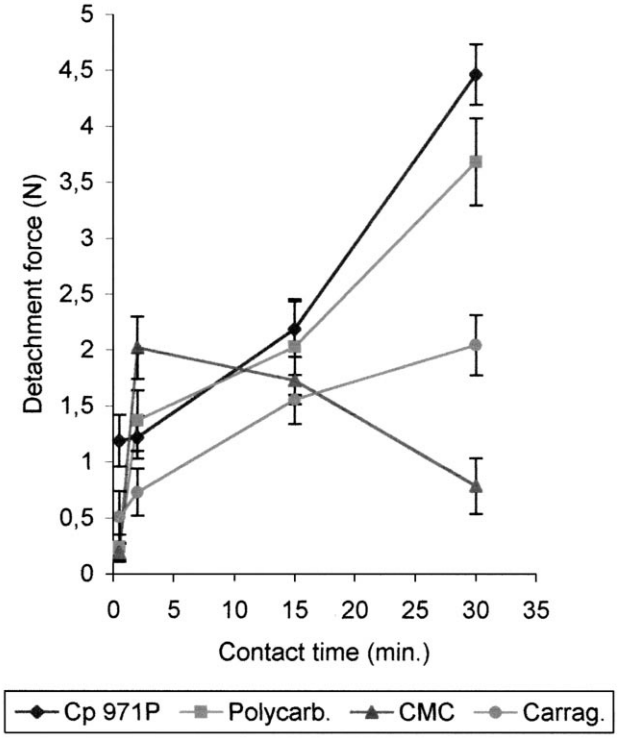

Fig. 8. Comparative maximum detachment force of prepared polymeric films at different contact times.

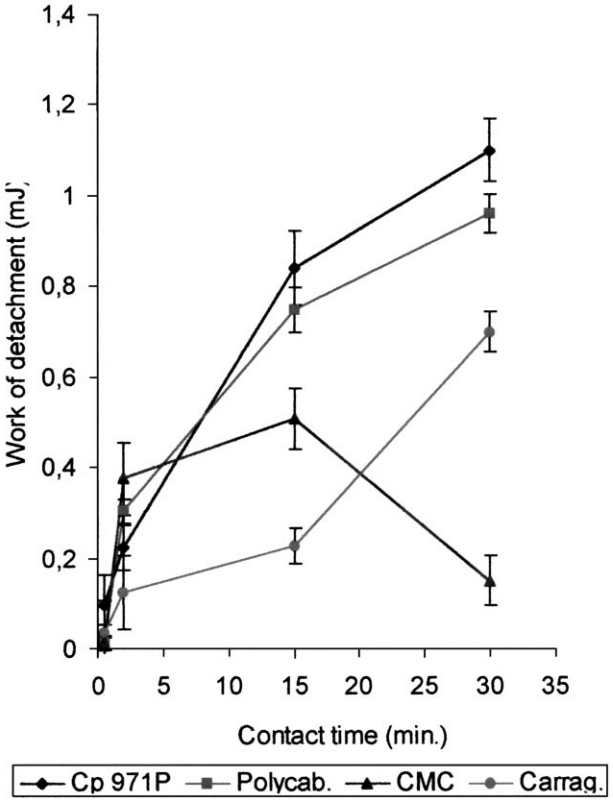

Fig. 9. Comparative work of adhesion of prepared polymeric films.

polymers as a function of contact time contributes to its bioadhesive behaviour [23]. It has been shown that hydrocolloids have an optimum contact time (15 min) at which they achieve maximal adhesion. During this time, hydration of the polymeric films resulted in a hydrated gel layer which allows the relaxation of the molecules, exposing their adhesive sites and facilitating interpenetration between the molecules of the substrate to a sufficient depth in order to create adhesive bonds [19]. This hypothesis is confirmed with that previously reported by Lehr et al. [24] and Mortazavi and Smart [25]. Accordingly, as a result of the hydration of hydrocolloids, capillary forces have been generated which might promote adhesion by tendency to dehydrate and consolidate an intermediate mucin layer.

Excessive hydration of CMC polymeric films, after a contact time of 15 min with mucus membrane resulted in a significant abrupt drop in the adhesive strength as compared with poly(acrylic polymers) $P < 0.05$ (Table 3, Fig. 8). This is clearly an indication of disentanglement at the hydrocolloid-tissue interface due to slippage of the macromolecular chains of the formulations, leading eventually to separation of the adhesive polymer and the substrate [6,8]. Fig. 6 shows that, carbopol 971P, polycarbophil as well as Carrageenan have reached a quasi-equilibrium state of swelling after 15 min, leading to an increase in mucoadhesive performance with further contact time as illustrated in Fig. 8. We can also deduce that the profile of the adhesion curves of the two polymers of poly(acrylic acid) (detachment force and work), are relatively close. But their results were not completely the same because of a higher absorption from the surrounding liquid by polycarbophil, shown in Fig. 6, and pH of the medium, these two factors contribute in the reduction of carbopol's potential. Also we have to consider the fact that polycarbophil forms more complex cross-linkage then carbopol 971P. The molecular structure of polycarbophil hides certain groups thus become unable to interact in the reinforcement of the adhesive link, contrary for carbopol 971P.

Fig. 9 shows that the work of detachment of the prepared polymeric films, at a contact time of 15 min., revealed the same rank order of viscoelastic parameters notably $\tan\delta$ (Table 2). Ponchel et al. [26], have discussed a model whereby the strength of mucoadhesive bond is considered to be a function of both the interaction energy (adhesion work) between the mucoadhesive polymer/mucosa and viscoelastic properties at the interfacial layer formed between the two surfaces.

The results of force as well as work of detachment tests within polymer-mucin systems are therefore almost certainly a function of swelling status together with viscoelastic moduli of the polymers themselves.

4. Conclusion

In summary, this work has examined an aspect of drug delivery, termed the persistence of bioadhesive vehicles at mucosal site. Different polymeric systems were tested as components of monolayer films, namely poly(acrylic acid) systems (carbopol 971P and polycarbophil), Carrageenan as well as CMC. In reference to the previous works we have concluded that the bioadhesive property of the polymeric systems is a function of their physical structure and their hydration state. The detachment test and the swelling behaviour test in combination provide an effective mean of characterizing mucoadhesive properties of the used polymeric systems. Generally, with the exception of CMC, polymers selected in this study were reported to be good buccal mucoadhesives. The measurements indicated that hydrogel of carbopol 971P has the highest elastic property and it's polymeric film present the lowest degree of hydration capacity followed by polycarbophil and Carrageenan. Although the viscoelastic analysis of the hydrogel does not show structurization of the polymeric chains, but it shows on one hand the collection of certain number of properties of the adherent(strong hydrogen-bonding groups, strong anionic charges, high molecular weight, sufficient chain flexibility, surface energy properties favoring spreading) and one the other hand configuration of the adhered surface and also that the environmental conditionscontribute significantly to the increment of the strength and duration of the mucoadhesive performance. The limited mucoadhesiveness obtained with CMC may be ascribed to the state of hydration of its polymeric film. The results suggest that such an approach may be viable to provide greater predictability in screening potential buccal mucoadhesive formulations prior to clinical testing.

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