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COMPARATIVE ASSESSMENT OF SURFACE PROPERTIES FOR SOME HYDROCOLLOID SYSTEMS BASED ON HYALURONIC ACID AND CARBOMER 940

LĂCRĂMIOARA POPA[1,2], MIHAELA VIOLETA GHICA[1,2,*], VALENTINA ANUȚA[1,2], MARINA-THEODORA TALIANU[1,2], MĂDĂLINA-MIHAELA-ADELINA ROȘU[1,2], MARIA-RALUCA VLĂSCEANU[1,2], LAVINIA-MILENA BOLOHAN[1,2], MATEI SITARU[2], CRISTINA-ELENA DINU-PÎRVU[1,2]

[1] *"Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, 6 Traian Vuia Str., 020956, Bucharest, Romania, *Corresponding author: mihaela.ghica@umfcd.ro*

[2] *Innovative Therapeutic Structures R&D Center (InnoTher), "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

The objective of the study was to develop hydrocolloid systems using hyaluronic acid and Carbomer 940, intended for buccal application, and explain their superficial characteristics by applying two different methods. Starting from the formulation of two macromolecular solutions of hyaluronic acid 0.3% and Carbomer 0.3%, four different blends were prepared in different ratios of 1:1, 1:2, 1:3, and 1:4. The goniometric analysis guided by the pendant drop model was performed to evaluate the surface tension of the samples, while the wettability behavior was explored through sessile drop model. Comparatively, the superficial characteristics were described using force tensiometer and explained through the Wilhelmy plate model. During goniometric analysis, surface tension depended upon the samples composition and varied between 42.07-76.48 mN/m. The comparative evaluation of the wettability behavior at contact with solid surfaces emphasized the hydrophilic structure of polymeric blends. The analysis conducted using the sessile drop technique in static mode revealed angles of 35.70°-61.05°. The dynamic contact angle fitted during Wilhelmy plate measurement varied between 45.35°-49.46° on the immersion side, being diminished to 43.97°-15.043° during emersion, in the sense of increasing Carbomer 940 ratio. The contact angle hysteresis defined by the difference in advancing and receding angles was related to the presence of Carbomer 940, which is responsible for maintaining the mucoadhesive action. The results obtained showed that Wilhelmy plate-based tensiometry provides an accurate technique to assess the wettability of hydrocolloids on various surfaces. The surface properties of the analyzed hydrocolloids play a significant role in explaining their influence on buccal application as therapeutic treatments for managing oral diseases.

Keywords: hydrocolloids, surface tension, wettability, goniometry, force tensiometer

INTRODUCTION

Nowadays, an outstanding interest is given in developing polymer-based materials for drug delivery intended for multiple applications in both local and systemic administration. The biomaterials tailored from natural-derived polymers in their simple and complex reticulated state, or grafted with new chemical groups are studied for their regenerative properties and capacity to adhere and create protective films with healing activity (Thang *et al*., 2023).

In oral disease management, the application of biocompatible supports is essential for the treatment of lesions produced by several affections like mouth sores (occurring in most cases as denture stomatitis or mucositis), periodontitis, oral lichen planus, or oral candidiasis, most of these pathologies being developed under individual exposure to mechanical stress induced by dentures, poor hygiene, immunological disorders, immunosuppressant drugs, antibiotics, or cancer chemotherapy (Chen *et al*., 2023; Garcia *et al*., 2024). Oral candidiasis is recognized as an oral fungi infection commonly triggered by pre-existent oral pathologies, such as the

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previously mentioned ones (Anuța *et al*., 2022). Cancer therapy and radiotherapy are tough interventions that increase the prevalence of oral infections with *Candida albicans* in cancer patients and seriously affect their life quality and forthcoming response to therapy (Sufiawati *et al*., 2019). Its evolution through the development of resistant mixed biofilms depends on the immediate initiation of antifungal therapy, concentrated on administering local and systemic drugs (Anuța *et al*., 2022).

Hydrocolloid carriers based on polymeric agents are used in the form of gels, hydrogels, mucoadhesive tablets or films, to assist an effective local therapy and regeneration of the mucosa (Ali *et al*., 2022; Anuța *et al*., 2022). Hyaluronic acid (HA), a biomacromolecule with powerful regenerative effects can be found in several commercial products for buccal application (Marques *et al*., 2024). Recent evidence proposed the development of mouthwashes containing vitamin E 0.2%, triamcinolone acetonide 0.1%, and hyaluronic acid 0.2% (Agha-Hosseini *et al*., 2021). The combination with a second polymer with mucoadhesive properties can be considered for the therapeutic valorization of HA.

Carbomer 940, a polyacrylic acid derivative with mucoadhesive attributes can enrich the physicochemical properties of polymeric-based systems with positive effects on viscosity, textural properties, surface characteristics and drug release. Mucoadhesive hydrogels tailored with Carbomer 940, carboxymethylcellulose, and different combinations of these were prepared to entrap a vegetable oil to increase the antifungal activity and reduce its volatilization (Nidhi *et al*., 2023).

The limited data coverage for HA and Carbomer 940 hydrocolloid combination oriented the study through the development of some macromolecular solutions using both polymers and their research centered on superficial characteristics related to the surface tension and wettability behavior. The importance of surface properties assessment in characterizing buccal formulations consists of formulation performance to adhere and create a protective film on the mucosa. In this respect, the quantification of surface tension and contact angle is essential in demonstrating the formulation compatibility with the tissue environment, hydrophilicity degree and spreading capacity (Menzies and Jones, 2010; Talianu *et al*., 2024)

The prior objective of the study was to develop hydrocolloid systems using hyaluronic acid and Carbomer 940, intended for buccal application, and explain their superficial characteristics by applying two methods based on goniometry and force tensiometry.

MATERIALS AND METHODS

Materials

All the ingredients were of analytical grade. Sodium hyaluronate 1200 kDa was acquired from Fagron, Carbomer 940 from Acrōs Organics, glycerin anhydrous from Chemical Company, Ultrapure Milli-Q water, with a specific resistance of 18.2 MΩ/cm, and a total organic carbon (TOC) of less than 5 µg/L was generated from a Milly-Q® Direct 8 Water Purification System (Merck Millipore), and was used as the aqueous phase.

Methods

Preparation of the Hydrocolloid Systems

To prepare the hydrocolloid systems, the two macromolecular solutions of HA 0.3% and Carbomer 940 0.3% were obtained. The two polymers were separately weighed and sprinkled on the aqueous phase previously mixed with a calculated amount of glycerin. The systems were placed for 24 h in a cold environment to permit polymers swelling, and then appropriately homogenized. In the case of the Carbomer 940 solution, triethanolamine was added to adjust the pH. In the final step, four hydrocolloid systems resulted by mixing different proportions of the two stock solutions, as presented in Table 1.

Table 1. Composition of the hydrocolloid systems with hyaluronic acid and Carbomer 940

Ingredients (w/w, %)	HA 0.3%	HAC 1 1:1	HAC 2 1:2	HAC 3 1:3	HAC 4 1:4	Carbomer 940 0.3%
Sodium hyaluronate	0.3	0.15	0.09	0.075	0.06	-
Carbomer 940	-	0.15	0.20	0.225	0.24	0.3
Glycerin	5	8.50	9.66	10.25	10.6	12
Distilled water	94.7	91.20	89.99	89.44	89.12	88.3

Surface Tension Determination Using Goniometry

The surface tension (ST) of the hydrocolloids was tested with a CAM 101 goniometer (KSV Instruments), equipped with a Hamilton syringe and a C209-30 needle as reported (Popa *et al.*, 2021). Young-Laplace equation (eq.1) was applied to estimate the ST and the determinations were recorded in triplicate, at 24 ± 0.5 °C.

$$p_{int} - p_{ext} = \gamma_{LG}\left(\frac{1}{r_1} + \frac{1}{r_2}\right) \quad (1)$$

where p_{int} - p_{ext} represents the Laplace pressure; γ_{LG} – superficial tension to liquid/gas (L/G) interface, and r_1, r_2 – the principal radii of curvature.

Contact Angle Determination Using Goniometry

As a first attempt on testing contact angle (CA), CAM 101 goniometer was used by applying the sessile drop model (Irimia *et al.*, 2019). CA was determined in triplicate, at 24 ± 0.5 °C using the Young equation (Talianu *et al.*, 2024).

$$\gamma_{SG} = \gamma_{SL} + \gamma_{LG} \cdot \cos(\theta) \quad (2)$$

where γ_{SG} is the interfacial tension to solid/gas (S/G) interface; γ_{SL}– interfacial tension to solid/liquid (S/L) interface; γ_{LG} – superficial tension to liquid/gas (L/G) interface, and θ – the contact angle made by the liquid drop with the solid surface.

Contact Angle Determination Using Force Tensiometry

Comparatively, the CA of the hydrocolloids was tested using a second equipment with a distinct methodology. Attension Sigma 700 force tensiometer (Biolin Scientific) was used in performing the measurement. A Wilhelmy plate was placed into the hook of the tensiometer, and used to analyze advancing and receding angles on the direction of plate immersion and emersion from the liquid samples (Daniel *et al.*, 2023). Wilhelmy equation was used to calculate the contact angle.

$$\cos(\theta) = \frac{F}{P \cdot \gamma_{LG}} \quad (3)$$

where θ represents the contact angle read at the solid surface, F – the buoyancy force, P – the plate perimeter, and γ_{LG} – the surface tension at the liquid/gas interface.

RESULTS AND DISCUSSION

The resulting hydrocolloid systems had a clear aspect and fluid structure, according to the composition. From Figure 1 the homogenicity of the two separate solutions of sodium hyaluronate 0.3% and Carbomer 940 0.3% can be seen, together with their macromolecular binary mixtures obtained in the four different ratios.

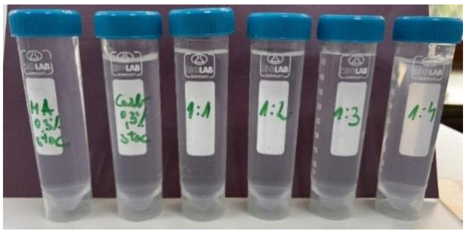

Figure 1. Hydrocolloid systems with hyaluronic acid, Carbomer 940, and their combinations resulted after preparation in the four ratios of 1:1, 1:2, 1:3, and 1:4

The variation in surface tension was dependent upon the composition of the macromolecular solutions, as can be noticed in Figure 2. The maximum value of the surface tension was specific for the hydrocolloid solution of hyaluronate 0.3%. With the addition of Carbomer solution, the ST diminished from 76.48 ± 0.39 to 42.07 ± 0.36 mN/m, being closer to the buccal surface tension.

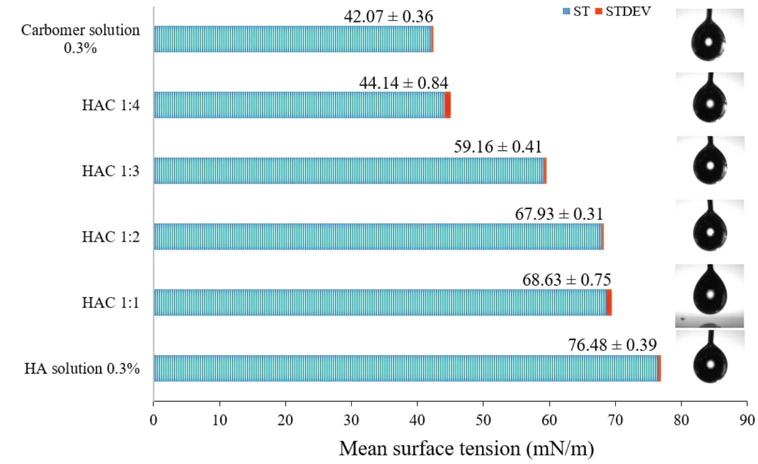

Figure 2. Graphical representation of the mean ST values for the hydrocolloid samples presented together with the corresponding drop shapes analyzed using the pendant drop model

Superficial tension represents a physical property affecting the release profile of a medicine from a pharmaceutical form. In this case, surface tension contributes to the understanding of the hydrocolloid spreadability to the mucosa and can be compared to the salivary fluid surface tension (Foglio-Bonda *et al*., 2018). The obtained results confirmed the literature evidence. Human saliva was analyzed as a drug release media, and the surface tension values determined on unstimulated and stimulated saliva were similar, without significant differences between experimental data sets. The ST of the saliva samples was found to vary between 54 and 65 mN/m (Gittings *et al*., 2015).

It is well known that the materials hydrophilicity is quantified by contact angle values of 0-90°. Over the analysis of the sessile drops fitted with the Young equation, the calculated values of the CA varied between 37.33 ± 0.57 and 61.05 ± 0.85°. The two edge values were specific for the solution of HA 0.3% and Carbomer 940 0.3%, respectively. As the Carbomer 940 ratio increased in the hydrocolloid solutions from HAC 1:1 to HAC 1:4, the calculated angles elevated from 44.47 ± 1.70 to 57.97 ± 1.87°, as can be noticed in Figure 3 in the analyzed sessile drops captured with the digital camera. The mean values of the CA tested through goniometry are additionally presented comparatively in Table 2, together with the experimental data assessed from the tensiometry study. Knowing the mucoadhesive effect of the polymer, the formulations with a higher concentration in Carbomer 940, namely HAC 1:2, HAC 1:3, and HAC 1:4 can display adhesive hydrophilic films on the mucosa, maintaining at the same time the hydrating activity of the HA.

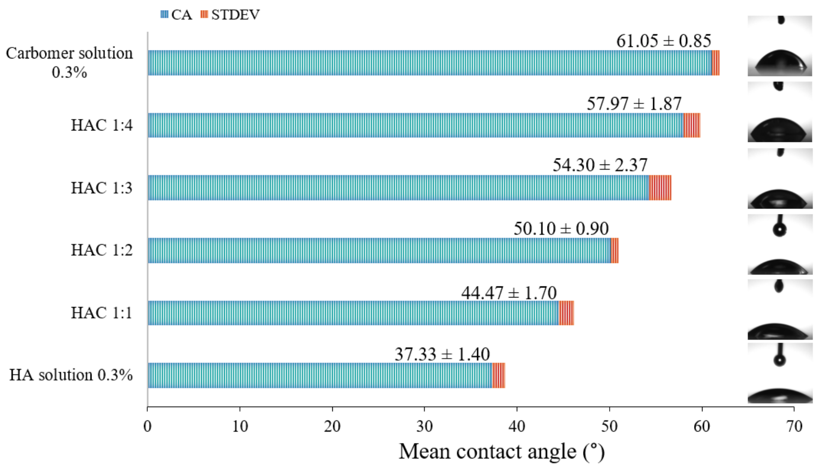

Figure 3. Graphical representation of the mean CA values for the hydrocolloid samples presented together with the corresponding drop shapes analyzed using the sessile drop model

The static goniometric analysis was emphasized in many studies, of which some important aspects were revealed. Thus, in a study conducted by Vorvolakos *et al.*, the wettability of HA ionically crosslinked with Fe^{3+} was studied to create a biodevice that can assure lubrication support in abdominal surgery. The CA values varied from 7 to 17°, relative to the increase in crosslinking grade (Vorvolakos *et al.*, 2011). Moreover, polymeric films containing hyaluronic acid, collagen, chitosan and their combinations were analysed following hydrophilicity, likewise, but at contact with glycerol or diiodomethane drops. Due to a marked hydrophilic character with CA values of 47°, HA contributed to the diminishing of collagen CA. In addition, the incorporation of chitosan into a polymeric blend made of collagen and HA (Col/HA) 80:20, respecting ascending weight fractions from 0.0 to 0.9, determined a decrease in CA of the Col/HA film from 72.3 to 46.6°, as the glycerol drop test suggested (Lewanodovska *et al.*, 2016).

It can be appreciated that the static CA analysis offered preliminary information concerning the initial contact of the sample with a surface, and can be followed by a dynamic CA analysis through the knowledge of intrinsic wettability behavior using the Wilhelmy plate model.

Following the tensiometry analysis of the hydrocolloid systems, the advancing and receding CAs were compared with the goniometric CA values. The CA results were obtained from graphical plots expressed as force versus the immersion depth calculated on each point of advancing and receding movement, as can be seen in the case of the four hydrocolloid binary mixtures of HAC 1:1- HAC 1:4 samples, and presented in Figure 4.

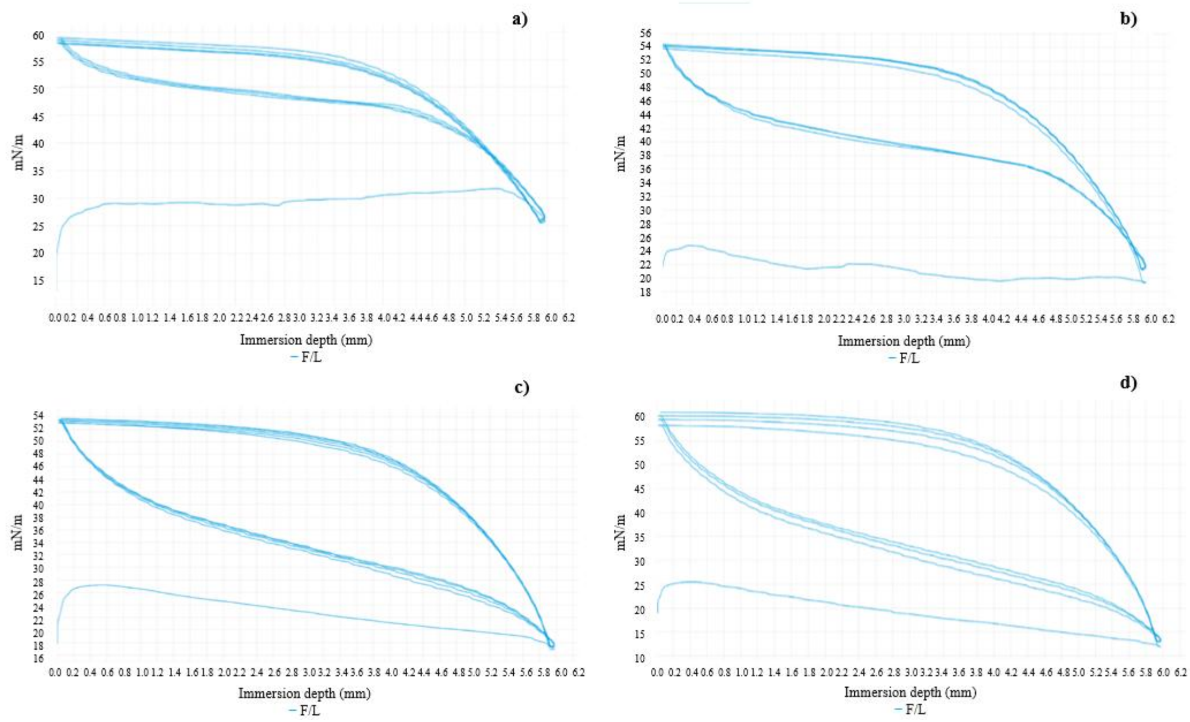

Figure 4. Advancing and receding profiles for the hydrocolloid samples tested using the Wilhelmy plate model: (a) HAC 1:1, (b) HAC 1:2, (c) HAC 1:3, and (d) HAC 1:4

Thus, in the immersion direction (advancing), contact angles varied from 45.35 ± 1.38 (angle specific for the HA 0.3% solution) to 49.46 ± 3.11° (for the Carbomer 940 0.3% solution). On the emersion (receding) direction, the angles diminished, from 43.97 ± 0.94 (HA solution 0.3%) to 15.04 ± 0.19° (Carbomer 940 0.3% solution). The experimental results from Table 2 present in a comparative manner the contact angles obtained using both methods. The angles measured at the plate immersion surface were similar to those obtained on the goniometric pathway. On the emersion direction, it can be noticed a reduction in the contact angles more obvious for the series HAC 1:1 - HAC 1:4, and Carbomer 940 0.3% hydrocolloid solutions. The difference calculated between advancing and receding angles was defined as the hysteresis angle, with values calculated for each formulation and expressed as mean values and standard deviation (Mohos *et al.*, 2014). The resulting hysteresis angles varied between 1.37 and 34.59°, according to the presented data from Table 2. Elevated values were specific for solutions with a good capacity of spreading and variation of the CA in time.

Table 2. Comparative results obtained through goniometric and tensiometric analysis of the hydrocolloid systems

Analysis model	Contact angle model			Wilhelmy plate model		
Code	CA (L) (°)	CA (R) (°)	CA (M) (°)	CA Adv (°)	CA Rec (°)	Hysteresis (°)
HA 0.3%	38.00 ± 1.30	36.67 ± 1.79	37.33 ± 1.40	45.35 ± 1.38	43.97 ± 0.94	1.374 ± 0.44
HAC 1:1	46.01 ± 0.42	42.94 ± 3.29	44.47 ± 1.70	42.12 ± 0.78	33.56 ± 0.39	8.56 ± 0.73
HAC 1:2	49.88 ± 0.89	50.32 ± 1.02	50.10 ± 0.90	45.48 ± 0.56	40.96 ± 0.13	4.52 ± 0.55
HAC 1:3	53.93 ± 1.35	54.68 ± 3.39	54.30 ± 2.37	51.60 ± 0.21	41.58 ± 0.26	10.01 ± 0.05
HAC 1:4	58.85 ± 1.16	57.10 ± 2.74	57.97 ± 1.87	49.52 ± 1.62	32.20 ± 1.14	17.32 ± 0.52
Carbomer 0.3%	62.32 ± 0.96	59.78 ± 1.34	61.05 ± 0.85	49.64 ± 3.11	15.04 ± 0.19	34.60 ± 2.92

The method was used as well to study the wettability phenomena in contact with hydrophilic and lipophilic surfaces of bicontinuous microemulsions prepared with tetradecane or methyl oleate as lipophilic phases stabilized with sucrose esters and pentanol (Vargas-Ruiz *et al.*, 2017). The increase of the hysteresis emphasized the affinity of the microemulsion for the analyzed substrate, explaining substance adsorption at the solid/liquid interface.

Wilhelmy plate method was considered a useful approach for measuring dynamic contact angles of the studied hydrocolloids, completing the information obtained in the goniometric study.

CONCLUSIONS

Based on the obtained results and observations, this study emphasized a complementary characterization method in the analysis area of superficial phenomena, applied in the formulation of liquid and semi-solid pharmaceutical systems with bioactive ingredients. The designed hydrocolloids aimed to offer an improvement in the management of oral pathologies and were characterized by adequate superficial characteristics. The surface tension values were specific for the oral cavity environment. Moreover, the comparative goniometric and tensiometric studies offered a comprehensive perspective on the contribution of the static and dynamic contact angle for the assessment of the hydrocolloids' wettability. In both analysis models, Carbomer 940 influenced the variation in contact angle, emphasizing its role in increasing the samples consistency and mucoadhesion effect. Wilhelmy plate model supported the results through the calculation of dynamic contact angle and hysteresis, being a mark for the estimation of the hydrocolloid spreadability on a surface and their practical application for buccal administration in oral candidiasis.

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