

XANTHAN GUM/CARRAGEENAN-BASED HYDROGEL PADS WITH OKRA FRUIT MUCILAGE POWDER FOR COSMECEUTICAL AND MEDICAL APPLICATIONS

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Abstract

The main component of mucilage found in the fruit of okra (*Abelmoschus esculentus*) is okra gum consisting of pectic polysaccharides reported to exhibit, *inter alia*, antibacterial and antioxidant characteristics. It was used in the pharmaceutical industry, e.g. as a stabilizer or a modifier drug release. In this work, various formulations of xanthan gum (XG)/ κ -carrageenan (CN)-based hydrogel with okra mucilage (OM) powder were examined to achieve the goal of developing OM-hydrogel pads that make good use of the advantages of OM polysaccharides relevant to drug delivery and/or stability. A straightforward cosmeceutical application of the OM-hydrogels is as under-eye masks since the OM itself is reported to contain diffusible small compounds with proven skincare benefits. OM from blended fresh okra pods without seeds was precipitated with ethanol. Preliminary studies showed that hydrogel pads prepared with XG, CN, glycerol, and NaCl at 0.5, 0.5, 13, and 4 wt%, respectively, possess a suitable hardness while exhibit the highest adhesive strength among other formulations tested. When OM powder was added at 0.02, 0.05, 0.06, 0.1, 0.2, 0.4, or 0.6 wt%, the OM-hydrogels' hardnesses substantially drop. Increases in hardnesses and adhesive strengths with increasing amounts of OM powder were observed. The upward trend of adhesive strengths continues only up to 0.2 wt% where the adhesive strength begins to drop. In OM-hydrogels containing 0.2 wt% OM powder, normalized rates of moisture loss are the lowest while water contents and water holding capacities are the highest. The formulation with 0.2 wt% OM powder is of highest potential for the fabrication of XG/CN-based OM-hydrogel pads for topical administration of active compounds.

Keywords: Hydrogel pad; κ -carrageenan; okra mucilage; rhamnogalacturonan I; xanthan gum

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Introduction

Okra (*Abelmoschus esculentus* (L.) Moench), also known as, among other names, lady's finger, green ginseng, or plant Viagra, is an economical vegetable crop originating from Africa. It is widely cultivated in the tropics, sub-tropical and temperature regions around the world including Asia, Africa and North America (Zhu *et al.*, 2020). Okra plants grow very fast, is grown in all soil types, and is among the most heat and drought-tolerant vegetables (Bakre and Jaiyeoba, 2009).

Okra is an important edible vegetable widely consumed due to its health benefits. Okra fruit is rich in nutrients and is a great source of vitamins and minerals. Apart from its nutritious characteristic, it is used in traditional medicine in the treatment of worms, dysentery, inflammation, and also irritation of the stomach, intestines, and kidneys (Dantas *et al.*, 2021).

Polysaccharides from natural sources were recently used in various purposes in food, pharmaceutical and cosmetic formulations. Crude okra polysaccharides are inexpensive and non-toxic biopolymer. Such characteristics open a wide range of applications for okras other than low-cost functional food.

In okra, carbohydrates are present mainly in the form of mucilage (Singh *et al.*, 2014). Okra mucilage is of high potential concerning health benefits. Its abilities as antitumor, antioxidant, antimicrobial, hypoglycemic, and antiulcerogenic agents were demonstrated (Dantas *et al.*, 2021).

The main component of mucilage found in the fruit of okra is okra gum consisting of pectic polysaccharides. Natural gums are non-toxic, chemically inert, low cost, and biodegradable (Biswas *et al.*, 2020). Okra polysaccharides are also biocompatible (Dantas *et al.*, 2021). The main component of Okra polysaccharides is branched polysaccharide called rhamnogalacturonan I (RG-I, Figure 1(a)). The backbone of RG-I is an alternating co-polymer synthesized from L-rhamnoses and D-galacturonic acids (Makshakova *et al.*, 2017). Both monomers are in 6-membered ring (pyranose) forms and represented as Rhap and GalpA, respectively. RG-I is highly branched and the branch points are almost exclusively at the hydroxyl group on C⁴ of the Rhap residues (Figure 1(b)) and both α - and β -(1,4)-linkages are possible. Although the GalpA residues do not generally bear side chains, it is demonstrated that they may be substituted with a single glucopyranose-based residue (Waldron and Faulds, 2007).

Zhang *et al.* (2018) analyzed the component of pectin extracted from okra pods and shown to be

rhamnose (21.4%), galacturonic acid (34.9%), galactose (29.6%), glucuronic acid (4.5%), glucose (5.9%), and arabinose (3.7%). They suggested that the RG-I's side chains are type-II arabinogalactan. Other possible side chains of RG-I include linear α -L-arabinan, linear β -D-galactan, branched α -L-arabinan, and type-I arabinogalactan (Waldron and Faulds, 2007).

In the pharmaceutical industry, okra gum was used to modifying drug release (Ghori *et al.* 2014; Zaharuddin *et al.*, 2014; Okunlola *et al.*, 2020). In addition, okra polysaccharide was used as a tablet binder, film-coating material, and as an emulsifier or stabilizer (Raj *et al.*, 2020). In the food industry, okra polysaccharides, as a pectin, can be used as emulsifier, thickeners, viscosity enhancers, gelling agents, texture modifiers and stabilizer (Nur Farhana *et al.*, 2017; Zhu *et al.*, 2020).

Hydrogels are three-dimensional cross-linked polymer networks, which can absorb and retain large amount of water (Wang *et al.*, 2020). Despite their high water contents, they are able to maintain well-defined structures because the polymer molecules forming the network do not typically dissolve due to chemical or physical cross-links and/or chain entanglements (Peppas *et al.*, 2012). Hydrogels have been considered promising biomaterials owing to their high water content, favorable structural features and biocompatibility

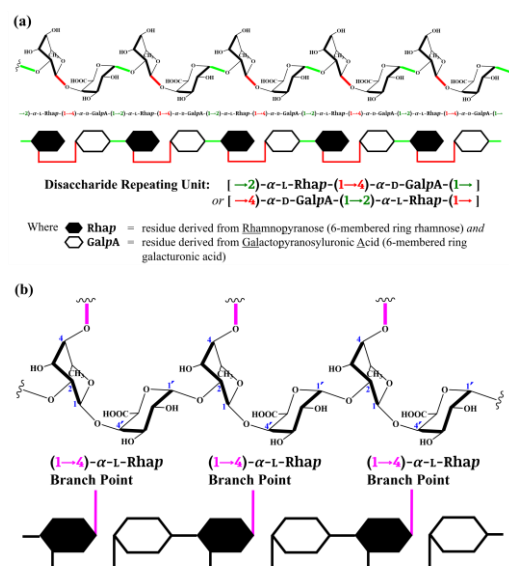


Figure 1. (a) Chemical structure of the backbone (5 repeating units) of rhamnogalacturonan I and (b) branch points on rhamnosyl residues of the backbone

(Balasubramanian *et al.*, 2018) and have been applied in a wide range of biomedical and engineering applications, ranging from tissue engineering and regenerative medicine to wastewater treatment and soft robotics (Wang *et al.*, 2020).

In this study, various formulations of xanthan gum (XG)/ κ -carrageenan (CN)-based hydrogel with okra mucilage powder additive were investigated in terms of hardness, adhesive force, weight-promoted downward creeping, water uptake, water holding capacity, and moisture loss for the use as hydrogel pads for topical administration of active compounds for cosmeceutical or biomedical applications. The focus is on biopolymers of the okra mucilage, not the small, easily diffusible bioactive compounds. Methodology and findings of the present study are summarized in Figure 2.

Materials and Methods

Materials

Xanthan gum and κ -carrageenan were supplied by Labo Chemie (India) and Cargill (USA), respectively. Glycerol, NaCl and phenoxyethanol (PhO(CH₂)₂OH) were supplied by Mercks. Fresh okra pods were obtained from local market.

Preparation of Okra Mucilage (OM) Powder

Okra mucilage powder was prepared as follows. Thoroughly-cleaned fresh okra pods were cut to small chunks and the seeds were removed. Water was added (1.2 mL/g) and the okra pulp chunks were blended for 2 min. Ethanol (85%) was added to the filtrate (50 mesh) obtained from the blended seedless okra pods (1:4 volume ratio) to precipitate OM. The OM precipitates were collected by centrifugation at 5,000 rpm at 0°C for 30 min and the sediment was freeze-dried and ground.

Preparations of OM-free Hydrogel Pads

Four formulations of OM-free hydrogel pads were prepared using ingredients given in Table 1. With continuous stirring at 300 rpm and temperature maintained at 95°C, xanthan gum (XG), κ -carrageenan (CN) and glycerol were dissolved in pre-heated water and kept stirred for 5 min before NaCl was added. After 1 min of further stirring, phenoxy ethanol (PhO(CH₂)₂ OH) was added. An additional 30 min of stirring was carried out to ensure homogenous mixing of the ingredients. 100 mL of the solution were casted into a 95-mm Petri dish and allowed to set at room temperature.

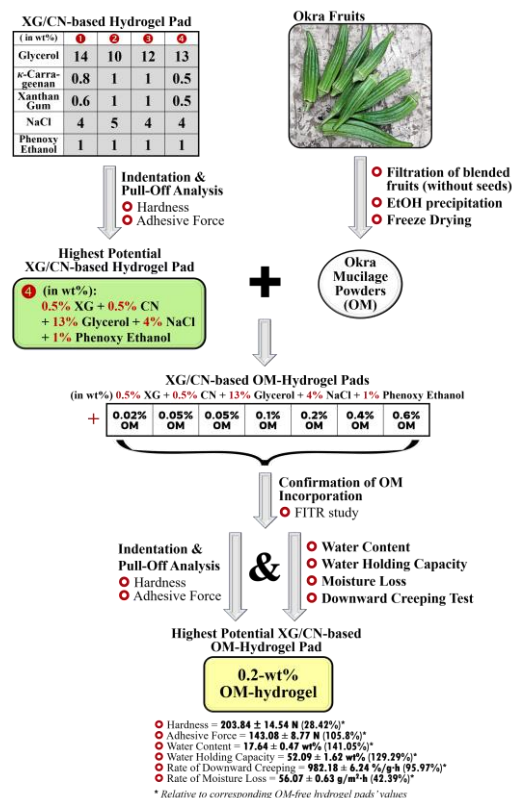


Figure 2. Schematic summary of the methodology and results of the present study

Table 1. Four formulations of OM-free XG/CN-based hydrogel pads

Chemical	Amount (wt%)			
	1	2	3	4
XG	0.6	1	1	0.5
CN	0.8	1	1	0.5
Glycerol	14	10	12	13
NaCl	4	5	4	4
PhO(CH ₂) ₂ OH	1	1	1	1

Preparations of OM-Hydrogel Pads

Eight formulations of OM-hydrogel are prepared based on Formulation-1 (Table 1). Following the same preparation steps of OM-free hydrogel pads, finely ground OM powder was added together with XG, CN and glycerol. The amounts of OM powder range from 0, 0.02, 0.05, 0.06, 0.1, 0.2, 0.4, and 0.6 wt%. The volume of water was adjusted accordingly to maintain the proper wt% of the ingredients. For each preparation, 30 mL and 100 mL of the solutions were casted into separate 95-mm Petri dishes and allowed to set at room temperature. 2 sets of 5 plates (5×thinner

(30 mL/plate) and 5×thicker (100 mL/plate), were made of each formulation. The thinner hydrogel pads were used in FTIR and downward creeping studies while the thicker ones were used in the other experiments.

SEM and FTIR Characterizations

Scanning electron microscopic (SEM) images of the OM powder was obtained using the Quanta250 (FEI) operating in high vacuum (HV) mode at 20 kV.

Fourier-transform infrared (FTIR) spectra was recorded with a Bruker ATR-FTIR spectrophotometer at a measuring range from 4,000 to 500 cm^{-1} using the thinner (30 mL/plate) hydrogel pads.

Determinations of Hardness and Cohesive Strength

Hydrogel pads' hardnesses and cohesive strengths were determined during a single cycle of indentation/pull-off using the CT3 texture analyzer (AMETEK Brookfield) with the TA38 (10-mm stainless steel spherical indenter) probe. The target compression is 1.0 mm with a test speed of 0.5 mm/s. The indentation/pull-off cycle was performed at 5 spots in each plate, i.e. at the center or on the top, right, bottom, and left areas.

Determinations of Rates of Weight-Promoted Downward Creeping

The extents of downward creeping due to gravity were determined on an acrylic substrate using $1 \times 1\text{-cm}^2$ hydrogel pads cut from the thinner (30 mL/plate) hydrogel. The OM-hydrogel pads were first weighed and dipped in water. After the excess water was removed using a tissue paper, each pad was placed on a separate lane at one of the substrate's ends. The pads were oriented so that 2 edges of the pads were parallel to the substrate's edge (Figure 3). The centers of each pad were



Figure 3. Positions and orientation of hydrogel pads on a clear acrylic substrate. Note that the horizontal lines are on a sheet of paper attached under the substrate

aligned and the pads were then pressed against the substrate for 5 s with the weight of a 50-g cylinder without additional applied force. The pads were rested horizontally on the substrate for a further 1 min. The substrate was then held vertically for 60 min and the creep depths (distances of downward creeping) were measured. A clear acrylic plate was used as the substrate. The paper protective layer of the acrylic plate was peeled off and the clean exposed surface was used without any treatment applied. A set of parallel lines with 1 cm spacing were printed on a sheet of paper and the paper was attached under the clear acrylic panel to facilitate hydrogel pads alignment.

Determinations of Water Contents and Water Holding Capacities

Water holding capacities were determined by immersing $1 \times 1\text{-cm}^2$ pads in water. To determine water contents, the initial weights of the square pad were recorded. After 15-min of immersion in 10 mL of water, excess water was removed from the swollen pads the swollen pads were weighed. The immersion solutions were filtered using a cellophane membrane that its dry weight was pre-determined. Each pair of swollen pad and filtered mass/membrane were dried at 80°C for 12 h. The dried pads and filtered mass/membrane were weighed again.

The pad's total dried weight is the sum of the dried pad weight and the calculated weight of the dried mass on the membrane. Water contents are the wt% of water in the untreated pads relative to their total "initial" weight. Water holding capacities were calculated relative to the "total dried" weight of the pads. They were estimated using the weight difference between the dried pads and the fully-imbibing pads.

Determinations of Rates of Moisture Loss

The rates of the moisture loss of the Formulation-4 and OM-hydrogel pads were determined using Tewameter TM300 according to the Manufacturer's procedure for transepidermal water loss (TEWL) test. The probe is a hollow cylinder of 1-cm inner diameter. The hydrogel pads were kept at room temperature in a closed high humidity chambers for 24 h before the test were carried out. At each spot, the measurement was carried for 10 sec at 1 measurement/sec and the last 5 rates were averaged. The rates of moisture loss were determined from 3 spots/ pad.

The normalized rates of water loss were estimated using the weight of water per 0.785398 cm^2 (area of the probe circular window) which in turn calculated from the pads' average water contents previously determined. The calculation

assumes that, for each formulation, the portions of hydrogel under the TM300 probe and the square pads used to determine water contents are of equal thicknesses.

Statistical Analyses

One-way analysis of variance (ANOVA) test were carried out followed by the Ryan-Einot-Gabriel-Welsch Range (REGW-Q) *post hoc* multiple comparison, when applicable. In experiments with a control group, Dunnett's multiple comparison was also performed and, if all of the treatment groups are significantly different from the control group, ANOVA/REGW-Q test were performed again with the control group data excluded. The numbers of data are $n = 3$ for the determination of water contents, water holding capacities and rates of downward creeping and $n = 5$ for the rest of the experiments.

An * is used to mark the treatments that their mean is significantly different compared to the that of the control group (the leftmost category of each bar chart except in Figure 4). The letter *a*, *b*, *c*, etc. are used to labeled homogeneous subset in the REGW-Q *post hoc* analyses. Treatment groups without any *post hoc* letter label in common are significantly different.

Results and Discussion

Mechanical Properties of OM-free Hydrogel Pads

Four formulations of XG/CN-based hydrogel pads were fabricated and their averaged hardnesses and adhesive forces are given in Figure 4. The hydrogel pads containing higher XG and CN and lower glycerol (Formulations-**2** and **3**) are harder. The XG/CN-based hydrogels are binary hydrogels since XG and CN are the only polymers among the hydrogel ingredients. Therefore, higher amounts of XG and CN leads to denser hydrogel polymeric networks which, in turn, lead to harder hydrogel pads. Mechanical strengths of κ -carrageenan hydrogel are reported to be affected by cation concentrations (Zabik and Aldrich, 1968). Higher Na^+ and lower glycerol in Formulations-**2** lead to higher pads' hardness compared to that of Formulations-**3**.

The hardnesses of the pads of other 2 formulations are not significantly different ($p > 0.05$). It is interesting that Formulations-**1** hydrogel pads are slightly softer than Formulations-**2** hydrogel pads despite the higher amounts of XG and CN in Formulations-**1**. The higher glycerol in

Formulations-**1** counteracts the effect of the higher XG/CN.

The Formulation-**4** pads exhibit the highest adhesive force (135.24 ± 8.20 N) which is substantially higher than those of the other formulation. The Formulation-**4** pads' average adhesive force is approx. 143.75% compared to that of the second rank group (Formulation-**3**). The Formulation-**4** pads' average hardnesses (717.36 ± 23.40 N) is approx. 82.62% of that the hardest group (Formulation-**3**). The Formulation-**4** was used in subsequent studies with OM power additive due to the good and balanced mechanical properties of the pads.

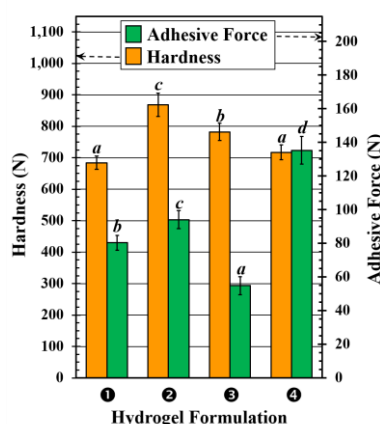


Figure 4. Hardnesses and adhesive forces of 4 formulations of OM-free hydrogel pads



Figure 5. SEM image of finely ground okra mucilage powder at $\times 5,000$ magnification

Morphology of OM Powder and Fabrications of OM-Hydrogel Pads

SEM image of the finely ground freeze-dried OM powder is given in Figure 5. The OM granules are globular in shape. The granules possess large surface areas due to their relatively rough surfaces



Figure 6. 100-mL/plate OM-hydrogel pads containing increasing amounts of OM powder, 0.01 wt% at the leftmost to 0.6 wt%

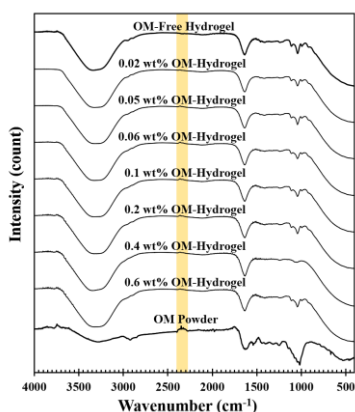


Figure 7. FTIR spectra of OM powder and hydrogel pads, with or without OM powder

possessing large numbers of deep grooves and holes. The granules' average diameter is approx. 25 μm .

OM-hydrogel pads were fabricated with 0.02, 0.05, 0.06, 0.1, 0.2, 0.4, or 0.6 wt% of OM powder. From the darker brownish colors of the OM-hydrogel pads (Figure 6), the incorporations of the OM are evident in the pads containing higher amounts of the additive. The presences of OM additive in the pads were also confirmed in FTIR spectra given Figure 7.

It is obvious from Figure 8 that the incorporation of OM powder results in OM-hydrogel pads that are much softer. However, the pads are slightly harder at higher amounts of OM additive. The hardest pads containing 0.6 wt% OM powder and their hardnesses are only 34.97% of the OM-free counterparts.

The adhesive forces drop to 60.87% in OM-hydrogel pads prepared with 0.02 wt% OM powder and continue to increase with increasing amounts of the additive. The adhesive forces reach the maximum value of 143.08 ± 8.77 N at 0.2 wt% of OM additive (Figure 8). The value is higher (105.80%) but not significantly different from that of the OM-free pads. Beyond 0.2 wt%, the adhesive forces substantially drop to <50% of that of the OM-free pads. 0.2-wt% OM-hydrogel pads are the only formulation exhibiting statistically comparable

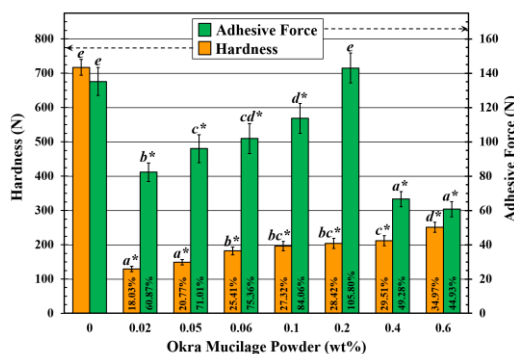


Figure 8. Hardnesses and adhesive forces of Formulation-④ hydrogel pads, with or without OM additive

value of adhesive force when compared with the OM-free counterpart.

OM consists mainly of pectic polysaccharide called as rhamnogalacturonan I (RG-I) which is a pectic polysaccharide. Dissolved OM polysaccharides are able to act as a gelling agent. However, the incorporations of OM powder do not result in ternary XG/CN/OM hydrogels since the OM granules do not fully dissolve. Each OM granule acts as a globular additive with rigid core covered with partially dissolved RG-I chain radiate from the center of the granule. The dissolved segments of RG-I exposed a large number of free hydroxyl ($-\text{OH}$) groups on the surface of OM granules. These free hydroxyl groups contribute to the OM granules very high water affinity. A portion of the OM granules' free hydroxyl groups help anchor the granules on the XG/CN hydrogel network. Therefore, the OM granules are loosely bound to the hydrogel network.

κ -Carrageenan is rigid hydrocolloids that was frequently used to prepared binary hydrogel via synergistic gel formation whereas xanthan gum is a non-gelling agent, unable to form gel networks on its own. The synergistic interactions induced gel formation of the hydrocolloids at non-gelling concentrations, and/or enhanced the gel properties at gelling concentrations. XG/CN hydrogel networks are formed via synergistic interaction between XG and CN molecules. CN is a linear unbranched polysaccharide. Synergistic interactions with CN occur by the binding of the CN's ordered helices to the smooth regions of the other polymer. (The smooth regions are the segments of the carbohydrate backbone that have no branch.)

Due to their size, OM granules prevent proper formations of synergistic interactions between XG and CN around them resulting in structural

irregularity in the hydrogel network. The number of cross-linking sites between XG and CN is substantially dropped and the hydrogel is much less firm. This leads to the observed extensive losses in OM-hydrogel pads' hardnesses. The OM granules' surface free hydroxyl groups (-OH) are able to form hydrogen bonds with the XG or CN segment located in close vicinity. These attractive interactions contribute to and partially recover OM-hydrogel pads' firmness and explain why higher amounts of OM additive results in higher pads' hardnesses.

Water Contents and Rates of Moisture Loss of OM-Hydrogel Pads

The wt% of OM-hydrogel pads' water content with respect to the pads' weights are given in Figure 9(a). Water contents follow a similar trend observed in the case of adhesive forces, i.e. the OM additive causes a reduction in water content at 0.02 wt% but water contents exhibit an upward trend until 0.2 wt% (17.66 ± 0.47 wt%) where the value begins to drop. However, in this case, the drops in water contents are much smaller and only the 0.02-wt% and 0.6-wt% OM-hydrogel pads exhibit lower water contents compared to that of the OM-free counterpart. The water contents of the other 5 formulations are significantly higher.

Water holding capacities were determined by immersion of the hydrogel pads in water and estimated with respect to the pads' total dried weights. On immersion, as evident by the color of immersion waters, the portions of the OM additive located near the surfaces of the pads begin to diffuse out to the surrounding water. The pads' fractions lost to the immersion water were collected using cellophane membranes. The pads' water holding capacity was estimated from the ratio of "the weight difference of the fully-imbibing pad and the same pad completely dried" to "the pad's total dried weight". The total dried weight is the sum of the pad's dried weight and the weight of the fraction diffused out from the pad. The estimated values (Figure 9(a)) are under estimated since it assumes that the fractions collected using membranes do not contribute to the pads' water holding capacity at all. Although such an assumption is unlikely to be hold true, the weights of the fractions are relatively tiny compared to the dried pad weights (data not shown) and, in most cases, does not results in ambiguities when the estimated values are interpreted.

Total water holding capacities follows a similar trend as that of water contents. The equivalent wt% of water contents calculated with respect to the pads total dried weights are also given in Figure 9(a) (labelled "° of water (dry weight)"). Despite their significantly different water contents, the 0.05-wt%, 0.06-wt%, 0.1-wt%, and 0.6-wt%

OM-hydrogel pads have comparable percentage points of additional water holding capacities compared to that of the OM-free pads. This means that these pads are able to absorbed comparable amounts of additional water since the total dried weights of hydrogel pads, with or without OM powder, are not much different (data not shown). The 0.2-wt% and 0.4-wt% OM-hydrogel pads not only have higher water contents than the OM-free pads but are also able to absorb more water resulting in much larger total water holding capacities.

At optimal concentration of OM additive, the presence of OM powder makes the XG/CN hydrogel network to be loose. This allow the pads to expand to absorb additional water to the largest extent. If OM concentrations are too high, free hydroxyl groups on the surface of OM granules help strengthen the hydrogel network interactions and resist pads expansion. As a result, less additional water can be absorbed. The hydrogel network interactions are also stronger if the OM concentration is too low because a large proportion of synergistic interaction between XG and CN is still present. Less additional water can be absorbed in this case.

The rates of moisture loss are given in Figure 9(b). Moisture is lost from the OM-hydrogel pads at

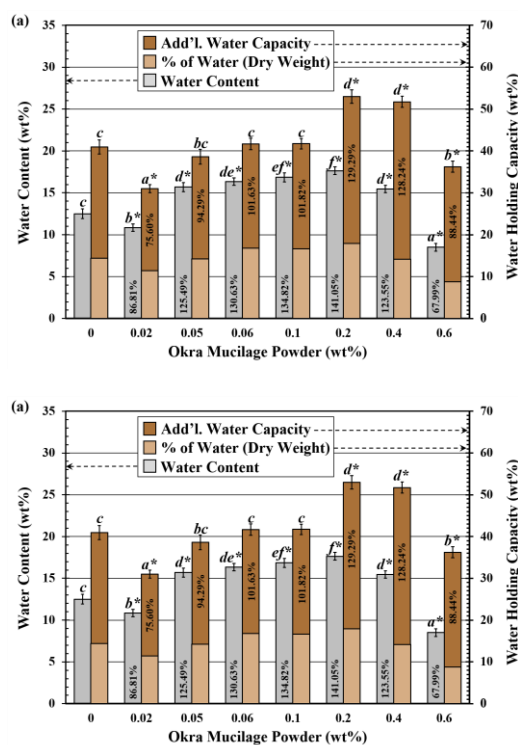


Figure 9. (a) Water contents and water holding capacities and (b) rates of moisture loss of the OM-hydrogel pads

much slower rates compare to that of the OM-free pads. Among OM-hydrogel pads, the highest rate of moisture loss is observed in the 0.6-wt% pads and the average rate is <50% of that of the OM-free pads. From 0.02-0.06 wt% OM powder, the rates of moisture loss exhibit an upward trend. Beyond that the rates slightly drop when they reach the “local” minimum value of $56.07 \pm 0.63 \text{ g/m}^2 \cdot \text{h}$ observed in 0.2-wt% pads and the rates begin to increase in the rest of the OM-hydrogel pads containing higher amounts OM. Among OM-hydrogel pads with harnesses more than 150 N, the 0.2-wt% pads exhibit the lowest average rate of moisture loss. The “global” minimum of the rates is observed in 0.02-wt% pads ($36.75 \pm 0.78 \text{ g/m}^2 \cdot \text{h}$).

As OM-hydrogel pads have significantly different water contents, we also calculated the normalized rates of moisture loss using the total amounts of water present in the cylindrical portions of the pads underneath the Tewameter TM300's hollow cylinder probe. Such total amounts of water are estimated from the pads' water contents. The normalized rates reveal that, even though the 0.02-wt% pads have the lowest average rate of moisture loss, the lowest normalized rates are observed in 0.05-wt% and 0.2-wt% pads. The average normalized rate of the 0.2-wt% pads is slightly lower than that of the 0.05-wt% pads but the values are not significantly different ($p > 0.05$).

Rates of Downward Creeping on Acrylic Substrate

The creep depths (distances of downward creeping) depend on (1) the physicochemical properties of the pads' surface, (2) the physicochemical properties of the substrate surface, (3) the contact area between the pads and the substrate, (4) the weight of the pads, and (5) the time intervals of creeping. When the hydrogel pads sticking on a flat surface are held vertically, the pads' weights promote the gradual and usually slow downward movement due to gravity call “creeping”. The weights of the pads act as shear forces that pull the pads downward against the adhesive forces act perpendicularly to hold the pads with the substrate and resist the creeping. The rates of downward creeping are given in Figure 10. To make it easier to comprehend, we also calculated the rates of creeping of pads of a fixed 1-cm width. The rates are reported as percentage of the creep depth relative to the pads' height per gram of pads' weight per hour since the creep depths and the pads' height are parallel.

As expected, stronger adhesive surfaces resist weight-promoted creeping to larger extents. Pads with higher adhesive forces exhibit slower rates of creeping. Both type of creeping rates reveal that the

pads adhesive forces are the major factor that resist the pads' downward creeping. The average rate of the 0.2-wt% hydrogel pads is significantly lower than that of the OM-free pads despite their insignificantly-higher adhesive forces. The OM-free pad (1-cm width) creeps continuously at approx. 10.23 times of its height per gram of the pad's weight per hour whereas the 0.2-wt% pad (1-cm width) creeps at a slightly lower rate of 9.82 times of its height per gram of the pad's weight per hour. Note that the pad's height refers the pad's dimension aligned vertically during the course of creeping, not the pad's thickness.

Effect of OM Additive on Adhesive Forces, Water Contents, Water Holding Capacities and Rates of Moisture Loss

At certain concentration of OM powder, the additions of OM powder lead to the increase in the number of “free” hydroxyl groups (-OH). In OM-hydrogel, there are 3 sources of free hydroxyl groups: (1) those on the surfaces of added OM granules, (2) those already present on XG or CN without the OM granules, and (3) those arising from the irregularity in the XG/CN hydrogel network caused by the presence of OM granules.

At lower OM concentrations, the total number of free hydroxy groups is small because most of Group 1 hydroxyl groups form hydrogen bond with the XG/CN network and are no longer free hydroxyl groups. A portion of Group 2 hydroxyl groups is hindered by the presence of OM granules. Group 3 hydroxyl group is also small in number because small structural irregularities in the hydrogel network are created with low concentration of OM. These concepts are summarized graphically in Figure 11(a).

When the concentration of OM granules is high enough (Figure 11(b)), there are free-floating OM granules with free hydroxyl groups. These free

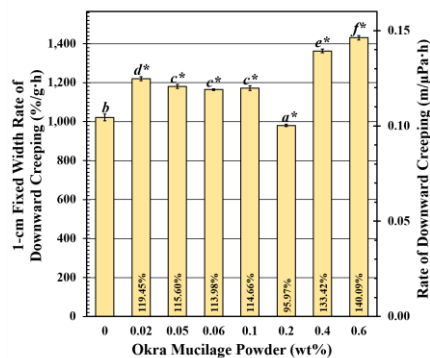


Figure 10. Rates of downward creeping of the OM-hydrogel pads on a clear acrylic substrate

hydroxyl groups contribute to pads' higher water affinity and are responsible for the higher water contents and the lower rates of moisture loss. They also contribute to stronger pads' adhesive force.

When the OM concentrations are too high (Figure 11(c)), OM granules can form hydrogen bond with each other and with the XG/CN hydrogel network and the number of total free hydroxyl groups decrease as a result. The reduction in number of free hydroxyl groups leads to the drops in water affinity which, in turn, lead to lower water contents and faster rates of moisture loss. Smaller number of free hydroxyl groups at the surface of the pads also make the pads less adhesive.

The too-low and too-high OM concentrations can cause the pads' adhesive force and/or water contents to drop below those of the OM-free counterpart.

Conclusions

XG/CN-based hydrogel formulation containing 0.5 wt% XG, 0.5 wt% CN, 13 wt% glycerol, 4 wt% NaCl and 1 wt% phenoxy ethanol is used to study the effects of OM powder on the hydrogel network. OM powder was added to the hydrogel colloidal solution and thoroughly mixed before casting. Amounts of OM additive ranges from 0.02 to 0.6 wt%. The incorporation of OM powder results in extensive losses of the pads' hardness whereas the average adhesive force of the 0.2-wt% pads (143.08 ± 8.77 N) is slightly higher than that of the OM-free reference pads although the 2 values are not significantly different. The water contents are highest in 0.2-wt% pads (17.66 ± 0.47 wt%) whereas the water holding capacities are highest in 0.2-wt% and 0.4-wt% pads (52.98 ± 1.63 wt% and 51.72 ± 1.31 wt%, respectively). Among OM-hydrogel pads with harnesses more than 150 N, the 0.2-wt% pads exhibit the lowest average rate of moisture loss. The average rate of weight-promoted downward creeping of the 0.2-wt% pads is also the lowest. Despite its relatively soft hydrogel network (203.84 ± 14.54 N), the XG/CN-based hydrogel formulation containing 0.2 wt% OM powder is of highest potential for topical administration of active compounds for cosmeceutical or biomedical applications

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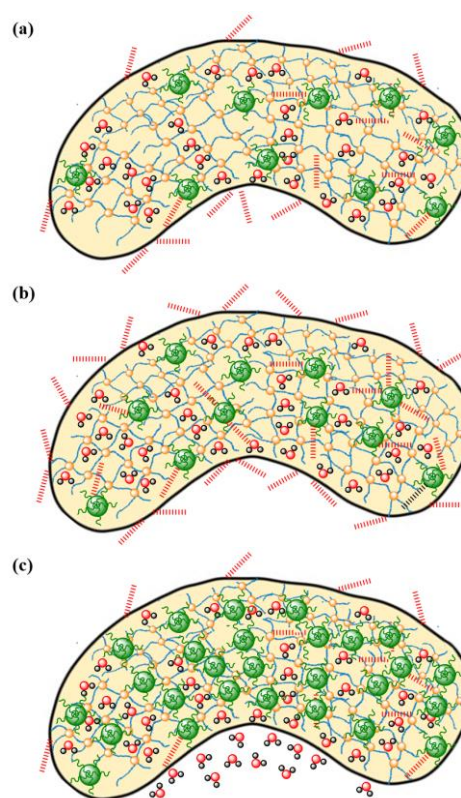


Figure 11. Chemical interactions among XG/CN hydrogel network, OM granules, and water molecules: (a) too-low, (b) optimal, and (c) too-high OM concentration

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