polysaccharides

Article

Formulation and Physical Characterization of a Polysaccharidic Gel for the Vehiculation of an Insoluble Phytoextract for Mucosal Application

Giovanna Pressi [1], Elisa Barbieri [1], Raffaella Rizzi [1], Giovanni Tafuro [2,*], Alessia Costantini [2], Elisa Di Domenico [3] and Alessandra Semenzato [3]

[1]   Aethera Biotech S.r.l., via Dell'innovazione 1, 36043 Camisano Vicentino, Italy
[2]   Unired S.r.l., via Niccolò Tommaseo 69, 35131 Padova, Italy
[3]   Department of Pharmaceutical and Pharmacological Sciences, University of Padova, via Marzolo 5, 35131 Padova, Italy
*   Correspondence: giovanni.tafuro@unired.it; Tel.: +39-334-6812046

Abstract: Maintaining insoluble plant-based ingredients in suspension and ensuring long-term physical stability is particularly challenging for formulators of green cosmetics. This study aimed to evaluate the structure and applicative properties of gel and gel-cream topical formulations suitable for delivering an insoluble phytocomplex on the vaginal mucosa and maintaining its integrity. For this purpose, we studied the compatibility of *Perilla frutescens* (L.) Britton phytocomplex (PFP), derived from in vitro plant cell cultures and presented as a powder finely dispersed in glycerin, with different classes of natural rheological modifiers (such as xanthan gum, sclerotium gum, succinoglycan, xyloglucan, diutan gum, hydroxypropyl guar gum derivative) in gel and gel-cream formulations, to meet the needs of the cosmetic market for naturalness and biodegradability. Through rheological and texture analyses, we studied the physico–mechanical properties of the samples, comparing the performances of the chosen polysaccharides to those of acrylic polymeric rheological modifiers, evaluating their contribution in terms of stability and applicative properties. Since a weak-gel rheological pattern proved to be the optimal one to keep the actives in suspension, the associations of tamarind seed polysaccharides with succinoglycan or scleroglucan were the most suitable for the formulation of mucoadhesive gels.

Keywords: green cosmetics; rheology; texture; stability; *Perilla frutescens*; phytocomplex; in vitro plant cell culture

1. Introduction

In recent years, when it comes to the purchase decision of cosmetic products, consumers are increasingly trying to make informed choices, not only in terms of safety and efficacy, but also in terms of respect for our environment. In this context, green cosmetics have become a popular trend and the use of plant-based actives is in great demand [1]. Plant-based ingredients have been known for many years in the pharmaceutical and cosmetic fields for their well-documented biological effects and their use in today's products is appealing [2]. Traditional plant extracts have extreme variability in the phytocomplex composition, depending on factors such as climate, soil, and cultivation techniques. This variability cannot always guarantee the efficacy of the extract in healthcare applications [3]. Plant cell culture technology is a technique for plant cell growth under strictly controlled environmental conditions that makes it possible to obtain preparations with a standardized content of active substances and a high consumer safety profile [4]. However, during the formulation process with these active ingredients, manufacturers may encounter some difficulties due to dispersion problems, instability phenomena, or the interaction with other components of the vehicle leading to long-term instability [5–8]. It is, therefore, extremely

important during the product development design to evaluate a rational inclusion of these actives in the formula, considering any incompatibility phenomena, to achieve the required stability and efficacy objectives [9,10]. The long-term stability of a cosmetic formulation is a compulsory requirement to guarantee product safety, but the stability testing protocols are time-consuming procedures.

Hydrophilic polymers are commonly used in cosmetic formulations for their stabilizing properties, acting as rheological modifiers and suspending agents for insoluble active ingredients. Hydrophobic particles, in fact, due to their non-polar chemical nature, tend to aggregate together with the aim of minimizing contact with the aqueous phase, causing instability phenomena, such as flocculation or sedimentation. Thanks to their ability to coordinate water molecules and form a thick three-dimensional network, Synthetic acrylic polymers have been used over the years to help the dispersion of the hydrophobic particles in water by increasing their wettability and solubility, forming protective colloids, and increasing the viscosity of the system to slow down the movement and aggregation of the particles, thus stabilizing the formula [11]. These properties strictly depend on the polymer molecular weight, cross-linking degree, and chemical substitution [12].

Alongside these numerous undoubted functional advantages, non-biodegradable acrylic polymers of synthetic origin are frowned upon by public opinion, especially now that the concern for environmental issues is continuously growing. If we consider that the European Chemicals Agency (ECHA), is currently considering whether to also include in the definition of microplastics many non-biodegradable non-solid synthetic polymers that can be dispersed or emulsified in cosmetic formulas with functional purposes, we understand the urgency for cosmetic industries to quickly find sustainable alternatives in a time and money-saving way [13]. Polysaccharides are biodegradable multipurpose ingredients widely used in green products for their functional characteristics, such as swelling and hydration. They have been proposed as moisturizing agents, thickeners, stabilizers, and texturizers in the cosmetic and pharmaceutical fields [14,15]. However, matching the performances of synthetic polymers, in terms of thickening, adhesive, and suspending properties, by using polysaccharides can be quite challenging. Synthetic polymers, in fact, are artificially created to play specific roles in a formulation. On the other hand, natural polymers must be calibrated and evaluated before being used in cosmetics, carefully choosing the ones that best fit the formulation design in terms of mechanical and sensorial properties. If not properly calibrated, in fact, many polysaccharides can negatively impact on the skin feel of the product, which can be sticky and unpleasant during application, showing a stringy behavior that has repercussions on consumers' acceptability [16].

In this context, the priority for manufacturers is to study and characterize, with time-saving and reproducible tools, these natural raw materials proposed on the market, evaluating the potentiality of their use as alternatives to synthetic polymers without losing the stability and applicative aspects. Physico–mechanical characterization of cosmetic formulas by means of rheological and texture analyses is useful to predict the contribution of new raw materials to the formulations, and they can be used successfully to help the cosmetic product design [17–20]. Rheological measurements, performed both in continuous and oscillatory flow conditions, are used to study the flow behavior and viscoelastic properties of semi-solid materials, and hence, evaluate the products' stability properties [21–23]. Texture analysis, commonly used in the food industry, has been introduced in the cosmetic field to study the mechanical properties of products during pick-up and application, such as firmness, consistency, adhesiveness, cohesiveness, and stringiness, which are linked to their usability and sensory characteristics [24–26].

The aim of this work was to evaluate the ability of different classes of natural hydrophilic rheological modifiers, used alone and in associations, to keep *Perilla frutescens* phytocomplex (PFP), a powder finely dispersed in glycerin, with anti-inflammatory and repairing activity, in suspension. *Perilla frutescens* (L.) Britton, also known as Shiso, is a specie of Perilla that belongs to the Lamiaceae family, commonly used as an aromatic and

medical plant. Perilla has historical importance in Chinese medicine, as it was recorded as a drug around 500 A.D. [27]. Some Perilla-based products are widely used to treat seasonal allergy symptoms and aphthae [28]. The presence of phenolic compounds, flavonoids, and anthocyanins in *Perilla frutescens* is amply documented in the scientific literature [29]. *Perilla frutescens* phytocomplex (PFP), produced by in vitro plant cell culture technology, is characterized by a high and standardized content of rosmarinic acid and anthocyanins and can be used as a new cosmetic ingredient with sustainable and safety features related to the production process, free from pesticides, contaminates and residual solvents, maintaining the same biological efficacy in all batches.

Starting from those concepts, our scope was to prepare cosmetic base formulas suitable for the preparation of cosmetic products intended to be applied on the vaginal external mucosa for hygiene, protection, and lenitive functions. The use of mucoadhesive polymers is common in vaginal semi-solid products with several advantageous features such as barrier effect, biocompatibility, and prolonged retention of active ingredients in situ [30]. Various synthetic polymers such as acrylic derivates, poloxamer, poly(vinyl alcohol), and poly(vinyl pyrrolidone) have conventionally been used for this scope, thanks to their ability to form strong hydrogen bonds with the mucosal layer [31]. Polysaccharides can also efficiently influence the mechanism of mucoadhesion; chitosan, alginate, and cellulose derivatives are the most common polysaccharides used as mucoadhesive ingredients in pharmaceutical and cosmetic products [32]. In this study, we prepared gel and gel-cream formulas using three different polymer classes: a synthetic polymer (carbomer), natural polysaccharides (xanthan gum, succinoglycan, sclerotium gum, diutan gum, and tamarindus seed polysaccharide) and a semi-synthetic polymer (C18–C22 hydroxyalkyl hydroxypropyl guar). Xanthan gum is an extracellular polysaccharide obtained by fermentation of the bacterium *Xanthomonas campestris* and consisting of a β-1,4-glycosidic bond-linked main chain and a trisaccharide side chain of two mannose and glucuronic acid. Noncarbohydrate substituents include an acetyl group on the inner mannose and a pyruvate group on the terminal mannose [33]. Succinoglycan is an octasaccharide produced by bacteria belonging to the family Rhizobiaceae (Rhizobium, Agrobacterium), composed of one galactose residue and seven glucose residues, with acetyl, succinyl, and pyruvyl substituents [34]. Sclerotium gum is a nonionic polysaccharide produced by fermentation of the filamentous fungus Sclerotium rolfsii and characterized by a linear chain of β-(1,3)-D-glucose with a single β-(1,6)-D-glucose every third unit [35]. Diutan gum is a natural gum produced by aerobic fermentation of Sphingomonas, consisting of a tetrasaccharide backbone of glucose, glucuronic acid, mannose, and rhamnose, and a side chain of two units of rhamnose [36]. Tamarind seed polysaccharide is a xyloglucan composed of a glucose backbone with xylose branches that are partially substituted with galactose and is obtained from the endosperm of the seed of the tamarind tree, *Tamarindus indica* L.; it was used in this work for its mucin-like structure to confer mucoadhesive properties to the formulations [37,38]. C18–C22 hydroxyalkyl hydroxypropyl guar is a chemically modified galactomannan with emulsifying properties, extracted from the seeds of Cyamopsis tetragonoloba, a native plant of India, consisting of a mannose backbone with side groups of galactoses (ratio of 1:2) branched on the six positions [39].

The first step was to prepare and analyze aqueous dispersions of the selected polymers used individually at increasing concentrations to study their physical–mechanical properties and their structuring capacity. Then we prepared binary associations of the aforementioned polymers with tamarind seed polysaccharide to confer mucoadhesive properties to the systems. We then evaluated the suspending capacity of the polysaccharides in the association and the effect of the insertion of the active PFP on the structure, texture, and stability properties of the system. In the second phase, the polysaccharides that showed greater suspending and stabilizing capacity were used in binary and ternary associations with an oily phase to prepare cream–gel systems. We evaluated the stability of the obtained systems, focusing on the compatibility between PFP and these polymers. The combined use of rheological and texture analyses in the cosmetic field is still not widespread and scientific

articles investigating the texture properties of polysaccharide mixtures are still limited. We studied the applicative properties of the systems in terms of spreading, viscoelastic, and adhesive properties by means of rheological and texture analyses, comparing the performances of the chosen polysaccharides to those of the acrylic polymer.

2. Materials and Methods

2.1. Materials

Perilla frutescens phytocomplex (PFP): ReSILiEMcare CROP®-G (INCI name: Glyceryn, *Perilla frutescens* Callus Lysate) supplied by Aethera Biotech s.r.l. (Camisano Vicentino, Italy), derived from in vitro plant cell cultures of meristematic cells of *Perilla frutescens* (L.) Britton [40].

To simplify comprehension of the results, the polymers are identified with a letter of the alphabet. Synthetic rheology modifier: U—Carbopol® Ultrez10 (INCI name: Carbomer) by Lubrizol (Wickliffe, OH, USA). Natural polymers: R—Rheozan® SH (INCI name: Succinoglycan gum) by Solvay Novecare (Princeton, NJ, USA); A—Actigum™ CS11 QD (INCI name: Sclerotium gum) by Cargill (Wayzata, MN, USA); X—Keltrol® TF (INCI name: Xanthan gum) by CP Kelco (Atlanta, GA, USA); D—KELCO-CARE™ Diutan gum (INCI name: Sphingomonas Ferment Extract) by Lubrizol; T—Xilogel® HS (INCI name: *Tamarindus indica* seed polysaccharides) by Indena (Milan, Italy). Semi-synthetic polymer: E—Esaflor® HM 22 (INCI name: C18–C22 Hydroxyalkyl Hydroxypropyl Guar) by Lamberti (Zanica, BG, Italy).

Emollients: Cetiol® Sensoft (INCI name: Propylheptyl Caprylate) by BASF (Ludwigshafen am Rhein, Germany); Dub™ MCT 5545 (INCI name: Caprylic/capric triglyceride) by Stearinerie Dubois (Boulogne-Billancourt, France).

Preservatives: Euxyl™ pe 9010 (INCI name Phenoxyethanol, Ethyhexylglycerin) by Ashland (Wilmington, DE, USA)

2.2. Perilla Frutescens Phytocomplex Preparation

The stabilized and highly selected cell line specified on the synthesis of rosmarinic acid and anthocyanins was obtained from dissected young *Perilla frutescens* leaves sanitized by means of treatment in sequence with 70% (v/v) ethanol (Honeywell, Wunstorfer Straße 40, D-30926 Seelze, Germany) in water for about 1 min, 2% (v/v) of sodium hypochlorite solution (6–14% active chlorine), (MERCK KGaA, 64,271 Darmstadt, Germany) and 0.1% (v/v) Tween 20 (Duchefa, Postbus 809, 2003 RV-Haarlem, The Netherlands) for 2–3 min and, finally, at least three washes with sterile distilled water. *Perilla frutescens* cell culture obtained at the end of the fermentation process in liquid selected cell culture medium was collected, filtered by 50 μm mesh filter, and the medium cultures were discarded. Cells were washed with a double volume of saline solution (0.9% w/v NaCl in sterile water) and added with 1.5% (w/w) of citric acid and then homogenized with ultraturrax at 15,000 rpm for 20 min. The biomass of homogenized cells was dried using a Mini Spray Dryer (BUCHI-B290) to obtain a powder of PFP (particle size range between 10 and 100 μm) with the content of total polyphenols expressed as rosmarinic acid equivalent ≥2.3%. The percentage of rosmarinic acid in total polyphenols was 85%. The PFP powder was suspended in vegetable glyceryn to obtain a standardized product with a content of total polyphenols expressed as rosmarinic acid equivalent ≥0.1%.

2.3. Samples Preparation

Gel formulations were prepared with different amounts of each rheology modifier, according to the concentration ranges reported in the technical data sheets: U at 0.25–0.5–0.75–1% w/w. R at 0.5–0.75–1–1.5% w/w; A at 1–1.25–1.5–2–2.5% w/w; X at 0.5–1–1.5–2% w/w; D at 0.25–0.5–0.75–1% w/w; T at 2–2.5–3% w/w; and E at 0.5–0.75–1–1.5% w/w. The rheology modifiers were added to the water under light stirring at room temperature.

Gel formulations with *Tamarindus indica* polysaccharides and the rheology modifiers with and without the plant-based active ingredient PFP were prepared, as indicated in Table 1. Water was weighed and heated at 60 °C, then glycerin was mixed with the rheology modifier and added to the water under light stirring. PFP glycerin suspension was added

and mixed with a stirrer. The preservative (Phase B) was added to phase A. Once the gel was cooled down, the pH was measured and adjusted at 5.5 with phase C, if necessary.

Table 1. Reference formula for gel formulations.

Phase	Ingredients	Composition %
	Water	Add until reaching 100
	Glycerin	3
A	*Tamarindus indica* seed polysaccharides	0.5
	Rheology modifier	Varies
	PFP	0–3
B	Phenoxyethanol, Ethyhexylglycerin	0.9
C	Buffering agent	Add until reaching pH 5–5.5

The active ingredient was also added in gel–cream formulations according to the reference formula in Table 2. Water was weighed and glycerin was mixed with the rheology modifiers and added to the water under light stirring. Phase B was added to phase A by stirring at 4200 rpm for five minutes by means of Silverson L5T homogenizer until complete homogeneity. PFP glycerin suspension (phase C) was added and mixed with a stirrer until well dispersed. The preservative (phase D) was added. Once the emulsion was cooled down, the pH was measured and adjusted with phase E, if necessary.

Table 2. Reference formula for gel–cream formulations.

Phase	Ingredients	Composition %
	Water	Add until reaching 100
	Glycerin	3
A	Esaflor HM 22	0.3–0.5–0.7
	Tamarindus indica seed polysaccharides	0–0.2
	Rheology modifier	0–0.2
B	Propylheptyl Caprylate	2
	Caprylic/capric triglyceride	0.5
C	PFP	0–3
D	Phenoxyethanol, Ethyhexylglycerin	0.9
E	Buffering agent	Add until reaching pH 5–5.5

A mechanical stress test was performed to check the samples' stability by using the centrifuge MPW-56 of MED at 4800 RPM for 30 min.

2.4. Rheological Analyses

The rheological tests were performed with a Rheometer MCR e302 from Anton Paar (Anton Paar GmbH, Graz, Austria) at a controlled temperature of 23 °C $\pm$ 0.05 °C. Tests were conducted both in continuous and oscillatory flow conditions using a CP50-1 sensor consisting in a parallel plate geometry with a fixed gap of 0.1 mm. The viscosity values (η) and the flow properties were measured with controlled shear rate tests (CSR), at increasing shear rate ranging from 0.001 to 1000 s^{-1}. The zero-shear viscosity, i.e., the viscosity of

the material at rest, was calculated by fitting the flow curves with the Carreau−Yasuda mathematical model applicable to shear-thinning materials [41].

$$\tau = \eta_\infty \dot{\gamma} + \frac{(\eta_0 - \eta_\infty)\dot{\gamma}}{\left[1 + (\lambda\dot{\gamma})^2\right]^{\frac{1-n}{2}}} \tag{1}$$

Amplitude sweep tests (AS) were performed, increasing strain (γ) from 0.01% to 1000%, at a fixed frequency of 1 Hz, to identify the samples' linear viscoelastic region (LVER) and the critical strain (γ G' = G''). Frequency sweep tests were performed decreasing frequency from 10 Hz to 0.01 Hz, at a fixed strain inside the LVER, to analyze the emulsions' inner structure and the trend of storage (G') and loss (G'') moduli.

2.5. Texture Analyses

An immersion/de-immersion test was conducted at room temperature by means of a Texture Analyzer TMS-Pro, from Food Technology Corporation (Sterling, VA, USA) equipped with a 2 cm diameter, nylon, spherical probe, using a load cell of 10N. The probe moved vertically to a depth of 10 mm at a rate of 80 mm min^{-1} inside the samples loaded in 50 mL containers (5.3 cm diameter) and then returned to its start position. Texture Lab Pro was used to collect the data and elaborate a curve plotted as load (N) vs. cumulative displacement (mm) (Figure S1). Firmness (N) is the maximum value of force; consistency (N.mm) is the area under the positive curve; cohesiveness (N) is the negative peak; adhesiveness (N.mm) is the area under the negative portion of the curve; stringiness (mm) is the extension of the filament the sample formed during the de-immersion phase [42,43].

3. Results and Discussion

3.1. Gel Formulations

Before approaching the formulation phase, the characterization of the physical and mechanical properties of the single raw materials through rheological measurements is useful to understand the contribution of each polymer to the final product. The mechanical spectra registered for the water dispersions of the different polymers at increasing concentrations are shown in Figure S2. The frequency sweep tests were conducted by choosing a strain value that falls within the linear viscoelastic region (LVER), in which the trend of both the elastic G' and the viscous G'' moduli does not change irreversibly. The higher the polymers' concentrations, the higher the moduli values since stronger intermolecular interactions between the polymeric chains and water molecules are possible. For the polymers U (carbomer), A (sclerotium gum), D (diutan gum), R (succinoglycan), and X (xanthan gum), G' was larger than G'' throughout the entire range of frequencies investigated, indicating that the elastic components of the networks formed always dominated over the viscous components. This structure is optimal to keep an active ingredient in suspension [44]. For the synthetic polymer. The storage modulus G' remained constant, while the loss modulus G'' showed a slight increase in the frequency, with a characteristic minimum at around 1 rad s^{-1} (Figure S2a). This behavior indicates that the microgel structure is held by strong ionic interactions, as reported in previous studies on cross-linked acrylic polymers [45]. The rheological moduli of the polysaccharides were significantly lower than those of the synthetic polymers and settled between the first and the second decades. They showed almost parallel moduli dependent on the frequency applied (Figure S2b–e). This behavior is typical of the so-called weak gels, whose structure is held by physical bonds. The moduli of polymer D tended to progressively approach as the oscillation frequency decreased, which could indicate a lower stabilizing capacity over time (Figure S2c). The polymer R was able to form stiffer and more elastic systems if compared to the other polysaccharides used at the same concentrations (Figure S2d). By increasing the amount of X, there were only a few variations of the moduli values because the system was saturated at 1.5% *w/w* of polymer concentration (Figure S2e). The viscoelastic moduli of the semi-synthetic

polymer E (C18–C22 hydroxyalkyl hydroxypropyl guar) were significantly dependent on the frequency (Figure S2f). G′ was predominant at higher frequencies and G″ modulus became higher than G′ when low frequencies were applied. By increasing the polymer concentration, a shift of the cross-over point to lower frequencies was detected, thus indicating an increase in the elastic character of the system. The dispersions of polymer T (*Tamarindus indica* seed polysaccharides) showed a liquid-like behavior with G″ always dominating over G′ (Figure S2g). As the concentration increased, the elastic components of the polymer became progressively greater at high frequencies. The rheological response of these last two polymers E and T is commonly associated with viscous and flowing systems with marked mucoadhesive properties.

To achieve the purpose of this work and formulate a system with adhesive properties and stable over time, gels were prepared containing binary associations between a weak gel polysaccharide, whose rheological profile is the most suitable for maintaining an insoluble active ingredient in suspension, and tamarind seed polysaccharide (T) with moisturizing and mucoadhesive properties. A comparison between the rheological curves obtained with the frequency sweep analyses performed on the monodisperse systems and the binary association with T at the same total polymer amount is reported in Figure 1. All the gels analyzed showed a mainly elastic behavior, as the G′ modulus was always greater than the G″ modulus in the frequency range considered. However, the partial replacement with 0.5% of T resulted in a modulation of the viscoelastic properties: a significant decrease in both modules could be observed, indicating a loss of elasticity and the structuring degree of the system. This reduction was less marked for the gel containing R, which, even in association with T, maintained its viscoelastic properties (Figure 1d).

To find the correct viscosity to maintain the active ingredient PFP at 3% w/w in suspension, gel formulations were prepared at a fixed concentration of polymer T (0.5% w/w) to provide mucoadhesion, with different concentrations of each rheology modifier. Centrifuge tests at 4500 rpm for 30 min were carried out to evaluate the stability of the gels, and the results are listed in Table 3. All the gels formulated with the synthetic acrylic polymer U were homogeneous and stable. Among the natural polymers, the only ones to allow homogeneous dispersion of the active and guarantee stability to the centrifuge test were sclerotium gum (A) at 2.5% w/w and succinoglycan (R) at 1% w/w. The gels that failed the centrifuge test had a precipitate of the powder of the active ingredient PFP.

Frequency sweep analyses were carried out on the gel samples that were stable in the centrifuge test or showed negligible, slight sedimentation. The analyses were performed, increasing the oscillation frequency and maintaining the amplitude strain constant at a strain within the LVE region previously determined by the amplitude sweep analysis. In Figure 2a comparison between the rheological parameters measured for the samples with and without the phytocomplex PFP is shown. The complex modulus (G*) and the loss factor (tanδ) values were taken at a frequency of 1.5 Hz. G* is defined as the ratio between the total stress and the strain to which the material is subjected at a given frequency and describes the entire viscoelastic behavior of the sample (Figure 2a). The gels with polymers U and A were those with the highest G* values, indicating more structured and stiffer systems. G* significantly decreased when PFP was added to the sample containing the polymer U, whereas it increased when PFP was added to the samples containing polymer D, R, and polymer X. Tanδ is a rheological parameter that describes the ratio between the viscous and the elastic modulus; values of tanδ < 1 correspond to viscoelastic or gel-like behavior. The lower the tanδ, the greater the influence of the elastic component; the higher the tanδ, the greater the influence of the viscous component (Figure 2b). The gels formulated with U, A, and R showed lower values of tanδ, thus indicating more elastic systems, and for this reason, they were stable in the centrifuge test when the active ingredient was added. Tanδ slightly increased when PFP was added to the samples containing U, A, and D, whereas it decreased when PFP was added to the samples containing R and X. The insertion of the phytocomplex determined both quantitative changes in the gel structure, as evidenced by the G* values, and qualitative, as shown by the tanδ values.
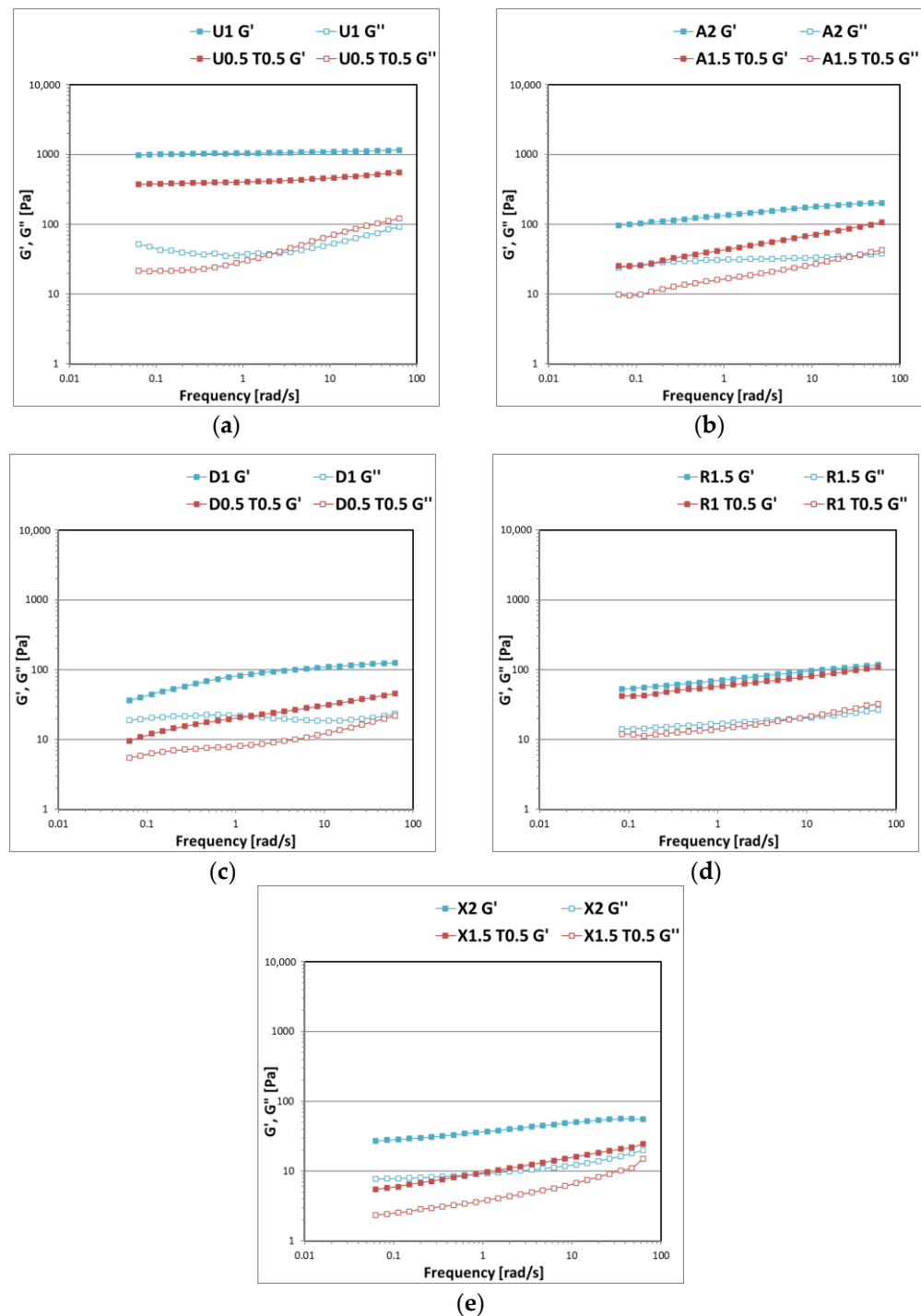
Figure 1. The trend of elastic G′ and viscous G″ moduli in the function of the frequency applied for samples containing a weak-gel polysaccharide alone and in association with tamarind seed polysaccharide (T): (**a**) comparison between the gel containing U at 1% *w*/*w* (U1) and the gel containing U at 0.5% *w*/*w* with T at 0.5% *w*/*w* (U0.5 T0.5); (**b**) comparison between the gel containing A at 2% *w*/*w* (A2) and the gel containing A at 1.5% *w*/*w* with T at 0.5% *w*/*w* (A1.5 T0.5); (**c**) comparison between the gel containing D at 1% *w*/*w* (D1) and the gel containing D at 0.5% *w*/*w* with T at 0.5% *w*/*w* (D0.5 T0.5); (**d**) comparison between the gel containing R at 1.5% *w*/*w* (R1.5) and the gel containing R at 1.5% *w*/*w* with T at 0.5% *w*/*w* (R1.5 T0.5); (**e**) comparison between the gel containing X at 2% *w*/*w* (X2) and the gel containing X at 1.5% *w*/*w* with T at 0.5% *w*/*w* (X1.5 T0.5).

Table 3. Summary of the gel formulations and results of centrifuge stability test.

Polymer	Polymer % *w/w*	T % *w/w*	PFP % *w/w*	Stability
U	0.25	0.5	3	homogeneous
	0.5			homogeneous
	0.75			homogeneous
A	1	0.5	3	sedimentation
	1.5			sedimentation
	2			sedimentation
	2.5			homogeneous
D	0.25	0.5	3	sedimentation
	0.5			sedimentation
	0.75			slight sedimentation
R	0.5	0.5	3	sedimentation
	0.75			sedimentation
	1			homogeneous
X	1	0.5	3	sedimentation
	1.5			sedimentation
	2			slight sedimentation
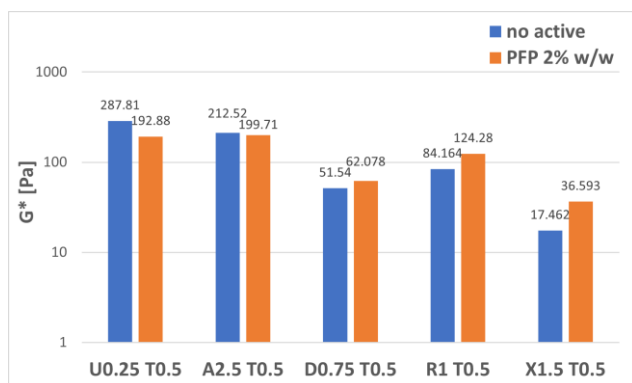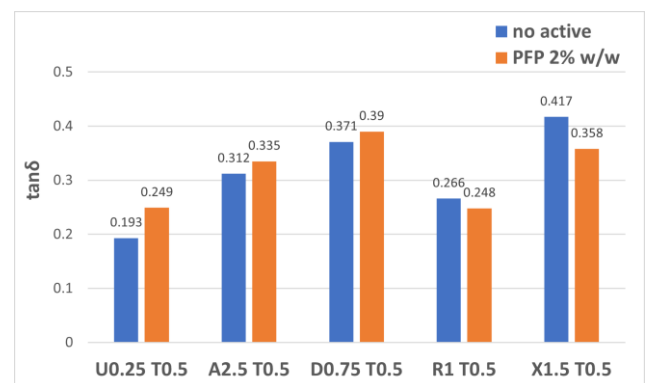
Figure 2. Comparison between the rheological parameters measured before and after adding 2% *w/w* of PFP for the gels U0.25T0.5 prepared with U at 0.25% *w/w* and T at 0.5%, A2.5T0.5 prepared with A at 2.5% *w/w* and T at 0.5% *w/w*, D0.75T0.5 prepared with D at 0.75% *w/w* and T at 0.5% *w/w*, R1T0.5 prepared with R at 1% *w/w* and T at 0.5% *w/w*, X1.5T0.5 prepared with X at 1.5% *w/w* and T at 0.5% *w/w*: (**a**) complex modulus G* and (**b**) damping factors tan δ calculated at 1.5 Hz.

This behavior was confirmed with the texture analyses performed on the gel formulations before and after the insertion of PFP in the formulation (Figure 3). The samples containing the polymers A and U showed the highest values of firmness, whereas the sample containing the polymer X showed the lowest values (Figure 3a). This texture parameter is directly connected with the spreadability of a product: the higher the firmness, the more difficult the application because higher forces are needed to make the product flow on the skin. In the presence of PFP, the firmness of the gels with U, A, and D decreased, whereas it increased for the gels formulated with R. The highest values of adhesiveness were registered for the samples containing U and R, after the insertion of the plant-based active in the formula (Figure 3b).
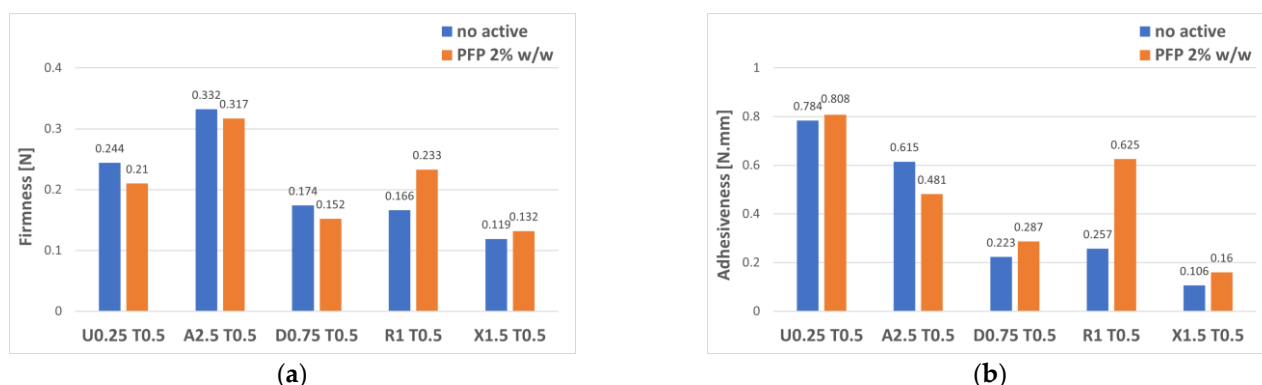
(a)   **(b)**

Figure 3. Comparison between the texture parameters measured before and after adding 2% *w/w* of PFP for the gels U0.25T0.5 prepared with U at 0.25% *w/w* and T at 0.5%, A2.5T0.5 prepared with A at 2.5% *w/w* and T at 0.5% *w/w*, D0.75T0.5 prepared with D at 0.75% *w/w* and T at 0.5% *w/w*, R1T0.5 prepared with R at 1% *w/w* and T at 0.5% *w/w*, X1.5T0.5 prepared with X at 1.5% *w/w* and T at 0.5% *w/w*: (**a**) firmness and (**b**) adhesiveness values obtained through an immersion test.

A comparison between the curves obtained with the texture analyses performed on the gel samples after the insertion of the phytocomplex PFP is reported in Figure 4. The sample formulated with polymer A showed the highest values of firmness and consistency. The sample formulated with U showed the highest values of cohesiveness and adhesiveness. The texture curves of the samples with U and R showed some differences in the negative part of the curve related to the products' adhesive and film-forming properties.
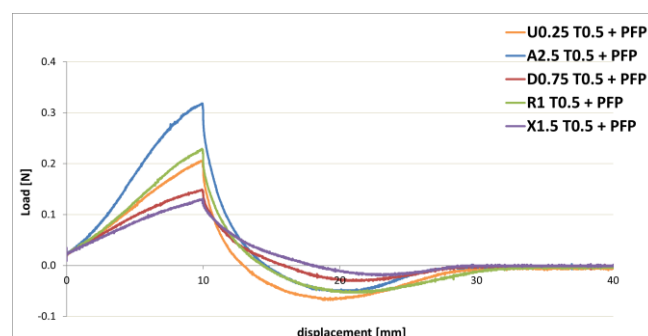

Figure 4. Texture curves obtained from an immersion/de-immersion test performed on the gel formulations containing 2% *w/w* of PFP: comparison between the samples U0.25T0.5 prepared with U at 0.25% *w/w* and T at 0.5%, A2.5T0.5 prepared with A at 2.5% *w/w* and T at 0.5% *w/w*, D0.75T0.5 prepared with D at 0.75% *w/w* and T at 0.5% *w/w*, R1T0.5 prepared with R at 1% *w/w* and T at 0.5% *w/w*, X1.5T0.5 prepared with X at 1.5% *w/w* and T at 0.5% *w/w*.

For the next steps of this work, the polymers D and X were not used since they did not confer the rheological and texture properties suitable for keeping the active in suspension, guaranteeing stability over time and formulating a vaginal gel with mucoadhesive properties. As assessed by the results obtained, A and R gave the system adequate viscosity and good adhesive and spreading properties, very close to those of the synthetic acrylic polymer U, and for this reason, these polysaccharides have been selected for the formulation of gel–cream.

3.2. Gel–Cream Formulations

Since C18–C22 hydroxyalkyl hydroxypropyl guar gum (E) is a synthetically modified polysaccharide with emulsifying properties, it was used as an emulsifier alone and in association with other rheological modifiers under study to formulate light gel–creams. The viscosity of the formulations was assessed by means of controlled shear rate analysis, and the zero-shear viscosity values (η_0) obtained with the Carreau–Yasuda equation are reported

in Figure 5. Comparing the sample with only E and the samples with the rheological modifiers, with the same total concentration of polymer (0.7% w/w), it can be seen how T determined a slight decrease in the viscosity values, while the presence of the weak-gel type polymers caused an increase in the viscosity values. More precisely, polymer R determined significantly higher values of zero-shear viscosity than polymer A.
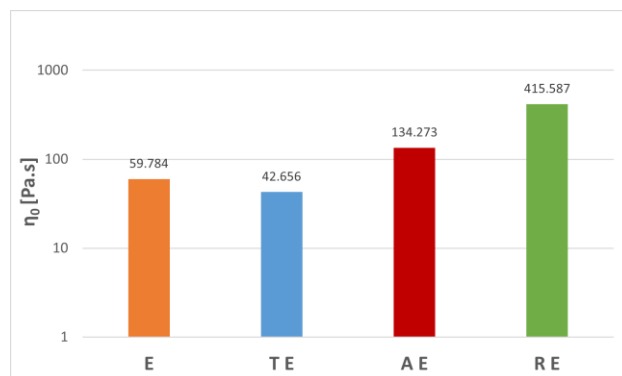

Figure 5. Comparison between the zero-shear viscosity values measured for the gel–creams E prepared with E at 0.7%, T E prepared with T at 0.2% w/w and E at 0.5% w/w, A E prepared with A at 0.2% w/w and E at 0.5% w/w, R E prepared with R at 0.2% w/w and E at 0.5% w/w.

The analyses carried out in oscillatory flow conditions confirmed the greater viscosifying and structuring capacity of the polymers R and A (Figure 6). The gel–cream formulations R E and A E showed the highest values of G* (Figure 6a) and the lowest values of tanδ (Figure 6b), indicating that the presence of these polysaccharides increased the elastic character of the products with respect to the sample prepared using E alone or the one prepared with T.
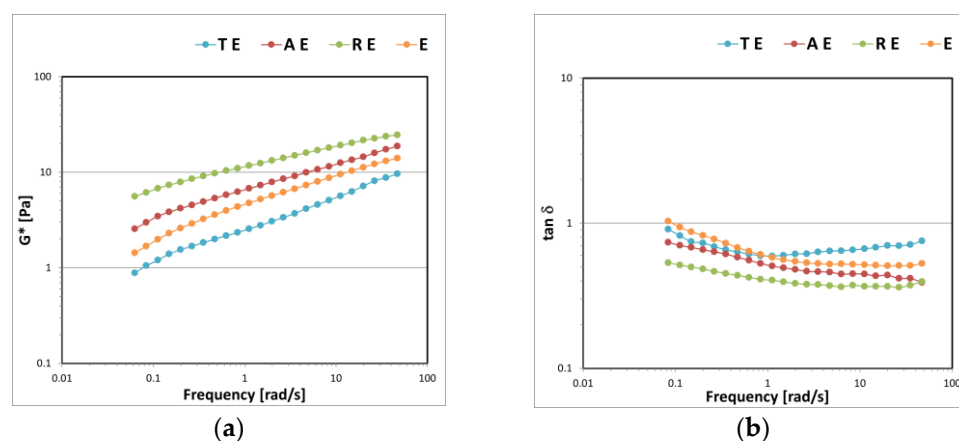

(a)

(b)

Figure 6. The trend of the rheological curves in the function of the oscillation frequency measured for the gel–creams E prepared with E at 0.7%, T E prepared with T at 0.2% w/w and E at 0.5% w/w, A E prepared with A at 0.2% w/w and E at 0.5% w/w, R E prepared with R at 0.2% w/w and E at 0.5% w/w: (**a**) complex modulus G* and (**b**) damping factor tanδ.

The texture analyses performed on gel–cream samples prepared at the same total polymer amount showed that the formulation with the polymer R reached higher values of firmness and consistency. Moreover, by observing the final part of the texture curves reported in Figure 7, it can be seen how the insertion of a rheological modifier determined a decrease in the stringiness values. For the formulations R E the lowest values of stringiness were registered, thus describing a compact, non-sticky, and elastic formulation in accordance with the results of the rheological analyses.
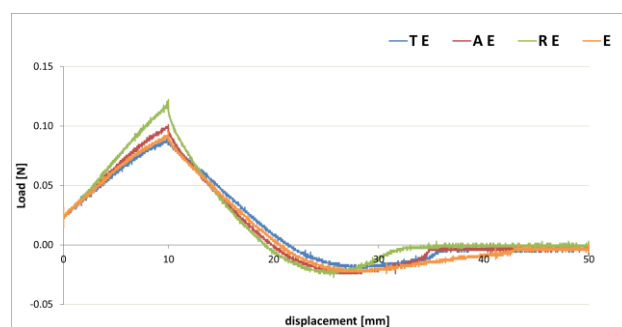
Figure 7. Texture curves obtained from an immersion/de-immersion test performed on the gel–creams E prepared with E at 0.7%, T E prepared with T at 0.2% *w/w* and E at 0.5% *w/w*, A E prepared with A at 0.2% *w/w* and E at 0.5% *w/w*, R E prepared with R at 0.2% *w/w* and E at 0.5% *w/w*.

After adding the plant-based active PFP at 3% *w/w* to the gel–creams formulations, some structural modifications could be seen (Figure 8). The tanδ values of the formulation T E were higher than the other gel–creams and became even higher when the active was added, confirming the liquid-viscous properties of the T polymer (Figure 8a). For the formulations A E and R E there was no significative variation of tanδ after the insertion of PFP. However, a slight decrease in the firmness was detected for all the samples in the presence of PFP, thus, indicating a greater spreadability (Figure 8b). All these samples were stable during the centrifuge test.
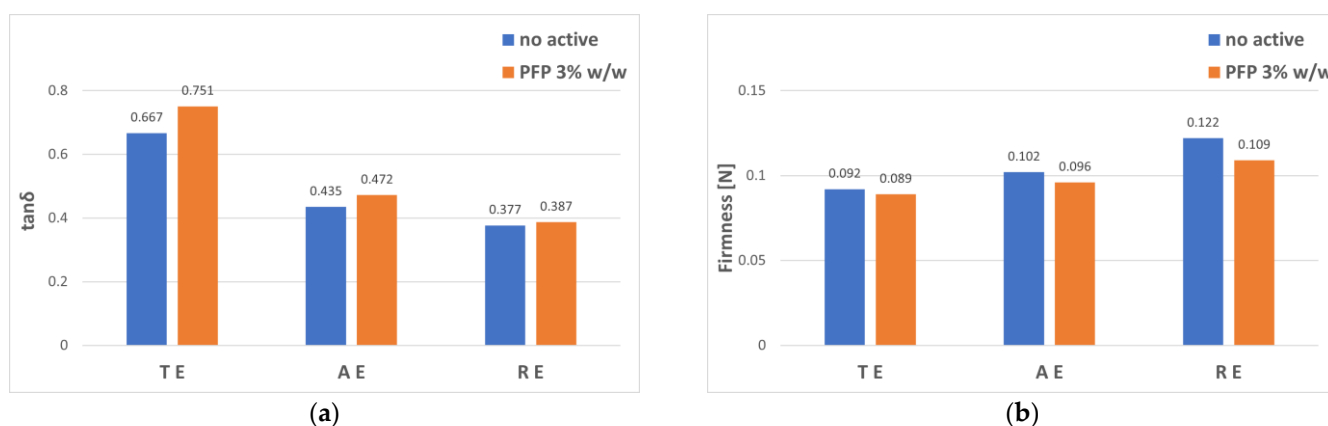

(**a**)

(**b**)

Figure 8. Texture and rheological parameters measured before and after adding 3% *w/w* of PFP for the gel–creams T E prepared with T at 0.2% *w/w* and E at 0.5% *w/w*, A E prepared with A at 0.2% *w/w* and E at 0.5% *w/w*, R E prepared with R at 0.2% *w/w* and E at 0.5% *w/w*: (**a**) damping factor tanδ at 1.5 Hz obtained from the frequency sweep analysis and (**b**) firmness obtained from the texture analysis.

Keeping the total amount of polymer concentration fixed at 0.7% *w/w* we prepared samples by using a ternary mixture of the polysaccharides in order to obtain the best fit in terms of stability of the product, sensorial and mucoadhesive properties. E (C18–C22 hydroxyalkyl hydroxypropyl guar gum) is the emulsifier polymer that allows creating the product's structure, T (tamarind seed polysaccharide) is the polymer that can guarantee mucoadhesion, while A (sclerotium gum) or R (succinoglycan gum) are two polymers that can optimize the stability of the product conferring elasticity to the bulk structure. In Figure 9, the complex G* modulus and the damping factor tanδ values in function of the oscillation frequency of samples prepared with TA E association (Figure 9a) and TR E association (Figure 9b) are reported in comparison with the binary systems. While the TA E system appeared very similar to the T E binary sample, the ternary sample TR E seemed to be the one with the best structural elastic properties, with intermediate viscoelasticity values between the binary gel–creams.
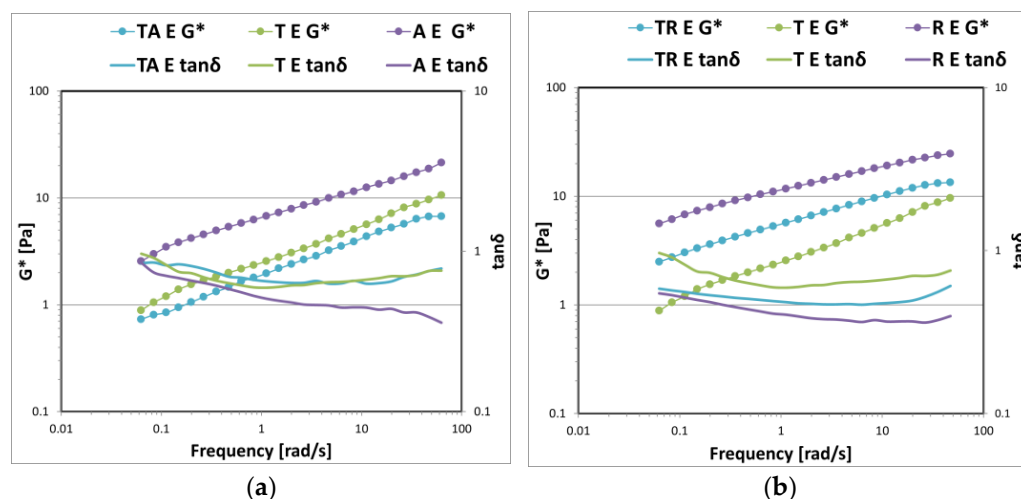
Figure 9. The trend of the complex G* modulus and the damping factor tanδ in the function of the oscillation frequency for the gel–creams prepared with ternary polysaccharides associations: (**a**) sample TA E prepared with T at 0.2% *w/w*, A at 0.2% *w/w* and E at 0.3% *w/w*, sample T E prepared with T at 0.2% *w/w* and E at 0.5% *w/w*, sample A E prepared with A at 0.2% *w/w* and E at 0.5% *w/w*; (**b**) sample TR E prepared with T at 0.2% *w/w*, R at 0.2% *w/w* and E at 0.3% *w/w*, sample T E prepared with T at 0.2% *w/w* and E at 0.5% *w/w*, sample R E prepared with R at 0.2% *w/w* and E at 0.5% *w/w*.

Figure 10 compares the flow curves obtained with a controlled shear rate test and the texture curves obtained with an immersion/de-immersion test performed on the gel–creams prepared with ternary polysaccharidic associations are reported. Both the samples showed a pseudoplastic behavior as viscosity progressively decreased under shear application (Figure 10a). TR E sample reached higher values of viscosity than TA E sample: the zero-shear viscosity values calculated with the Carreau–Yasuda equation in the so-called Newtonian plateau region where the viscosity remained almost constant were 228.264 Pa·s for TR E and 23.065 Pa·s for TA E. The values of firmness, corresponding to the positive load peak measured with the texture analysis, were greater for the TR E association (0.102 N) than for the TA E association (0.087 N), demonstrating the greater structuring power of the R polymer (Figure 10b). TR E also showed higher values of adhesiveness and cohesiveness than TA E. The values of stringiness, on the other hand, did not show significant differences.
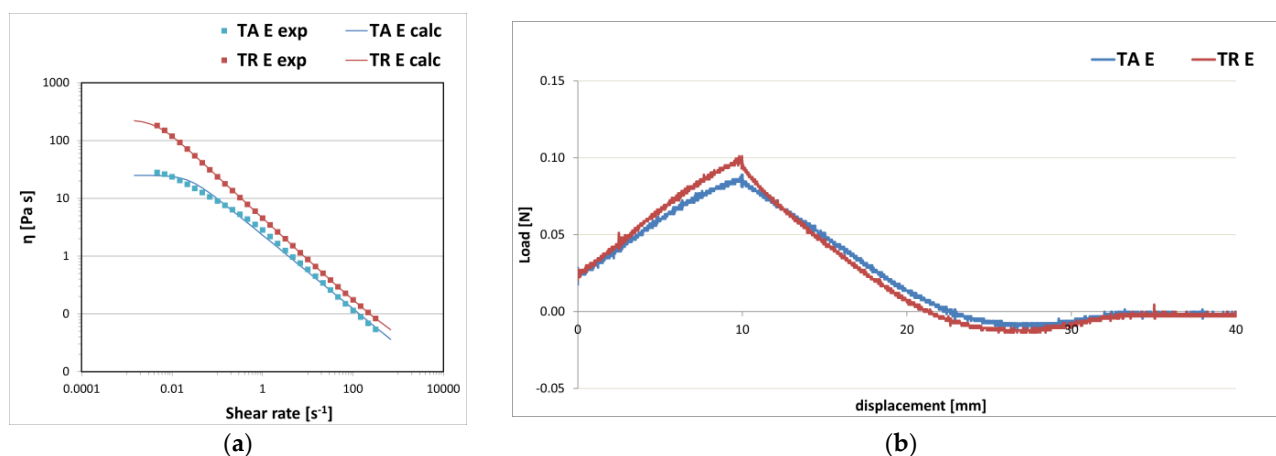

Figure 10. Rheological and texture curves obtained for the gel–creams samples TA E prepared with T at 0.2% *w/w*, A at 0.2% *w/w* and E at 0.3% *w/w* and TR E prepared with T at 0.2% *w/w*, R at 0.2% *w/w* and E at 0.3% *w/w*: (**a**) viscosity curves (exp) as a function of the shear rate fitted with the Carreau−Yasuda model (calc); (**b**) texture curves obtained with an immersion test.

In all the ternary systems, the presence of PFP glycerin suspension did not significantly change the characteristics of the inner structure (Figure 11). The G* values and the tanδ values measured with the frequency sweep rheological tests performed on the associations of TA E (Figure 11a) and TR E (Figure 11b) did not show a significative difference when adding the active phytocomplex PFP. These gel–cream formulations were also stable to the centrifuge test, indicating that these associations of polysaccharides are suitable for keeping the active in suspension.
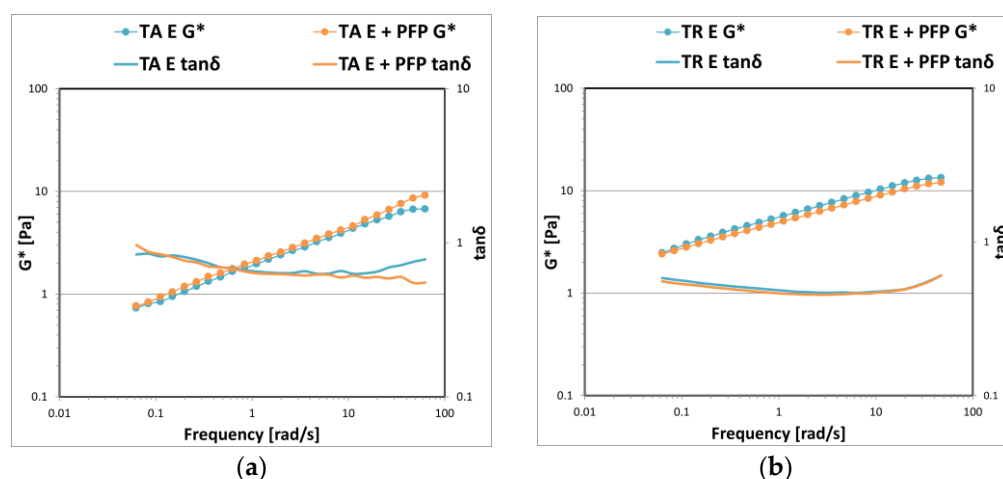

Figure 11. The trend of the complex G* modulus and the damping factor tanδ in the function of the oscillation frequency for the gel–creams before and after adding 3% *w/w* of PFP: (**a**) TA E prepared with T at 0.2% *w/w*, A at 0.2% *w/w* and E at 0.3% *w/w* and (**b**) TR E prepared with T at 0.2% *w/w*, R at 0.2% *w/w* and E at 0.3% *w/w*.

The influence of the active ingredient on the texture properties of the polysaccharidic associations was investigated (Figure 12). The insertion of the active ingredient PFP did not affect the firmness of the samples (Figure 12a); however, a marked decrease in adhesiveness was registered (Figure 12b).
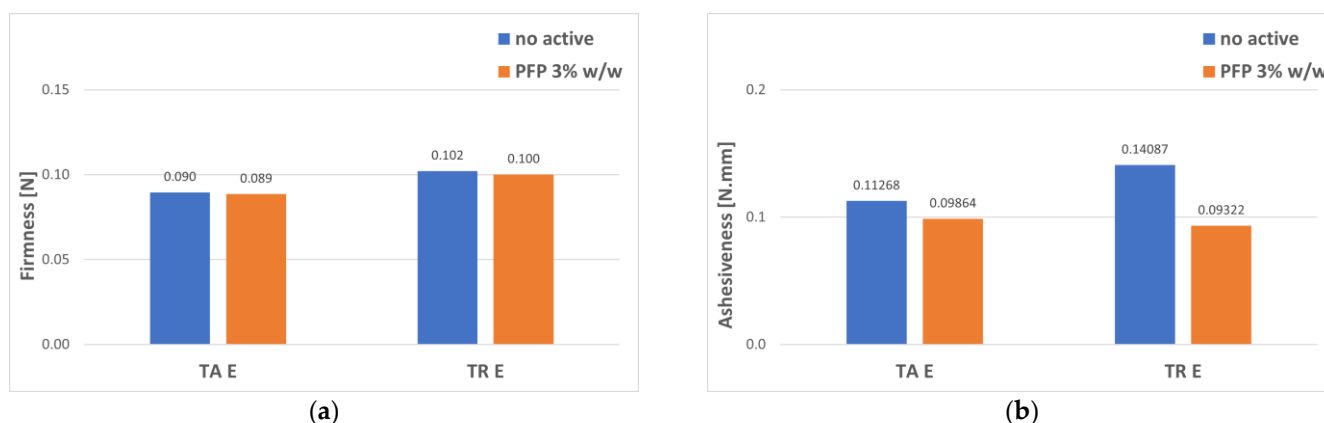

Figure 12. Texture parameters measured before and after adding 3% *w/w* of PFP for the gel–creams TA E prepared with T at 0.2% *w/w*, A at 0.2% *w/w*, and E at 0.3% *w/w* and TR E prepared with T at 0.2% *w/w*, R at 0.2% *w/w* and E at 0.3% *w/w*: (**a**) firmness and (**b**) adhesiveness.

4. Conclusions

In this work, we studied the compatibility of the active ingredient PFP, presented as a powder finely dispersed in glycerin, with different classes of rheological modifiers to formulate an intimate cosmetic gel. We prepared gel and gel–cream formulations evaluating the possibility of using naturally-derived polymers as alternative suspending

agents to synthetic acrylic polymers. Through the centrifuge stability test, we evaluated the stability of the polysaccharidic systems before and after the insertion of PFP. Rheological analyses showed that in a more liquid-like structure, the contribution given to the system by PFP was stronger in structural terms, while in gels with weak-gel characteristics, the contribution given by PFP was hardly perceptible. Moduli values between 10 and 1000 Pa, typical of a weak-gel structure, resulted in being optimal to keep the active in suspension. Succinoglycan gum and sclerotium gum proved to be the most suitable natural polymers for the formulation of gels with this type of active ingredient, giving a contribution to the elastic component of the system by increasing its stability. The presence of tamarind seed polysaccharides, a polymer with moisturizing and mucoadhesive properties, gave the gel and gel-cream formulations a contribution to the viscous component. Ternary associations of polymers, in which there was a correct balance between elastic and viscous modulus, seemed to be the most suitable for obtaining products with the required characteristics of texture and stability, and maintaining PFP in suspension. The association between tamarind seed polysaccharides, sclerotium gum, and the hydroxypropyl guar gum derivative was the one with the best structural properties in which the active ingredient did not significantly change the characteristics of the structure and was stable in the formulation.

The combined use of rheology and texture analysis has proved to be a useful protocol during the research and development phase to characterize the applicative properties of cosmetic formulas, evaluating the influence of the vehicle composition and the replacement of raw materials on spreading properties and adhesive characteristics. These two complementary techniques could provide scientific support for cosmetic industries to easily formulate cosmetic products in a green and sustainable perspective without losing the applicative performances impaired by conventional synthetic ingredients. The replacement of non-biodegradable and high environmental impact ingredients is a priority for cosmetic industries and must be done in a truly brief time. An instrumental protocol is needed that easily allows to objectively measure cosmetic products' applicative and sensory properties, rationalizing the choice of raw materials and avoiding stability tests and sensory panel tests that take a long time to be carried out.

Author Contributions: Conceptualization, G.P. and R.R.; investigation, E.B., G.T. and E.D.D.; resources, G.P.; project administration A.C.; formal analyses, G.T. and E.D.D.; writing—original draft preparation, G.T.; writing—review and editing, A.C.; supervision, A.S. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: Not applicable.

Data Availability Statement: Not applicable.

References

1. Ribeiro, A.S.; Estanqueiro, M.; Oliveira, M.B.; Sousa Lobo, J.M. Main benefits and applicability of plant extracts in skin care products. *Cosmetics* **2015**, *2*, 48–65. [CrossRef]
2. Amit, G.; Ashawat, M.S.; Shailendra, S.; Swarnlata, S. Phytosome: A novel approach towards functional cosmetics. *J. Plant Sci.* **2007**, *2*, 644–649. [CrossRef]
3. Fkiri, S.; Mezni, F.; Ouarghi, A.; Ghazghazi, H.; Larbi Khouja, M.; Khaldi, A.; Nasr, Z. Variability of phenolic compounds and antioxidant efficacy in needles extracts of *Pinus nigra* Arn. *J. New Sci.* **2018**, *53*, 3528–3535.

4. Mulabagal, V.; Hsin-Sheng, T. Plant cell cultures—An alternative and efficient source for the production of biologically important secondary metabolites. *Int. J. Appl. Sci. Eng.* **2004**, *2*, 29–48.

5. Hong, D.Y.; Lee, J.S.; Lee, H.G. Chitosan/poly—Glutamic acid nanoparticles improve the solubility of lutein. *Int. J. Biol. Macromol.* **2016**, *85*, 9–15. [CrossRef] [PubMed]

6. Ribeiro, R.C.d.A.; Barreto, S.M.A.G.; Ostrosky, E.A.; Rocha-Filho, P.A.d.; Veríssimo, L.M.; Ferrari, M. Production and Characterization of Cosmetic Nanoemulsions Containing *Opuntia ficus-indica* (L.) Mill Extract as Moisturizing Agent. *Molecules* **2015**, *20*, 2492–2509. [CrossRef]

7. Olejnik, A.; Goscianska, J.; Zielinska, A.; Nowak, I. Stability determination of the formulations containing hyaluronic acid. *Int. J. Cosmet. Sci.* **2015**, *37*, 401–407. [CrossRef]

8. Matusiak, J.; Grządka, E.; Bastrzyk, A. Stability, adsorption and electrokinetic properties of the chitosan/silica system. *Colloids Surf. A Physiochem. Eng. Asp.* **2018**, *554*, 245–252. [CrossRef]

9. Filipović, M.; Lukić, M.; Krstonošić, V.; Đorđević, S.; Pantelić, I.; Gledović, A.; Vuleta, G.; Savić, S. Feasibility of a Natural Surfactant as a Stabilizer for Cosmetics with Liposome-Encapsulated Plant Stem Cells: Pre-Formulation and Formulation through Stability Studies. *Tenside Surf. Det.* **2016**, *53*, 214–226. [CrossRef]

10. Semenzato, A.; Costantini, A.; Meloni, M.; Maramaldi, G.; Meneghin, M.; Baratto, G. Formulating O/W Emulsions with Plant-Based Actives: A Stability Challenge for an Effective Product. *Cosmetics* **2018**, *5*, 59. [CrossRef]

11. Goddard, E.D.; Gruber, J.V. Principles of Polymer Science and Technology in Cosmetics and Personal Care. In *Cosmetic Science and Technology*; Marcel Dekker: New York, NY, USA, 1999.

12. Varges, P.R.; Costa, C.M.; Fonseca, B.S.; Naccache, M.F.; De Souza Mendes, P.R. Rheological characterization of Carbopol dispersions in water and in water/glycerol. *Fluids* **2019**, *4*, 3. [CrossRef]

13. Kentin, E.; Kaarto, H. An EU ban on microplastics in cosmetic products and the right to regulate. *RECIEL Rev. Eur. Comp. Int. Environ. Law* **2018**, *27*, 254–266. [CrossRef]

14. Kanlayavattanakul, M.; Lourith, N. Natural polysaccharides for skin care. In *Polysaccharides of Microbial Origin*; Oliveira, J., Radhouani, H., Reis, R.L., Eds.; Springer: Cham, Switzerland, 2021; pp. 1–23.

15. Noralian, z.; Gashti, M.P.; Moghaddam, M.R.; Tayyeb, H.; Erfanian, I. Ultrasonically developed silver/iota-carrageenan/cotton bionanocomposite as an efficient material for biomedical applications. *Int J. Biol. Macromol.* **2021**, *180*, 439–457. [CrossRef] [PubMed]

16. Tafuro, G.; Costantini, A.; Baratto, G.; Francescato, S.; Busata, L.; Semenzato, A. Characterization of Polysaccharidic Associations for Cosmetic Use: Rheology and Texture Analysis. *Cosmetics* **2021**, *8*, 62. [CrossRef]

17. Gilbert, L.; Picard, C.; Savary, G.; Grisel, M. Rheological and textural characterization of cosmetic emulsions containing natural and synthetic polymers: Relationships between both data. *Colloids Surf. A Physiochem. Eng. Asp.* **2013**, *421*, 150–163. [CrossRef]

18. César, F.C.S.; Maia Campos, P.M.B.G. Influence of vegetable oils in the rheology, texture profile and sensory properties of cosmetic formulations based on organogel. *Int. J. Cosmet. Sci.* **2020**, *42*, 494–500. [CrossRef]

19. Gómez, I.; Calvo, F.; Gómez, J.M.; Ricardez-Sandoval, L.; Alvarez, O. A multiscale approach for the integrated design of emulsified cosmetic products. *Chem. Eng. Sci.* **2022**, *251*, 117493. [CrossRef]

20. Kulawik-Pióro, A.; Ptaszek, A.; Kruk, G. Effective tool for assessment of the quality of barrier creams—Relationships between rheological, textural and sensory properties. *Regul. Toxicol. Pharmacol.* **2019**, *103*, 113–123. [CrossRef]

21. Tadros, T. Application of rheology for assessment and prediction of the long-term physical stability of emulsions. *Adv. Colloid Interface Sci.* **2004**, *108–109*, 227–258. [CrossRef]

22. Yokokoji, A.; Kitayama, W.; Wichai, K.; Urakawa, O.; Matsumoto, A.; Vao-Soongnern, V.; Inoue, T. Viscoelastic relaxation of polymerized ionic liquid and lithium salt mixtures: Effect of salt concentration. *Polymers* **2021**, *13*, 1772. [CrossRef]

23. Zainal, N.F.A.; Lai, S.A.; Chan, C.H. Melt rheological behavior and morphology of poly(ethylene oxide)/natural rubber graft-poly(methyl methacrylate) blends. *Polymers* **2020**, *12*, 724. [CrossRef] [PubMed]

24. Calixto, M.S.; Maia Campos, P.M.B.G. Physical–Mechanical characterization of cosmetic formulations and correlation between instrumental measurements and sensorial properties. *Int. J. Cosmet. Sci.* **2017**, *39*, 527–534. [CrossRef] [PubMed]

25. Vergilio, M.M.; de Freitas, A.C.P.; da Rocha-Filho, P.A. Comparative sensory and instrumental analyses and principal components of commercial sunscreens. *J. Cosmet. Dermatol.* **2022**, *21*, 729–739. [CrossRef]

26. Vieira, G.S.; Lavarde, M.; Fréville, V.; Rocha-Filho, P.A.; Pensé-Lhéritier, A. Combining sensory and texturometer parameters to characterize different type of cosmetic ingredients. *Int. J. Cosmet. Sci.* **2020**, *42*, 156–166. [CrossRef] [PubMed]

27. Hiwa, M.A. Ethnomedicinal, Phytochemical and Pharmacological Investigations of *Perilla frutescens* (L.) Britt. *Molecules* **2019**, *24*, 102.

28. Igarashi, M.; Miyazaki, Y. A Review on Bioactivities of Perilla: Progress in Research on the Functions of Perilla as Medicine and Food. *Evid. Based Complement. Altern. Med.* **2013**, *2013*, 925342. [CrossRef]

29. Dhyani, A.; Chopra, R.; Garg, M. A Review on Nutritional Value, Functional Properties and Pharmacological Application of Perilla (*Perilla frutescens* L.). *Biomed. Pharmacol. J.* **2019**, *12*, 649–660. [CrossRef]

30. Valenta, C. The use of mucoadhesive polymers in vaginal delivery. *Adv. Drug Deliv. Rev.* **2005**, *57*, 1692–1712. [CrossRef]

31. Lam, H.T.; Zupancic, O.; Laffleur, F.; Bernkop-Schnurch, A. Mucoadhesive properties of polyacrylates: Structure–Function relationship. *Int. J. Adhes. Adhes.* **2021**, *107*, 102857. [CrossRef]

32. Roy, S.; Pal, K.; Anis, A.; Pramanik, K.; Prabhakar, B. Polymers in Mucoadhesive Drug-Delivery Systems: A Brief Note. *Des. Monomers Polym.* **2009**, *12*, 483–495. [CrossRef]

33. Lapasin, R.; Pricl, S. *Rheology of Industrial Polysaccharides, Theory and Application*; Blackie Academic & Professional: London, UK, 1995; pp. 38–39.

34. Vinarta, S.C.; Francois, N.J.; Daraio, M.E.; Figueroa, L.I.C.; Farina, J.I. *Sclerotium rolfsii* scleroglucan: The promising behavior of a natural polysaccharide as a drug delivery vehicle, suspension stabilizer and emulsifier. *Int. J. Biol. Macrom.* **2007**, *41*, 314–323. [CrossRef] [PubMed]

35. Rinaudo, M.; Tinland, B. Relation between Molecular Structure and Physicochemical Properties for Some Microbial Polysaccharides. In *Novel Biodegradable Microbial Polymers*; Dawes, E.A., Ed.; Kluwer Academic Publishers: Norwell, MA, USA, 1990; pp. 349–370.

36. Xu, L.; Gong, H.; Dong, M.; Li, Y. Rheological properties and thickening mechanism of aqueous diutan gum solution: Effects of temperature and salts. *Carbohydr. Polym.* **2015**, *132*, 620–629. [CrossRef] [PubMed]

37. Semenzato, A.; Costantini, A.; Baratto, G. Green Polymers in Personal Care Products: Rheological Properties of Tamarind Seed Polysaccharide. *Cosmetics* **2015**, *2*, 1–10. [CrossRef]

38. Kulkarni, A.D.; Joshi, A.A.; Patil, C.L.; Amale, P.D.; Patel, H.M.; Surana, S.J.; Belgamwar, V.S.; Chaudhari, K.S.; Pardeshi, C.V. Xyloglucan: A functional biomacromolecule for drug delivery applications. *Int. J. Biol. Macrom.* **2017**, *104*, 799–812. [CrossRef] [PubMed]

39. Lapasin, R.; De Lorenzi, L.; Pricl, S.; Torriano, G. Flow properties of hydroxypropyl guar gum and its long-chain hydrophobic derivatives. *Carbohydr. Polym.* **1995**, *28*, 195–202. [CrossRef]

40. Pressi, G.; Bertaiola, O.; Guzzo, F.; Biagi, M. Phytocomplex and Extract of a Meristematic Cell Line Selected of *Perilla frutescens*. Patent ITA102020000028230/PCT/IB2021/057560, 24 November 2020.

41. Yasuda, K.; Armstrong, R.C.; Cohen, R.E. Shear flow properties of concentrated solutions of linear and star branched polystyrenes. *Rheol. Acta* **1981**, *20*, 163–178. [CrossRef]

42. Tai, A.; Bianchini, R.; Jachowicz, J. Texture analysis of cosmetic/pharmaceutical raw materials and formulations. *Int. J. Cosmet. Sci.* **2014**, *36*, 291–304. [CrossRef]

43. Estanqueiro, M.; Amarak, M.H.; Sousa Lobo, J.M. Comparison between sensory and instrumental characterization of topical formulations: Impact of thickening agent. *Int. J. Cosmet. Sci.* **2016**, *38*, 389–398. [CrossRef]

44. Bais, D.; Trevisan, A.; Lapasin, R.; Partal, P.; Gallegos, C. Rheological characterization of polysaccharide–surfactant matrices for cosmetic O/W emulsions. *J. Colloid Interface Sci.* **2005**, *290*, 546–556. [CrossRef]

45. Medina-Torres, L.; Calderas, F.; Sanchez-Olivares, G.; Nunez-Ramirez, D.M. Rheology of Sodium Polyacrylate as an Emulsifier Employed in Cosmetic Emulsions. *Ind. Eng. Chem. Res.* **2014**, *53*, 18346–18351. [CrossRef]