

Hand sanitizer gel formulations: Influence of polymer type on the rheological properties

Formulações de gel higienizante de mãos: Influência do tipo de polímero nas propriedades reológicas

Formulaciones de gel desinfectante para manos: Influencia del tipo de polímero en las propiedades reológicas

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Gardenia Barbosa Carrijo Rodrigues

ORCID: <https://orcid.org/0000-0002-6034-3705>
Instituto Federal de Educação, Ciência e Tecnologia Goiano, Brasil
E-mail: gardenia.rodrigues@estudante.ifgoiano.edu.br

Josemar Gonçalves de Oliveira Filho

ORCID: <https://orcid.org/0000-0001-9755-7128>
Universidade Estadual Paulista, Brasil
E-mail: josemar.gooliver@gmail.com

Adriano Jakelaitis

ORCID: <https://orcid.org/0000-0003-0093-9846>
Instituto Federal de Educação, Ciência e Tecnologia Goiano, Brasil
E-mail: adriano.jakelaitis@ifgoiano.edu.br

Elton Clementino da Silva

ORCID: <https://orcid.org/0000-0002-3217-5222>
Universidade de Brasília, Brasil
E-mail: eltosilva@unb.br

Geovana Rocha Placido

ORCID: <https://orcid.org/0000-0002-3028-7191>
Instituto Federal de Educação, Ciência e Tecnologia Goiano, Brasil
E-mail: geovana.placido@ifgoiano.edu.br

Suzana Maria Loures De Oliveria Marcionilio

ORCID: <https://orcid.org/0000-0001-7177-380X>
Instituto Federal de Educação, Ciência e Tecnologia Goiano, Brasil
E-mail: suzana.loures@ifgoiano.edu.br

Raphaella Gabri Bitencourt

ORCID: <https://orcid.org/0000-0002-0675-0609>
Instituto Federal de Educação, Ciência e Tecnologia Goiano, Brasil
E-mail: raphaella.bitencourt@ifgoiano.edu.br

Abstract

COVID-19 increased the demand for alcohol-based hand sanitizer in establishments. The present study aimed to characterize different polymers and/or polymer mixtures with the potential to be used to produce alcohol-based gel hand sanitizers and evaluate the different formulations of alcohol gel as to their rheological properties. Polymers and polymer blends (natural and/or synthetic) were characterized by DSC and FTIR/NIR analysis. Six were polymers or blends of polymers efficient to production of this product in the concentration of 70% ethanol (w/w). Alcohol-based hand sanitizer gel formulations were stored at two different temperatures (25 °C and 40 °C) and subjected to rheological analysis over the storage time (0, 7, 14, and 28 days). The rheological profile indicated a behavior of pseudoplastic fluid of the samples, and they remained stable throughout the days of storage at 25 °C. Formulations containing natural polymers derived from cellulose are good alternatives to replace the carbomer gelling agent, with limitations related to the reduction of the gel apparent viscosity.

Keywords: Alcohol gel; COVID-19; Gelling agents; Polymers; Stability.

Resumo

A COVID-19 aumentou a procura por desinfetantes para as mãos à base de álcool nos estabelecimentos. O presente estudo teve como objetivo caracterizar diferentes polímeros e/ou misturas de polímeros com potencial para serem utilizados na produção de álcool em gel para higienização das mãos e avaliar as diferentes formulações de álcool gel quanto às suas propriedades reológicas. Polímeros e misturas de polímeros (naturais e/ou sintéticos) foram caracterizados por análises de DSC e FTIR/NIR. Seis polímeros ou misturas de polímeros foram eficientes para a produção deste produto na concentração de 70% de etanol (m/m). As formulações de gel antisséptico para as mãos à

base de álcool foram armazenadas em duas temperaturas diferentes (25 °C e 40 °C) e submetidas à análise reológica ao longo do tempo de armazenamento (0, 7, 14 e 28 dias). O perfil reológico indicou comportamento de fluido pseudoplástico nas amostras, que permaneceram estáveis ao longo dos dias de armazenamento a 25 °C. Formulações contendo polímeros naturais derivados de celulose são boas alternativas para substituir o agente gelificante carbômero, com limitações relacionadas à redução da viscosidade aparente do gel.

Palavras-chave: Álcool em gel; COVID-19; Agentes gelificantes; Polímeros; Estabilidade.

Resumen

El COVID-19 incrementó la demanda de desinfectante para manos a base de alcohol en los establecimientos. El presente estudio tuvo como objetivo caracterizar diferentes polímeros y/o mezclas de polímeros con potencial para ser utilizados para producir desinfectantes para manos en gel a base de alcohol y evaluar las diferentes formulaciones de alcohol en gel en cuanto a sus propiedades reológicas. Los polímeros y mezclas de polímeros (naturales y/o sintéticos) se caracterizaron mediante análisis DSC y FTIR/NIR. Seis eran polímeros o mezclas de polímeros eficientes para la producción de este producto en una concentración de 70% de etanol (p/p). Las formulaciones de gel desinfectante para manos a base de alcohol se almacenaron a dos temperaturas diferentes (25 °C y 40 °C) y se sometieron a análisis reológico durante el tiempo de almacenamiento (0, 7, 14 y 28 días). El perfil reológico indicó un comportamiento de fluido pseudoplástico de las muestras, y se mantuvieron estables durante los días de almacenamiento a 25 °C. Las formulaciones que contienen polímeros naturales derivados de la celulosa son buenas alternativas para reemplazar el agente gelificante carbómero, con limitaciones relacionadas con la reducción de la viscosidad aparente del gel.

Palabras clave: Alcohol en gel; COVID-19; Agentes gelificantes; Polímeros; Estabilidad.

1. Introduction

On March 11, 2020, COVID-19 was characterized by the World Health Organization (WHO) as a pandemic. Vaccine research and other ways to combat and prevent contagion began. The use of alcohol-based hand sanitizer has greatly increased as a way to help the disinfection of the hands. Increasing the demand for alcoholic preparations at 70% w/w, the National Health Surveillance Agency of Brazil (ANVISA) reduced the bureaucracy in the production of this type of product. Technical Note No. 3 of 2020 exceptionally authorized companies interested in carrying out the manufacture, donation, and transport of Ethyl Alcohol 70% w/w, with the purpose of application in the services of the National Unified Health System and other public institutions (ANVISA, 2020).

Alcohol-based hand sanitizer is a colloidal solution in the form of a denatured gel, composed of alcohol, water, gelling agent, a denaturing agent, and a neutralizing agent (Brasil, 2019; Brasil, 2012). This material can be considered a cosmetic, domissanitary or medicinal preparation (degerming antiseptic). Ethyl alcohol gel as a cosmetic product is considered a risk grade II product, being registered as antiseptics, with the purpose of hand hygiene, with no proposal to replace the use of soap or proper hand washing (Correia, 2013).

In formulations with alcohol contents greater than or equal to 68% w/w, the dynamic viscosity of alcohol gel at the temperature of 25 °C shall be greater than or equal to 8000 cP and greater than or equal to 4000 cP for formulations with ethanol concentration less than 68% w/w. Products formulated based on hydrated ethyl alcohol sold with graduations below or equal to 54° GL (54% v/v) at a temperature of 20 °C must contain a denaturing agent in order to prevent its misuse (Brasil, 2002).

Several companies in the cosmetic, pharmaceutical, sanitary, and magisterial sectors have started or have increased the production of this type of product supported by Technical Note N° 3 of 2020. However, with the closure of ports, it was observed the lack of essential raw materials for production of alcohol-based hand sanitizer gel, as carbomer thickening agent. Thus, new polymers have been studied and a potential was found mainly in natural biomacromolecules that are biodegradable, biocompatible, and environmentally sustainable (Kang et al., 2016).

Sodium carboxymethylcellulose (CMC) is a cellulosic ether of anionic character, and it is non-toxic, odorless, and biodegradable, which can be dissolved in hot or cold water (Yang & Zhu, 2007). Hydroxyethylcellulose (HEC) is also a water-soluble, non-ionic cellulosic ether and, like CMC, it is used for a variety of applications in several industries, including food,

personal care, pharmaceutical, petroleum, and paper industries due to its superior properties as a binder, thickener, and stabilizing agent. The main advantage of using CMC and HEC in formulations is that they come from renewable and biodegradable sources. Cellulose derivatives, alone or in mixtures, can also be used in the preparation of gels without the need for neutralization. Also, they are among the recommended polymers to be applied to increase the viscosity of formulations by SIFAP (Italian Society of Compounding Pharmacists) during the COVID-19 pandemic (Perinelli et al., 2021).

Among the class of synthetic carbomers is Carbopol 940, which is a copolymer of polyacrylic acid often used as a gelling agent to form transparent and bioadhesive gel. The concentration of Carbopol 940 as a gelling-agent can be varied to produce preparations that meet the criteria for gel physical properties such as pH, viscosity, adhesion, spreadability, organoleptic, and stability. The main advantages of using carbopol is that it is a non-toxic material, can be applied at room temperature, and produces gels with a wide viscosity range by varying its concentration (Safitri et al., 2021; Mou et al., 2008).

Given this context, the present study aimed to characterize different polymers and/or polymer mixtures with the potential to be used to produce alcohol-based gel hand sanitizers and evaluate the different formulations of alcohol gel as to their rheological properties.

2. Methodology

2.1 Materials

10 different samples of polymers purchased from companies that supply gelling agents were used, among natural and synthetic materials, including materials formed by a mix of polymers, as shown in Table 1. In addition, double-distilled glycerin, triethanolamine-based solution, and VPQ neutralizer (Aminomethyl propanol and Triisopropanolamine solution) were used for the alcohol gel formulations. The ethyl alcohol used had a concentration of 96 °GL (equal to 96% v/v or 92.8% w/w) and was purchased from the company Itajá (Brazil).

Table 1 - List of evaluated polymers.

Sample	INCI* composition	Degree of purity
I	Hydroxyethylcellulose	Pharmaceutical
II	Carbomer	Pharmaceutical
III	Xanthan Gum	Pharmaceutical
IV	Sodium Carboxymethyl Cellulose	
V	Hydroxypropylmethylcellulose; Hydroxyethylcellulose	Pharmaceutical
VI	Methylhydroxyethylcellulose; Hydroxypropylmethylcellulose; Hydroxyethylcellulose	Pharmaceutical
VII	Methylhydroxyethylcellulose;	Pharmaceutical
VIII	Guar Hydroxypropyltrimonium Chloride	Pharmaceutical
IX	Cassava Starch	-
X	Acrylates Copolymer	Pharmaceutical

*INCI: International Nomenclature of Cosmetic Ingredients. Source: Authors.

2.2 Characterization of polymers

The polymers were subjected to DSC analysis and the thermograms were obtained using the Netzsch DSC 204 F1 Nevio equipment, using aluminum crucible (30-40 μ L). The measurements were carried out in the temperature range between -70 and 300 °C. The measurement started at 20 °C, then the system was cooled to -70 °C, kept constant for 30 minutes, and finally the system was heated to 300 °C. The heating rate was 10 °C/min, and the nitrogen flow was 40 mL/min.

In addition, the functional groups of the surfaces of adsorbents were studied using the Fourier-transform infrared spectroscopy (FTIR/Nir, Perkin Elmer Frontier) with attenuated total reflectance (ATR) mode, covering the spectral range from 650 to 4000 cm^{-1} .

2.3 Preparation of alcohol-based gel formulations

The formulations containing xanthan gum, CMC, quaternized guar gum, and cassava starch formed gel only up to the following alcohol contents: 60, 60, 40, and 30% (w/w), respectively. In the study by Perinelli et al. (2021) in which gels formed by cellulose-derived polymers at different ethanol/water concentrations were evaluated, only hydroxypropyl cellulose formed transparent dispersions across the entire range of ethanol concentrations and CMC showed an important decrease in solubility when reaching a concentration of 60% (w/w), with quick sedimentation of insoluble particles being observed.

The other polymers formed gels with an alcohol content of 70% (w/w) and were tested in different formulations, varying their concentrations as shown in Table 2. The definition of the concentrations to be evaluated are in accordance with the specifications given by the suppliers of the polymers and/or from preliminary tests.

Table 2 - Codification of alcohol-based gel formulations.

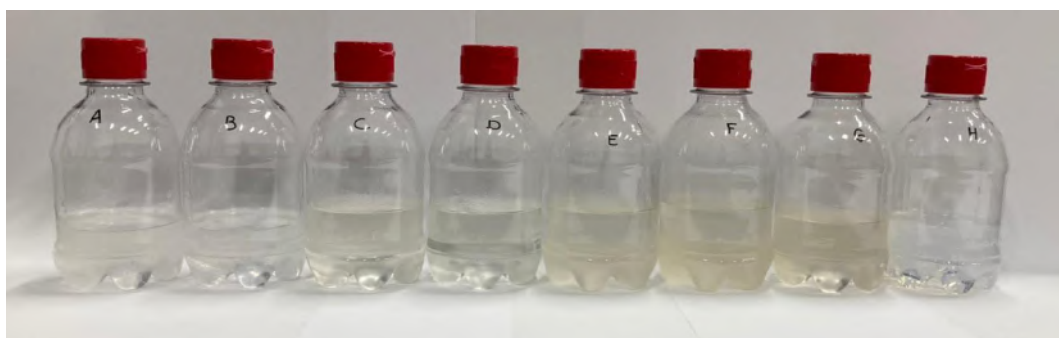
Formulation	Polymer Type (INCI*)	Polymer concentration (% w/v)
A	Carbomer	1.0
B	Carbomer	0.5
C	Hydroxyethylcellulose	1.0
D	Hydroxyethylcellulose	0.5
E	Methylhydroxyethylcellulose;	1.0
F	Methylhydroxyethylcellulose; Hydroxypropylmethylcellulose; Hydroxyethylcellulose	1.0
G	Hydroxypropylmethylcellulose; Hydroxyethylcellulose	1.0
H	Acrylates Copolymer	6.0

*INCI: International Nomenclature of Cosmetic Ingredients. Source: Authors.

The preparation of samples A to G of alcohol in gel started by diluting the polymer in distilled water and then adding the corresponding amount of ethyl alcohol 92.8% (w/w) to form a polymeric solution with alcohol content of 70% (w/w), with the aid of a glass rod. Finally, the solutions were neutralized by using triethanolamine-based solution. Only the sample containing carbopol was neutralized with the VPQ neutralizer.

Sample H was prepared by solubilizing the polymer in ethanol 92.8% (w/w) and then adding distilled water. Neutralization was carried out in a similar way with the use of the solution based on triethanolamine. After neutralization, double-distilled glycerin was added to all samples at a concentration of 1% (v/v). The samples were stored in plastic packaging at 25 °C and 40 °C, as shown in Figure 1.

Figure 1 - Alcohol gel samples obtained.



Source: Authors.

2.4 Characterization of alcohol-based gel formulations

The samples were stored at two different temperatures (25 °C and 40 °C) and were subjected to rheological analysis over the storage time (0, 7, 14, and 28 days). Rheological analyses of alcohol gel samples were performed in a rheometer (Physica, MCR 101, Ostfildern, Germany) through flow curves performed in duplicate in plate-cone geometry, at a temperature of 25 °C. The shear rate was evaluated in three steps/intervals: in the first step (climb 1) the deformation rate was increasing from 0.1 to 500 s⁻¹; the second (descent) was performed with a decreasing rate of 500 to 0.1 s⁻¹; and the third (rise 2), with rising rate again at 0.1 to 500 s⁻¹ to eliminate thixotropy effect. At each stage, 50 data experimental points were obtained.

The rheology model of the Law of Power (Equation 1) and Herschel-Bulkley (Equation 2) were adjusted to the experimental data using Origin pro 8.5 software.

$$\tau = k \cdot \dot{\gamma}^n \quad (1)$$

$$\tau = \tau_0 + k \cdot \dot{\gamma}^n \quad (2)$$

Where τ is shear stress (Pa), $\dot{\gamma}$ is a shear rate (s⁻¹), k is consistency index (Pa.sⁿ), τ_0 is residual stress (Pa), and n is fluid behavior index (nondimensional).

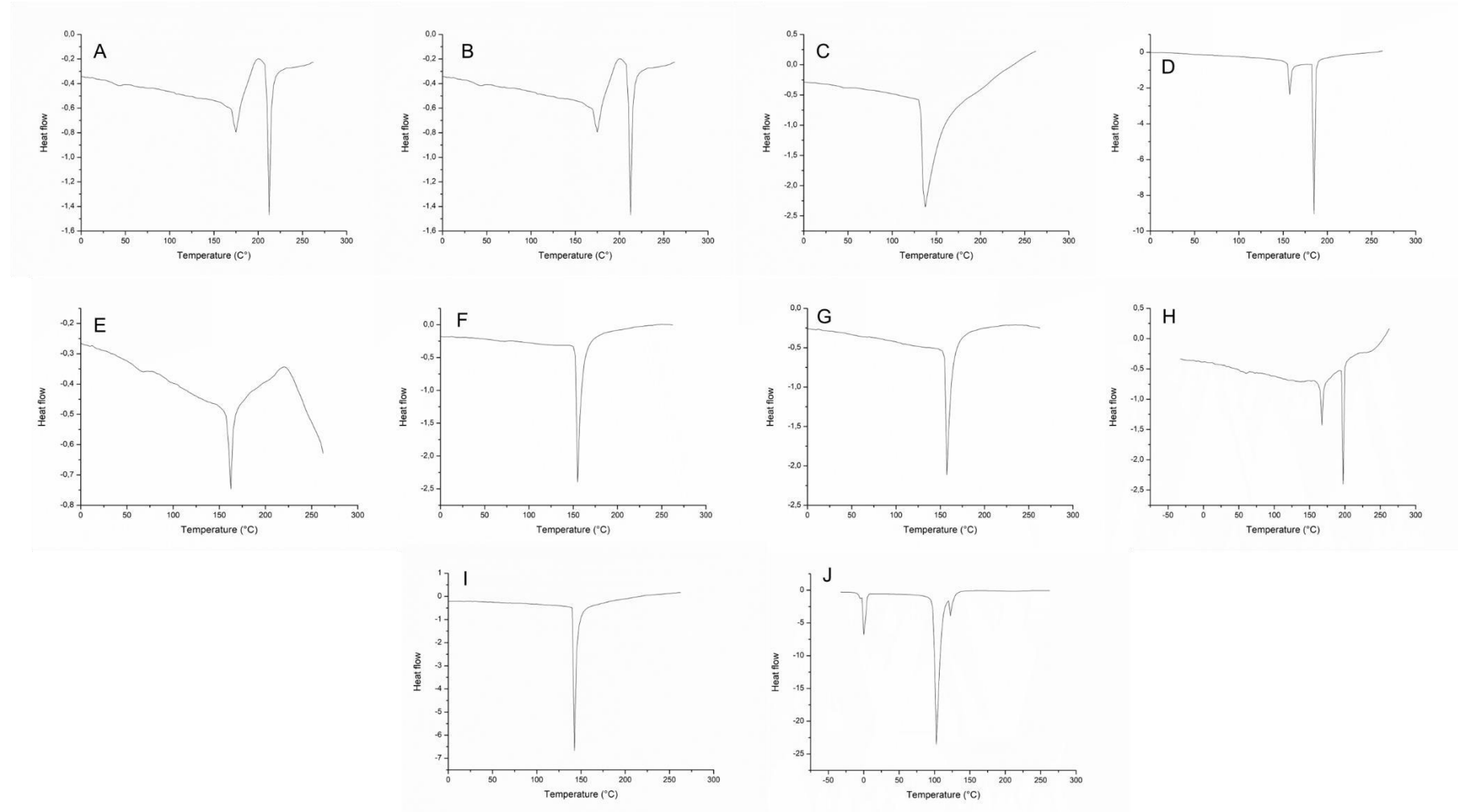
3. Results and Discussion

3.1 Characterization of polymers

3.1.1 DSC

Figure 2 shows DSC thermograms of the polymers. Hydroxyethylcellulose DSC thermogram showed two endothermic peaks: one at 173.8 and another at 210.7 (Figure 2A). Carbomer DSC thermogram showed three endothermic peaks: at 43.8 °C, 170 °C, and 208.8 °C (Figure 2B). Xanthan gum exhibited a broad endothermic bank of 132.5 °C to 152.7 °C (Figure 2C). Sodium carboxymethyl cellulose DSC thermogram showed two endothermic peaks: at 155.0 and 184.4 °C (Figure 2D). The mixture of hydroxypropylmethylcellulose and hydroxyethylcellulose showed two endothermic peaks: at 161.5 °C and 288.8 °C (Figure 2E). The blend of methylhydroxyethylcellulose biopolymers; hydroxypropylmethylcellulose hydroxyethylcellulose had a single endothermic peak near 154.8 °C (Figure 2F). Methylhydroxyethylcellulose showed an endothermic peak at 157.5 °C (Figure 2G). The biopolymer guar hydroxypropyltrimonium chloride showed two endothermic peaks: at 166.7 and 196.5 °C (Figure 2H). Cassava starch DSC thermogram showed an endothermic peak at 141.5 °C (Figure 2I). Finally, the acrylates copolymer showed three endothermic peaks: at 0.5 °C, 102.7 °C and 122.2 °C (Figure 2J). The DSC thermograms for the studied polymers agreed with what is reported in the literature for these compounds (Regiani et al., 2000; Khonsari et al., 2014; Sandeep et al., 2014; Sathiyarayanan et al., 2015; Wang et al., 2020; Kumar et al., 2018).

Figure 2 - DSC thermograms of the polymers. A: Hydroxyethylcellulose, B: Carbomer, C: Xanthan Gum, D: Sodium Carboxymethyl Cellulose, E: Hydroxypropylmethylcellulose and Hydroxyethylcellulose, F: Methylhydroxyethylcellulose; Hydroxypropylmethylcellulose; and Hydroxyethylcellulose, G: methylhydroxyethylcellulose, H: Guar hydroxypropyltrimonium chloride, I: cassava starch, J: acrylates copolymer.



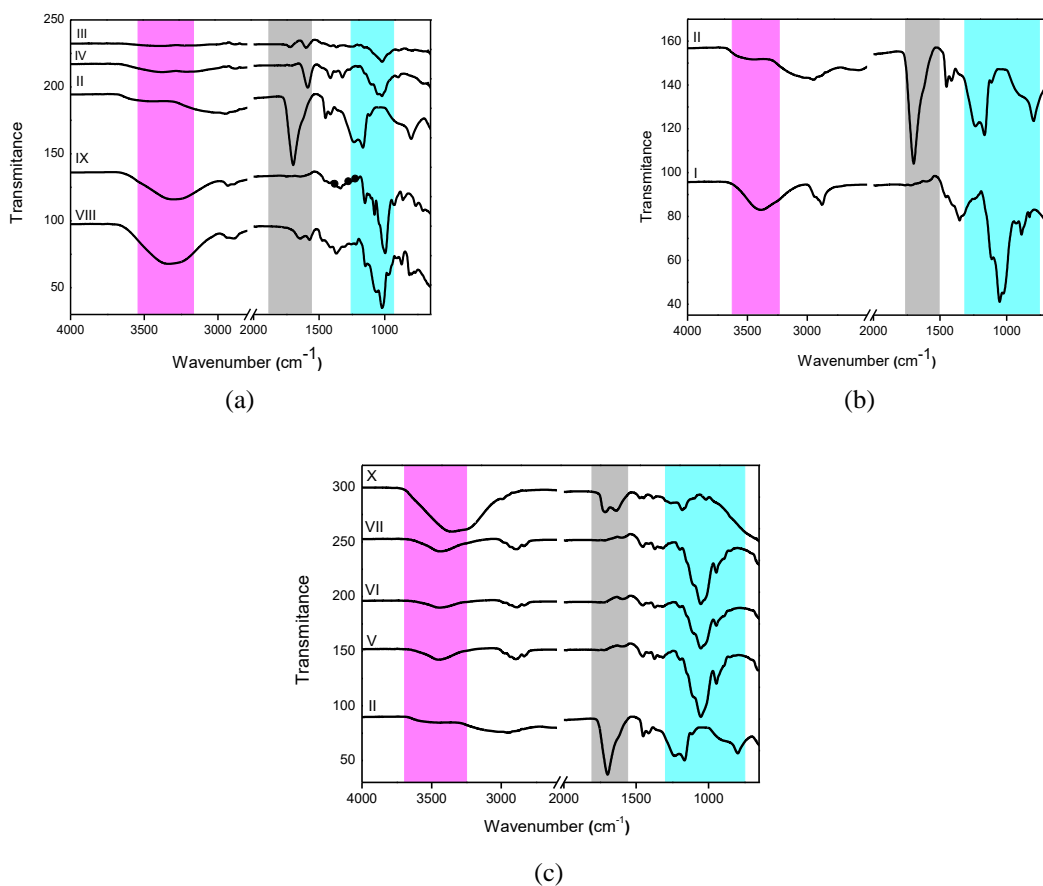
Source: Authors.

3.1.2 FTIR

Infrared spectroscopy provides direct information about the vibrational modes of the molecules of a substance. Since the set of bands in the spectrum is specific to each substance, in particular, the isolated bands are linked to vibrations of a certain functional group or a type of bond of the studied compound (Silverstein, 1997). The identification of the vibration frequency of the corresponding bond, the so-called band marking, is obtained by comparing these with spectroscopy tables (Silverstein, 1997). The FTIR technique is increasingly used in the quality control of industrial processes and products (Blanco et al., 1994), mainly because the measurements are fast, use a small amount of sample, and involve quick and simple sample preparation.

Figure 3 shows FTIR spectra of powdered samples, which all presented very similar spectra, a typical polysaccharide profile - except for carbomer. Briefly, the peaks in the range of 900 to 1100 cm^{-1} are characteristic of C-O e C-C bonds and those that occurred in 1404-1410 cm^{-1} are due to OH bonds. The broadband in the region 3420-3424 cm^{-1} is characteristic of hydrogen bond to the hydroxyl group (OH), that is, associated with intra- and intermolecular hydrogen bonds (Shalviri et al., 2010; Silverstein & Weber, 2000).

Figure 3 - FTIR spectra of (a) II: Carbomer; III: Xanthan Gum; IV: Sodium Carboxymethyl Cellulose; VIII: Guar Hydroxypropyltrimonium Chloride; IX: Cassava Starch. (b) I: (Hydroxyethylcellulose) and II (Carbomer); (c) II: Carbomer; V: Hydroxypropylmethylcellulose and Hydroxyethylcellulose; VI: Methylhydroxyethylcellulose, Hydroxypropylmethylcellulose and Hydroxyethylcellulose; VII: Methylhydroxyethylcellulose; X: Acrylates Copolymer.



Source: Authors.

All raw materials except carbomer (2960 cm^{-1}) analyzed by FTIR show peaks of OH groups in the region of 3424 cm^{-1} (red region). The analysis of the spectral profile of ATR-FTIR (Figure 3a) of the natural samples allowed identification that most of the signals of groups of the samples' chemical constituents were concentrated in the region between 700 to 1700 cm^{-1} , indicating the presence of proteins (1650-1550 cm^{-1}) in the gray region and carbohydrates (1250 to 999 cm^{-1}) in the blue region. In the starch sample, the presence of peaks at 1018 and 999 cm^{-1} stands out, which correspond to the diagnostic signs of amylopectin and amylose (Silverstein & Weber, 2000; Pavia et al., 2001; Cerná et al., 2003). Amylose and amylopectin are responsible for water retention in the gelatinization process with heating, and the required water content is 65%, irreversibly.

Guar gum is formed by linear chains of D-mannopyranosyl units linked together through links of β -1,4 and D-galactopyranosyl units, linked together by links of α -1,6 (Goldstein et al., 1973). The guar gum spectrum shows polysaccharides characteristic bands and is comparable to other galactomannan spectra reported in the literature, such as: a wide band at 3424 cm^{-1} (gray region), vibrational stretch characteristic of the OH group; bands at 869 and 814 cm^{-1} , assigned to the (C-O-C) glycosidic bond of the units of β -D-mannopyranose and α -D-galactopyranose, respectively; band at 1076 cm^{-1} , relating to the stretching of primary alcohol (CH₂OH), blue region indicated (Figueiró et al., 2004; Cerqueira et al., 2011).

The xanthan gum consists of a main chain of D-glucose units joined together by links of β -1,4, with alternating residues of D-mannose and D-glucuronic acid, in a molar ratio of 2:1, forming the side chain, and also having acetyl and pyruvic groups (Jansson et al., 1975). Due to this structure, the xanthan gum molecule has pseudoplastic rheological behavior and is soluble in cold water. In FTIR, xanthan gum range presents a fingerprint between the range of 1800-1200 cm^{-1} , the peak being at 1715-1730 cm^{-1} (gray region), indicating ester and pyruvate or acetate grouping at 1730 cm^{-1} . Xanthan gums have absorption bands around 1,027 cm^{-1} which may be associated with the elongation of the C-C and C-O groups and the typical C-H polysaccharide band, blue region (Hashemi et al., 2014). In the spectra of xanthan gum, the vibration bands of hydrogen bound to O-H and C-H are observed at 3416 cm^{-1} and 2902 cm^{-1} (red region), respectively (Pooja et al., 2014). In this region, a wide band is commonly found, corresponding to the axial deformation of hydroxyl groups of intermolecular polysaccharide hydrogen bonds. Absorptions to 1,656 cm^{-1} and 1,438 cm^{-1} are related to asymmetric and symmetrical elongation vibrations of carboxylic anion, which is present in the trisaccharide side chain of xanthan gum obtained with sugarcane bagasse and lineages 254 (Hashemi et al., 2014).

As shown in Figure 3a, Sodium Carboxymethyl Cellulose (CMC – sample IV) contains hydrophobic polysaccharide groups and many hydrophilic carboxyl groups and hence shows amphiphilic characteristics. Also, CMC is an ionic polymer which in general, cellulose is made up of glucose rings that are connected by -C(1)-O-C(4) ether bonds known as RMB-1.4 glycoside linkages with an extensive intermolecular hydrogen bonding characteristic peak at 2922 cm^{-1} C-H anti-symmetric stretching, while peaks at 1422 and 1624 cm^{-1} appear due to the carboxylate groups stretching vibrations (symmetric and asymmetric). Due to the presence of intermolecular and intramolecular hydrogen bonds and -OH groups, a visible band is seen at 3434 cm^{-1} (Singh & Khatri, 2012).

Figure 3c shows the FTIR bands for commercial carbomers, with bands characteristic of a carbomer of natural origin, widened band at 3424 cm^{-1} and then bands between 700 and 1100 cm^{-1} , fingerprints similar and even equal to of Figure 3a and HEC, shown in Figure 3b.

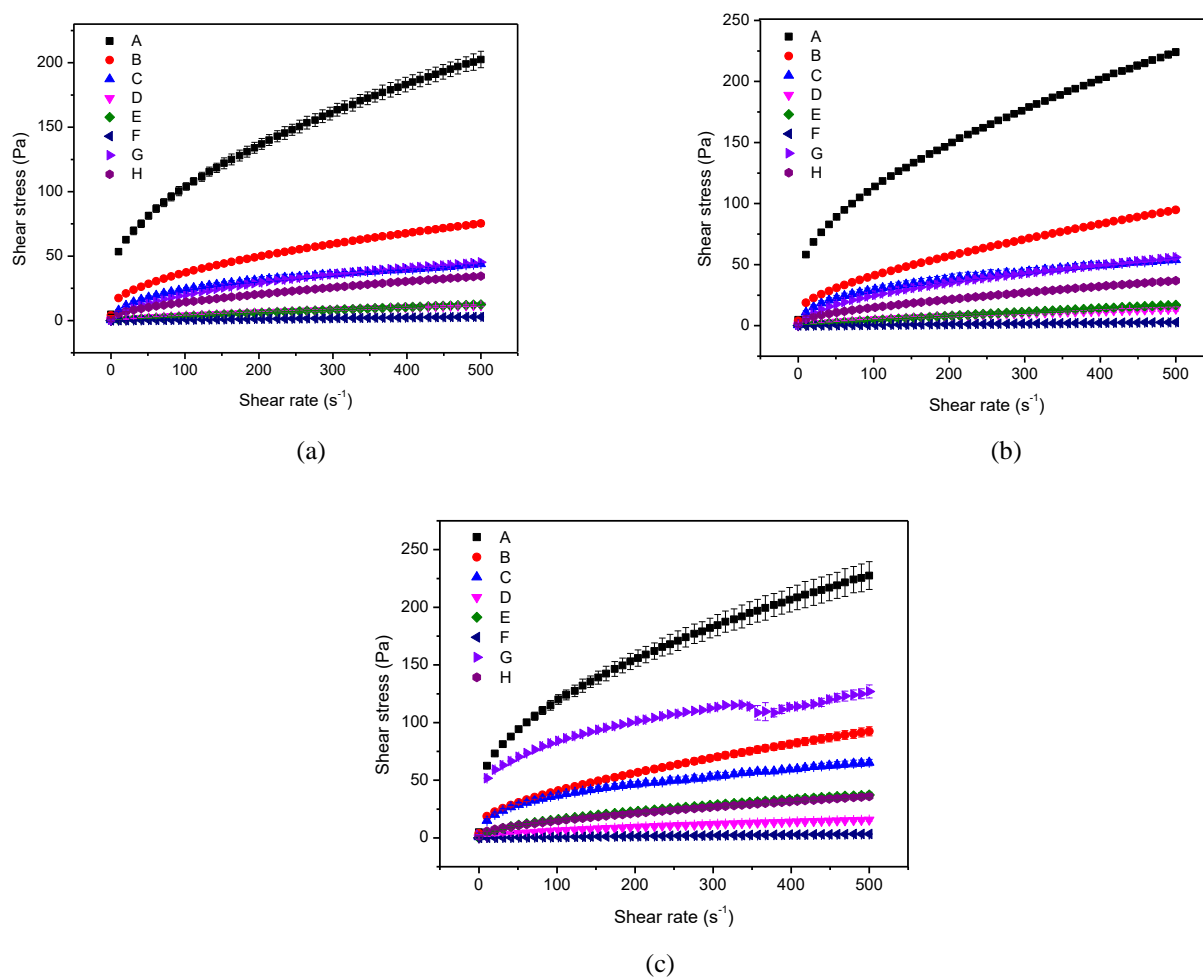
3.2 Characterization of alcohol-based gel formulations

3.2.1 Rheological analyses

In all formulations studied, pseudoplastic behavior was verified, which allows ease of application of the product due to low resistance to flow in the use of alcohol gel (Figure 4). However, formulation F presented the slope of the points of the shear

stress versus shear rate curves much less variable than the other formulations in the evaluated shear rates, which results in apparent viscosity values less dependent on the shear rate and corresponds to a behavior closest to a Newtonian fluid, as can be seen in Figure 5f.

Figure 4 - Rheological profile of the formulations after (a) 0 days of storage; (b) 30 days of storage at 25 °C; (c) 30 days of storage at 40 °C.



Source: Authors.

It can be verified that the rheological behavior of the formulations was influenced by the type of polymer and the concentration used. The formulations with carbomer (A and B) were the only ones that presented, in all conditions evaluated, initial/residual shear stress, that is, significantly high stress value to start its flow, thus showing a Herschel Bulkley fluid behavior. Formulation G showed the same behavior, but only after 30 days of storage at 40 °C (Figure 4C). All other formulations can be considered as pseudoplastic fluids, for which the parameters of the corresponding mathematical models have been adjusted and are presented in Table 3. Good quality of the model of the Law of Power adjustment, with values of R² ranging from 0.980 to 0.999 was verified. Hydrophilic gels formulated with carbomer, CarbopolUltrez, and Pemulen polymers are reported in the literature as pseudoplastic fluids (Corrêa et al., 2005).

Table 3 - Herschel-Bulkley and pseudoplastic fluid model parameters.

Sample	Time	Parameters			
		n	k (Pa.s ⁿ)	τ_0 (Pa)	R ²
A	T0	0.4746	9.4609	23.0977	0.99048
		0.38477	18.4414	-	0.98538
B	T0	0.52838	2.53802	6.78139	0.99269
		0.44507	4.63829	-	0.98917
C	T0	0.41673	3.24097	-	0.98052
D	T0	0.70458	0.14848	-	0.98939
E	T0	0.82929	0.07181	-	0.99921
F	T0	0.9686	0.00670	-	0.98830
G	T0	0.47933	2.32796	-	0.99455
H	T0	0.53377	1.24274	-	0.99484

Source: Authors.

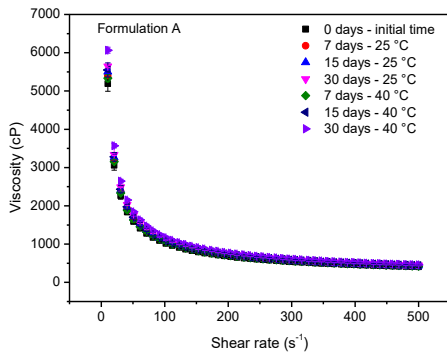
According to Perinelli et al. (2021), the viscosity of gels formed by cellulose polymers is variable as a function of the concentration of ethanol in the hydroalcoholic solution and the molecular mass of the polymer. The author evaluated the consistency index of formulations containing Hydroxyethylcellulose and Hydroxypropylmethylcellulose and verified higher values with Hydroxypropylmethylcellulose, a similar behavior to that obtained in the present study, when comparing formulations C and G, which are formed by these polymers. It is not possible to compare the magnitude of this parameter since the concentration used of polymers was not the same in both studies, but most hydroalcoholic gels with 70% of ethanol formed by these polymers presented a pseudoplastic profile.

Analyzing the magnitude of the apparent viscosity in small deformation rate conditions, it is verified that the samples gelled with carbopol (formulations A and B) and Topgel 8010 (formulation G) were the ones with the highest averages, while sample F presented the lowest apparent viscosity values. According to the RDC (Resolution of the Collegiate Board of Directors - ANVISA) n° 46/2002 (Brasil, 2002), the viscosity of alcohol gel at 70% should be greater than 8,000 cP at 25 °C to reduce the risk of accidents due to burning or ingestion of the product, however, this measure should be made under experimental conditions different from those performed in the present study. Though, it was possible to observe that the samples formulated with carbomer (Carbopol 940) presented the highest viscosities than all the others.

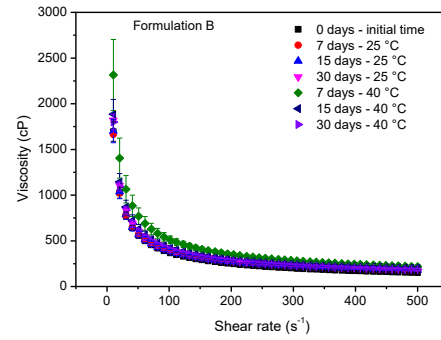
When evaluating the effect of temperature and storage time on formulations' viscosity, the behaviors were diverse (Figure 5). Formulations A, B, and H, which were produced using acrylic polymers, were more stable, since they maintained the viscosity behavior with the constant shear rate even when varying the storage time and at both temperatures. The same behavior was not observed in the other formulations. In general, the other formulations (C, D, E, and G) showed a tendency to increase apparent viscosity with increasing storage temperature. This was probably due to the fact that the gel production process was not done with heating of the sample, which is a common process for polymers derived from celluloses, indicating that the sample had not completed its gelatinization process when it was stored.

Comparing the apparent viscosity of the samples at time 0 and over the 30 days of storage, the profiles are very similar when the storage is evaluated at 25 °C, indicating the stability of the formulations in this temperature condition, which can be observed in both Figure 4 and Figure 5.

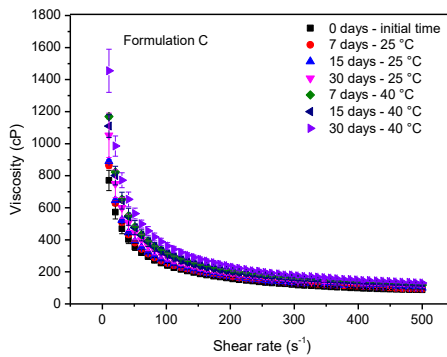
Figure 5 - Viscosity of formulations: (a) A; (b) B; (c) C; (d) D; (e) E; (f) F; (g) G; (h) H.



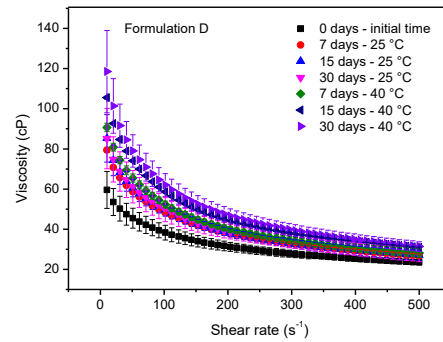
(a)



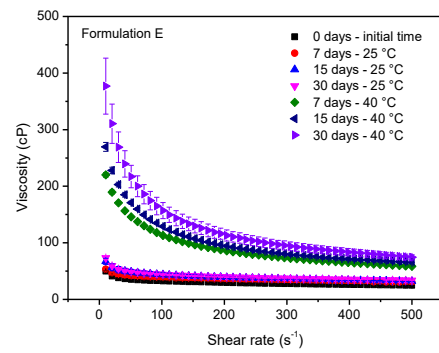
(b)



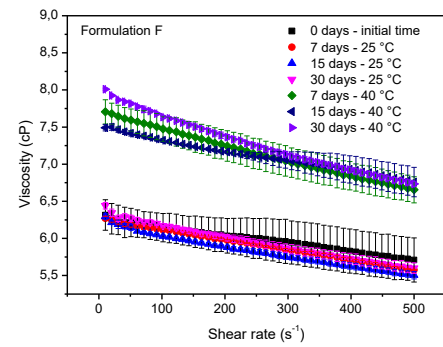
(c)



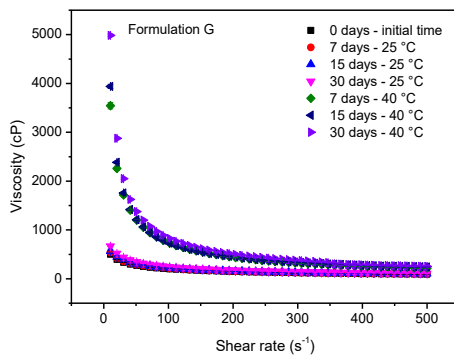
(d)



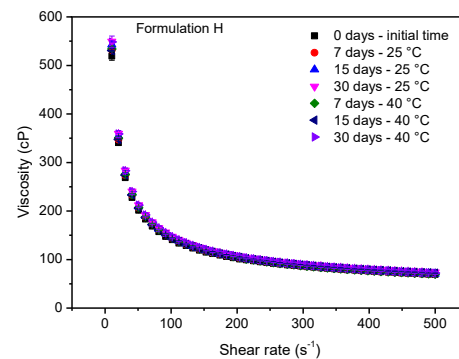
(e)



(f)



(g)



(h)

Source: Authors.

4. Conclusion

Of the 10 polymers or blends of polymers with the potential to be applied as a gelling agent for the production of alcohol-based hand sanitizer, six of them were considered efficient for the production of the product at an ethanol concentration of 70% (w/w). The formulations containing xanthan gum, CMC, quaternized guar gum, and cassava starch formed gel only up to the following alcohol contents: 60, 60, 40, and 30% (w/w), respectively. Similarities in FTIR spectra were detected in these polymers, such as the presence of proteins in xanthan gum and CMC (1650-1550 cm⁻¹), and carbohydrate (1250 to 999 cm⁻¹) in the samples of quaternized guar gum and cassava starch.

All formulations obtained have a characteristic odor and homogeneous appearance, without the presence of lumps. The rheological behavior indicated a characteristic behavior of pseudoplastic fluid of the samples and they remained stable throughout the 30 days of storage at 25 °C. However, at higher storage temperature, formulations that were produced using acrylic polymers were more stable when compared to samples produced with polymers or blends of natural polymers derived from cellulose, which showed a slight increase in apparent viscosity with increasing storage temperature.

As future work, we suggest a detailed study to optimize the amount of use of polymers derived from cellulose to meet the viscosity requirements established by the National Health Surveillance Agency and its impacts on the acceptance of this product by the consumer.

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References

- Blanco, M., Coelho, J., Iturriaga, H., Masposh, S., de la Pezuela, C., & Russo, E. (1994). Control analysis of a pharmaceutical preparation by near infrared reflectance spectroscopy. A comparative study of a spinning module and fibre optic probe. *Analytica Chimica Acta*, 298, 183-191.
- Brasil. Nota Técnica Nº 3/2020/SEI/DIRE3/ANVISA: Orientações gerais sobre a doação de álcool 70%. (2020, march 24). Brasília: Agência Nacional de Vigilância Sanitária.
- Brasil. Ministério da Saúde (2019). Formulário nacional da farmacopeia brasileira. Brasília: Agência Nacional de Vigilância Sanitária.
- Brasil. Ministério da Saúde (2012). Formulário nacional da farmacopeia brasileira. Brasília: Agência Nacional de Vigilância Sanitária.
- Brasil. Resolução da Diretoria Colegiada (RDC) nº 46. (2002, february 20). Brasília: Agência Nacional de Vigilância Sanitária.
- Cerná, M., Barros, A. S., Nunes, A., Rocha, S. M., Delgadillo, I., Copíková, J., & Coimbra, M. A. (2003). Use of FT-IR spectroscopy as a tool for the analysis of polysaccharide food additives. *Carbohydrate Polymers*, 51 (4), 383-389.
- Carqueira, M. A., Bourbon, A. I., Pinheiro, A. C., Martins, J. T., Souza, B. W. S., Teixeira, J. A., & Vicente, A. A. (2011). Galactomannans use in the development of edible films/coatings for food applications. *Trends in Food Science & Technology*, 22 (12), 662-671.
- Corrêa, N. M., Camargo Júnior, F. B., Ignácio, R. F., & Leonardi, G. R. (2005). Avaliação do comportamento reológico de diferentes géis hidrofílicos. *Revista Brasileira de Ciências Farmacêuticas*, 41 (1). <https://doi.org/10.1590/S1516-93322005000100008>.
- Correia, L. M. P. C., Justi, J. S., & Andersen, M. V. (2013, april 19). Retrieved from https://www.saude.pr.gov.br/sites/default/arquivos_restritos/files/documento/2020-05/alcool_gel.pdf
- Figueiró, S. D., Góes, J. C., Moreira, R. A., & Sombra, A. S. B. (2004). On the physicochemical and dielectric properties of glutaraldehyde crosslinked galactomannan-collagen films. *Carbohydrate Polymers*, 56 (3), 313-320.
- Goldstein, A. M., Alter, E. N., & Seaman, J. K. (1973). Guar gum In Whistler, R. L, (Eds), *Industrial gums* (pp. 303-321). New York: Academic Press.
- Hashemi, M. M., Aminlari, M., & Moosavinasab, M. (2014). Preparation of and studies on the functional properties and bactericidal activity of the lysozyme-xanthan gum conjugate. *Food Science and Technology*, 57 (2), 594-602.
- Jansson, P. E., Kenne, L., & Lindberg, B. (1975). Structure of the extracellular polysaccharide from *Xanthomonas campestris*. *Carbohydrate Research*, 45 (1), 275-282.

- Kang, H., Liu, R., & Huang, Y. (2016). Cellulose-Based Gels. *Macromolecular Chemistry and Physics*, 217 (12), 1322-1334. DOI: 10.1002/macp.201500493
- Khonsari, F., Zakeri-milani, P., & Jelvehgari, M. (2014). Formulation and evaluation of in-vitro characterization of gastic-mucoadhesive microparticles/discs containing metformin hydrochloride. *Iranian Journal of Pharmaceutical Research*, 13(1), 67-80.
- Kumar, Y. M., Kayyrapu, B., Neeruganti, O. G., & Chekuri, R. (2018). Thermal and Conductivity Studies of VO₂⁺ Doped Methacrylic Acid-Ethyl Acrylate (MAA: EA) Copolymer Films. *Materials Research*, 21 (1), 1516-1439. <https://doi.org/10.1590/1980-5373-mr-2017-0328>.
- Mou, D., Chen, H., Du, D., Mao, C., Wan, J., Xu, H., & Yang, X. (2008). Hydrogel-thickened nanoemulsion system for topical delivery of lipophilic drugs. *International Journal of Pharmaceutics*, 353 (1-2), 270-276. 10.1016/j.ijpharm.2007.11.051.
- Pavia, D. L., Lampman, G. M., & Kriz, G. S. (2001). Introduction to Spectroscopy. Brooks/Cole-Thomson Learning.
- Perinelli, D. R., Berardi, A., Bisharat, L., Cambriani, A., Ganzetti, R., Bonacucina, G., Cespi, M., & Palmieri, G. F. (2021). Rheological properties of cellulosic thickeners in hydro-alcoholic media: The science behind the formulation of hand sanitizer gels. *International Journal of Pharmaceutics*, 604, 120769. <https://doi.org/10.1016/j.ijpharm.2021.120769>.
- Pooja, D., Panyaram, S., Kulhari, H., Rachamalla, S. S., & Sistla, R. (2014). Xanthan gum stabilized gold nanoparticles: characterization, biocompatibility, stability and citotoxicity. *Carbohydrate Polymers*, 110, 1-9.
- Regiani, A. M., Tambelli, C. E., Pawlicka, A., Curvelo, A. A. S., Gandini, A., Lenest, J. F., & Donoso, J. P. (2000). DSC and solid state NMR characterization of hydroxyethylcellulose/polyether films. *Polymer International*, 49, 960-964.
- Safitri, F. I., Nawangsari, D., & Febrina, D. (2021). Overview: Application of Carbopol 940 in Gel. Proceedings of the International Conference on Health and Medical Sciences (AHMS 2020). *Advances in Health Sciences Research*, 34. <https://doi.org/10.2991/ahsr.k.210127.018>.
- Sandeep, C., Deb, T. K., & Shivakumar, H. G. (2014). Cationic guar gum polyelectrolyte complex micro particles. *Journal of Young Pharmacists*, 6(4), 11-19.
- Sathiyarayanan, P., Karunakaran, R. J., Gomathi, T., & Sudha, P. N. (2015). Synthesis and characterization of carboxymethyl cellulose/polyethylene glycol/montmorillonite clay blends. *International Journal of Novel Trends in Pharmaceutical Sciences*, 5(2), 36-41.
- Shalviri, A., Liu, Q., Abdekhodaie, M. J., & Wu, X. W. (2010). Novel modified starch-xanthan gum hydrogels for controlled drug delivery: Synthesis and characterization. *Carbohydrate Polymers*, 79 (4), 898-907.
- Silverstein, R. M. & Webster, F. X. (2000). Identificação Espectrométrica de Compostos Orgânicos. Rio de Janeiro: LTC Editor.
- Silverstein, R. M., Bassler, G. C., & Morrill, T. C. (1997). *Spectrometric Identification of Organic Compounds*. New York: John Wiley.
- Singh, R. K. & Khatri, O. P. (2012). A scanning electron microscope based new method for determining degree of substitution of sodium carboxymethyl cellulose. *Journal of Microscopy*, 246 (1), 43 -52.
- Wang, Z., Zhao, Y., Zhou, L., Xu, L., Diao, G., & Liu, G. (2020). Effects of hydroxyethyl methyl cellulose ether on the hydration and compressive strength of calcium aluminate cement. *Journal of Thermal Analysis and Calorimetry*, 140 (2), 545-553.
- Yang, X. H. & Zhu, W. L. (2007). Viscosity properties of sodium carboxymethylcellulose solutions. *Cellulose*, 14, 409-417.