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Qualitative Physical Assessment on The Effects of Salt on Potential Hydrogels Used in Nanoparticle Drug Delivery

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Abstract

The prevalence of oral cancer cases worldwide has urged scientists to revise topical drug formulations meant for oral application improving drug locality. This alternative treatment helps to minimise the side effects from the current available treatment. The physicochemical properties of the material need to be assessed when designing a new topical drug. Therefore, this paper aims in developing formulation and characterise hydrogels with the addition of different salt concentrations. In this project, the hydrogels studied are iota-carrageenan and kappa-carrageenan. As salt is the common ingredient used in drug formulation, the effects of salt on the physical properties of carrageenan are studied. Each concentration of the carrageenan is formulated with four different concentrations of salt at 0.5%, 1.0%, 1.5%, and 2.0%. The pH of the solution is maintained at pH 7. The results show that both concentrations of kappa-carrageenan are not suitable to be used as a carrier for nano-topical drugs due to their hard and rigid texture. Based on the physical properties, the suitable formulation for nano-matrix would be the 0.5% iota-carrageenan added with 1.5% and 2.0% NaCl, as well as the 1.0% iota-carrageenan added with 0.5% NaCl.

Keywords: Oral cancer, drug delivery, nanotechnology, carrageenan, salt

Abstrak

Kelaziman kes kanser mulut di seluruh dunia telah menggesa para saintis untuk menyemak semula formulasi ubat topikal yang bertujuan untuk aplikasi oral meningkatkan lokaliti ubat. Rawatan alternatif ini membantu meminimumkan kesan sampingan daripada rawatan sedia ada. Sifat fizikokimia bahan perlu dinilai dalam pembuatan ubat topikal baharu. Oleh itu, kertas kerja ini bertujuan untuk membangunkan formulasi dan mencirikan hidrogel dengan penambahan kepekatan garam yang berbeza. Dalam projek ini, hidrogel yang dikaji ialah iota-karageenan dan kappa-karageenan. Oleh kerana garam adalah bahan biasa yang digunakan dalam perumusan ubat, kesan garam terhadap sifat fizikal karagenan dikaji. Setiap kepekatan karagenan dirumuskan dengan empat kepekatan garam yang berbeza pada 0.5%, 1.0%, 1.5%, dan 2.0%. pH larutan dikekalkan pada pH Keputusan menunjukkan bahawa kedua-dua kepekatan kappa-carrageenan tidak sesuai digunakan sebagai pembawa ubat topikal nano kerana teksturnya yang keras dan tegar. Berdasarkan sifat fizikal, formulasi yang sesuai untuk nano-matriks ialah 0.5% iota-karageenan ditambah dengan 1.5% dan 2.0% NaCl, serta 1.0% iota-karaginan ditambah dengan 0.5% NaCl.

Kata Kunci: Kanser mulut, penghantaran dadah, nanoteknologi, karagenan, garam

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Introduction

The prevalence of oral cancer globally is alarming as the number of cases is disturbingly high. Oral cancer also known as one of the factors of mortality worldwide, mainly because of late detection. International Agency for Research on Cancer & Organization (2019) reported that there are more than 350,000 new oral cancer cases to date, with countries in Asia recording the highest number of new cases for more than 200,000 cases. The common factors contributing to the disease are the habit of tobacco chewing, smoking, and alcohol consumption. Other than that, recent studies show that many patients who do not practice these habits were diagnosed (Kim & Kim, 2020). The growing health problem has become a concern, and scientists are working on developing better treatments for oral cancer.

The current treatments for oral cancer are surgery, radiotherapy, and chemotherapy, but these treatments have some drawbacks to the patient's quality of life. These therapies typically present a variety of side effects for the patients. For example, patients may experience facial disfigurement, speech difficulties, loss of nutrition due to loss of appetite, and risk of cancer cell metastases to other parts of the body (Nandini et al., 2020). To reduce the side effects, newer treatment methods such as targeted therapy may become the alternative. Sankar et al. (2011) mentioned the potential of topical drugs such as creams, gels, or ointments as targeted therapy for oral cancer. Such topical drugs provide effective targeted drug delivery and ultimately improve the treatment outcome. The topical drug faces some challenges in its therapeutic action in the aspects of controlling and determining the therapeutic concentration of its bioactive pharmaceuticals ingredients onto the target site (Chaudhari, 2012).

The formulation of the nanoparticle drug delivery system can control and sustain the release of the drug to the target site hence offering site-specific delivery (Seeni, Krishnamurthy, & Chan, 2015). The sizes of nanoparticles range from 10-100nm, and they are relatively small particles in size. The small particle sizes provide advantages to the drug delivery system as it can penetrate the skin barriers deeper through fine capillaries and allow cells to take up the active compound of the drug efficiently (Hornig, Bunjes, & Heinze, 2009; Patel, Patel, Shah, & Modasiya, 2011). Nonetheless, the small particle size also can be a limitation contributing to its fragility. Therefore, nanoparticles research is often associated with nanoparticles or matrix to be included in the formulation acting both as protector and carrier. Hydrogels are currently being assessed as potential nanocarriers. The use of hydrogels in pharmaceutical industries is widely known. The hydrogel is a polymer that has so many unique properties that are useful in drug delivery development study. Lopez Hernandez, Grosskopf, Stapleton, Agmon, and Appel (2019) stated among the unique properties of hydrogels are having the tissue-like mechanical properties, its biocompatibility, and its ability to retain high water content. These properties make hydrogels a suitable candidate for nanocarrier used in oral cancer treatment. Gonçalves, Pereira, and Gama (2010) also acknowledged the advantages of hydrogels for the drug study, which offer site-specific delivery and able to reduce the toxicity of the drug that can improve the drug's effectiveness. Other than that, hydrogels have non-Newtonian fluid properties which means that the viscosity is independent of the shear rates. Thus, the hydrogels can be formulated so that the viscosity is suitable for oral drug texture.

The integration of hydrogel and nanoparticles is known as hydrogel nanoparticles which is also interchangeably used with the term nanoparticles-hydrogels. There is rising attention towards hydrogel

nanoparticles in some fields of medicine, such as the use of hydrogel nanoparticles in improving cell viability (Lopez Hernandez et al., 2019) and as a treatment for leukaemia disease (Senthil et al., 2010). Hydrogel nanoparticles also have a bright future in topical drug design for oral cancer. For instance, they could retain their shape in the aqueous environment of the oral cavity. Thus, it can maximize the diffusion efficiency while the nanoparticle drug is being released to the target site (Patel et al., 2011; Saha & Bhattacharya, 2010; van Aken, Vingerhoeds, & de Hoog, 2007). Hydrogels also have been widely used as food additives as gelling agents; thus, they can be considered as safe to be applied orally.

However, the study of a topical drug with hydrogel nanoparticles specifically for oral treatment is minimal. The current study for topical drugs using hydrogel nanoparticles only adopted for skin disease treatment. The formulation adopted for dermatological conditions might become a challenge when applied orally because of the mouth condition that is different from human outer skin layer. Hence, detailed insight into the characteristics of hydrogels needs to be studied. Material characterisation allows researchers to understand the physical, chemical, and mechanical properties of the materials. Researchers can also gain knowledge on the behaviour of the materials in different conditions and any potential adverse biological effects of the materials. In the effort to develop a novel topical nanoparticle drug for oral treatment, salt is one of the ingredients that is usually used to alter the taste and characteristics of the materials. In this study, the hydrogels are added with common salt, sodium chloride (NaCl), and the effects of the salt addition to the characteristics of the hydrogels are studied.

This paper aims to study the effects of salt addition on the physical characteristic of the hydrogels used for nanoparticle drug delivery to treat oral cancer. For this project, the natural polymer-based hydrogels, which are kappa-carrageenan and iota-carrageenan, are studied. These two types of carrageenan are chosen as they are non-toxic, biodegradable, and biocompatible (Król, Malik, Marycz, & Jarmoluk, 2016). Other than that, carrageenan is extracted from the edible red seaweed; therefore, it can reduce the halal concerns among Muslim consumers. Four different salt concentrations are added to the hydrogels, and the effects on the characterization of hydrogels are studied.

Material and Methods Materials

Chemicals

The powder gels used were kappa-carrageenan sulphated plant polysaccharide (Sigma-Aldrich, Denmark) and commercially grade iota-carrageenan type II (Sigma-Aldrich, United States of America, USA). Phosphate buffer saline solution (0.05 M) was prepared using potassium dihydrogen phosphate anhydrous (KH_2PO_4, ChemAR System, Malaysia), disodium hydrogen phosphate anhydrous (Na_2HPO_4, R&M Chemicals, United Kingdom), sodium chloride (NaCl, Merck, Germany), and distilled water. The adjustment of buffer pH was made by using 1.0 M sodium hydroxide (NaOH, Merck, Germany) and 1.0 M hydrochloric acid (HCl, Nacalai Tesque, Japan). All sample concentration was measured in per cent weight per volume (% w/v).

Chemicals Preparation

Phosphate Buffer Saline solution (PBS)

The 0.05 M PBS solution was prepared using 0.05 M potassium dihydrogen phosphate (KH_2PO_4), 0.05 M disodium hydrogen phosphate (Na_2HPO_4), and 0.05 M sodium chloride (NaCl). All the chemicals were added to 1000 mL of distilled water and stirred with a hotplate until it becomes completely dissolved. The

pH was adjusted to pH 7 by adding either sodium hydroxide (1.0 M, NaOH) or hydrochloric acid (1.0 M, HCl) and measured using a pH meter (Eutech pH 510) and stirred on a hotplate. 1.0 M NaOH and 1.0 M HCl were prepared in a fume hood. The PBS was filtered using filter papers to remove any impurities in the solution. PBS was stored in a 1000 mL Schott bottle at room temperature.

Gels Preparation

Two concentrations of carrageenan samples, which are 0.5 w/v% and 1.0 w/v%, were prepared using weight per volume percentage (w/v%). Dry kappa-carrageenan powder was weighed using an analytical balance and transferred into a beaker. Sodium chloride salt was weighed and added to the same beaker. The concentrations of the salt were set at 0.5 w/v%, 1.0 w/v%, 1.5 w/v%, and 2.0 w/v%. κ-Carrageenan samples were formulated by adding 50 mL total volume of 0.05 M PBS solution prepared previously into the beaker. The beakers with respective sample concentrations were covered using aluminium foil, stirred at 100 rpm using a magnetic stirrer and heated to approximately 70°C then left to dissolve for 30 minutes. The samples were then poured into 50 mL falcon tubes, covered with parafilm, and chilled at 4 °C. All sets of samples were prepared in triplicate. For each concentration of carrageenan, a set of controls was prepared with no presence of additional NaCl. The samples' texture and consistency were observed and recorded. ι-carrageenan samples were prepared using the similar method. Figure 1 illustrates the formulation of iota-carrageenan and kappa-carrageenan prepared in this study.

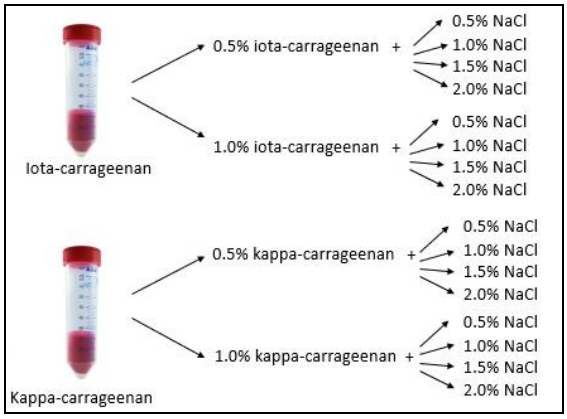

Figure 1. The formulation of iota-carrageenan and kappa-carrageenan prepared for the study.

Result and Discussion

In this study, the pH of the solution for all concentrations of carrageenan to become gel is maintained at pH 7, and the gelling temperature is standardized to 70°C. This condition is a general condition in the gelling process of carrageenan. Ali and Ahmed (2019) explained in their review paper that carrageenan, especially kappa- and iota-carrageenan have thermally reversible properties in which they can melt to a solution during heating and turn back to gel upon cooling. However, these two types of carrageenan are stable in pH 7 and do not undergo hydrolysis in a neutral condition. In the paper, Ali and Ahmed (2019) also mention that the gelling temperature of kappa-carrageenan and iota-carrageenan is high because they need to be heated to solubilise and the preferred heating temperature is more than 40°C-60°C. 70°C is the preferred gelling temperature in most carrageenan preparation. Similar statements are mentioned by Hotchkiss, Brooks, Campbell, Philp, and Trius (2016) by explaining the heating of kappa-carrageenan and iota-carrageenan allows the polymer chains to exist as random coils and upon cooling, the chains will form double helixes and aggregated further to

turn into gel if monovalent ions or divalent such as K^+ or Ca^{2+} ions are present. For this project, the monovalent and divalent cations are present from the buffer used which are the phosphate buffer saline solution.

During the preparation of the gels, a total of 48 samples of carrageenan were prepared for the triplicate result. From the result, kappa-carrageenan and iota-carrageenan show significant texture variations to each other. Figure 2 shows the texture of 0.5% kappa-carrageenan when different NaCl concentrations are added. (A) is the control as no additional NaCl is added to the solution during preparation. Whereas (B), (C), (D), and (E) are the result of NaCl addition at concentration of 0.5%, 1.0%, 1.5%, and 2.0% respectively. Based on the observation, the kappa-carrageenan forms brittle gels with no NaCl addition, but the gels become more elastic as the concentration of NaCl increases. 0.5% kappa-carrageenan added with 2.0% NaCl is the hardest compared to the rest. The difference in the texture of (A) and (E) are obvious as the latter appear more solid as compared to the control. Similar characteristics are also observed for the 1.0% kappa-carrageenan samples shown in Figure 3.

Figure 3 displays the appearance of 1.0% kappa-carrageenan. The comparison of the controls for 1.0% and 0.5% kappa-carrageenan shows that the increase in the kappa-carrageenan concentration will also increase the gel strength. 1.0% kappa-carrageenan appears as harder gels when compared to 0.5% kappa-carrageenan. An increase in the concentration of carrageenan causes the gels to become more apparent. Furthermore, the addition of sodium chloride salt also influences the texture and consistency of the gels. For example, the addition of 2.0% NaCl to the 1.0% of kappa-carrageenan shows that the resulting gels are rigid and there is almost no excess moisture present when the gel is placed on a piece of paper. On the other hand, the same concentration of NaCl at 0.5% kappa-carrageenan illustrates an almost similar appearance as the 1.0% kappa-carrageenan with no NaCl addition. In short, the higher the kappa-carrageenan concentration and salt concentration, the gels will become harder.

Generally, kappa-carrageenan is well-known as an excellent gelling agent. Therefore, the clear, brittle, and hard gel formation of kappa-carrageenan is expected. The hardness and brittle properties of kappa-carrageenan are influenced by the presence of K^+ ions obtained from the PBS solution. Hotchkiss et al. (2016) mentioned that kappa-carrageenan forms brittle gels with the presence of potassium salt as kappa is potassium ion-sensitive. It is also supported by Li, Ni, Shao, and Mao (2014), in which they agreed that different salts have different effects on the gelling and phase transition of kappa-carrageenan. The researchers emphasized that kappa form stronger gels with the presence of potassium salt compared to sodium and calcium.

However, the temperature of the gel-sol transition of kappa is closely related to the NaCl content. Li et al. (2014) further stated that the increase in salt concentration and cations in kappa might increase the storage modulus. Higher storage modulus indicates an increase in strength and mechanical rigidity. Other than that, the addition of NaCl increases the ionic strength of the carrageenan and may cause syneresis by kappa-carrageenan. Syneresis is the spontaneous contraction of gels that can results in the removal of water onto the surface when the gels are at rest (Scherer, 1989).In this study, 0.5%

kappa-carrageenan with the addition of 0.5%, 1.0%, 1.5%, and 2.0% NaCl shows some syneresis actions as shown in Figure 2. Excess moisture from the gels can be observed in the piece of the black paper. Based on the observation, the formulation of 0.5% and 1.0% kappa-carrageenan and NaCl is not suitable to be developed as a topical drug due to the texture of the gels which are very rigid and brittle. The texture indicates that the storage modulus of these formulations is high, and it will cause the gels to have limited swelling properties. When swelling is limited, the transfer of nanoparticles drug orally can become a challenge because of the aqueous environment can cause the hydrogels to burst.

Next, the formulation of 0.5% iota-carrageenan in Figure 4 shows different gelling characteristics as compared to 0.5% kappa-carrageenan and 1.0% kappa-carrageenan. 0.5% iota-carrageenan has a soft texture and closely resembling to semi-solid properties. Based on the observation, 0.5% iota-carrageenan exhibits gel-solution texture, and when added with sodium chloride, they turn into a jelly texture. The higher concentration of the salt will increase the gelling ability of iota-carrageenan. The flow behaviour of 0.5% iota-carrageenan added with 2.0% NaCl is slightly different from the control as the former is more elastic and viscous compared to the latter. However, the formulation of 1.0% iota-carrageenan has a different appearance compared to 0.5% iota-carrageenan. From Figure 5, the turbidity of 1.0% iota-carrageenan is higher than 0.5% iota-carrageenan. Not only that, 1.0% iota-carrageenan with the increase of salt concentration illustrates a smoother and softer texture. The thickness of 1.0% iota-carrageenan is thicker as compared to 0.5% iota-carrageenan and both concentrations of kappa-carrageenan. When different salt concentrations were added to each concentration of iota-carrageenan, the texture of the gels become more elastic. The increase in the concentration of iota-carrageenan also contributes to the elasticity. For example, 0.5% iota-carrageenan added with 0.5% NaCl salt in Figure 4 (B) when compared with 1.0% iota-carrageenan with 0.5% NaCl salt from Figure 5 (B) are distinct in appearance. The former barely formed gel and has liquid-like consistency, whereas the latter shows the appearance of gel, and the colour is slightly cloudy compared to it.

Unlike kappa-carrageenan, iota-carrageenan is preferred as the thickening agent should have an elastic and soft texture (Blakemore, 2016). These observations follow the underlying gelling mechanism and characteristics of kappa-carrageenan and iota-carrageenan accordingly. Gelling of carrageenan formed when a single helix of carrageenan combined with another similar single helix to form a double helix and eventually promote aggregation into a 3-D network (Carneiro-Da-Cunha et al., 2011). However, gelling is only possible with the presence of the 3,6-anhydrous bridge and lower sulphate esters group. Higher sulphate ester content will have lower gel strength. According to Ali & Ahmed (2019), the ester sulphate content of kappa and iota is 25% and 32%, respectively. The higher sulphate ester content of iota explained the softer texture of gels formed.

Besides, iota-carrageenan presents lesser to no syneresis compared to kappa with the increase in salt concentration. It is because the additional sulphate group in the iota structure could increase its ability to inhibit syneresis due to the higher hydrophilicity of iota compared to kappa. (Popescu, Iordan, & Boscornea, 2007). Furthermore, Popescu et al. (2007) also

explained that the increase in salt concentration added to iota-carrageenan would increase the hydration temperature and allow the solution to be converted into the gel at a specified yield point.

Based on illustration in Figure 5, it is shown that 1.0% of iota-carrageenan has higher turbidity with the increasing NaCl salt concentration as compared to other concentrations of carrageenan. According to Nguyen et al. (2014), sodium salt or Na^+ ions will increase the turbidity of the material. Nevertheless, kappa-carrageenan remains transparent with increasing NaCl salt because NaCl help to reduce the electrostatic repulsion between helixes of kappa and facilitates the association with K^+ ions to induce gelling.

Often, kappa-carrageenan and iota-carrageenan have almost similar properties due to the presence of 3,6-anhydrobridges and sulphate group at position four in their chemical structure. The latter, however, has an additional sulphate group at position number 2. While they both are biocompatible, non-toxic, and have a bright future in drug delivery, the slight difference in the chemical structure could influence their gel strength, texture, solubility, and melting temperature (Ali & Ahmed, 2019). Other than that, the presence of cation and salt concentration could also affect the gelling mechanism of kappa-carrageenan and iota-carrageenan. Necas and Bartosikova (2013) stated that kappa- and iota-carrageenan require the presence of potassium and calcium ions for them to form gels, whereas lambda-carrageenan does not. Moreover, studies done by Nguyen, Nicolai, Benyahia, & Chassenieux (2014) show that the stiffness rate increases as the concentration of NaCl salt increases.

From the result, the texture of kappa-carrageenan and iota-carrageenan are contrasting with each other. Both 0.5% and 1.0% kappa-carrageenan form a clear, hard, and brittle gel. On the other hand, similar concentrations of iota-carrageenan are softer, cloudy, opaque, and elastic. The addition of four different concentrations of NaCl salt to kappa-carrageenan increases the hardness of the gel. Based on the observation, 1.0% kappa-carrageenan with the addition of 2.0% NaCl salt is the hardest as compared to the other mixture of kappa-carrageenan, whereas 1.0% iota-carrageenan with 2.0% NaCl seems to have the highest elasticity. The ionic strength of salt is responsible for determining the texture and viscosity of the gels.

Not only that, but the increase in the concentration of the carrageenan itself could also affect their physical properties. For instance, the syneresis action from kappa-carrageenan at 1.0% concentration is visibly lower than that of 0.5% concentration. Similarly, the syneresis action of iota-carrageenan also agrees with that of kappa. This observation is supported by a study done by Foegeding and Ramsey (2006) that aims to study the rheological properties of gelled meat batters using iota and kappa-carrageenan. The study reveals that the addition of carrageenan concentration increases the water-holding ability of the batters, and batters added with iota-carrageenan result in the true shear strain as the batter does not deform. The kappa-carrageenan, on the other hand, has shown effective to increase the hardness of the batters. The principles of the water-holding capacity of the batters can be applied in this study. It is because the situation happens due to the increase in hydrophilic properties of carrageenan. As the concentration increases, the number of hydroxyl groups that can form ionic interaction with the water is also increased (Garcia, Yamashita, Youssef, Prudencio, & Shimokomaki, 2013). The addition of NaCl also contributes to the increase of the

water holding capacity as NaCl can increase the ionic strength of the carrageenan structure. As the water holding capacity increases, the expulsion of moisture when the gels are at rest decreases.

Next, the viscosity characterizes the physical properties of kappa and iota-carrageenan based on their flow behaviour. The viscosity of a material can be classified as Newtonian and non-Newtonian fluids. Kappa and iota-carrageenan are chosen as the hydrogels to be studied because of their non-Newtonian fluid properties. The graph in Figure 6 (George & Qureshi, 2013) displays the relationship between shear stress and shear rate for Newtonian and other non-Newtonian fluids when mechanical force is applied. From the graph, the shear stress of Newtonian fluids increases linearly with the shear rate. The ratio of shear stress and shear rate indicates the viscosity. The viscosity of non-Newtonian fluids, as shown in the graph, is not constant and dependent on the shear rate. This is the reason carrageenan is suitable as a carrier for topical drug. For carrageenan to be designed as a topical drug carrier for oral cancer, they need to be formulated so that it can withstand a particular force. It is so that the oral drug does not destroy when squeezed out of the packaging, during the application, or due to the mastication activity in the mouth. Thus, the suitable viscosity for a topical drug is when it is reduced as the shear rate increases.

Based on the flow properties of the carrageenan, 0.5% and 1.0% kappa-carrageenan could exhibit shear-thickening flow behaviour. It is because of the viscosity of kappa-carrageenan that is higher as the concentration increases, and upon deformed, kappa-carrageenan could not return to its original shape. Conversely, 0.5% of iota-carrageenan has fluid-like properties, but the addition of salt improves the elasticity of the gels. Unlike 0.5% iota-carrageenan, 1.0% iota-carrageenan is elastic even without the addition of salt. The elasticity could indicate shear-thinning flow behaviour which is suitable for the topical drug as the viscosity decreases when the force increases. The shear-thinning and shear-thickening of a gel indicate non-Newtonian fluid's behaviour. Physically, iota-carrageenan has better flow properties as nanocarriers for topical drug. However, for accurate classification as shear-thinning or shear-thickening, it is recommended to test the carrageenan using a rheometer so that the value of the viscosity and the force can be obtained.

All in all, 0.5% and 1.0% kappa-carrageenan added with NaCl are not suitable as nanoparticle-matrix for topical drugs. This is because the texture of the gels is too rigid, and it does not have the normal pasty texture of topical drugs such as lotions or creams. In contrast, iota-carrageenan has the potential to be used as a matrix for nanoparticle drug delivery in oral conditions. The formulation of iota with NaCl creates smooth, soft, and elastic gels.

Conclusion

In conclusion, the objectives of the study were achieved when the observations show that the different formulations of the carrageenan concentration and salt concentration exhibit different physical properties. The formulation of kappa-carrageenan and NaCl results in a clear, hard, and brittle gel, whereas the iota-carrageenan added with NaCl has a softer texture and is more elastic. The formulation of kappa-carrageenan with NaCl was found not suitable to be used as the matrix of nanoparticles for topical administration due to its hard texture.

However, the formulation of iota-carrageenan and NaCl has the potential to be used in designing novel topical drugs. For 0.5% iota-carrageenan, the addition of 1.5% and 2.0% NaCl has the desired texture for topical drug administration. Whereas for 1.0% iota-carrageenan, the addition of the lowest concentration of salt, which is 0.5% is another suitable candidate for topical drug design.

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TABLES AND FIGURES

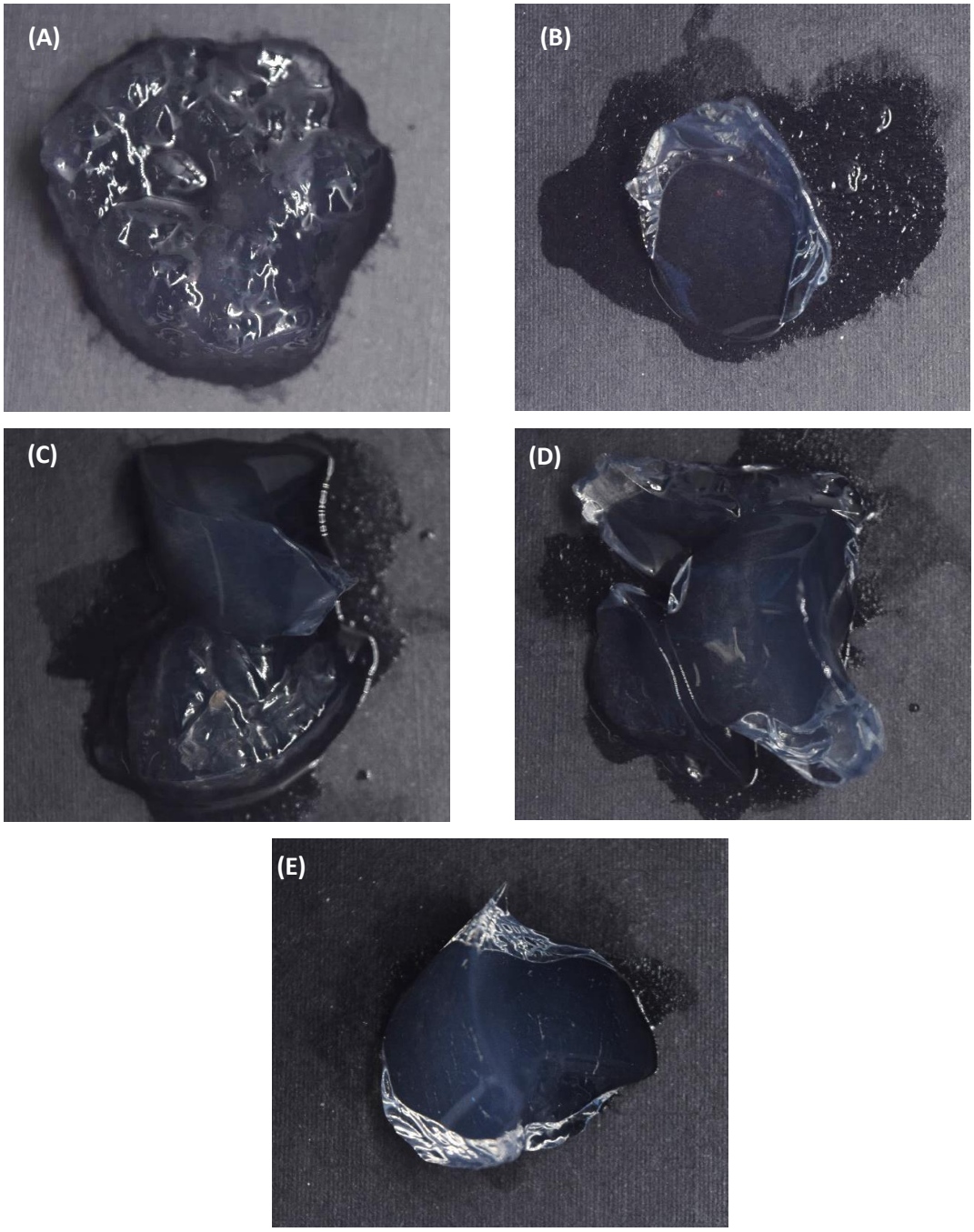

Figure 2. The texture of 0.5% κ-carrageenan with addition of different NaCl concentration. (A) Control, with no salt addition. (B) Addition of 0.5% NaCl. (C) Addition of 1.0% NaCl. (D) Addition of 1.5% NaCl. (E) Addition of 2.0% NaCl.

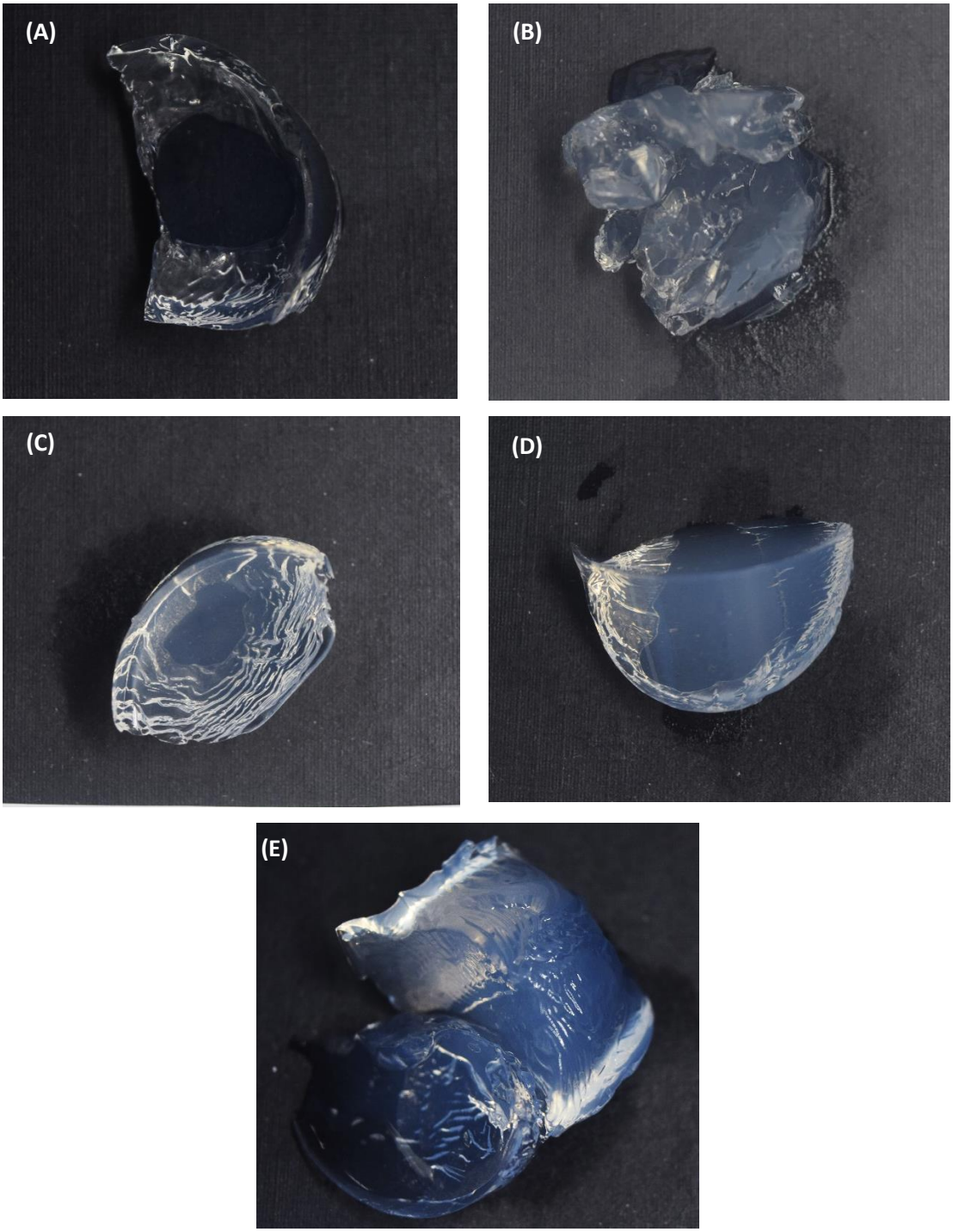

Figure 3. The texture of 1.0% κ-carrageenan with addition of different NaCl concentration. (A) Control, with no salt addition. (B) Addition of 0.5% NaCl. (C) Addition of 1.0% NaCl. (D) Addition of 1.5% NaCl. (E) Addition of 2.0% NaCl.

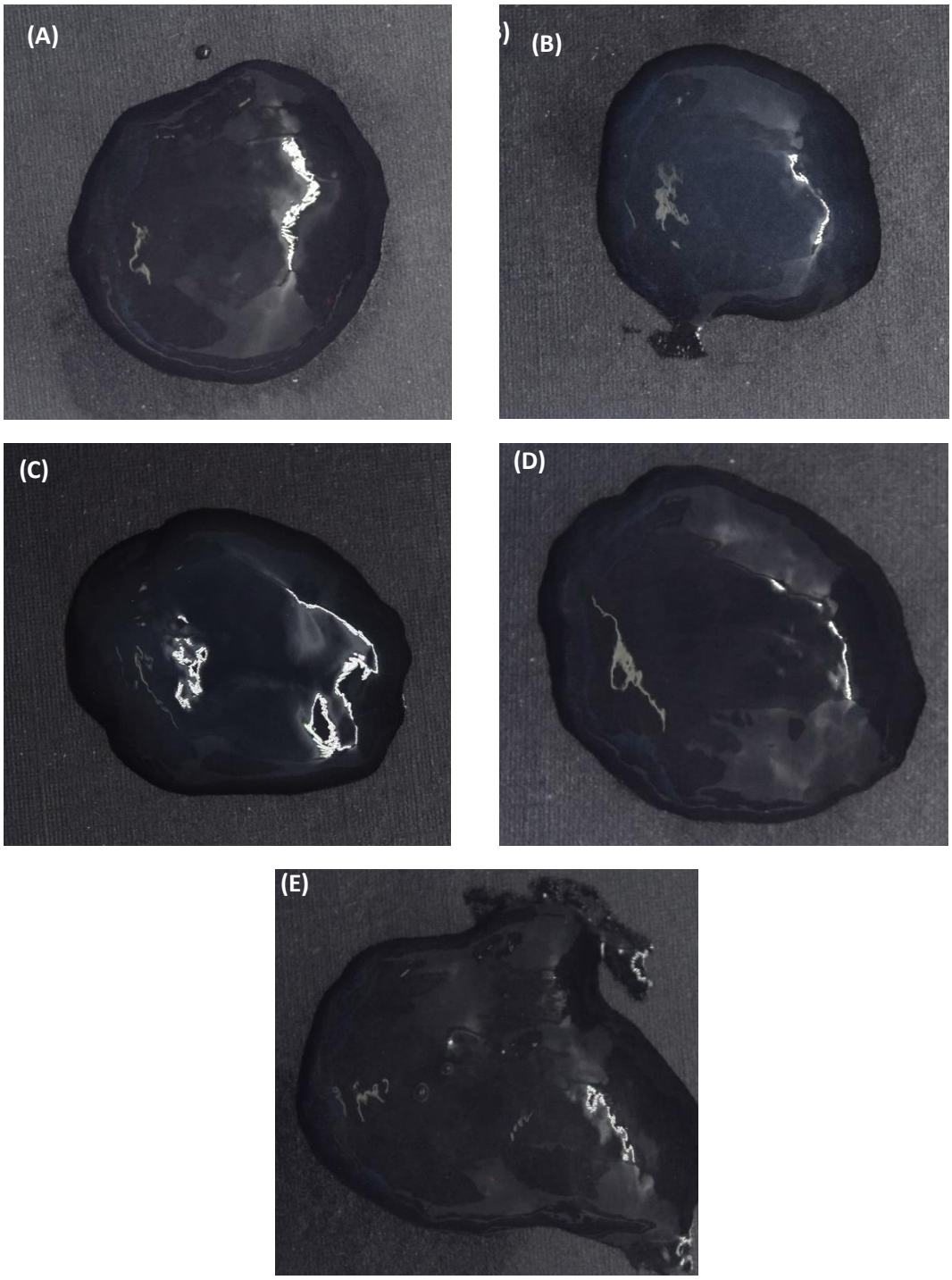

Figure 4. The texture of 0.5% ι-carrageenan with addition of different NaCl concentration. (A) Control, with no salt addition. (B) Addition of 0.5% NaCl. (C) Addition of 1.0% NaCl. (D) Addition of 1.5% NaCl. (E) Addition of 2.0% NaCl.

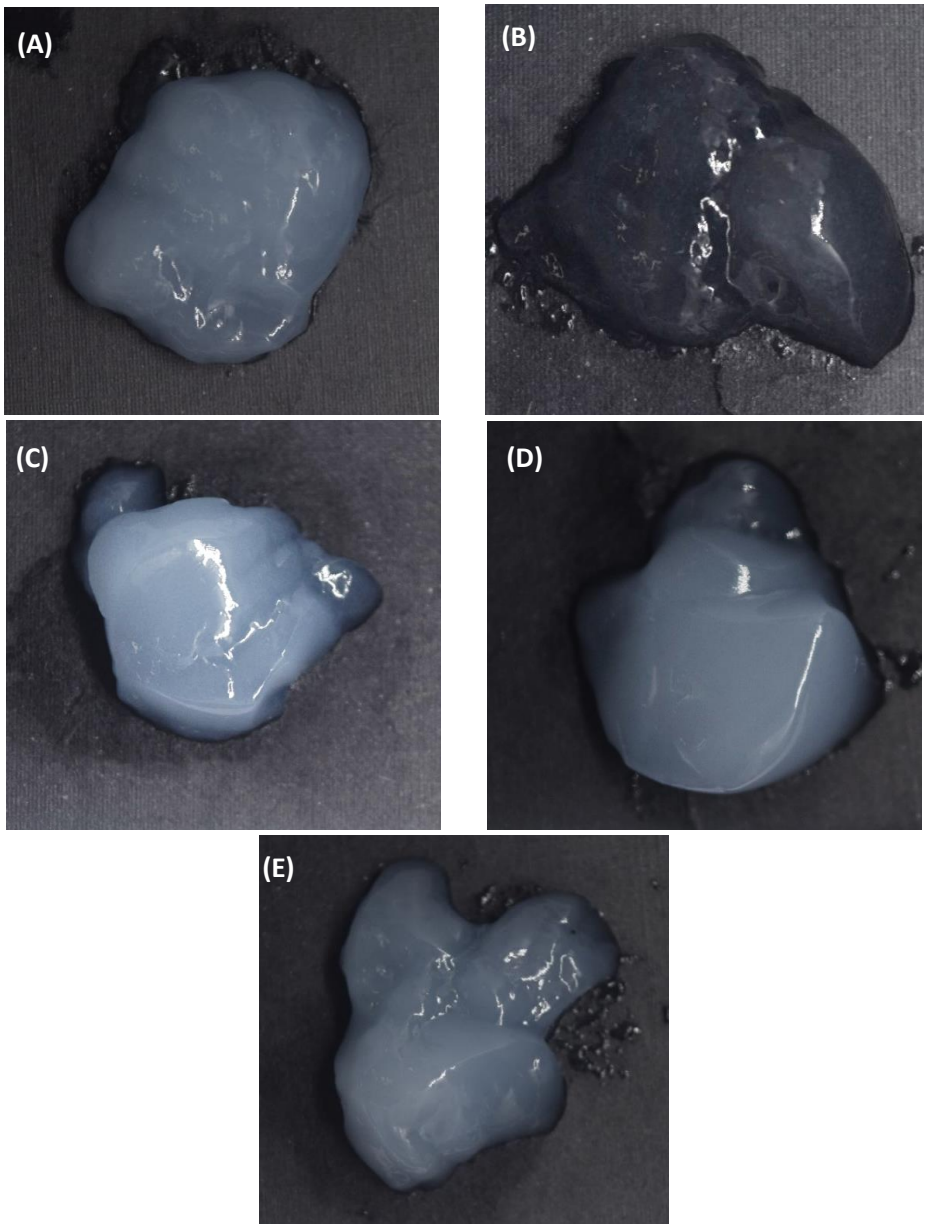

Figure 5. The texture of 1.0% ι-carrageenan with addition of different NaCl concentration. (A) Control, with no salt addition. (B) Addition of 0.5% NaCl. (C) Addition of 1.0% NaCl. (D) Addition of 1.5% NaCl. (E) Addition of 2.0% NaCl.

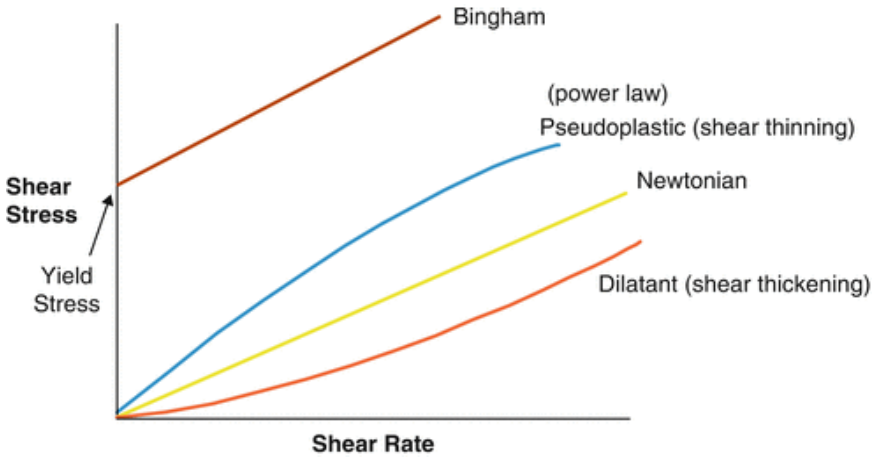

Figure 6: The relationship between shear stress and shear rate for Newtonian and non-Newtonian fluids (George & Qureshi, 2013).