Characterization of Alginate with Natural Polymers Combination for Drug Encapsulation

Viviane Annisa*, Teuku Nanda Saifullah Sulaiman**, Akhmad Kharis Nugroho** and Agung Endro Nugroho**,1

*Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia, 55281
**Departement of Pharmaceutics, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia, 55281

Abstract

Alginate is one of the natural biopolymers that is widely used for drug formulations, combination of alginate with other polymers, such as gum acacia, pectin, and carrageenan can increase mechanical strength, therefore, can reduce leakage of the encapsulated active pharmaceutical ingredient from the polymer matrix. Interaction of alginate and these polymers can occur via intermolecular hydrogen bonds causing synergism, which is determined from the viscosity of polymer mixture.

Alginate was combined with gum acacia/pectin/carrageenan in different blending ratios (100:0, 75:25, 50:50, 25:75, and 0:100) with and without addition of $CaCl_2$. The synergism effect is obtained from the design of experimental (DoE), and calculation the percentage value of viscosity deviation viscosity synergism index, then the strength of gel was analyzed. The interaction between two polymers was observed using FTIR spectroscopy. In distilled water, the synergistic effect was found in the combination of alginate-carrageenan at ratios 25:75 and 50:50. Otherwise, in $CaCl_2$ solution, synergistic effect appears in alginate-gum acacia (75:25), alginate-pectin (50:50 and 75:25), and alginate-carrageenan (50:50 and 75:25). The synergistic effect and strength of gel polymers increased, with the addition of $CaCl_2$.

Keywords: Synergistic interactions, alginate, pectin, carrageenan, polymer viscosity

Introduction

The combinations of alginate with some electronegative polymers such as pectin, gum acacia, carrageenan, etc. have been widely used in drug formulation. to encapsulate active ingredients to prevent degradation [1], improve thermal and chemical stability [2–5], reduce toxicity [6,7], increase the effectiveness of active substances [7,8], control the release of the active substance [9–12], improve mechanical properties of microbeads [13], and as a carrier for drug targeting [14].

Alginate as biopolymer material does not have sufficient mechanical properties, and this makes it difficult to use in specific products. To overcome this, it can be resolved by combining alginate with other polymers. Alginate can dimerize to form bridges with other chains and produce hydrogel networks [15]. Alginate and other poly-electronegative polymers will interact via intermolecular hydrogen bonds [16,17]. The combination with polymers, such as gum acacia, pectin, and carrageenan can increase their synergistic effect compared to the single polymer. The synergistic ability of polymers can be characterized through changes in viscosity that occur when polymers are combined [18]. The determination of synergy effect is very useful for the fabrication of the matrix used for drug encapsulation.

An approach using experimental design has been studied by Jadhav, et al (2018) to identify polymeric synergy. The benefit of using the design of experiment tool is an experiment can be more effective with a smaller sample [19]. Marimuthu et al (2017) have calculated the synergism index to determine the synergy effect on the combination of carrageenan with several natural polymers [18]. On the other hand, Nkenmogne et al (2020) have calculated using percentage deviation calculation the synergy effect of a combination of alginate and hydrocolloids from tropical vegetal species [20]. The synergism between two polymers can be determined from experimental design or mathematical equations.

The objective of this study was the characterization of alginate combination with pectin, gum acacia, or carrageenan with and without the addition of Calcium Chloride ($CaCl_2$) solution. The interaction of two polymers combination would be observed using calculation of synergy effect ability. Synergism will be determined using viscosity data obtained from an experimental design, and mathematical equation including viscous synergism index and percentage deviation of viscosity. FTIR spectroscopy was used to show the bands of interaction in the polymer's mixture.

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Materials and Methods

Materials

Sodium alginate ALG was manufactured by Shandong Jiejing Group Corporation (China), gum acacia GA was manufactured by Spectrum Chemical MFG Corporation (California), pectin PC was manufactured by Danisco USA Inc (USA), kappa-carrageenan CR was manufactured by Top P&P Co (China), $CaCl_2$ was manufactured by PT. Smart-Lab Indonesia and deionized water was supplied from CV. Alfa Kimia.

Preparation of polymer mixture solution

A polymer solution with a concentration of 1% was prepared by weighing 1.0 g and dissolved slowly into 100 ml deionized water then stirred until homogenous. The solution of alginate (ALG) mixed with each gum acacia (GA), pectin (PC), or carrageenan (CR) that weighted with a total weight of 50 g (w/w). The ratio of ALG-GA, ALG-PC, and ALG-CR were 100:0, 75:25, 50:50, and 0: 100. The aqueous solution of combination ALG with other polymers was mixed under stirred 500 rpm for 30 minutes together continuously until polymer mixture solution is completely mixed. Then, the polymers mixture solution was added to 50 mL 0.2% w/v $CaCl_2$ solution.

Design of experimental (DoE)

The Simple Lattice Design (SLD) software Design Expert Version 10 was applied to determine the ratio of mixture between two polymers then be used to identify the combination synergistic polymers. The SLD is one of the types of DoE that have been used to address formulation exercises and follow two major constraints, equality, and non-negatively. The model F ratio was found statistically significant (a<0.0001) indicating that there is only a 0.01% chance that an F-value this large could occur due to noise. The p-value for lack of fit was not significant because a>0.05 indicates the model is good to fit.

The SLD can describe mixtures with proportions ranging from zero to 100% for the components under study [21]. In this study, the ratios were obtained from SLD software. The independent factors are the ratio of alginate (X_1) and pectin/gum acacia/carrageenan (X_2), which are 100:0, 75:25, 50:50, 25:75, and 0:100. The dependent factor is viscosity as a response (Y) from polymers mixture (total concentration 1%). The total runs for each combination were 8 runs conducted with 2 replicates. The equation for SLD is described as follows:

$$Y = b\_1 X\_1 + b\_2 X\_2 + b\_12 X\_1 X\_2 + b\_12 X\_1 X\_2 (X\_1 - X\_2) + b\_12 X\_1 X\_2 (X\_1 - X\_2)^2 \quad \text{(Equation 1)}$$

Characterization of polymers mixture

Determination of viscosity and rheological analysis

Viscosity was measured using a viscometer Brookfield at 50°C±5°C following stirring with spindle no. 02 or 03, at 100 rpm for 15 s for each mixture solution. The data was determined in triplicate in mPa.s.

Equation 2 described the synergistic effect of combination polymers, but it doesn't predict the viscosity of the mixture solution. Equation 3 was first used by Miller and Mann (1994) to calculate the power requirements for agitation of mixtures of immiscible liquids and predict a geometric mean viscosity which provided a better approximation to the experimental value for the viscosity of polymer mixture [22].

$$\eta_{mix} = X_A \eta_A + X_B \eta_B \qquad \text{(Equation 2)}$$
$$\eta_{mix} = \eta_A{}^{X_A} \times \eta_B{}^{X_B} \qquad \text{(Equation 3)}$$

The determination of percentage deviation was calculated by Equation 4. The negative value indicates an antagonistic effect, while the positive value indicates a synergy effect that shows the interaction of coupled network form [20]. The theoretical viscosity in this equation is used from equation 1.

$$\%deviation = \left(\frac{\eta_{exp}}{\eta_{theori}} () \right) \qquad \text{(Equation 4)}$$

The viscous synergism index was calculated by Equation 5. Index value between 0-0.5 means there is antagonistic interaction. Index value = 0.5 means no interaction occurs. Index value between 0.5-1.00 or > 1 indicates interaction in mixture solution is higher than the sum of two polymers, hence referring to the synergistic effect [18].

$$Synergism \ index = \frac{\eta_{mix}}{\eta_A + \eta_B} \qquad \text{(Equation 5)}$$

Gel strength

Gel strength was measured using texture analyzer AMETEK with type TA1 in duplicates.

Fourier transforms infrared (FT-IR) spectroscopy analysis

Samples were dried by freeze dryer to powder and analyzed as KBr pellets using FT-IR Spectroscopy Thermo Scientific Nicolet Is10 (USA). Spectral scanning was measured between the wavelength region 4000 to 400 cm^{-1}.

Result and Discussion

Design of experimental

The Simple Lattice Design was selected to calculate of combination polymer in with and without $CaCl_2$ solution with viscosity as a response change (Table 1).

Table 1. Design of experimental for combination polymers

Run	Ratio	Viscosity (mPa.s)					
		Without CaCl$_2$			With CaCl$_2$		
		ALG:GA	ALG:PK	ALG:CR	ALG:GA	ALG:PK	ALG:CR
1	0:100	12.4	8.8	32.8	10.4	9.2	17.2
2	0:100	11.6	8.4	36	11.2	11.6	17.2
3	25:75	26	22	188.8	34	36	39
4	40:60	42	-	-	48.4	164	-
5	50:50	43.2	38.8	145.2	78	210	263
6	75:25	52.4	70.4	75.2	216	229	332
7	100:0	152.8	146.4	146.4	202	209	209
8	100:0	146.4	150.8	150.8	209	234	202
9	100:0	150.8	152.8	146.4	234	202	234

The result of the equation of experimental was represented in Table 2. We need additional data for the combination of alginate-gum acacia and alginate-pectin due to the model did not show a lack of fit value. Therefore, to obtain a lack of fit value, we fabricated an addition ratio of polymers combination which is aimed at a 40:60 ratio. The model could determine the synergistic of polymer combination. A positive sign of AB refers to a synergistic effect, while a negative sign of AB refers to an antagonistic effect. The polymer combination that showed synergies effect only alginate-carrageenan in distilled water. Whereas, in CaCl$_2$ solution, the synergy effect has been found not only in alginate-carrageenan, but also in alginate-pectin. The determination of synergism with the design of experimental did not know specific at ratio specifically, to found out the ratio we need equation methods such as viscosity deviation and viscosity index.

Table 2. Model design of experimental

Mixture		Lack of Fit	Equation	R-Squared	Model
Alginate : Gum Acacia	Without CaCl$_2$	0.4762	$Y_{viscosity} = +150.012 \times A + 11.973 \times B - 145.915 \times AB - 231.753 \times AB (A-B) - 304.351 \times AB (A-B)^2$	0.9982	Quartic
	With CaCl$_2$	0.9189	$Y_{viscosity} = +215.008 \times A + 10.781 \times B - 135.93 \times AB + 422.971 \times AB (A-B) + 804.437 \times AB (A-B)^2$	0.9848	Quartic
Alginate : Pectin	Without CaCl$_2$	0.3989	$Y_{viscosity} = +149.894 \times A + 8.442 \times B - 169.073 \times AB - 119.074 \times AB (A-B)$	0.9983	Cubic
	With CaCl$_2$	0.5486	$Y_{viscosity} = +215.052 \times A + 10.284 \times B + 411.622 \times AB + 464.414 \times AB (A-B) -1208.3 \times AB(A-B)^2$	0.9825	Quartic
Alginate : Carrageenan	Without CaCl$_2$	0.9087	$Y_{viscosity} = 147.879 \times A + 34.4184 \times B + 217.089 \times AB - 908.428$	0.9987	Cubic
	With CaCl$_2$	0.0644	$Y_{viscosity} = +213.42 \times A + 14.830 \times B + 481.763 \times AB - 1033.09 \times AB (A-B)$	0.9648	Cubic

Viscosity synergism index and percentage deviation of viscosity

Combination of alginate with other anionic polymers could form an intermolecular association via hydrogen bonding. The synergies effect were shown by viscosity characterization as a result of multicomponent gel [23]. Alginate gave a major contribution to increase the viscosity of polymer combination. The synergies effect in both polymer combinations could be known from percentage deviation (Equation 4) and viscous synergism index (Equation 5). If alginate was combined with another polymer, a semi-interpenetrating polymer network (s-IPN) could be formed which increased the mechanical strength of the mixture gel [24]

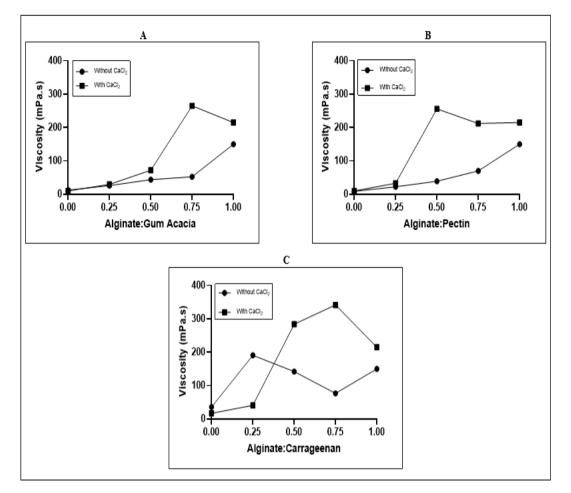.

Figure 1. The viscosity of mixture solution polymer with presence and absence CaCl₂. (a) alginate with gum acacia; (b) alginate with pectin; and (c) alginate with carrageenan. data shown are the average values and standard deviation (n=3).

In distilled water, the highest viscosity of polymers combination would be the highest alginate composition ratio (Fig. 1a and 1b). However, viscosity in the combination of alginate-carrageenan (Fig. 1c) would increase if the composition of carrageenan increases. The dispersion of carrageenan could be able to form gel briefly. This gelling ability leads to increase in the viscosity of combination carrageenan with alginate. In CaCl₂ solution, the viscosity could increase at all polymers combination and their ratio specifically compared with using distilled water without CaCl₂ (Fig. 1). The cation (Ca^{2+} from CaCl₂) can cross-link with alginate so that an egg-box network is formed. This could increase the viscosity in the combined solution, proportional to an increasing composition ratio of alginate.

Generally, viscosity from experimental and theoretical did not always have the same value, which concludes the mixture was not much fit (Table 3 and 4) due to specific interaction such as synergism.

Table 3. Estimation of the apparent viscosity of alginate mixture without CaCl₂

Ratio	Gum Acacia (mPa.s)			Pectin (mPa.s)			Carrageenan (mPa.s)		
	Exp.	Eq. 1[ab]	Eq. 2[a]	Exp.	Eq. 1[ab]	Eq. 2[a]	Exp.	Eq. 1[ab]	Eq. 2[a]
100:0	150.0	150	150	150	150	150	150	150	150
75:25	52.4	115.6	80.4	70.1	114.7	73.5	76.8	121.4	104.8
50:50	43.7	81.2	43.1	39.1	79.3	36.1	142.3	92.9	73.2
25:75	26.0	46.8	23.1	22.4	44	17.7	190.8	64.3	51.1
0:100	12.4	12.4	12.4	8.7	8.7	8.7	35.7	35.7	35.7

[a]p > 0.05 indicate no significant difference in mixture ratio that compared to exp. group
[b]p > 0.05 indicate no significant difference in mixture ratio that compared to equation 2

Table 4. Estimation of the apparent viscosity of alginate mixture with CaCl₂

Ratio	Gum Acacia (mPa.s)			Pectin (mPa.s)			Carrageenan (mPa.s)		
	Exp.	Eq. 1[ab]	Eq. 2[a]	Exp.	Eq. 1[ab]	Eq. 2[a]	Exp.	Eq. 1[ab]	Eq. 2[a]
100:0	215	215	215	215	215	215	215	215	215
75:25	265.3	163.8	100.5	212.3	163.7	99.8	341.67	165.55	114.3
50:50	72.3	112.6	47	256.3	112.5	46.4	284	116.1	60.8
25:75	29.7	61.4	22	33.3	61.25	21.5	40.67	66.65	32.3
0:100	10.3	10.3	10.3	10	10	10	17.2	17.2	17.2

[a] $p > 0.05$ indicate no significant difference in mixture ratio that compared to exp. group
[b] $p > 0.05$ indicate no significant difference in mixture ratio that compared to equation 2
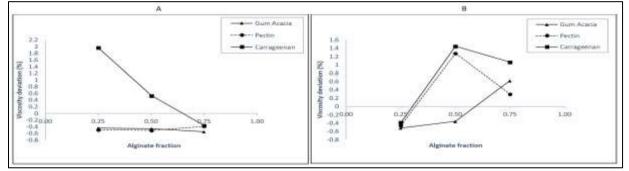

Figure 2. Viscosity deviation of alginate in combination with gum acacia/pectin/carrageenan. (a) in distillate water and (b) in cacl₂ solution.

In distilled water, combination of alginate with carrageenan at 25:75 and 50:50 have a positive value (Fig. 2a). Meanwhile, combination alginate with gum acacia and pectin at all weights the ratio showed a negative value, which means no synergy effect occurs. Alginate and pectin were able to form a synergistic mixed gel at low pH even in the absence of CaCl₂. However, in this study, no synergistic effect was found in the combination of alginate and pectin due to the degree of esterification (DE) of pectin being categorized as high DE. Synergism between alginate and pectin depended on a heterogeneous association between galacturonic acid region of alginate and degree of esterification of pectin. Both regions could form twofold crystalline arrays [13]. The more the degree of esterification, the higher carboxylic groups that were methylated and the lower available carboxylic groups so that the binding pectin with the region of alginate was limited. The presence of CaCl₂ could make an egg-box network on each pectin and alginate that could enhancement viscosity in mixed combination, so synergies effect occurs.

In CaCl₂ solution, the positive value of viscosity deviation was found in combination of alginate and gum acacia at ratio 75:25, alginate and pectin at ratio 50:50 and 75:25, also alginate and carrageenan at 50:50 and 75:25 (Fig. 2b). The synergies effect in CaCl₂ solution was more than in distilled water due to the cation interaction effect from Ca²⁺.

The synergistic effect result in CaCl₂ solution was a combination of alginate-gum acacia (75:25), alginate-pectin (75:25 and 50:50), and alginate-carrageenan (75:25 and 50:50). Otherwise, only a combination of alginate-carrageenan (50:50 and 25:75) had good synergy distilled water. There was no different result from the viscosity index equation compared with the deviation index (Table 5). Therefore, we could use one of the equations to determine the synergistic effect, either deviation index or viscosity index.

Table 5. Viscous synergism Index of alginate mixture in with and without CaCl₂

Ratio	Viscosity Index					
	Gum Acacia		Pectin		Carrageenan	
	Without CaCl₂[a]	With CaCl₂	Without CaCl₂[a]	With CaCl₂	Without CaCl₂[a]	With CaCl₂
100:0	-	-	-	-	-	-
75:25	0.32	**1.18**	0.44	**0.94**	0.41	**1.47**
50:50	0.27	0.32	0.25	**1.14**	**0.77**	**1.22**
25:75	0.16	0.13	0.14	0.15	**1.03**	0.18
0:100	-	-	-	-	-	-

[a] $p > 0.05$ indicate no significant difference in mixture ratio that compared to a solution with CaCl₂

Gel strength

The combination of the polysaccharide was an effective method to improve the physical properties and interactions of these biomacromolecules[25]. The combination of alginate with other polyelectrolyte polymers could create strong complex bonds in gels forming with the addition of divalent ions, such as Ca^{2+} from $CaCl_2$ solution. The mechanical strength and chemical stability of alginate beads would result [26]. The hydrophilic effect in these natural polymers leads to formation of a viscous gel structure due to their capability to hydrate in water. This is advantageous in encapsulating the drug and forming a viscous layer around the drug hindering the diffusion and causing a prolonged release of the drug, which is proportional with the viscosity and molecular weight of the polymer [11]. The gel strength is shown in Fig. 3.
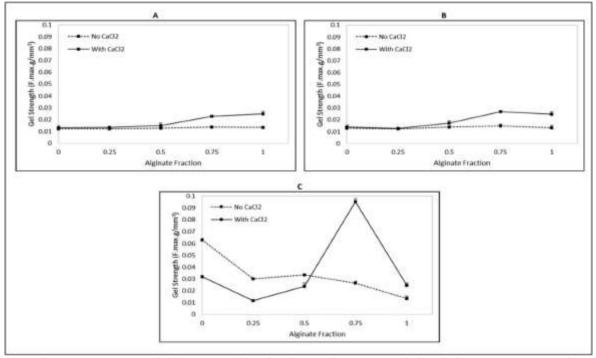

Figure 3. The gel strength of mixture solution of alginate with gum acacia/pectin/carrageenan. a: alginate with gum acacia; b: alginate with pectin; and c: alginate with carrageenan. data shown are the average values and standard deviation (n=2).

The structure created by the interaction of Ca^{2+} with alginate is known as the egg-box (Fig. 4) [27,28]. The Ca^{2+} ion interacts with a guluronic acid residue of alginate and carboxyl group groups of alginate and gum acacia (about 17% Glucuronic acid) which were negatively charged ions. The Ca^{2+} ion could not form an egg-box structure like alginate with gum acacia [4], this could be represented by the viscosity value of gum acacia alone that did not change on the addition of $CaCl_2$.
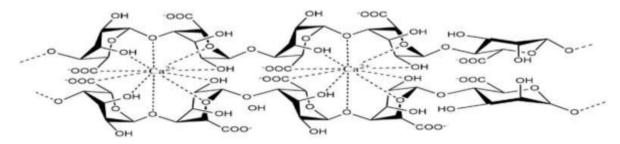

Figure 4. Egg-Box Alginate Cross-linking with $CaCl_2$

However, in polymer combination of gum acacia with alginate, the higher the alginate fraction, the greater the strength of gel (Fig. 5). This interaction occurred via the ionotropic gelation technique by cross-linking between hydroxy groups of both polymers [9]. The addition of gum acacia into alginate in $CaCl_2$ solution could reduce side-by-side aggregation that can lead to alginate swelling due to electrostatic repulsive force between carboxylate anions [4].
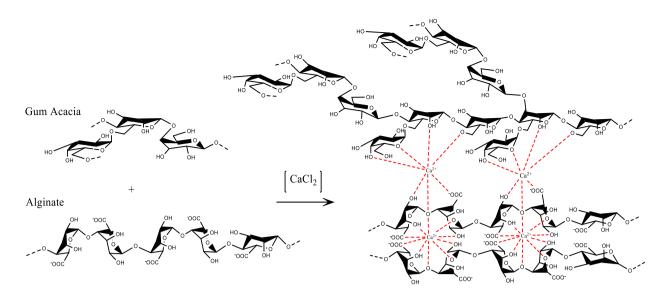
Figure 5. Interaction between alginate and gum acacia in CaCl$_2$ solution

Pectin could form an egg-box structure in the presence of Ca^{2+} ions as well as alginate. Therefore, increasing gel strength after addition of CaCl$_2$ (Fig. 3b). Gel formation was preferable if pectin had a low degree of esterification (DE) instead of a high DE. The lower DE, the more carboxylic groups that were not methylated so they could bind more Ca^{2+}. The pectin that was used in this study had a high DE, which was 70%. Therefore, the addition of Ca^{2+} did not significantly affect gel strength. The higher the alginate fraction in the mixture solution, the greater gel strength, because Ca^{2+} did not have a significant influence on pectin. The interaction between Ca^{2+} with carboxyl groups of alginate and pectin may cause cross-linking that could reduce electrostatic repulsion between polymers. The character of the gel formed depends on the degree of esterification of pectin and guluronic acid residue of alginate. The synergistic interaction between pectin and alginate in mixed gels was not fully known (Fig. 6) [29].
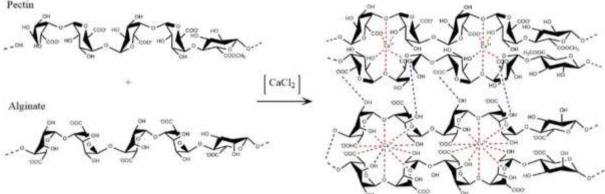

Figure 6. Interaction between alginate and pectin in CaCl$_2$ solution

Carrageenan could undergo ionic gelation with monovalent or divalent ions, such as K$^+$ or Ca^{2+} ions. The interaction of carrageenan with Ca^{2+} ion underwent electrostatic attractions which then formed an intramolecular bridge between oxygen and -OSO$_3$ groups of carrageenan. After that, the cross-linking network between carrageenan was formed. Cation could induce conformation in the polymer through the coil-helix transition, then the aggregation of helix form a gel [30]. In this study, the gel strength in a solution of sole carrageenan with the presence of CaCl$_2$ was lower than without CaCl$_2$. This was probably because divalent ion did not have a major effect on kappa-carrageenan, but had a major influence with iota-carrageenan which has two sulfate groups [31]. In the combination of alginate and carrageenan, the addition of CaCl$_2$ could increase the gel strength along with the increase in the alginate ratio. The interaction was formed between the carboxyl groups of alginate and the sulfate and carboxyl groups of carrageenan (Fig. 7) [32].
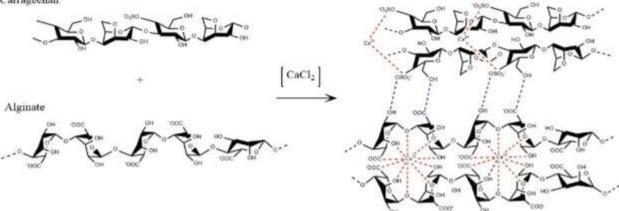
Figure 7. Interaction between alginate and carrageenan in CaCl₂ solution

FT-IR analysis

FT-IR spectra determine intermolecular interactions and specific vibrations of each functional group in the sample of alginate and other polymers. Before FTIR, the samples of the hydrogel mixture have been freeze-dried. This step could also initiate or reinforce the potential interactions between the two polymers [33].

The FTIR spectra of alginate and gum acacia showed similar bands. Fig. 8a presents spectra of alginate and gum acacia. In mixture solution, the sharp peaks at 1420 cm^{-1} along with increasing alginate ratio. The absorption band of the OH moiety has shifted to lower wavenumbers. This change could occur due to there being the interaction of intermolecular hydrogen bonding between alginate and gum acacia[34]. The specific peak at region 1035-1072 cm^{-1} showed a difference on all combinations of the ratio of alginate and gum acacia, depending on the ratio of each polymer, which could be useful to distinguish all ratios. In mixture solution alginate/gum acacia 25:75, the intensity absorption bands at 1635 cm^{-1} decreased with decreasing of alginate ratio. In mixture solution alginate/gum acacia 75:25, the absorption bands at 1420 cm^{-1} showed low intensity due to the ratio of gum acacia decreased. The spectra of alginate showed the bands at 1622 cm^{-1} and 1417 cm^{-1} that correspond to asymmetric and symmetric C=O stretching vibrations of the carboxylate groups, respectively [9,34]. This result described that all mixed ratios of alginate and gum acacia were successfully blended. FTIR spectra of sole alginate with the presence of CaCl₂ (Fig. 8b) showed a sharper peak than absence due to carboxylate groups being affected. The sole gum acacia showed the sharper peak at 1073-1036 cm^{-1} that represented C=O stretching vibrations that attributed to glycosidic linkages. That impact to all ratio combination showed more intense peak than without presence CaCl₂.

Spectra of alginate and pectin in distillate water were presented in Fig. 8c have specific absorption bands between 1000-1200 cm^{-1} range correspond to ring vibrations overlapping with the stretching vibrations of C-OH side groups and C-O-C glycosidic bond vibration [35]. The region between 1600-1800 cm^{-1} was specific interest that did not show in alginate to compare pectin sample with other polymers [13]. The combination of alginate and pectin in CaCl₂ solution (Fig. 8d) showed the typical spectra with some differences compared with a single polymer. Although the differences were not significant. In mixture solution, alginate/pectin 75:25 showed two bands between 1077 and 1144 cm^{-1} similar with bands in single alginate [13]. The absorption bands at 1600 cm^{-1} increased with increasing alginate ratio due to alginate having more carboxylate groups than pectin. In mixture, solution alginate/pectin 25:75 showed the intensive absorption at 1144 cm^{-1} that correspond to glycosidic pectin vibration. The spectra at 1738 cm^{-1} increased with increasing pectin ratio due to the presence of methyl-esterified carboxyl group [35]. This result described that all mixed ratios of alginate and pectin were successfully blended.

The FTIR spectra of alginate and carrageenan showed similar bands. Fig. 8e presents spectra of alginate and carrageenan. The specific peak of carrageenan showed at 1381 cm^{-1} and 1234 cm^{-1} assigned to the stretching vibration band of sulfate presence (S-O) [24,36]. FTIR spectra of sole alginate with the presence of CaCl₂ (Fig. 8f) showed a sharper peak than absence due to carboxylate groups being affected. The sole carrageenan showed a sharper peak at 1149 cm^{-1} that correspond to glycosidic linkage. That impact to all ratio combination showed more intense peak than without presence CaCl₂. In mixture solution alginate/carrageenan 75:25, there were two spectra similar with bands in single alginate. The intensity absorption bands of single carrageenan at 1421 cm^{-1} decreased with increasing alginate ratio due to alginate have more carboxylate groups than carrageenan. In mixture solution alginate/carrageenan 25:75, the absorption bands at 1637 cm^{-1} showed low intensity, otherwise, the

intensity would be high following the increased ratio of alginate. This result described that all mixed

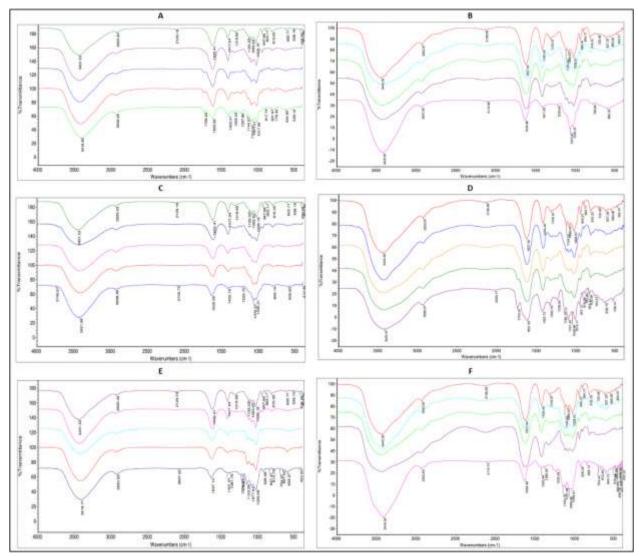ratios of alginate and carrageenan were successfully blended.

Figure 8. FT-IR spectra in CaCl₂ solution (a) alginate with gum acacia (c) alginate with pectin (e) alginate with carrageenan, in absence CaCl₂ (b) alginate with gum acacia (d) alginate with pectin (f) alginate with carrageenan.

Conclusion

The result of synergic effect in combination polymers used the design of experimental in distilled water have been found in alginate-carrageenan. Whereas, in CaCl₂ solution, the synergy effect has been found not only in alginate-carrageenan, but also in alginate-pectin. The determination of synergism using the design of experimental cannot show the specific ratio of polymer combination that have synergic effect, so that the synergism should be determined by mathematical equation including viscous synergism index and percentage deviation of viscosity too.

Determination of synergy effect from percentage value of viscosity deviation and viscous synergism index equation have a similar result. In

distilled water, the synergies effect was found in the combination of alginate-carrageenan at ratios 25:75 and 50:50. On the other hand, the addition of CaCl₂ to alginate-gum acacia (75:25), alginate-pectin (50:50 and 75:25), and alginate-carrageenan (50:50 and 75:25) showed more synergistic effect. The synergistic effect is confirmed with data of strength of gel polymers that increased with the addition of CaCl₂.

Conflict of Interest

The authors have no conflicts of interest regarding this investigation.

Acknowledgments

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