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Solid Dispersion Powder of *Sargassum cristaefolium* extract by solvent evaporation technique

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ABSTRACT

Sargassum cristaefolium is one of 782 types of seaweed/macroalgae that grows in Indonesia and is known as one of the macroalgae with bioactive compounds having an important role in the development of nutraceuticals for disease prevention and health maintenance. *Sargassum cristaefolium* extract (SCE) is known for its various beneficial activities such as antimigraine by reducing levels of CGRP and inhibitor of tyrosinase activity in anti-melanogenetics. Nevertheless, due to its hygroscopic viscous extract consistency and fishy odor, a suitable formulation is required to prepare a powder form of SCE and thus could be applied in a suitable dosage form. Our current study aims to develop the extract into suitable powder raw material by applying a solid dispersion technique. The solid dispersion of SCE was initially prepared by selecting suitable carrier agents such as Aerosil, Microcrystalline cellulose (MCC) PH 101, maltodextrin, and PVP K30 with the extract in a ratio of 1:1, and continued by the combination of the carrier agents. The best powder formula was characterized by its powder characteristic, solubility and powder flow was assessed by its angle of repose, Carr's index and Hausner ratio. The experiment results that the optimum formulation for solid dispersion of SCE was obtained by the combination of SCE:PVP: MCC at a ratio of 1:1:3 with a less fishy smell, and excellent powder properties. The composite mixture was estimated due to the formation of hydrogen bonds between the carbonyl group of PVP and the hydroxyl group of SCE's compound and MCC. In conclusion, solid dispersion of SCE by employing a combination of PVP and MCC can be an alternative to prepared SCE powder with optimum humidity protection and good flowability thus suitable to proceed as solid dosage form.

Keywords: *Sargassum cristaefolium*, solid dispersion, PVP K30, Microcrystalline cellulose PH101

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1.Introduction

Indonesia is known as the world's largest archipelago, where two-thirds of its territory is marine with 95,181 km of the second-longest coastline in the world[1]. Seaweed (macroalgae) is one of the biological resources that is very abundant in Indonesia's coastal ecology. There are 8,000 species of seaweed in the world, and among them, there are 782 types of seaweed, namely 134 brown algae, 196 green algae, and 452 red algae found in Indonesia[2]. One of the abundant and easily harvested seaweed in Indonesia is *Sargassum* sp., which belongs to the type of brown algae (Phaeophyceae)[3]. There are approximately 400 species of *Sargassum* identified throughout the world and 15 of them are found in Indonesia. One of the *Sargassum* species that grows in Indonesia is *Sargassum cristaefolium*. Chemical analysis shows the presence of bioactive compounds from various groups in the *Sargassum* sp. extract, such as fucoidan and sulfate polysaccharides, laminarin, alginate, fukosterol, phlorotannin, sargachromenol, and fucoxanthin[4] . The biological Effects of *Sargassum* sp. reported include antioxidant, anti-inflammatory, antidiabetic, antitumor, immunomodulatory, gastroprotective, osteoprotective, and antimicrobial activities. Therefore, *Sargassum* sp. is considered a potential naturally derived raw material to be developed as a supplement product [5]

Supplement products are mostly given orally and can be designed in various dosage forms including solid dosage forms (powder, tablet, or capsule) and liquid (tincture, syrup, suspension, emulsion). Therefore, preparing a good formulation by employing excipients with a good capacity to adsorb and improve their flow properties is necessary. Solid dispersions can be designed in various novel polymers or other excipients and technology, as alternatives applied to increase the solubility, dissolution rate, and bioavailability of active pharmaceutical ingredients (API). Moreover, it could transform the API into granules with good flow properties for tablets or capsule dosage forms[6] . Solid dispersion is the dispersion of one or more active ingredients in an inert matrix. Inert carriers can be water-soluble polymers such as polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), and methylcellulose. Solid dispersions increase the dissolution rate and solubility of active substances through size reduction, increased wettability, and amorphous transformation[7]. Solid dispersion can be done by various methods, the most common of which are solvent evaporation, spray drying, melt extrusion, and lyophilization [8]In the solvent evaporation method, the active ingredient is forced into close contact with the carrier by dissolving it in a common solvent. The homogeneous solution is then converted into a solid by rapidly removing the solvent[7].

The current study focussed on finding a suitable excipient and its ratio for solid dispersion to obtain a good powder of SCE that can be utilized in several dosage forms by employing aerosil, Microcrystalline cellulose (MCC) PH101, maltodextrin, and PVP K30. Therefore, people may gain beneficial activity from SCE to manage their health.

2. Method

Materials

The brown algae *S. cristaefolium* was collected from the western coast of Lombok, Batu layar coast. Maltodextrin DE 10-12 was purchased from Lihua, China. Aerosil, MCC PH101,

and PVP K30 were purchased from a local distributor in Indonesia.

The instrument used were *Flow Tester*, Microskop CKX53 (Olympus, Japan), *Moisture Analyzer MB35* (OHAUS, USA), *Rotary Evaporator (IKA*, Germany), UV-VIS Spectrophotometer UV-1700 PharmaSpec (Shimadzu, Japan), Tap Density Tester (Varian, USA), Analytical Balance AR2140 (OHAUS, USA), Waterbath WTB (Memmert, Germany)

Determination of S. cristaefolium

The *voucher specimen of* ***S. cristaefolium was*** *deposited in* Pusat Unggulan Biosains dan Bioteknologi, Universitas Mataram for plant determination.

Preparation of the extract (SCE*)*

The dried *S. cristaefolium* was chopped and mashed using a blender and was sieved using a sieve shaker until a powder size of 125 μm – 250 μm was obtained. The extraction process is carried out using the maceration method by 96% ethanol, with a powder: solvent ratio = 1:10, and stirred using a magnetic stirrer at 600 rpm for 24 h. Take the solvent after 24 h, and extraction continued 3 times, with the addition of new solvent. The liquid extract obtained was concentrated using a rotary evaporator with a temperature of 40°C – 45°C and a flask rotation speed of 40 – 45 rpm. The viscous extract was collected and placed in a suitable container.

Phytochemical screening

Qualitative analysis for alkaloid was conducted by dissolving 50 mg SCE in 5 drops of HCl, and separately adding *Dragendorff*, *Mayer*, and Wagner's reagent. The positive result of indicated by a red-to-orange precipitate formed in the Dragendorf reaction, a yellowish-white precipitate in the Meyer reagent, and a brown precipitate formed in Wagner's reagent [9,10.] The phenolic qualitative analysis was analyzed by dissolving 0.1 g of SCE in water and heat for 5 minutes and filtering into a test tube. It was reacted with 3 drops of FeCl3 5%. The positive result was indicated by the formation of a green color in the mixture[11]. The qualitative flavonoid test was conducted by adding 2 mg of SCE with 1 mL of 2N NaOH. A positive result was indicated by the formation of a yellow color in the mixture[12]. A Triterpenoid/Steroid test was conducted by dissolving 0.1 g of SCE in 2 ml of chloroform, furthermore, it reacted with 10 drops of acetate anhydrate and 3 drops of sulfuric acid. A positive result of triterpenoid was indicated by the formation of a brown ring on the surface of the mixture and a green ring indicating the presence of steroids [11,12]. The saponin test was conducted by dissolving 50 mg of SCE in 5 ml of hot water, shaking vigorously for 10 seconds, and adding 1-2 drops of 2N HCl. A positive result is indicated by the formation of 1-10 cm persistent foam[9,13]. The qualitative analysis of tannin was conducted by dissolving 50 mg of SCE in ethanol, and reacting with the addition of 2−3 drops of 5% $FeCl_3$. A positive result is indicated by the formation of a bluish-black or green color[9,12].

Solubility evaluation of SCE

The maximum solubility of SCE in water and ethanol was performed by placing an accurate weight of SCE into a vial, a quantity of added water was transferred to the vial, gently shaken, and the solubility was visually observed. The addition of water continued until SCE was completely dissolved and finally the required volume of water to dissolve an accurate weight of SCE was recorded. The same procedure was also applied to evaluate the solubility of SCE in ethanol.

Optimation of SCE with a single carrier agent

Solid dispersion of SCE was first optimized by using a variation of carriers, namely Aerosil, MCC, Maltodextrin, and PVP as F1, F2, F3, and F4 respectively. The solvent evaporation technique was chosen to remove the solvent and allow it to form a dry solid dispersion. The SCE is mixed with the carrier at a ratio of 1:1, then dissolved with 96% ethanol until it becomes a homogeneous solution or dispersion. The mixtures were then evaporated in a water bath at 70°C until dry. The resulting solid was collected and then ground in a mortar. The particle size was homogenized by sieving the powder through #40 mesh. Store in a desiccator for 24 hours before evaluation of organoleptic (shape and special features, odor, and color) and solubility.

Preparation of Solid Dispersion of SCE with a combination of two carrier agents

The experiment was carried out by a combination of SCE: PVP:MCC at ratios of 1:1:1, 1:1:2, and 1:1:3 as F5, F6, and F7 respectively. Similar to the preparation in F1-F4, all the material was mixed and dissolved in sufficient 96% ethanol. The mixtures were then evaporated in a water bath at 70°C until dry. The resulting solid was collected and then ground in a mortar, and homogenized by sieving the powder through #40 mesh. Store in a desiccator for 24 hours for further organoleptic (shape and special features, odor, and color), solubility, and hygroscopicity. Further microscopic and flowability characteristics were evaluated only for F7.

Evaluation of the SCE Powder

Solubility Test

A quantity of samples equivalent to 50 mg of extract was placed in a vial and 1 ml of water, gently shaken, and allowed to stand for 20 minutes, and observed whether the precipitation occurred and the color of the solution. The change in the color of the solution from colorless to green indicates the presence of SCE soluble in water.

Hygroscopicity test

A quantity of 1 g solid dispersion of SCE was weighed and placed in an uncovered porcelain evaporating dish. Allow the exposure of room humidity and evaluate the form and color of powder in 2 hours, 3 days, and 7 days. Visually observe the change in physical properties of the powder, including changes in color and form.

Microscopic Observations

The particle characteristics of viscous SCE, PVP, MCC, and solid dispersion of SCE powder were observed microscopically using an optical microscope at 400x magnification, especially in particle shape and color.

Angle of repose

A quantity of 25 g of powder was put into the funnel. Open the closure of the funnel. The angle of repose is calculated by measuring the diameter (d) and height (h) of the powder, using formula

$$\text{Tan } \alpha = \frac{h}{0.5\ d}$$

Compressibility index

A quantity of 100 g of powder was weighed and put into a 250 ml graduated cylinder on a tapped density tester, the initial powder volume was recorded as bulk density. Run the tapped density tester and record the height of the powder as tapped density.

Calculate the Compressibility index and Hausner ratio with the below formula:

$$Compressibility = \frac{\rho_T - \rho_B}{\rho_T} \; x \; 100$$

$$Hausner\ Ratio = \frac{\rho_T}{\rho_B}$$

Where: ρ_T *is tapped density (g/ml) and* ρ_B is bulk density (g/ml)

1.Result

Determination and preparation of SCE

The *S. cristaefolium* obtained from the western coast of Lombok had been determined and based on the results it was directed to *S. cristaefolium*. The extraction of dried *S. cristaefolium* yielded 20.30% of the extract. The extract, SCE, has a viscous consistency, dark green color, and less fishy characteristic odor as seen in Figure 1A.

Phytochemical screening of SCE

The phytochemical screening analysis revealed that it is positive for tannin, triterpenoid, and steroids, weak for flavonoids, and negative for phenolic compounds, saponin, and alkaloids as seen in Figure 2.

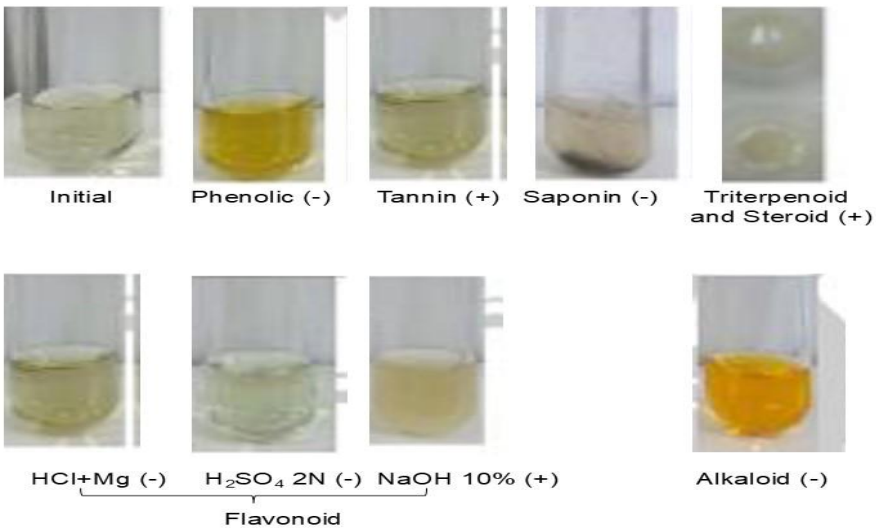

Figure 2. Phytochemical screening analysis of SCE

Solubility of SCE

The results showed that 1 gram of SCE was soluble in 100 mL of water, which is in the range of solubility of 1 part soluble in 30-100. Meanwhile, the 1 g of SCE soluble in 30 mL of 96% ethanol, referred to the USP guideline is in the range of 1 part soluble in 10-30 parts solvent. Indicate that SCE is sparingly soluble in water and soluble in 96% ethanol.

Optimation of SCE with a single carrier agent

Solid dispersion with 96% ethanol results in different powder characteristics. It required different quantities of solvent to completely dissolve the mixture and drying time as seen in table 1. The F1, mixture of SCE with aerosil (1:1) required a larger amount of solvent thus requiring a longer time for solvent evaporation. Nevertheless, the carrier agent can transform the viscous extract into a dried bulky powder similar to aerosil and MCC characteristics. The F2, mixture of SCE with MCC (1:1) results in flour-like dry powder with less solvent and a short time for solvent evaporation among other formulas. Meanwhile, F3 and F4, a mixture of SCE with maltodextrin and PVP result in a sticky mass. The F3 results in a hard sticky agglomerate mass and F4 results in a soft sticky mass (Figure 1A).

Table 1. Effect of carrier agent in solid dispersion

Formula	Carrier agent	Ratio of SCE:carrier agent	Solvent required (mL)	Time for solvent evaporation (minutes)	Powder condition	Solubility in water
F1	Aerosil	1:1	9	40	Dry and fine bulky powder (compared to F2) with a light green color	Insoluble
F2	MCC	1:1	5	25	Dry and fine powder with a dark green color	Insoluble
F3	Maltodextrin	1:1	4*	100	Sticky, hard agglomerate mass with dark green color	Soluble
F4	PVP K30	1:1	4	60	Sticky with dark green color	Soluble

Note : *=maltodextrin was not soluble in 96% ethanol
SCE = *Sargassum cristaefolium* extract

The solubility of each formula reveals that F1 and F2 were not soluble in water, and precipitation occurred in less than 20 minutes. The precipitation has a more intense green color in F1 than in F2, on the contrary, the green color in the solution given by F2 was slightly more intense than in F1. This indicates that the carrier in F1 binds the SCE and reduces its solubility. Interestingly F3 and F4 were soluble in water with similar intensity of green color solution, and no precipitation occurred after 20 minutes, observed visually. This indicates that both dissolve the SCE at a similar level (Figure 1B and 1C).

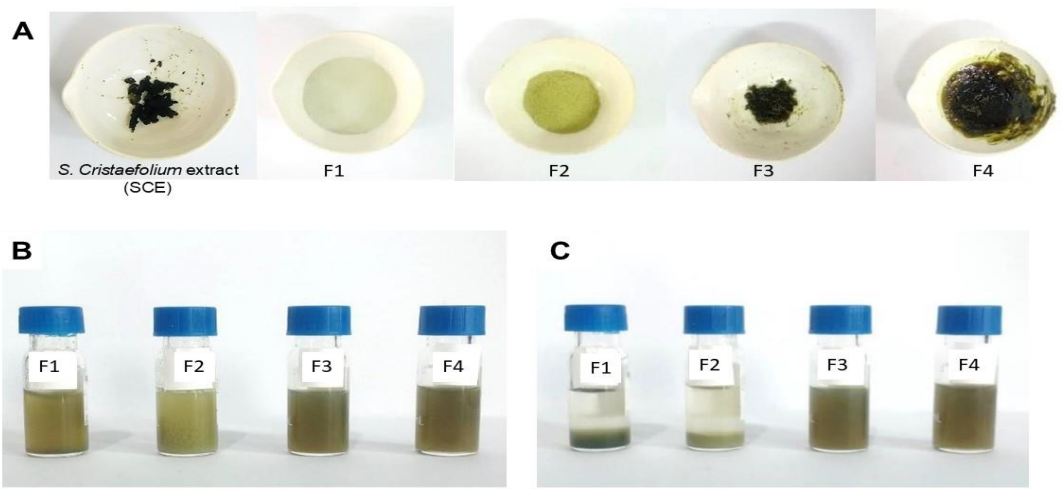

Figure 1. Physical characteristics of solid dispersion of SCE prepared with a single carried agent. The solid dispersion was prepared by using Aerosil, MCC, Maltodextrin, and PVP K30 as F1, F2, F3, and F4 respectively resulting in different characteristics of powder (A) and solubility (B). F1 and F2 were not soluble in water, meanwhile, F3 and F4 were soluble in water (C).

Preparation of solid dispersion of SCE in two combinations of carrier agent

The solid dispersion prepared by a combination of SCE: PVP K30:MCC at different ratios of MCC revealed that F7 with a ratio of 1:1:3 resulted in a good powder characteristic as dry and fine powder, with a light green color. Meanwhile, F5 and F6 with less MCC result in darker sticky powder (Figure 3A).

Albeit the solubility of F7 was less than F5 and F6, the intensity of green color in solution and precipitation were similar, indicating that a higher quantity of MCC did not affect the solubility of SCE-PVP complex (Figure 3B).

The exposure of F5, F6, and F7 powder to room humidity (72±5%) reveals that longer exposure to humidity increases the water content in powder resulting in a darker color and agglomerate of powder. Nevertheless, F7 showed lower hygroscopicity compared to F5 and F, indicated by less sticky and agglomeration (Figure 3C).

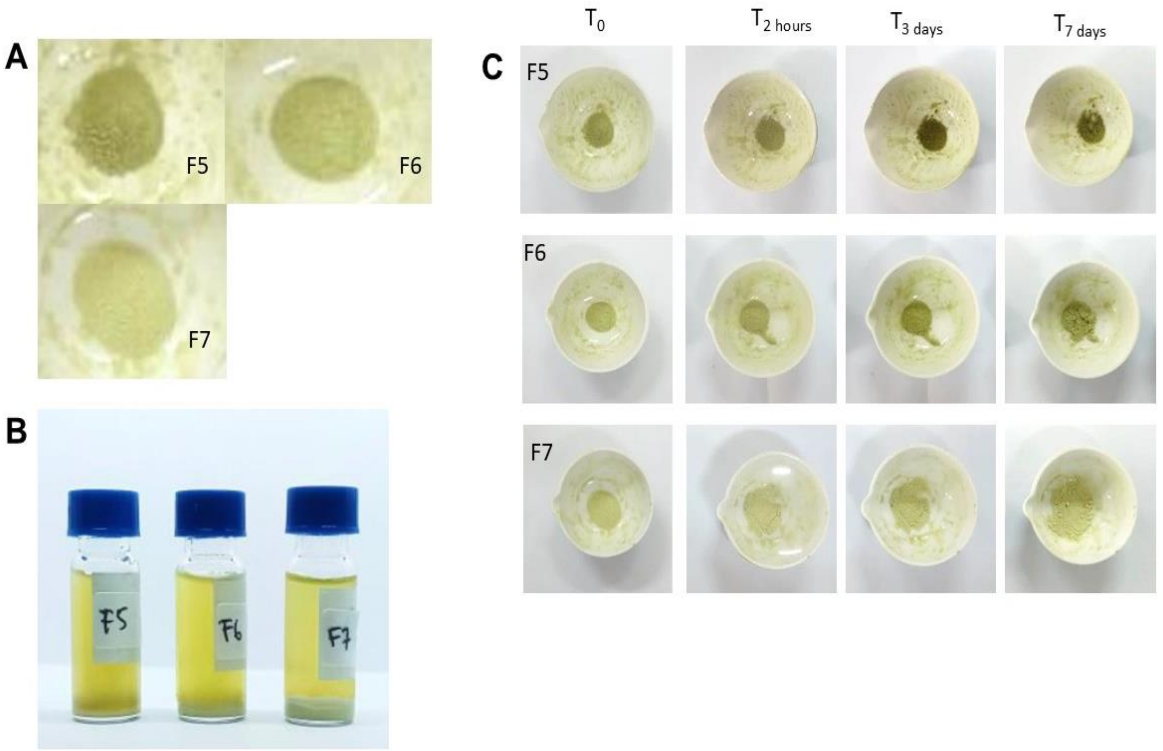

Figure 3. Solid dispersion of SCE prepared in combination with two carrier agents.
The solid dispersion of SCE prepared in SCE: PVP K30: MCC, in combination of MCC as 1:1:1, 1:1:2, 1:1:3 as F1, F2 and F3 respectively. Resulted in the variation of powder characteristics (A) and solubility (B). The presence of advice could improve the stability of SCE against humidity in 7 days as seen in F7 compared to F5 and F6(C)

Powder evaluation of SCE solid dispersion F7

Visual observation of F7 solubility as seen in Figure 2B showed the white precipitation of MCC, and the green color in solution, indicating the SCE was soluble in water. The SCE powder had a moisture content of 5.51±0.015% and a flow rate of 14.16±0.306 (g/second). It also has good density and flowability as seen in Table 2

Table 2. Physical characteristic of Solid dispersion of SCE

Evaluation	x̄±SD	Result
The angle of repose (°)	42.73±0.850	Flow property is Passable—may hang up[34]
Bulk density (g/ml)	0.484±0.005	Good density
Tapped density (g/ml)	0.536±0.007	Good density
Carr's index (%)	9.678±0.109	Flowability is Excellent (1-10)[35]
Hausner ratio	1.107±0.001	Flowability is Excellent (1.00-1.11)[35]

Microscopic evaluation of F7 and its excipient

The SCE, PVP, MCC, and the solid dispersion of SCE containing those excipients observed under the microscope reveal that SCE has a yellowish-green constituent. Interestingly round liposome-like shape of the constituents observed, indicates the shelf-formation of liposom may occurred naturally due to the numerous constituents in the extract (Figure 4A). The PVP was observed as a colorless round particle, with a smooth surface (Figure 4B). Meanwhile, the MCC was observed as an irregular shape of the particle with uneven surface texture (Figure 4C). The microscopic analysis of solid dispersion of SCE revealed the composite particle PVP containing extract. This changes the round shape of PVP into an oval shape of a particle with a firm boundary line due to the presence of the MCC (Figure 4D). This gives the macroscopic evaluation of F7 solid dispersion of SCE as a light green fine powder as seen in Figure 4E.

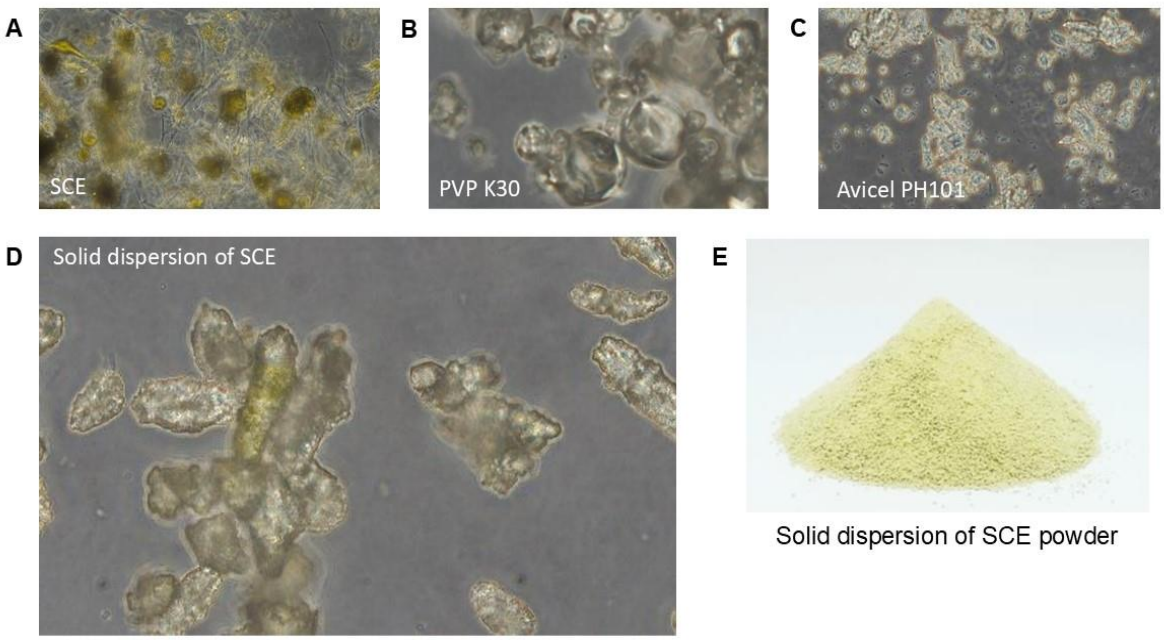

Figure 4. Microscopic evaluation of solid dispersion of SCE, carrier agents, and its physical characteristics.

The SCE observed under a microscope at 400x magnification revealed it has a yellowish-green constituent and the natural formation of a liposome-like structure was observed (A). The round shape of PCP K30 (B) and, the irregular shape of MCC (C) were also observed. The Solid dispersion of SCE forms an oval structure (D) in microscopic evaluation and physical characteristics as dry and fine powder with a light green color (E).

4. Discussion

Extraction is the activity of withdrawing secondary metabolites from plants using appropriate solvents. Several solvents can be used according to the character of the material to be obtained. This research uses a solvent of 96% ethanol because it can attract a wide range of bioactive molecules, as seen in Figure 1A. The 96% ethanol as a solvent may attract such as polyphenols, flavones, tannins, flavonoids, and pigments[14,15.] A study conducted by Susilo *et al* (2022), also informed that most of the phytochemical in seaweed tends a polar, thus polar solvents such as methanol or ethanol are more suitable for high yields of *S. cristaefolium* extract than non-polar solvents [16,17.] The first process reduces the size of dried S. Cristaefolium powdered simplex to 125 µm – 250 µm. to maximize the contact surface area between the sample and the solvent and also help break down the thick cell walls of macroalgae thereby increasing the transfer/withdrawal of bioactive compounds from the biological material to the solvent and increasing the total yield of *S. cristaefolium* extract[18–20.] Maceration was chosen to avoid damage to the secondary metabolite content which is thermolabile or not resistant to heat This means that the process and tools are simple, and the costs are relatively more affordable[21]. The yield results were above 10%, thus the effective extraction process was achieved.

Phytochemical screening results show that SCE contains mainly triterpenoids and steroids (Figure 2), this is in line with the study conducted by Adam *et al*, 2022 which said that the 70% ethanol extract of SCE contains mainly triterpenoids and steroids and was tested to have the activity of reducing levels and expression of calcitonin gene-related peptide (CGRP), a Neuropeptide that plays a role in the formation of headaches and other migraine symptoms, as well as reducing TNF at a dose of 500 mg/kg and increasing the expression of anti-inflammatory cytokine IL-10[22]. Also in line with Lailiyah *et al*, 2014 who said it mainly contains steroids and negatively contains flavonoids, with moderate antioxidant activity compared to vitamin C, namely reduction of the DPPH radical 80.68% at 400 ppm of the extract[23]. Moreover, the previous study also revealed that 150 µg/mL SCE effectively inhibited tyrosinase activity, thus potential as anti-melanogenetic[18]. Thus SCE is promising to be further developed as an active material as an example for supplements to enhance human health.

Preparation of powder extract by solid dispersion can be an alternative to transform from viscous to powder, and depending on the substance carried, it may also cover the unpleasant fishy odor and maintain the stability of the active substance. Therefore, it can be applied as a supplement in tablet or capsule dosage form. The current study applied Aerosil, MCC, Maltodextrin, and PVP since those materials are generally applied in solid dosage form. Aerosil or fumed silica has a main function as rheology control and optimized flow of powder, it also has anti-settling properties and is applied in

less than 2% in formula. MCC has a characteristic suitable as a binder-filler in the formulation of conventional tablets[24]. Aerosil and MCC can function as adsorbents and can be used alone or in combination with both in drying extracts and can reduce the water content of extract powder and make extracts with good flow rate characteristics.[25]. Maltodextrin is a carbohydrate, nutritive saccharide polymer available in various ranges of dextrose equivalent (DE) of usually less than 20. Low DE of maltodextrin has similar properties to native starch. It is widely applied in food mixtures to improve dry properties due to thermoreversible gel properties. These properties allow maltodextrin as a carrier agent to dry the extract and can also be used for fat replacement. It is usually applied to 1-35% of food.[26] . Polyvinylpyrrolidone k30 (PVP k30) is a water-soluble viscoelastic polymer. [27]. Depending on the polymerization of monomer N-vinylpyrrolidone, it is available in various ranges of molecular weight from 2500–30,00,000 Da and is distinguished by its K-value calculated by Fikentscher's equation which is related to relative viscosity determination of the polymeric solution. The grade of PVP indicated by the K-value is 1000 times the Fikentscher parameter. PVP is a non-toxic, pH-stable, biocompatible, biodegradable polymer and thus suitable for encapsulating lipophilic and hydrophilic substances. PVP is usually applied as a coating material for tablet, granule, and solid dispersion [28].

Solid dispersion by using aerosil and MCC suitable for impregnation of the extract, creates good powder properties, similar to initial aerosil and MCC without changing its properties (Figure 1A). Aerosil and MCC are not soluble in water and did not increase the solubility of the extract, where the extract and its carrier precipitate at the same time (Figure 1 B and 1C). Meanwhile, the solid dispersion of SCE with maltodextrin and PVP changes the initial powder form of the carriers into agglomerate mass (Figure 1A). Nevertheless, impregnation of extract to this carrier increases SCE solubility (Figure 1 B and 1C). Compared to maltodextrin which results in a hard agglomeration mass, the PVP-30 results in a soft sticky agglomeration thus considered potential to be further developed into a dried powder in addition to MCC. MCC was selected because it has a higher-density powder than aerosil.

Preparation of SCE with a combination of PVP:MCC at ratios 1:1:1 (F5), 1:1:2 (F6), and 1:1:3 (F7) improves the solid dispersion properties from sticky agglomerate into powder (Figure 3A). The addition of MCC did not affect the SCE solubility, as observed by the green color in the solution. Moreover, F7 which contains a higher content of MCC among others, showed higher white MCC precipitation with the same intensity of green color with F5 and F6 (Figure 2B). The protection capacity of the formulation using different ratio was observed against environmental humidity. It was observed that F7 with a higher ratio of MCC protects the powder from humidity (Figure 3C). Microscopic evaluation revealed that sticky green extract observed as a yellowish green mass microscope (Figure 4A), the composite solid dispersion of SCE:PVP:MCC at a ratio 1:1:3 showed a green color of powder (Figure 4E), with microscopic evaluation observed as yellowish green irregular shape of particles, different with its initial particle shape. Indicating the SCE is successfully encapsulated within PVP and the presence of the MCC emphasizes the particle boundaries (Figure 4B-D). PVP is a polymer of N-vinylpyrrolidone with

each monomer containing a hydrophilic moiety of pyrrolidone and a hydrophobic moiety of the alkyl group. the carbonyl groups of pyrrolidone allow interaction by the formation of hydrogen bonds between PVP and hydroxyl groups of bioactive substances of SCE as depicted in Figure 5A[28–30]. PVP and MCC are also miscible creating a hydrophilic property of the composite. MCC is a type of cellulose comprised of linear chains of β1-4-linked glucose monomers. The secondary -OH groups at C-2 or C-3 of the glucose ring are important in creating interfacial interaction via hydrogen bonding with the oxygen of the carbonyl group (C=O) of PVP (Figure 5B)[31,32]. Interestingly, a study revealed that the PVA/MCC interaction increased the availability of the hydrophilic groups thus affecting increased interactions with water molecules thus increasing the solubility. A similar interaction is predicted to occur between PVP and MCC in this experiment. Thus, composite solid dispersion can be depicted as in Figure 5C. Nevertheless, the limitation of the study is the lack of instrumentation analysis to evaluate the solubility of SCE in single and interaction with carrier. This is due to the major bioactive substance as a marker not yet determined in this experiment.

The current study assesses the suitability of SCE solid dispersion powder for tablets or capsules by angle of repose, and compressibility through Carr's index and Hausner ratio. The angle of repose has been widely used to characterize the flow properties of solids. In powder flow analysis, it characterizes the movement of powder over powder or interparticulate friction. This demonstrates the flow of powder in the hopper of the tableting machine or capsule-filling machine. Meanwhile, compressibility through Carr's index and Hausner ratio is useful as an indirect method to measure bulk density, surface area, moisture, and cohesiveness of material influence the compressibility index[33]. This method evaluates bulk density and tapped density of powder, which represent the ability of the powder to be compacted into a tablet or fill the capsule shell. This experiment reveals that the SCE extract powder prepared by solid dispersion is effective in preparing the stabile composite powder against humidity with an excellent property of the powder flowing and promising to be proceed further in solid dosage forms such as tablets or capsules.

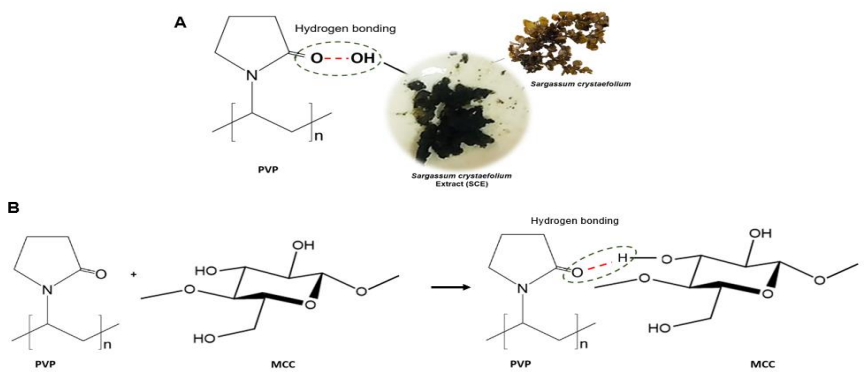

Figure 5. Interaction of PVP with substances in SCE and MCC. The interaction of PVP occurs via hydrogen bonding between carbonyl group with hydroxyl groups of substances contained in SCE (A) and hydroxyl group in glucose (B)

5. Conclusion

S. cristaefolium is a natural source of material promising to be developed as a supplement to augment human health. The extract is mainly composed of triterpenoid/steroid with activity as antimigraine by reducing levels of CGRP and TNF and increasing IL-10, it also has anti-melanogenetic properties by inhibiting tyrosinase activity, it has antioxidant activity and low cytotoxic effect against several cancer cell line. The extract is hygroscopic, sparingly soluble in water, and has a fishy odor which limits its application, especially in solid dosage form. Preparation of SCE powder with the combination of PVP/MCC at a ratio of 1:1:3 successfully created a composite via hydrogen bonding among the molecules to form a powder with good solubility in water and flowability, also less fishy odor. This powder is suitable to be further developed as a tablet or capsule dosage form.

6. Acknowledgements

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