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Research Article

Optimization of HPMC and Na-CMC as Gelling Agents on Physical Properties and Stability in Sunflower Seed Oil Gel Formulation

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Abstract: In recent years, skincare with natural ingredients is being developed for it has fewer side effects and is relatively suitable for all skin types. One of the potential ingredients from the natural ingredients is sunflower seed oil, which has proven to have potential as a skin moisturizer and fight acne bacteria. The purpose of this study was to make a gel formulation of sunflower seed oil by optimizing the combination of the gelling agent of HPMC and Na-CMC. The Simplex Lattice Design method was used to optimize the gel base with Design Expert software version 13. There were 8 gel formulas made and evaluated including organoleptic, homogeneity, pH, viscosity, spreadability, and adhesion. The independent variables in SLD were the amount of HPMC and Na-CMC, while the responses included pH, viscosity, and spreadability. The optimal formula suggested by SLD is a combination of 1.451% HPMC and 1.549% Na-CMC. The optimal formula has a pH of 6.813 ± 0.041, a viscosity of 194.8 ± 2.94 dPas, an adhesion of 6.29 ± 0.50 seconds, and a spreadability of 21.5 ± 10.05 cm2. The optimum prediction formula from the software has no significant difference from the test results which show that the method can be used to predict the physical properties of sunflower seed oil gel preparations. The results of the physical stability test also stated that its physical properties were stable in terms of pH, viscosity, spreadability, and adhesion.

Keywords : gel, stability, optimation, HPMC, Na-CMC

1. INTRODUCTION

Sunflower or *Helianthus annus L.* contains several compounds that have the potential to be applied in skincare products [1]. Its oil has the potential to be used as a moisturizer as it contains triacylglycerol and a small portion of phospholipids, tocopherols, and sterols [2]. The sunflower seed oil is scientifically proven to have a MIC (Minimum Inhibitory Concentration) of 1.5% and a Minimum Inhibitory Power of 15.28 mm, hence it has the potential as an antibacterial to fight acne [3]. Sunflower seed oil with the DPPH method has strong antioxidant activity with an inhibition percentage value of around 51.57% and an IC50 of 90 ± 11.56 µg/ml. [4]. However, sunflower seed oil that is applied directly onto the skin as skincare will cause discomfort because it can leave a greasy effect on the face and is considered impractical. In this research, the researchers aimed to increase comfort and convenience in utilizing sunflower seed oil by formulating sunflower seed oil in the gel dosage form.

Gel preparation is a form of semi-solid topical preparation designed with a high water content so it can provide moisture to the skin and penetrate better than other topical preparations [5]. Gel preparations also have good spreadability, are easy to wash, and have a good release of active substances [6].

This research is carried out to obtain the physical properties and stability of the gel which are influenced by the selection of the right gelling agent in the formulation. The researchers used a combination of Na-CMC and HPMC gelling agents in the preparation of the gel preparations. Na-CMC is widely used in the cosmetic field because it has good adhesion to the skin [7]. Meanwhile, HPMC is a gelling agent used in topical formulations as it solves with good clarity. HPMC acts as an emulsifier, suspender, and stabilizer in gel preparations [8].

The method used was SLD (Simplex Lattice Design), which is an optimization method that uses several samples to form an equation that expresses the relationship between the physical properties of the preparation and the variation in the composition of the ingredients. Through the equation formed by the SLD method, it can be seen the effect of the concentration of each component on the response of the physical properties observed and the combination of gelling agent levels to determine optimal physical properties [9].

2. MATERIALS AND METHODS

2.1. Materials

Instruments: Analytical balance (Adventurer™ Ohaus), glassware (Iwaki, Pyrex), pH meter stirrer (HANNA), spreadability test kit (Faculty of Pharmacy UGM), stickiness test kit (Faculty of Pharmacy UGM), stopwatch (Alba), ultra turrax (IKA T25 digital ultra turrax), and viscometer (Brookfield DV- 1 Prime). Materials: Sunflower seed oil (Ecowa Oil Distributors), propylene glycol (pharmaceutical quality), DMDM hydantoin (pharmaceutical quality), sodium carboxymethylcellulose (pharmaceutical quality), and HPMC (pharmaceutical quality).

2.2. Course of Research

The sunflower seed oil gel formula which can be seen in Table 1.

Table 1. Sunflower seed oil gel formula from the SLD method

Materials	R1	R2	R3	R4	R5	R6	R7	R8
Sunflower seed oil	5	5	5	5		5	5	5
Na-CMC	1.75	2	1.75	1,625	1,875	1.5	2	1.5
HPMC	1.25	1	1.25	1,375	1,125	1.5	1	1.5
Propylene Glycol	10	10	10	10	10	10	10	10
DMDM hydantoin	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Aquadest	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100	Ad 100

The base gel was dispersed first, weighed with Na CMC, then added 40 mL of distilled water, and heated to 70 ^{0}C, then Na CMC was put in and added to the heated aquadest while stirring until it was homogeneous and formed a gel mass. In another container, HPMC was dispersed using 30 mL of hot distilled water at 70^{o}C while homogenizing until a gel mass was formed. The gel mass that had been formed was then mixed in a beaker glass and sunflower seed oil was added. Then propylene

glycol and DMDM hydantoin were added and homogenized using ultra turrax at 8000 rpm for 10 minutes. Finally, the rest of the water was slowly added until the preparation became 100 mL.

2.3. Physical Properties Test

2.3.1. Organoleptic

The organoleptic test was carried out visually, and macroscopically without any aids. The observations recorded included the color, smell, shape, and texture of the gel made [10].

2.3.2. Homogeneity Test

The homogeneity of the preparation was tested by applying the gel to an object glass, then the color uniformity, the mixability of the ingredients, and whether there were small particles that had not been mixed were observed.

2.3.3. pH Test

The pH test was carried out for all formulas made by inserting the pH stick into the gel that had been placed in the container, the pH obtained was then recorded and adjusted to safe pH requirements for topical preparations [11].

2.3.4. Viscosity Test

The test was carried out using a Brookfield viscometer. The gel was put into a tubular container on a viscotester. The rotor was installed until it was immersed in the gel, the tool was turned on, and the rotor that was immersed in the gel was made sure it could rotate. The viscosity value was found by observing the movement of the pointer on the viscometer screen after 15 seconds which showed a certain number and then recording [12].

2.3.5. Adhesion Test

The gel was placed on an object glass and another object glass was placed on it which was then pressed with a load of 1 kg for 5 minutes. The object glass that had been attached to each other was attached to the test equipment. As much as 80 g of weight was released and the time was recorded until the two glass objects were detached [13].

2.3.6. Spreadability Test

A total of 0.5 grams of gel was weighed and placed in the middle of a round glass scale. Another round glass was placed on top of the gel and was let stand for 1 minute, then the spread was recorded. 50 grams of weight was placed on a round glass and left for 1 minute, and the distribution was recorded repeatedly for 100 grams, 150 grams, 200 grams, and 250 grams. Spreadability is considered as the wide area covered by the sample [14].

2.3.7. Cycling Test of Sunflower Seed Oil Gel

The stability test of gel preparation was carried out using the cycling test method. The gel was placed in a tightly closed glass container, then put in the refrigerator for 24 hours at 8 °C, and then transferred to the oven for 24 hours at 40 °C (1 cycle). This process was repeated for 3 cycles or 6 days

[16]. The instability that may occur is characterized by a gel that changes color, odor, a change in texture, or phase separation [15].

3. RESULTS AND DISCUSSIONS

The organoleptic observations showed that the 8 gel formulas did not show any different results in terms of color, smell, and shape, where all the formulas had a milky white color, a characteristic odor of oil, and a slightly viscous shape.

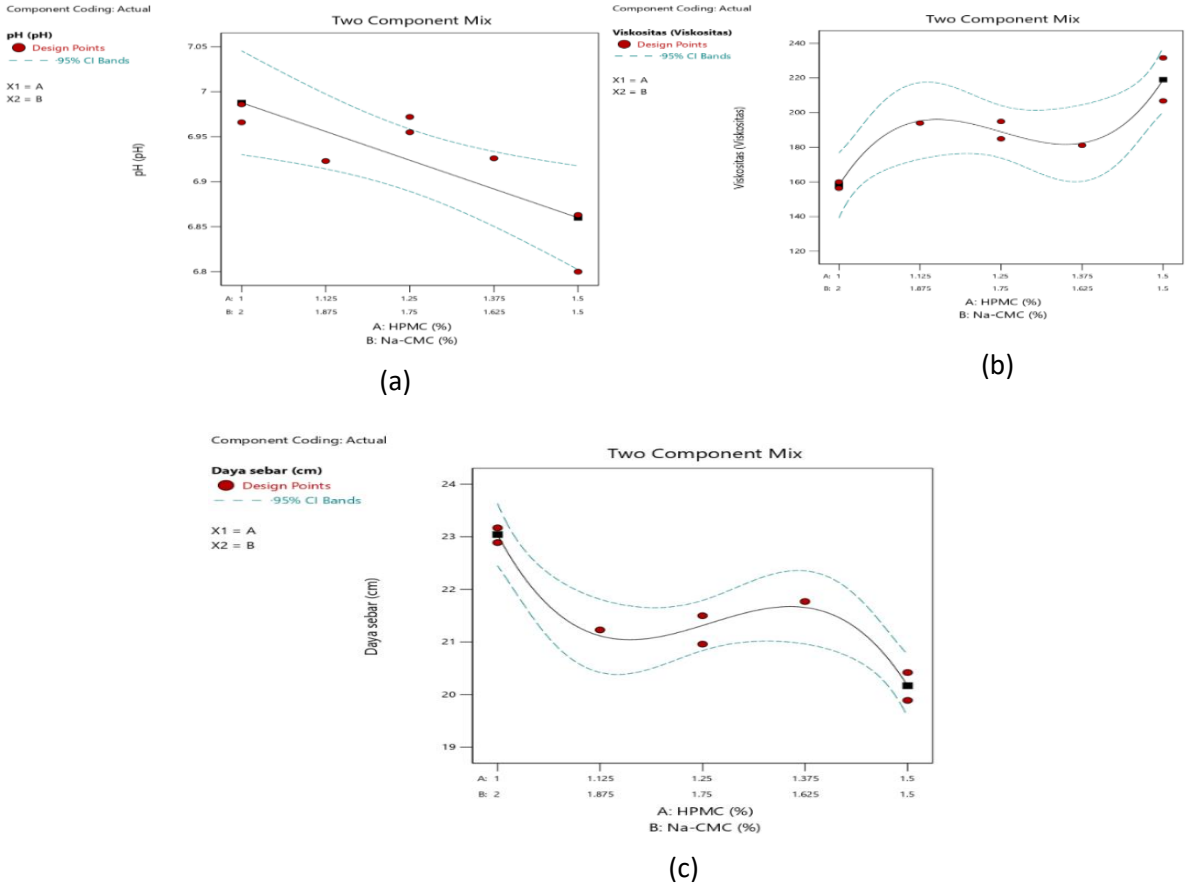

Figure 3. HPMC and Na-CMC graphs versus (a) pH; (b) viscosity; (c) spreadability

The results of the homogeneity test showed that the gel was homogeneous because coarse grains were not visible on the object glass. A homogeneous gel indicates that the active substance has been mixed evenly and it is hoped that the gel will have the same activity when used.

The pH test was carried out to determine the suitability of the topical preparations required between 4.5-7. Topical preparations in which the pH is too low can irritate the skin and if the resulting pH is too alkaline it will make the skin look scaly [16]. The results showed that HPMC and Na-CMC affected increasing the pH of the gel preparation which was indicated by a positive coefficient. This is following the theory where HPMC and Na-CMC both produce neutral gels [7,17].

A viscosity test was performed to determine the thickness of a fluid. The viscosity of the gel preparation should not be too high because it will make it difficult to remove the gel from the package and also result in low spreading power. The viscosity of the gel should not be too low because it will complicate the application process to the skin. Good gel preparations have a viscosity in the range of 150-300 dPas [18]. The results of the equation obtained show that the two gelling agents used gave a

positive response to the viscosity of the sunflower seed oil gel preparation, meaning that each addition of each gelling agent can increase the viscosity of the preparation.

The spreadability test aims to show the ease with which the gel preparation spreads after being applied to the skin. Preparations that have good spreading power will increase patient comfort in their use [19]. A good gel preparation has a spreading power of up to 5-7 cm in diameter [17]. Both gelling agents gave a positive response to the increase in spreadability. CMC-Na had a greater positive response than HPMC so the addition of CMC-Na had a greater effect on the increase in spreadability. The results of this analysis are inversely proportional to the viscosity response, where HPMC has more influence on the increase in viscosity than CMC-Na.

Table 2. Test results for pH, viscosity, and spreadability of sunflower seed oil gel

Run	pH	Viscosity (dPas)	Spreadability (cm2)
1	6,972 ± 0,0300	184,93 ± 3,002	20,96 0,468
2	6,986 ± 0,0250	160 ± 5,091	22,89 1,188
3	6,955 ± 0,0392	194,93 ± 2,203	21,5 0,473
4	6,926 ± 0,0490	181,2 ± 2,263	21,77 0,473
5	6,923 ± 0,0720	194 ± 3,394	21,23 0,815
6	6,8 ± 0,0740	231,6 ± 2,828	19,89 0,456
7	6,966 ± 0,200	156,4 ± 3,274	23,17 0,497
8	6,863 ± 0,003	206,8 ± 4,454	20,42 0,790

Table 3. Equation of pH, viscosity, and spreadability of sunflower seed oil gel

Response	Equation
pH	Y = 6.86A + 6.99B
Viscosity	Y = 219.04A + 158.04B + 1.75AB – 230.93(AB(A-B)
Spreadability	Y = 20.17A + 23.04B -1.17AB + 10.55(AB(A-B)

3.1. Optimum Formula

The optimum formula for sunflower seed oil gel preparations was determined using the Design Expert software with the simplex lattice design method. The selected target for the pH response was *minimize*. This is because the pH obtained was close to the upper limit of pH requirements for topical preparations so it was expected that the pH in the optimum formula would reach a minimum according to the range of the 8th run of the formula. The target set for the viscosity response was maximized to get the best range from the data obtained, which is around 200 dPas, because in this range the gel is not too thick and not too liquid. The selected target for the spreading power response was *maximize*. This is because a high spreadability will increase the patient's comfort. The degree of importance shows the magnitude of the importance of response in determining the optimum formula. Importance used has the same value (+++), except for pH which has importance (++++) because pH is an important requirement for the safety of topical preparations.

3.2. Optimum Formula Verification

The optimum formula of sunflower seed oil gel produced from prediction software was formulated and tested for its physical properties. The results of the physical properties test obtained

are listed in the table, where the table shows that there is no significant difference between the predictions and the experimental results.

3.3. Optimum Formula Cycling Test Results

In the organoleptic test results, no differences were found in color, odor, or homogeneity of the optimum formula. This shows that the gel preparation was stable for 3 cycles at extreme temperatures because there was no change in color, odor, and homogeneity.

Based on the results of the pH test, the optimum formula of sunflower seed oil gel did not change the pH value during 3 storage cycles with a cycling test. This means that the optimum formula for sunflower seed oil gel has good stability against temperature changes in the pH test.

The results of the adhesion and spreadability tests showed that there was no significant difference during the 3 test cycles.

Table 4. Determination of targets, lower, upper, and importance of the response of sunflower seed oil gel

Response	Lower Limit	Upper Limit	Target	*Importance*
pH	6.8	6,986	*Minimize*	++++
Viscosity	156.4 dPas	231.6 dPas	*Maximize*	+++
Spreadability	19.89 cm^2	23.17 cm^2	*Maximize*	+++

Table 5. Comparison of the predicted results of the optimum formula with experimental results

Response	Prediction	Test	Sig (2 tailed)	Summary
pH	6,873	6,813	0,062	Not significantly different
Viscosity (dPas)	196,689	194,800	0,289	Not significantly different
Spreadability (cm^2)	21,102	21,502	0,209	Not significantly different

Table 6. Test results for pH, spreadability, and viscosity of the optimum gel formula for 3 cycles of storage

Physical Properties	Storage Period			
	0 cycle	1st cycle	2nd cycle	3rd cycle
pH	6,813 ± 0,041	6,792 ± 0,022	6,746 ± 0,015	6,757 ± 0,076
Viscosity (dPas)	194,8 ± 2,94	194,8 ± 2,55	196,8 ± 1,93	200,5 ± 4,06
Spreadability (cm2)	21,5 ± 0,50	21,34 ± 0,70	20,76 ± 0,56	20,63 ± 0,77
Spreadability ((second)	6,29 ± 0,50	7,08 ± 1,00	7,35 ± 1,40	7,65 ± 1,81

The same thing also happened in the viscosity test where there was no difference in viscosity after the cycling test was carried out for 3 cycles of storage.

4. CONCLUSION

Variations of HPMC and Na-CMC bases affect the physical properties of sunflower seed oil gel preparations, namely pH, viscosity, and spreadability. The optimum formula composition of sunflower seed oil gel obtained is 1.451% HPMC and 1.549% Na-CMC. Sunflower seed oil gel has a pH of 6.813 ± 0.041, a viscosity of 194.8 ± 2.94 dPas, an adhesion of 6.29 ± 0.50 seconds, and a spreadability of 21.5 ± 10.05 cm2. Sunflower seed oil gel is stable at extreme temperatures (cycling test) for 3 cycles.

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