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Original Article

DETERMINATION OF THE STABILITY OF CATECHIN FROM GAMBIR (*UNCARIA GAMBIR* (HUNTER) ROXB) THROUGH SOLUBILIZATION MECHANISM

SEFRIANITA KAMAL[1,2*], FEBRIYENTI[1], ERIZAL ZAINI[1], DACHRIYANUS HAMIDI[1]

[1]Faculty of Pharmacy, Andalas University, Limau Manis, Pauh, Padang, West Sumatera, 25163, [2]Pharmacy Study Program, Dharma Andalas University, Sawahan 103 A, Simpang Haru Padang, West Sumatera, 25127
*Email: dachriyanus@gmail.com

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ABSTRACT

Objective: This study aims to obtain the solubility of catechins in water through the solubilization mechanism and determine their stability.

Methods: The research was conducted using the method of making spontaneous solubilization.

Results: Thermodynamically stable 0.5% catechin W/O solubilization formulation can be formulated using the oil phase, namely Tween 80 (15% and 10%) as a surfactant, 15% propylene glycol and 10% glycerin and is quite stable against shaking (centrifugation) and testing. freeze-thaw or cycling test.

Conclusion: Good solubility of catechins in water by solubilization mechanism. Based on the characterization and stability testing of the formed catechin solubilization system, the solubilization system of catechins was obtained which was more stable.

Keywords: Solubility, Catechin, Solubilization, Stability

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INTRODUCTION

Gambir (*Uncaria gambir* (Hunter) Roxb) is a plant belonging to the Rubiceae family. This plant comes from the Southeast Asian region, especially Indonesia and Malaysia [1, 2]. The main chemical content of gambir is catechin (7-33%) and tannic catechu acid (20-50%). The solubility properties of catechins are soluble in cold alcohol, ethyl acetate, hot water and glacial acetic acid and acetone [3]. Catechins are relatively poorly soluble in cold water and esters. Insoluble in $CHCl_3$, methyl ether and benzene. In the air, catechins are unstable and easily oxidized at a near-neutral pH of 6.9 and more stable at a low pH of 2.8 and 4.9. The benefits of catechins as antioxidants and antiaging are very suitable as cosmetic preparations. Meanwhile, pH of preparations that are suitable for the skin is close to normal (pH 6,9) [4].

An important physicochemical property of a drug substance is its solubility, especially the solubility of the system in water. If the solubility of the drug substance is less than desired, consideration should be given to improving its solubility [5]. From the problem of solubility of catechins which are difficult to dissolve in cold water, this research was carried out with the aim of making catechin formulations through the solubilization mechanism. Solubilization is defined as the maximum amount of a substance that can actually be dissolved in a certain amount of solvent. In addition, solubilization is a dosage form in the form of liquid or semi-solid, clear and isotropic, which consists of incorporation or solution in water of a substance that is insoluble or slightly soluble in water with the help of a surfactant [6].

The solubilization method has long been known and can only be obtained at certain concentrations of various substances mixed. Because the product obtained is thermodynamically stable, this method is expected to play a large role in the pharmaceutical and cosmetic fields [7].

The aims of this research are: To determine the solubilization of catechins can be formed and can be characterized, to determine the stability of catechins in the form of solubilization and to determine the level of solubilization of catechins that have been formed.

MATERIALS AND METHODS

Materials

The materials used in this study include Catechins (Gambir), Tween 80, Span 80, Propylene glycol, Glycerin, Alkohol 70%, Aquadest.

Instruments

The tools used in this study include Analytical Digital Scale (PrecisaXB 220A, Switzerland), UV–VIS Spectrophotometer (Shimadzu UV Mini-1240, Japan), Hot plate (Thermo, USA), Oven (Memmert, Germany), Refrigerator (Toshiba, Japan), Centrifuge (Hettich® Centrifuge EBA 280, Germany), Viscometer (Brokfield, USA), pH meter (Hanna, Romania).

Methods

Organoleptic test

The purpose of this analysis is to look at the physical visual solubilization. In this test, the observed color, odor, phase separation and clarity of solubilization [8].

Homogeneity test

Is carried out by means of sample solubilization smeared on a piece of glass or other suitable transparent material; the preparation should show a homogeneous and imperceptible arrangement presence of coarse grains [9].

Viscosity test

Measurements were made with a Brookfield Viscometer with speeds of 5, 10, 20 and 30 rpm. Observation of solubilization viscosity carried out in the initial state (zero weeks) and in the state forced (accelerated stability or after a cycling test). The purpose of this analysis is to see the flow properties of solubilization preparation formed [10].

Centrifugation test

The solubilization preparation is put into a centrifugation tube then shaken or centrifuged at a speed of 3000 rpm for 30 min. The purpose of this analysis is to show the stability of the solubilized preparation that has been formed. The results are seen whether cracking flocculation is formed and creaming [11].

Specific gravity

Specific gravity was measured using a pycnometer at a temperature of 25 °C. At room temperature, a clean, dry pycnometer weighed (A_0). Then filled with solubilization until full and weighed (A_1). The density of the dosage form is calculated using the formula as following Eq1:

$$\text{Specific gravity} = \frac{A_1 - A_0}{V_{pycno}} \quad \text{.... (Eq.1)}$$

pH measurement

The solubilization preparation was tested for pH using a pH meter at room temperature and after cycling test.

Freeze-thaw test or cycling test

The solubilization preparation was stored at cold temperature of 4 °C for 24 h then removed and placed at 40 °C for 24 h. This process is counted as 1 cycle. This experiment was repeated up to 7 cycles. The results of this cycling test are compared with the previous preparations [12].

Solubilization methods

The research was conducted using the method of making spontaneous solubilization (table 1). Type W/O solubilization was made by dissolving catechins with a small amount of alcohol in a 250 ml beaker. Put span 80, tween 80 and glycerin into the catechin solution, then place it on a hot plate at 70 °C. Stir until homogeneous using a magnetic stirrer at a speed of 200 rpm. Next, slowly drop the aqua dest mixture with propylene glycol while homogenizing it with a magnetic stirrer at a speed of 200 rpm until all substances are dissolved and homogeneous. The solubilization that has been formed is then stored at room temperature for 24 h before use. After that, the solubilization characterization was carried out.

RESULTS AND DISCUSSION

In the initial optimization stage, 0.5% catechin solubilization (for all formulas) was made using surfactant as a single oil phase with 2 concentration variations, namely 15% and 10%. The surfactants used were Span 80 and Tween 80. The reason for choosing Span and Tween surfactants was due to the potential for irritation and low toxicity [13].

The solubilization system is characterized by a clear (transparent) [14]. Fomula 2 and formula 4 only form a solubilization system. Both formulas contain Tween 80 with concentrations of 15% and 10% per formula, respectively. While in formulas 1 and 3 that contain Span 80, each formula is not formed a solubility system. In the formula looks cloudy and when left for±5 min will form 2 phases. This is due to the polarizing nature of span that is lipophilic anionic (non-polar) so it is not suitable to be used as a surfactant in the formulation of oil type in water [15].

Solubilization characterization

Solubilization characterization includes color, odor, phase separation and clarity. This characterization is carried out during the evaluation process until stability testing is accelerated. The first evaluation carried out on solubilization was an organolpetic and visual homogeneity test (table 2). The results from the initial observations before and after the accelerated stability test, the solubilization preparation remained organoleptically stable and homogeneous.

Table 1: Catechin solubilization formula composition

No.	Material name	Concentration (% w/v)			
		F1	F2	F3	F4
1.	Catechins	0.5	0.5	0.5	0.5
2.	Span 80	15	-	10	-
3.	Tween 80	-	15	-	10
4.	Propylene glycol	15	15	15	15
5.	Glycerin	10	10	10	10
6.	70% alcohol	qs	Qs	qs	Qs
7.	Aquadest ad	100	100	100	100

Table 2: Organoleptic test results

Parameter	F1	F2	F3	F4
Color	yellowish	yellowish	yellowish	yellowish
Smell	Typical	Typical	Typical	Typical
Phase separation	2 phase	There is not any	2 phase	There is not any
clarity	cloudy	Clear	cloudy	Clear

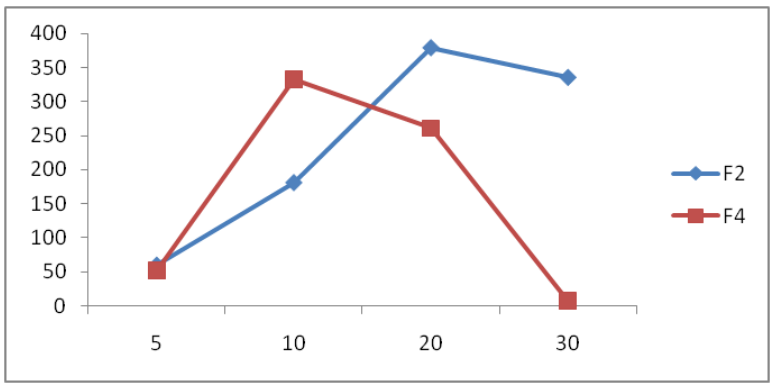

Fig. 1: The relationship between formula viscosity and rotational speed

Viscosity analysis

Viscosity testing was carried out at the initial state; the results obtained a stable viscosity at a speed of 20 rpm (fig. 1). Meanwhile, in the forced state, the viscosity of the solubilization becomes unstable. This is due to the extreme temperature exchange carried out on the solubilization preparation for 7 cycles.

The ideal solubilization has criteria similar to that of a solution where the solubilization has a low viscosity value. The flow type of solubilization is included in the pseudoplastic flow type. This means that in pseudoplastic flow, there is an increase in shearing stress which results in a continuous decrease in viscosity. As the shearing stress increases, the disordered molecules will arrange a long axis in the direction of flow.

pH measurement

Measurement of solubilization pH was carried out at the initial state and at the time of accelerated stability testing. From the measurements made, it was found that the solubilization results were stable in the initial state. And in the accelerated stability test, the pH of the solubilization did not increase significantly, so it can be said that the solubilization remained chemically stable (fig. 2). In addition, the increase in pH that occurs is still within the safe range for skin pH [16].

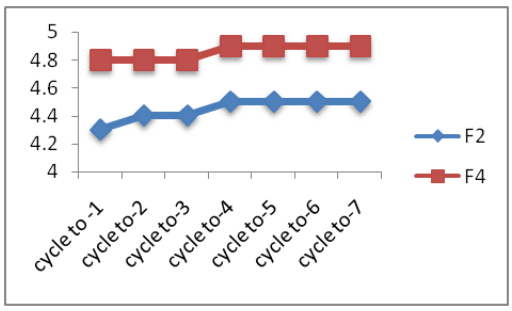

Fig. 2: Relationship between formula pH and cycle in forced condition

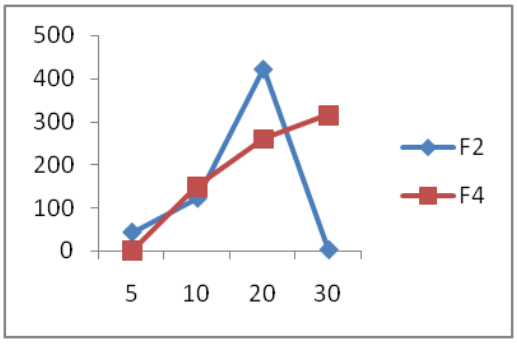

Fig. 3: The relationship between formula viscosity and rotational speed in forced conditions

CONCLUSION

Thermodynamically stable 0.5% catechin W/O solubilization formulation can be formulated using the oil phase, namely Tween 80 (15% and 10%) as the surfactant, 15% propylene glycol and 10% glycerin. The solubilization of catechins formed was stable to shaking (centrifugation) and freeze-thaw or cycling tests. There was no significant change in levels during the freeze-thaw test or cycling test and storage for±14 d.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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