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Testosterone Undecanoate Hormone Microemulsion Formulation Optimization

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ABSTRACT

Testosterone undecanoate, sometimes known as TU, is a medication that is hydrophobic. A microemulsion is a type of dispersion system that can boost the medications' solubility, especially those that are hydrophobic. In this investigation, the optimization of microemulsion formulations was carried out using a wide variety of surfactants, oils, cosurfactants, and water in their respective proportions. After that, a microemulsion was created with the following components: 30% tween 80 and 10% tween 20 as surfactant components, 24% isopropyl myristate (IPM) and 24% castor oil (CO) as oil phase, 10% n-butanol as a cosurfactant, and 2% water. The oil phase consisted of isopropyl myristate and castor oil. The findings obtained from the TU After being stored at 40 C and 270 C for two months, the examination of the microemulsion revealed that it remained in a stable condition.

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1. INTRODUCTION

In order to design a dosage form correctly, it is necessary to take into account the physical, chemical, and biological properties of all of the drug substances and pharmaceutical ingredients that are going to be utilized in the production of the product. The medications and pharmaceutical components that are going to be utilized have to be combined with one another in order to produce a solution that is reliable, effective, appealing, simple to produce, and risk-free (Ansel, 1989).

In recent years, there has been a lot of worry directed toward the solubility of hydrophobic medications that have a low solubility in water. The clinical application of hydrophobic medications becomes ineffective when they have a poor solubility, which will result in the drug having a modest penetration of the body (Lawrence, 2000). Because the solubility of a medicine and its dissolution rate are strongly related to one another, the solubility of a nutritional substance that is less than 1 mg/ml has a tiny dissolving rate. Increasing the amount of solvents and surfactants that are used in conjunction with tinkering with the pH is one of the many different solubility methods. Both traditional methods, such as the employment of extra solvents as oil carriers, and contemporary methods, such as the mixing of micelles, liposomes, complexation with cyclodextrins, and emulsions, have a number of drawbacks (Date AA, 2008).

Microemulsions, a novel type of vehicle, have been developed as a means of transporting medications that are hydrophobic. A dispersion system that is generated from emulsion preparations is known as a microemulsion. This preparation is appealing for use as a drug delivery method because, in comparison to emulsions, microemulsions possess a greater number of desirable properties.

Microemulsion is a colloidal dispersion that is thermodynamically stable, transparent, isotropic, and has a low viscosity. It consists of microdomains of oil and/or water that are stabilized by an interfacial layer of exchange of surfactant and cosurfactant molecules. Microemulsions can be sterilized by filtration, have a high solubility, and have a good penetrating ability. Carriers of choice due to desirable characteristics include spontaneous creation, ease of production, high solubility capacity, and self-defense characteristics (Date AA, 2008). Microemulsions can be made for preparations that are to be used topically, intradermally, pulmonaryly, ocularly, intramuscularly, or orally.

As a drug model, testosterone undecanoate (TU) will be used in the tests that will be carried out in this research. These experiments will result in the creation of microemulsion formulations. Because its log value (P) is 7.24, the hormone known as 17–hydroxyl–4 androsten–3–one 17–undecanoate, also known as testosterone undecanoate, is classified as a hydrophobic compound. After oral administration, testosterone undecanoate is an aliphatic fatty acid ester that is composed of testosterone. After oral administration, testosterone undecanoate is partially absorbed through the colon and is contained by the lymphatic system. Oral testosterone undecanoate has also been evaluated for use in male fertility control as a standalone oral contraceptive or in combination with other oral contraceptives, such as cyprotene acetate (CPA). There are a few factors that contribute to the ineffectiveness of TU when it is taken orally as a method of birth control. These factors include the frequency of administration, the amount of testosterone found non the serum, and the absence of inhibition of gonadotropins and spermatogenesis. (Ilyas S).

There was another research that was discovered in China; specifically, injections of testosterone undecanoate (TU), which has effects that last for a long time. Injection of TU 500mg and TU 1000mg dissolved in tea seed oil every four weeks, with the result that eleven out of twelve men who were injected with TU 500mg attained azoospermia, and one reached a sperm concentration of one million/ml. In the meantime, each of the 12 males became azoospermic after receiving an injection of 1000 mg of TU (Gu, et all, 2004)

At the moment, testosterone undecanoate is made in the form of a solution that is suspended in castor oil. The downside of using oil carriers in preparations is that they are more likely to go rancid, and the viscosity of the preparations will increase as a result. Because of this, a novel preparation known as a microemulsion was developed. This microemulsion dosage form has a number of benefits, including being thermodynamically stable, having a high solubility, having a good penetration ability, and being simple to produce. In the course of this study, an investigation into the microemulsion's stability will be carried out, and optimization of microemulsion formulations containing the active component testosterone undecanoate will be carried out utilizing a variety of surfactant and oil compositions.

2. RESEARCH METHOD

Time and Place of Research

This research was conducted at the Laboratory of Pharmaceutical Technology for ± 8 months.

Tools and materials

a. Tool

The equipment used is becker glass, pipette mumps, magnetic stirrer, analytical balance, microlite pipette, pycnometer, pH meter (Delta 320), centrifuge (Hettich Centrifuge EBA 20), Delta™ Nano C Particle Analyzer, Visco Tester 6R HAAKE, oven, homogenizer.

b. Ingredients

The materials used were testosterone undecanoate (Xianju Pharma), tween 80 (Merck), tween 20 (Merck), tween 60 (Merck), span 80, isopropyl myristate (Merck), castor oil (Sigma), n-butanol (Merck), PEG 400 (Merck), glycerin (Merck), distilled water.

3. RESULTS AND DISCUSSIONS

Results

Preparation of microemulsion preparations

After the preliminary experiments, it was found that the best conditions for making clear and stable microemulsion preparations were at a stirring speed of ± 300 rpm with a stirring time of 3 minutes and at room temperature, which was 27º C. Of the 10 formulas made in this experiment with variations in the concentration of the oil phase , surfactant, water as well as various ingredients used to obtain the ME 10 formula which produces a clear and transparent microemulsion preparation.

The best composition of ingredients to produce clear and stable microemulsion preparations is 30% tween 80, 10% tween 20, 24% castor oil, 24% IPM, 10% n-butanol and 2% water.

Table 1. Experimental Results for Making Microemulsion Preparations

Formulas	Material composition	Results
ME 1	IPM, CO, Tween 60, Glycerin, Water	Milky white emulsion
ME 2	IPM, CO, Tween 60, Glycerin, Water	Milky white emulsion
ME 3	IPM, CO, Tween 20, Glycerin, Water	Milky white emulsion
ME 4	HDI, Tween 80, PEG 400, Span 80, Water	Clear, 2 phase
ME 5	HDI, Tween 80, Tween 20, n–butanol, Water	Clear, 2 phase
ME 6	IPM, Tween 80, n–butanol, Span 80, Water	Clear, 2 phase
ME 7	HDI, Tween 80, PEG 400, Span 80, Water	Clear, 2 phase
ME 8	IPM, CO, Tween 80, Tween 20, n–butanol, Water	Clear, there is a precipitate
ME 9	IPM, CO, Tween 80, Tween 20, n–butanol, Water	Cloudy emulsion
ME 10	IPM, CO, Tween 80, Tween 20, n–butanol, Water	Microemulsion which is clear yellow and transparent

Evaluation of microemulsion preparations

a. Microemulsion specific gravity measurement

The specific gravity of the microemulsion was measured on the ME 10 microemulsion which was stored at 3 different temperatures, namely 27º C, 40º C and 4º C. The specific gravity was measured using a pycnometer. The pycnometer weight (A) is 11.5484 grams. The weight of the pycnomometer filled with water (A1) is 21.6922 grams. The weight of the pycnometer containing the microemulsion at 4º C is 21.2060 grams. The weight of the pycnometer containing the microemulsion at 27º C is 20.2867 grams. The weight of the pycnometer containing the microemulsion at 40º C is 21.1791 grams. From the calculation results, the specific gravity of the microemulsion is obtained, namely the temperature of 4º C is 0.952 g/ml, the temperature of 27º C is 0.861 g/ml, the temperature of 40º C is 0.949 g/ml.

b. pH test

The pH test was carried out for 8 weeks, with measurements taken every 2 weeks. The pH test was carried out on ME 10 microemulsion preparations which were stored at 4º C, 27º C and 40º C. The complete results can be seen in table 3 and figure 8.

Table 2. Microemulsion pH ME 10 at 4º C, 27º C and 40º C for 8 weeks

Sunday	pH at temperature (º C)		
	4	27	40
2	6,24	6,19	6,40
4	6.06	6,19	6,40
6	6,16	6,14	6,12
8	6,22	6,17	6,20

c. Centrifugation test

The microemulsion preparations tested by centrifugation were those that existed at 4º C, 27º C and 40º C. The preparations were centrifuged at 3000 rpm for 30 minutes. After centrifugation the ME 10 microemulsion remained stable, no separation occurred, no precipitation occurred and remained clear.

d. Microemulsion macroscopic observation

Low temperature (4º C), After 8 weeks of observation, the microemulsion stored at 4º C remained clear, the color and smell did not change and was thicker when compared to week 0. Results of microemulsion macroscopic observations at low temperatures.

Table 3. Results of Macroscopic Observation of ME 10 Low Temperature Microemulsion Preparations

Sunday	Temperature (ºC)	Organoleptic			
		Color	Smell	Clarity	precipitate
I	4	Clear Yellow	Typical	Clear	-
II	4	Clear Yellow	Typical	Clear	-
III	4	Clear Yellow	Typical	Clear	-
IV	4	Clear Yellow	Typical	Clear	-
V	4	Clear Yellow	Typical	Clear	-
VI	4	Clear Yellow	Typical	Clear	-
VII	4	Clear Yellow	Typical	Clear	-
VIII	4	Clear Yellow	Typical	Clear	-

Room temperature (27º C). After 8 weeks of observation, the microemulsion stored at 27º C remained clear, the color and smell did not change when compared to week 0. Results of microemulsion macroscopic observations at room temperature.

Table 5. Results of Macroscopic Observation of Microemulsion Preparations ME 10 Room Temperature

Sunday	Temperature(ºC)	Organoleptic			
		Color	Smell	Clarity	precipitate
I	27	Clear Yellow	Typical	Clear	-
II	27	Clear Yellow	Typical	Clear	-
III	27	Clear Yellow	Typical	Clear	-
IV	27	Clear Yellow	Typical	Clear	-
V	27	Clear Yellow	Typical	Clear	-
VI	27	Clear Yellow	Typical	Clear	-
VII	27	Clear Yellow	Typical	Clear	-
VIII	27	Clear Yellow	Typical	Clear	-

High temperature (40º C), After 8 weeks of observation, the microemulsion stored at high temperature remained clear, the color and smell did not change but a precipitate appeared.

Table 5. Results of Macroscopic Observation of Microemulsion Preparations ME 10 Room Temperature

Sunday	Temperature(ºC)	Organoleptic			
		Color	Smell	Clarity	precipitate
I	40	Clear Yellow	Typical	Clear	There is
II	40	Clear Yellow	Typical	Clear	There is
III	40	Clear Yellow	Typical	Clear	There is
IV	40	Clear Yellow	Typical	Clear	There is
V	40	Clear Yellow	Typical	Clear	There is
VI	40	Clear Yellow	Typical	Clear	There is
VII	40	Clear Yellow	Typical	Clear	There is
VIII	40	Clear Yellow	Typical	Clear	There is

e. Test cycling test
After passing 7 cycles of the cycling test, the microemulsion was physically observed including odor, color and clarity. And the result obtained is a yellow microemulsion, has a characteristic odor and remains clear.

f. Determination of microemulsion particle size
Microemulsion preparations that were measured were preparations at week 4 which were stored at 4º C, 27º C, 40º C and preparations that had been exposed to the cycling test. From the measurement results it was found that ME 10 at 4º C measured 62.2 nm. ME 10 at 27º C measures 73.6 nm. ME 10 at 40º C measures 62.5 nm. ME 10 results of the cycling test measuring 82 nm.

g. Viscosity test
The results of measuring the viscosity of microemulsion preparations at room temperature showed an increase in viscosity from the oth to the 8th week, from 93.1675 cps to 100.585 cps. The results of measuring the viscosity of microemulsion preparations at week 0 and week 8 can be seen in the following table:

Table 6. Microemulsion Viscosity ME 10 Week 0

Rpm	cp	%
5	87.33	1,1
10	92.67	2,3
20	96,67	4,8
30	96	7,2

Table 7. Microemulsion Viscosity ME 10 Week–8

Rpm	cp	%
5	95.67	1,1
10	98.67	2,4
20	103,67	5.0
30	104,33	7,5

h. Qualitative analysis of testosterone undecanoate
After conducting a qualitative analysis using the TLC method, the results were 3 spots, namely 1 sample spot taken from the prepared microemulsion and 2 spots of comparator, namely Nebido and Testosterone Undecanoate Xianju Pharma. The three spots each have an Rf value, namely Rf sample 0.793, Rf standard Nebido 0.777, Rf standard hormone Testosterone Undecanoate 0.826.

Discussion

a. Microemulsion preparation

Conditions that must be considered in the manufacture of microemulsion preparations are the speed of stirring, stirring time and temperature. The composition of the material that must be considered is the concentration of the oil phase, surfactant and water phase.

Microemulsions can be prepared by stirring. The stirring process can disperse the dispersed phase. This is because it provides kinetic energy which can cause the dispersed phase to split into small globules. This stirring process should not be too fast or too slow. If it is too fast, turbulence will occur which can cause the size of the dispersed globules to become uneven and also result in a larger particle size. Meanwhile, stirring that is too slow will cause the ingredients to be difficult to become homogeneous (Maya L).

Previously, at the beginning of the experiment, stirring was done with a homogenizer with varying speeds between 5000–17000 rpm and a milky white preparation with globules on the surface was obtained. Then the stirring was carried out using a magnetic stirrer, the stirring speed was varied from speed 1-5. Microemulsion was formed at speed 5 (± 300 rpm). The duration of stirring also affects the formation of microemulsions. If it is too short, the clear microemulsion will become cloudy due to the clumping of the particles (Leon L, 1994). If the stirring is too long, the opportunity for the globules to combine will be greater and coalescence will occur because the smaller diameter change will produce a high surface free energy so that the system becomes unstable. In this experiment, the microemulsion

was stirred for 2–5 minutes at 300 rpm. A microemulsion is formed when stirred for 3 minutes. In the manufacture of this microemulsion nonionic surfactants are used. Therefore must pay attention to the temperature used. At low temperatures, nonionic surfactants become hydrophilic and form an O/A system. At high temperatures, they are lipophilic and form A/M systems. At medium temperature, which is called the HLB temperature, the hydrophilic–lipophilic interactions become balanced (Swarbrick J, 1994).

In this experiment, microemulsions were made at room temperature 27º C. Previously, microemulsions were made by heating, the preparations that formed tended to separate. This is because an increase in temperature can cause each phase to separate (Leon L, 1994). In addition to the conditions of manufacture, it is also necessary to pay attention to the composition of the materials used for the manufacture of microemulsions. Generally, microemulsions consist of oil, surfactant, cosurfactant and water phases. The oil phases used in this experiment were IPM and CO with varying concentrations of IPM from 2–68% and CO from 24–40%. The surfactants used were tween 80, tween 20, tween 60 and span 80 with variations

tween 80 concentration from 7.5–30%, tween 20 from 0.05–10%, tween 60 0.05–10% and span 80 5%. The cosurfactants used were PEG 400, n- butanol and glycerin with varying concentrations of PEG 400 from 24-30%, n- butanol 10% and glycerin 20-25%. In preliminary experiments it was found that ME 1, 2 and 3 produced colored preparations. milk white. While ME 4, 5, 6, 7 produce clear preparations and separate into 2 phases. This is probably caused by the lack of surfactant concentration so that it is not strong enough to inhibit the coalescence of the inner phase droplets (Maya L). ME 8 forms a clear preparation but there is a precipitate at the bottom. This is because the protective layer is not strong enough to prevent the coalescence of the inner phase droplets (Leon L, 1994). ME 9 produces a turbid emulsion, but after 24 hours it will become clear and separate into 2 phases. ME 10 produces clear and transparent microemulsion preparations. This microemulsion is formed because the surfactant concentration has reached or exceeded the critical micelle concentration.

From the results of the preliminary experiments, it was found that the concentration and composition of the ingredients for ME 10 were 30% tween 80, 10% tween 20, 24% IPM, 24% castor oil, 10% n-butanol and 2% water. This ME 10 microemulsion formula will later be evaluated either physically or chemically for 2 months. The boundaries of the microemulsion region can be determined with the help of phase diagrams (Moreno, 2003). By plotting the data on the concentration of the ingredients that have been prepared, it will be seen which areas are microemulsions and which are not. The phase diagrams depict the properties of the many components that have been used in the optimization formulation, although a large amount of data must be generated if an adequate diagram is to be made. Without the use of phase diagrams, the characterization of the properties of the emulsion components in a multiphase system cannot be predicted (Block, 1989).

b. Microemulsion specific gravity measurement

Specific gravity is the ratio of the weight of a substance in the air at a predetermined temperature to the weight of water with the same volume and temperature (Ministry of Health, 1995). Specific gravity was measured using a pycnometer at room temperature. From the calculation results, the specific gravity of the microemulsion stored at 4º C, 27º C and 40º C were 0.952 g/ml, 0.861 g/ml and 0.949 g/ml respectively.

c. pH test

The pH test was carried out for 8 weeks with measurements made every 2 weeks on microemulsion preparations stored at 4º C, 27º C and 40º C. This pH measurement aims to observe changes in pH that may occur in microemulsions during the storage period. During the storage period, the pH of the microemulsion decreased and increased. At 4º C, the pH decreased in the 4th week, then the pH increased when measured in the 6th week. At temperatures of 27º C and also 40º C, the pH decreased in the 6th week, then the pH increased in the 8th week. At a temperature of 40º C the decrease in pH is greater when compared to temperatures of 4º C and 27º C. Castor oil is an unsaturated fatty acid, if castor oil is hydrolyzed it will produce carboxylic acids (Sastrohamidjojo H, 2005).

Although there was a decrease and increase in pH, the decrease and increase was not too drastic. It can be said that microemulsion preparations stored at these three temperatures are chemically stable, there is no interaction with containers or other materials and there are no significant chemical reactions.

d. Centrifugation test

This centrifugation test was carried out to evaluate the stability of the microemulsion. It is generally accepted that the lifetime of a microemulsion under normal storage conditions can be quickly predicted by observing the separation of the dispersed phase due to the formation of creaming or clumping when the microemulsion is exposed to centrifugation (Leon L, 1994). As with emulsions, microemulsions are said to be stable if they do not show any serious damage when centrifuged at 3000 rpm for 30 minutes at room temperature (Idson B, 1989).

This centrifugation test was carried out on microemulsions which were stored at 4º C, 27º C and 40º C. This test was carried out at 3000 rpm for 30 minutes. After centrifugation, the microemulsion remained clear, no phase separation or precipitate formed. This shows that the microemulsion preparation still shows a solution that is perfectly dispersed and can still flow well.

e. Microemulsion macroscopic observation

The stability of microemulsion preparations was observed physically which included odor, color and clarity. The thermodynamic stability of the generally postulated type for dissolved or microemulsion systems is generally temperature dependent (Leon L, 1994). The microemulsion was stored at 4º C, 27º C and 40º C for 8 weeks.

f. Low temperature (4º C)

When stored at low temperatures, microemulsions do not change physically when compared to preparations before storage at low temperatures. But the microemulsion becomes thicker than the preparation before being stored at low temperatures because the viscosity of the microemulsion at cold temperatures increases. This is because the solution tends to shrink at low temperatures and the oil phase also tends to freeze at low temperatures. So that the particles will tend to combine to form bonds between particles that are denser, as a result the viscosity increases and the flow rate decreases. But when the microemulsion is returned to room temperature, the microemulsion will return to its original state, where the microemulsion becomes runny and easy to pour.

This thickening can be excessive if the microemulsion is not agitated during the cooling cycle. Freezing can damage a microemulsion more than heating, because the solubility of emulsifiers, both in the oil phase and in the water phase, is more sensitive to cooling than to moderate heating. In addition, the formation of ice crystals develops pressure which can deform the spherical shape of the microemulsion droplets (Leon L. 1994).

g. Room temperature (27º C)

When the microemulsion was stored at room temperature, the microemulsion did not show any physical changes during the 8 weeks of observation. The microemulsion remains clear and transparent, and the color and odor do not change. This indicates that the microemulsion is thermodynamically stable.

h. Determination of microemulsion particle size

The particle size of a microemulsion is usually expressed as the diameter of the globules in the internal phase. The particle size depends on the type and amount of emulsifier and the addition of additives. If the particle size of the inner phase is smaller, the microemulsion becomes more stable (Idson B, 1989).

The microemulsion whose particle size was measured was a microemulsion which had been stored for 4 weeks at 4º C, 27º C, 40º C and which had been subjected to a cycling test. Sequentially the particle size of the microemulsion stored at 4º C, 27º C, 40º C and which had been tested by the cycling test were 62.2 nm, 73.6 nm, 62.5 nm and 82 nm. The particle size of the microemulsion that has been tested in the cycling test is larger when compared to the microemulsion stored at 4º C, 27º C and 40º C. This is due to the fact that during the cycling test process droplets coalesce which can cause

coalescence. From the results of observations it can be seen that during storage there may be coalescence between particles which will form larger particles.

i. Viscosity test

Viscosity is a statement of the resistance of a liquid to flow, the higher the viscosity the higher the resistance (Martin A, 1993). Viscosity is a physical benchmark that is usually measured to assess the effect of pressure conditions on microemulsions (Leon L, 1994). Viscosity changes during storage are the main criteria for emulsion stability. The results of microemulsion measurements at week 0 and week 8 showed that microemulsion preparations experienced an increase in viscosity from 93.1675 cps to 100.585 cps. As with emulsions, this is because usually the viscosity of microemulsions increases with increasing age of the preparation (Leon L, 1994).

j. Qualitative analysis of testosterone undecanoate

TLC is a method of separating components on the basis of differences in adsorption or partitioning by a stationary phase under the movement of a solvent developer or a mixed expansion solvent (Mulja M; Suharman, 1995). At the beginning of the experiment, a mixture of Acetonitrile (ACN) and water was used in various ratios. This developer solvent mixture is divided into two, namely those that are given phosphoric acid and those that are not. It turned out that the developer solvent mixture could not elute the sample. This is because the components of the sample being separated are non-polar or hydrophobic substances that do not dissolve in water (Mulja M; Suharman, 1995). Then the water is replaced with methanol (MeOH), so the mixture becomes ACN and MeOH. This developer solvent mixture is made with a ratio of 69: 31. It turned out that this developer solvent mixture could elute the sample components and the reference standard, so that 3 spots were obtained. The choice of expansion solvent or mixed expansion solvent is greatly influenced by the type and polarity of the chemicals being separated (Mulja M; Suharman, 1995). The purpose of the analysis using TLC was to find out whether the active substance testosterone undecanoate in the microemulsion was still present or not during the 2 months of storage. From the results of the TLC it was known that the active substance testosterone undecanoate was still present in the microemulsion preparation for 2 months of storage. So it can be concluded that TU is stable in this microemulsion formula. The choice of expansion solvent or mixed expansion solvent is greatly influenced by the type and polarity of the chemicals being separated (Mulja M; Suharman, 1995). The purpose of the analysis using TLC was to find out whether the active substance testosterone undecanoate in the microemulsion was still present or not during the 2 months of storage. From the results of the TLC it was known that the active substance testosterone undecanoate was still present in the microemulsion preparation for 2 months of storage. So it can be concluded that TU is stable in this microemulsion formula. The choice of expansion solvent or mixed expansion solvent is greatly influenced by the type and polarity of the chemicals being separated (Mulja M; Suharman, 1995). The purpose of the analysis using TLC was to find out whether the active substance testosterone undecanoate in the microemulsion was still present or not during the 2 months of storage. From the results of the TLC it was known that the active substance testosterone undecanoate was still present in the microemulsion preparation for 2 months of storage. So it can be concluded that TU is stable in this microemulsion formula. The purpose of the analysis using TLC was to find out whether the active substance testosterone undecanoate in the microemulsion was still present or not during the 2 months of storage. From the results of the TLC it was known that the active substance testosterone undecanoate was still present in the microemulsion preparation for 2 months of storage. So it can be concluded that TU is stable in this microemulsion formula. The purpose of the analysis using TLC was to find out whether the active substance testosterone undecanoate in the microemulsion was still present or not during the 2 months of storage. From the results of the TLC it was known that the active substance testosterone undecanoate was still present in the microemulsion preparation for 2 months of storage. So it can be concluded that TU is stable in this microemulsion formula.

4. CONCLUSION

Microemulsion with the active substance testosterone undecanoate can be prepared at room temperature, namely 27º C with a stirring speed of ± 300 rpm and a stirring time of ± 3 minutes. The best material composition for making microemulsions with the active ingredient testosterone undecanoate is 30% tween 80, 10% tween 20, 24% castor oil, 24% ipm, 10% n-bultanol and 2% water, this formula is stable for 2 months of observation. , no significant change in pH and no significant increase in viscosity. This formula is stable if stored at 27ºC and 4ºC.

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