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Formulation and Characterization of Mefenamic Acid Self Nanoemulsifying Drug Delivery System (SNEDDS) Preparations

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ABSTRACT

Mefenamic acid is included in BCS (biopharmaceutical classification system) class II, namely high permeability and low solubility. This research aims to obtain a good formula for oleic acid oil, tween 80, and PEG 400 according to the characterization test of emulsification time, % transmittance, drug loading, globule size, and zeta potential. This research was an experimental study by formulating mefenamic acid in the form of SNEDDS which was made 1 formula was made in the form of SNEDDS with the composition of oleic acid, tween 80, and PEG 400 and characterization tests were carried out for emulsification time, % transmittance, drug loading, globule size, zeta potential. The yield of the oleic acid formula is 1%, tween 80 is 8%, and PEG 400 is 1%. The emulsification time characterization test resulted in 17 seconds, % transmittance of 97%, drug loading of 179.81 mg, globular size of 85.8 nm and zeta potential of -1.6 mV.

1. Introduction

Mefenamic acid is a non-steroidal anti-inflammatory drug that is used to treat pain by preventing inflammation and stimulating the immune system in patients with arthritis and arthrosis. This drug is used to treat various complaints such as pain, menstrual pain, headaches, toothache, and rheumatism. Mefenamic acid is a BCS class II drug that has good permeability in the body but has low solubility. Several systems have been developed for the formulation of lipid-based preparations, especially the self-emulsifying drug delivery system (SEDDS), to increase the oral solubility of lipophilic drugs. SNEDDS (self-nanoemulsifying drug delivery system) is one of the SEDDS preparations. The advantage of

SNEDDS preparations is the ability to form nanoemulsions effectively. spontaneously in the digestive tract, and the resulting droplets are nanometers in size. The SNEDDS formulation is a preparation consisting of oil, surfactant, and co-surfactant with a suitable composition to produce a stable isotropic mixture. SNEDDS is a drug delivery system consisting of an isotropic mixture of drug, oil, surfactant, and co-surfactant. SNEDDS is a stable system in the digestive tract.¹⁻⁵

In this research, the pure active substance mefenamic acid, formulated in the dosage form (self-nanoemulsifying drug delivery system) SNEDDS using oleic acid and surfactant uses tween 80, and cosurfactant uses PEG 400. PEG 400 was chosen as

the cosurfactant phase. These cosurfactants can help reduce surface tension so that they can reduce particle size and increase the mobility of the hydrocarbon tails of the surfactant so that they dissolve more easily on the oil surface. The results of the preparation were then characterized, including emulsification time, transmittance value, size and size distribution of nanoemulsion droplets, and zeta potential of nanoemulsion.⁶⁻¹⁰

2. Methods

The type of research used is pure experimental research, namely by making SNEDDS preparations containing mefenamic acid and then testing the SNEDDS characterization. The tools used in this research are analytical balance, magnetic stirrer, UV-Vis spectrophotometer, particle size analyzer (PSA), ultrasonicator, and glassware. The materials used in this research include mefenamic acid, oleic acid, tween 80, PEG 400, aquades, and methanol P.a. Pipette each component of SNEDDS, namely oleic acid, tween 80, and PEG 400, according to the formula, then mix using an ultrasonicator and stirred with a magnet stirrer for 5 minutes with 300 rpm rotation until SNEDDS is formed. SNEDDS, the formed mefenamic acid, is added little by little until saturation conditions are reached, which is indicated by turbidity in the SNEDDS. SNEDDS mefenamic acid in saturated conditions was then centrifuged at 5.00 rpm for 45 minutes. Results supernatant SNEDDS mefenamic acid is stored in a microtube protected from exposure to sunlight and stored at room temperature. Results of supernatant Characterization tests were carried out, including emulsification time, drug loading, percent transmittance, and measurement of globule size. Formulation: Mefenamic acid 100 mg, oleic acid 1%, tween 80 8% and PEG 400 1%.

Emulsification time is the time required for SNEDDS to form an emulsion spontaneously when diluted in water media (1 part SNEDDS added to 100 parts distilled water) at a temperature of $37 \pm 2^\circ\text{C}$ and stirred with a magnetic stirrer at 100 rpm. Optical clarity is assessed by % transmittance (1 part SNEDDS

added to 100 parts distilled water) at a temperature of $37 \pm 2^\circ\text{C}$ and stirred with a magnetic stirrer at 100 rpm. The absorbance of each formulation was measured by spectrophotometer UV-Vis at 650 nm using distilled water as a blank. Determination test drug loading was carried out using a UV-Vis spectrophotometer. First, be careful in a pipette of 1 ml of the mefenamic acid SNEDDS formulation sample into a 10 ml volumetric flask, then fill with 10 ml of methanol to the line mark and shake gently until the solution is clear. Second, carefully read the absorbance of the solution on a UV-Vis spectrophotometer according to the maximum length of mefenamic acid with methanol as a blank. Third, the levels of the mefenamic acid formulation were calculated using a linear regression equation with a Determination calibration standard curve drug loading used to calculate the levels of Mefenamic Acid in the composition of SNEDDS. Determination of globule size by diluting into water media (1 part SNEDDS added to 100 parts distilled water) at a temperature of $37 \pm 2^\circ\text{C}$ and stirring with a magnetic stirrer at 100 rpm. Determination of zeta potential diluted into water media (1 part SNEDDS added to 100 parts distilled water) at a temperature of $37 \pm 2^\circ\text{C}$ and stirred with a magnetic stirrer at 100 rpm.

3. Results and Discussion

Results of mefenamic acid SNEDDS preparation

A nanoemulsion formulation is considered stable and meets the requirements of the visual observation. It is clear there is no phase separation, there is an oil/water nanoemulsion type, the formation time is less than 1 minute, the % transmittance is close to 100%, the drug loading value is higher, and the particle size is less than 200 nm, and the zeta potential is approximately -31 mV. Characterization of SNEDDS fenofibrate was carried out using a magnetic stirrer to determine the emulsification time, a UV-Vis spectrophotometer to determine the % transmittance, drug loading and PSA (particle size analyzer) to determine globule size and zeta potential.^{11,12}

Table 1. Results of SNEDDS characterization.

SNEDDS components			Characterization of SNEDDS				
Oleic acid	Tween 80	PEG 400	Emulsification time	% Transmittance	Drug loading	Particle size	Zeta potential
1	8	1	17 seconds	97 %	179,18 mg	85,8 nm	-1,6 mV

Results characterization self nanoemulsifying drug delivery system mefenamic acid

Emulsification time: The emulsification time test is carried out by reading using a stopwatch. Emulsification time is used to determine how quickly a formulation forms an emulsion. Formulation SNEDDS must be able to form spontaneously after interacting directly with gastric fluid. This is an important parameter in SNEDDS formulation. If the resulting emulsification time is less than 1-2 minutes, the SNEDDS formula can form an emulsion directly through the stomach by creating a fairly clear emulsion. The results of the formula test for the emulsification time of mefenamic acid SNEDDS of 17 seconds are in Table 1. The results show that this formula can form mefenamic acid SNEDDS because it can be dispersed in less than 1 minute.¹³

Transmittance value: SNEDDS has good clarity and a transmittance value greater than 90%. The % transmittance test was carried out by reading at a wavelength of 650 nm using a UV-Vis spectrophotometer. Table 1 shows that the SNEDDS formula for mefenamic acid has a transmittance value of 97%. This value shows that it is classified as good because the good transmittance value is close to 100%, according to the literature. The transmittance value of 97% is close to 100%, indicating that the SNEDDS formula is made transparent and clear. Apart from that, the clarity of the solution also shows that the particle size in the SNEDDS formula is nanometers.¹⁴

Drug loading: The drug loading test aims to determine the amount of mefenamic acid formulated in SNEDDS. The results of the SNEDDS formula for mefenamic acid can be seen in Table 1. It is known that the SNEDDS formula for mefenamic acid has a drug loading result of 179.18 mg.¹⁵

Globule size: Globule size is very important in making nanoparticles. Therefore, particle size observation can be done using a PSA (particle size analyzer). The globule size can be influenced by the type of stabilizer concentration, homogeneity, and polymer concentration. The globule size results from this research can generally be seen in Table 1. The globule size of the formulation is in the nanoparticle range with a size of 85.8 nm, where the results show smaller than 100 nm, so it can be said that the size is a nanoparticle.¹⁶

Zeta potential: Zeta potential indicates the stability of the colloid. Interactions between particles have an important role in the stability of a colloid. Zeta potential is a measure of the repulsion between particles. Since most colloidal systems in water are stabilized by electrostatic repulsive forces, the greater the repulsive forces between particles, the less likely the particles are to combine and form aggregates. Nanoparticles with zeta potential values greater than +/- 30 mV have been proven to be stable in suspension as inhibitors of charge agglomeration. The results of the SNEDDS Formula for the mefenamic acid zeta potential test are -1.6 mV.¹⁷

4. Conclusion

Mefenamic acid SNEDDS preparation formulation meets the physical quality of the preparation and produces a homogeneous phase. Emulsification time characterization test results 17 seconds, % transmittance of 97%, drug loading of 179.18 Mg, globule size of 85.8 Nm, and zeta potential of - 1.6 Mv.

5. References

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