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Formation and Characterization of Liquid Crystals of Aceclofenac for Transdermal Delivery

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ABSTRACT: Aceclofenac is a phenylacetic acid derivative classified as a nonsteroidal anti-inflammatory drug (NSAID) used to relieve pain caused by inflammation. It has potential for topical application through a transdermal delivery system. One promising approach is the use of liquid crystals as carriers in transdermal dosage forms. This study aims to develop a simple liquid crystal cream formulation for aceclofenac, using glyceryl monostearate as a mesogen and Pluronic as a stabilizer. The aceclofenac liquid crystal cream was characterized using Polarized Light Microscopy (PLM), Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy (ATR-FTIR), and Differential Scanning Calorimetry (DSC). Evaluations included drug release, permeation, viscosity, flow properties, zeta potential, and freeze-thaw stability. The optimal formulation consisted of oil: glyceryl monostearate-Pluronic P123: water in a 5:15:80% ratio. PLM results showed birefringence and a lamellar phase texture. FTIR analysis confirmed no new chemical bonds, while DSC indicated a reduced melting point and increased enthalpy of fusion. The release and permeation of aceclofenac after 6 hours were 27.849 ± 0.5479 µg/cm² and 21.093 ± 0.5761 µg/cm², respectively-higher than non-liquid crystal preparations. The cream exhibited thixotropic flow behavior, a zeta potential of -50.8 mV, and remained stable after six freeze-thaw cycles. In coclusion, Aceclofenac can be formulated into a liquid crystal cream with glyceryl monostearate as a mesogen, showing a birefringent lamellar phase that enhances its release and permeation.

Keywords: **aceclofenac; transdermal; liquid crystals; release; permeation.**

Introduction

Aceclofenac, 2-[2,6-dichlorophenyl) amino] phenyl acetoxyacetic acid, is a derivative of phenylacetic acid which is classified as a nonsteroidal anti-inflammatory drug (NSAID) [1]. Aceclofenac is useful in various pathological conditions such as osteoarthritis, rheumatoid arthritis and ankylosing spondylitis as a treatment for pain associated with inflammation [2].

Aceclofenac is practically insoluble in water and based on the Biopharmaceutical Classification System (BCS) is included in BCS class II [3]. The low solubility and dissolution of aceclofenac are rate limiting steps that have a negative impact on its bioavailability when administered orally. Therefore, through this study aceclofenac will be developed as an anti-inflammatory therapy with a transdermal delivery system. However, to achieve therapeutic effects, the drug must be able to penetrate the skin barrier in order to reach the target of drug action without injuring the skin. This system has the advantage of being able to avoid first-pass metabolism, allowing controlled release, and increasing patient compliance [4].

Several studies on aceclofenac as a transdermal preparation have previously been conducted, including using the nanoemulsion system, the results of which indicate that the nanoemulsion system has great potential to increase the transdermal delivery of aceclofenac [5]. In addition, the microemulsion system has also been conducted, the results of which indicate that the transdermal aceclofenac microemulsion system can increase skin permeability and efficacy for the treatment of muscle damage [6]. However, no research has been found on the liquid crystal system as a transdermal delivery system for the active substance aceclofenac. Liquid crystals are a state of matter that is between crystalline solids and amorphous liquids. The formation of liquid crystals can be done by 2 methods, namely the thermotropic and lyotropic methods. The thermotropic method forms liquid crystals by heating the crystalline solid or cooling the isotropic liquid and is highly dependent on temperature, while the lyotropic method is influenced by increasing the concentration of mesogen [7]. Currently, lyotropic liquid crystals are promising candidates as transdermal delivery systems for various drugs. The carrier can provide increased drug solubility, relative protection of the dissolved drug, and controlled drug release, The presence of mesophase structures can disrupt the stratum corneum lipid barrier,

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increasing skin permeability [8].

Liquid crystals can be formed by mesogens. Mesogens in pharmaceuticals are surfactants, drug molecules themselves and polymers [9]. Mesogens are divided into 2 categories, namely: i) non-amphiphilic anisometric mesogens which often display thermotropic liquid crystal phases; ii) amphiphilic mesogens which usually show lyotropic liquid crystal phases such as surfactants [10]. Surfactant-based liquid crystal systems are excellent potential formulations to improve drug dissolution and bioavailability [11]. Liquid crystal systems that are bioadhesive and physically stable have been developed for transdermal dosage formulations [12].

Based on the description above, researchers are interested in forming aceclofenac liquid crystals as a transdermal dosage delivery system by forming lyotropic liquid crystals using surfactant mesogens. The surfactant to be used in this study is glyceryl monostearate (GMS). Glyceryl monostearate is reported to form a liquid crystal system only at low concentrations [13]. The liquid crystal preparation of aceclofenac formed was characterized using Polarized Light Microscopy (PLM), Fourier Transformed Infrared Spectroscopy (FT-IR), and Differential Scanning Calorimetry (DSC), then the evaluation of the transdermal preparation included in vitro drug release, permeation tests, determination of viscosity and flow properties, zeta potential, and stability tests.

Methods

Materials

Aceclofenac C16H13Cl2NO4 (BOC Sciences, USA), ethanol pro analysis (Merck, Germany), glyceryl monostearate (PT Sumber Berlian Kimia, Indonesia), Pluronic P123 (Sigma Aldrich, USA), sunflower oil (Mazola, Indonesia), Aquadest (Kafarma, Indonesia), stearic acid (Zonakimia, Indonesia), triethanolamine (CV Kimia Jaya Labor, Indonesia), glycerin (Zonakimia, Indonesia), KH2PO4 (Merck, Germany), NaOH (Merck, Germany), and Shed snake skin. (*Python reticulatus*).

Methods

Formation of Aceclofenac Liquid Crystal Cream

The manufacture of aceclofenac liquid crystal cream begins with the optimization of the cream formulation, so that a liquid crystal cream is formed when viewed under a polarizing microscope (Axioscope 5, Germany). Optimization is carried out by varying the concentration of glyceryl monostearate (GMS), Pluronic P123, sunflower oil, and distilled water. The ingredients of the liquid crystal cream can be seen in the table 1.

To make liquid crystal cream, GMS is dissolved in sunflower oil (as the oil phase) at a temperature of 80°C, then the Pluronic P123 stabilizer solution and distilled water (as the water phase) are heated on a hotplate magnetic stirrer (Thermo Scientific, US) to a temperature of 80°C. Mixing is done by pouring the water phase into the oil phase slowly at the same temperature on a magnetic stirrer (Thermo Scientific, US) at a speed of 500 rpm. After all the water and oil phases are mixed, the cream is homogenized using Ultra-Turrax (IKA, Tiongkok) at a speed of 6000 rpm for 3 minutes, then the cream is stirred until cold. Before being observed birefringence with a polarizing microscope (Axioscope 5, Germany), the cream is left for 24 hours. A small amount of each sample is then placed on a microscope slide and covered with a coverslip for observation under a polarizing light microscope equipped with crossed polarizers. The presence and type of liquid crystalline phases are identified based on their characteristic birefringent textures, such as the Maltese cross for lamellar phases or fan-like patterns for hexagonal phases. The results are then used to construct a ternary phase diagram, mapping the mesophase regions within the system.

Formula 1 to 6 were tested for stability using the centrifugation (Joanlab, China) for 30 minutes at a speed of 3000 rpm. Formulas that showed no separation after the centrifugation test were made into aceclofenac liquid

Table 1. Liquid crystal cream formula.

No	Formula	Sunflower oil (%b/b)	GMS (%b/b)	Pluronic P123 (%b/b)	Aquadest (%b/b)
1	F1	5	4	1	90
2	F2	10	4	1	85
3	F3	5	8	2	85
4	F4	10	8	2	80
5	F5	5	12	3	80
6	F6	10	12	3	75

crystal cream preparations.

The best formula that meets the requirements of the centrifugation test is then made by mixing 1% w/w of aceclofenac into the oil phase and heating it to a temperature of 80°C. Then the Pluronic P123 stabilizer solution is also heated to the same temperature and then the solution is poured into the oil phase slowly to avoid phase separation. This finished preparation is called aceclofenac liquid crystal cream and will then be characterized and evaluated.

Preparation of Aceclofenac Non-Liquid Crystalline Cream

The non-liquid crystal cream in this study was made by modifying the vanishing cream formula, an o/w type emulsion. The aceclofenac vanishing cream formula can be seen in Table 2.

The manufacture of aceclofenac vanishing cream is done by dissolving the active substance in the oil phase (stearic acid and sunflower oil) at a temperature of 80℃, then the water phase solution (TEA and distilled water) is heated to a temperature of 80℃. Mixing is done by pouring the water phase into the oil phase slowly at the same temperature on a magnetic stirrer at a speed of 500 rpm.

Mesophase Analysis with Polarized Light Microscopy (PLM)

The liquid crystal sample to be tested was placed on a glass slide and covered with a cover glass, then examined under PLM (Axioscape 5, Germany) at room temperature (25°C ± 0.5°C) with a magnification of 50x [21].

Analysis with Fourier Transformed Infrared Spectrophotometry (FTIR) (Shimadzu IR-Tracer 100 AH, Japan)

IR spectrophotometer (Shimadzu, Japan) analysis was carried out with the sample placed on top of the ATR crystal so that it covered all the crystal surfaces.. The sample was closed by applying a little pressure, then tested in the 650-4000 cm^{-1} waveform [8].

Differential Scanning Calorimetry (DSC) Analysis

The liquid crystal sample was tested for its thermal properties with a DSC (Shimadzu DSC-60 Plus, Japan) device programmed in the temperature range of 20-200°C with a heating rate of 10°C/min under atmospheric conditions. The sample was placed on a closed aluminum holder as much as 2-14 mg and used an empty aluminum holder as a reference. The thermal profile of the sample was carried out by analyzing the endothermic or exothermic peaks obtained [8].

In vitro Release Test

The release test in the study was carried out using a static Franz diffusion cell (modification) device where the recipient fluid can only be taken at 1 time and then must be replaced completely. The release test used cellulose acetate as a membrane with a diffusion area surface area of 1.910376 cm^2. The hydration process was carried out first before using the membrane by inserting it into a pH 7.4 phosphate buffer solution. The receptor compartment was filled with 13.5 mL of pH 7.4 phosphate buffer which was stored in a water bath with a temperature maintained at 37 ± 0.5. The test membrane was placed between the donor cell and the receptor cell. Aceclofenac liquid crystal cream and aceclofenac vanishing cream to be tested were placed on the donor component as much as 1000 mg. After 6 hours the receptor fluid was taken and measured using the UV-Vis spectroscopy (Shimadzu UV-1700, Japan) method at maximum wave length of aceclofenac (277nm) [22].

The cumulative amount of active substance permeated per unit area of the membrane (Q) in µg/cm2 is calculated using the following formula [23].

$$Q = (Cn \times V)/A$$

Description:
Cn = Concentration of active substance (µg/mL)
V = Volume of Franz diffusion cell (mL)
A = Membrane area (cm^2)

After that, the flux calculation is carried out based on Fick's I law with equation [23]:

Table 2. Aceclofenac vanishing cream formula.

No	Material	Formula (%b/b)
1.	Aceclofenac	1
2.	Stearic acid	12
3.	Sunflower oil	5
4.	Triethanolamine (TEA)	3
5.	Aquadest	ad 100

$$J=Q/t$$

Description:
J = Flux (µg/cm^2 hour)
Q = Cumulative amount of aceclofenac released per area (µg/cm^2)
t = Time (hour)

The release of aceclofenac in liquid crystal cream was compared with aceclofenac in vanishing cream as a comparison of non-liquid crystal preparations. Data analysis was carried out using an independent sample T-test using SPSS 29.

In vitro Permeation Test

The permeation test in the study was conducted using a static Franz diffusion cell device where the recipient fluid can only be taken at 1 time and then must be replaced completely. The permeation test used a shed snake skin (*Python reticulatus)* as a membrane with a diffusion area surface area of 1.910376 cm^2. The hydration process was carried out first before using the membrane by inserting it into a pH 7.4 phosphate buffer solution. The receptor compartment was filled with 13.5 mL of pH 7.4 phosphate buffer which was stored in a water bath on modification of Franz diffusion cell with a temperature maintained at 37 ± 0.5. The test membrane was placed between the donor cell and the receptor cell. Aceclofenac liquid crystal cream and aceclofenac vanishing cream to be tested were placed on the donor component as much as 1000 mg. After 6 hours the receptor fluid was taken and measured using the UV-Vis spectroscopy (Shimadzu UV-1700, Japan) method [22].

The permeation of aceclofenac in liquid crystal cream was compared with aceclofenac in vanishing cream as a comparison of non-liquid crystal preparations. Data analysis was carried out using an independent sample T-test using SPSS 29.

Determination of Viscosity and Flow Properties

Determination of viscosity was measured using a Brookfield viscometer (DV2T, USA) with spindle 5 at 50 rpm. Prepare 50 mL of sample in a beaker, dip the spindle into it for 5 minutes. Then take a reading (24). The speed of the tool is set at 0.5; 1; 2; 5; 10; 20; 50; 100 rpm, then reversed 100; 50; 20; 10; 5; 2; 1; 0.5 rpm sequentially. Flow properties can be obtained by making a curve between shear stress (dyne/cm^2) and shear rate (second^{-1}).

Determination of Zeta Potential

The zeta potential value of the sample was determined using a Particle Size Analyzer (Horiba Scientific SZ-100, Japan). The sample was diluted and the zeta potential value was estimated from the electrophoretic mobility [25].

Stability Test

The stability of the samples was determined using the freeze-thaw method or cycling test for 6 cycles. In each cycle, the samples were stored at 4℃ for 24 hours and at 40℃ for 24 hours [24]. After 6 cycles, the samples were tested including physical observation, zeta potential, and characterization by polarization microscopy.

Result and Discussion

Liquid crystal cream is made using glyceryl monostearate (GMS) as a single-tailed amphiphilic substance, where GMS is able to self-assemble through intra- and intermolecular interactions, one of which is by forming hydrogen bonds. The presence of hydrogen bonds will encourage the formation of vesicles because hydrogen bonds have hydrophilic head groups for hydration will be reduced [14]. In this study, with a concentration of GMS-Pluronic P123 used as much as 5%, birefringence has occurred. Birefringence is a phenomenon in which light passing through a material is split into two perpendicular polarized rays. The six formulas that have been made appear to have a birefringence texture after being observed under a polarizing microscope which indicates the formation of an anisotropic liquid crystal phase. The six formulas are plotted into a ternary phase diagram to describe the cream phase that is formed which can be seen in Figure 1. Figure 1 is completed by displaying the birefringence texture of six liquid crystal cream formulas. All the formulas were shown the Maltese cross that indicating lamellar mesophase was formed. Birefringence from the biphasic structure of liquid crystals adjacent to isotropic areas can usually be detected by PLM. In previous studies, birefringence events have also been reported with a GMS concentration of 5% [13].

Six liquid crystal cream formulas were made, then centrifugation tests were carried out to see the stability of each liquid crystal cream formed. This centrifugation test was carried out to see whether or not there was a phase separation in the cream formed, so that the most optimal formula could be selected to proceed to the evaluation stage. From the results of the centrifugation test of the 6 cream formulas, five of them showed a separation of the water and oil phases. The formula that showed a

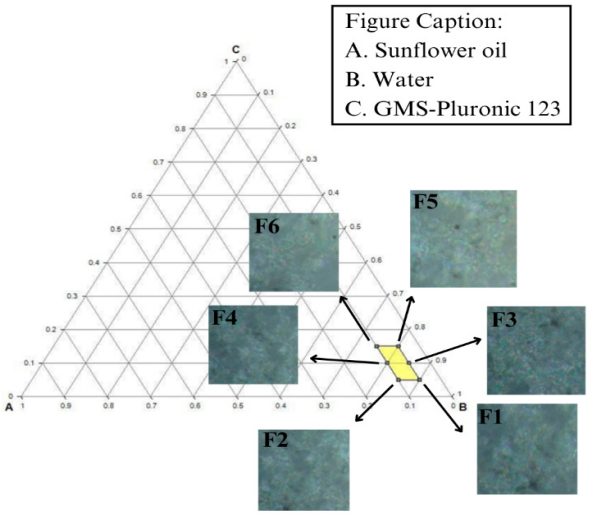

Figure 1. Ternary phase diagram of 6 liquid crystal cream formulas and observation under polarizing microscope.

homogeneous preparation without phase separation was formula 5. Formula 5 which had been added with active substances was then called aceclofenac liquid crystal cream.

In this study, the non-liquid crystal cream made was vanishing cream with the aim of being a comparison. Aceclofenac vanishing cream is made with the same treatment as making aceclofenac liquid crystal cream.

From the polarization microscope analysis in Figure 2, it can be seen that the birefringence event still occurs after the active substance is added to the liquid crystal. This event is supported by the results of the vanishing cream only showing an isotropic area under the PLM. Based on the results of observations under the PLM, in this study the liquid crystals formed are thought to form a lamellar phase. This is supported by the observation of lamellar liquid crystals from GMS which have a birefringence form by previous studies [13].

FTIR analysis was conducted to identify and confirm the presence of intra- and intermolecular interactions, particularly hydrogen bonding, involved in the formation of liquid crystals with glyceryl monostearate as an amphiphilic substance. In Figure 3, the FTIR spectrum of the formation of aceclofenac liquid crystals can be seen. In the liquid crystal spectrum, several typical peaks are visible, such as at 3354.44 cm^{-1} indicating the presence of an O-H stretch, at 2913.85 cm^{-1} indicating C-H stretch, at

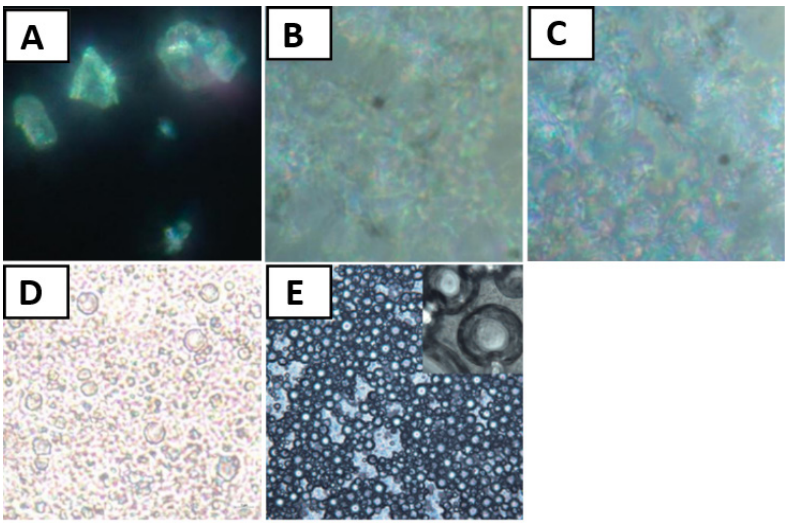

Figure 2. PLM observations of (A) aceclofenac, (B) liquid crystal cream formula 5, (C) liquid crystal cream aceclofenac, (D) vanishing cream aceclofenac, and (E) GMS literature lamellar liquid crystal [13].

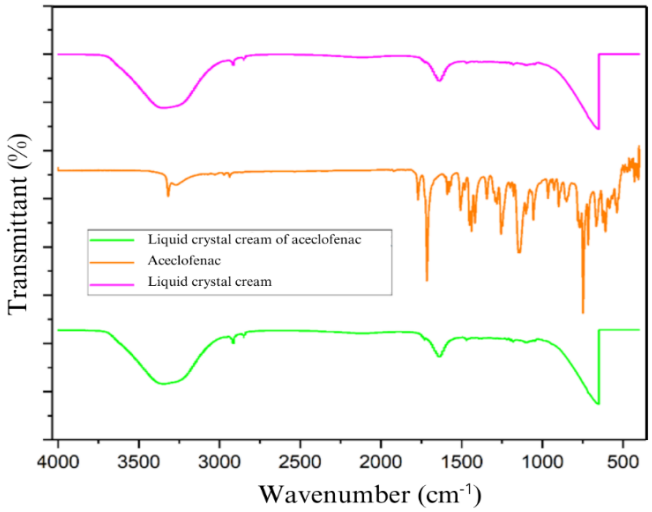

Figure 3. FT-IR spectra of (A) liquid crystal cream formula 5, (B) aceclofenac, and (C) aceclofenac liquid crystal cream.

1635.13 cm^{-1} indicating C=O stretch, and at 1471.19 cm^{-1} indicating C-H bending. The manufacture of liquid crystals with glyceryl monostearate as an amphiphilic substance occurs through intra- and inter-molecular interactions, one of which is by forming hydrogen bonds [14]. Because of the interaction through hydrogen bonds, this causes the emergence of a typical O-H stretch spectrum in the area of 3750-3000 cm^{-1} in liquid crystals. The active substance aceclofenac added to liquid crystals is expected not to have interactions that result in new bonds. Because the active substance will be absorbed between the oil phases, without changing the structure of the active substance or liquid crystals [15]. This can be seen in the spectrum which shows the absence of the typical aceclofenac peaks seen in aceclofenac liquid crystals, only a shift in several absorption peaks.

DSC testing is carried out to determine the heat changes in samples when heated or cooled. In Figure 4, it can be seen that there is a decrease in the melting point and an increase in the fusion enthalpy value in aceclofenac liquid crystals. The decrease in the melting point is in the pure substance 153.79°C to 99.73°C. This can occur due to the physical interaction between aceclofenac and the liquid crystal components. Then there is an increase in the fusion enthalpy value, namely in the pure substance 132.4 J/g to 1408.0129 J/g. This indicates that the amount of energy

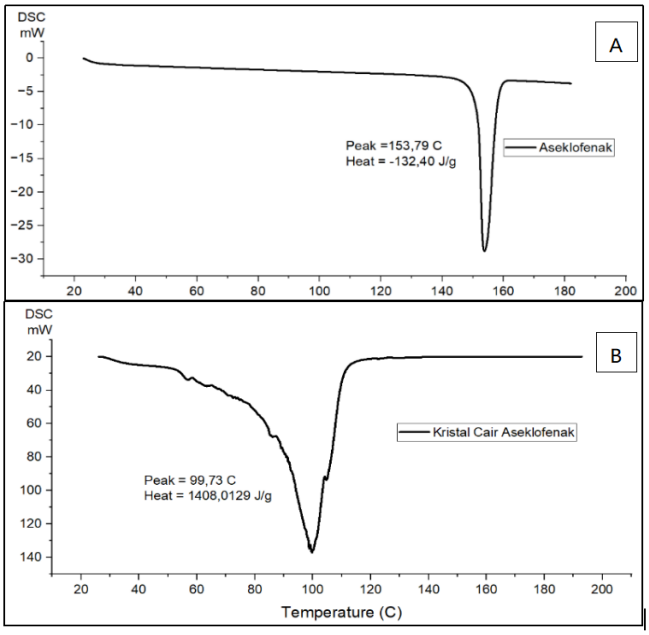

Figure 4. Overlay thermogram (A) Aceclofenac, (B) Aceclofenac liquid crystals.

Table 3. Release test result data.

Sample	Average concentration (µg/mL)	Average amount of substance (µg)	Average Q (µg/cm²) ± SD	Average J (µg/cm² hour ± SD
Aceclofenac liquid crystal cream	3.941	53.202	27.849 ± 0.5479	4.641 ± 0.0913
Aceclofenac vanishing cream	2.192	29.598	15.493 ± 0.785	2.582 ± 0.1308

needed by liquid crystals to melt the compound is greater than pure aceclofenac [16].

Aceclofenac liquid crystal cream as a transdermal drug needs to be tested forrelease to determine the drug's ability to release form dosage form..This test is carried out in vitro using a Franz diffusion cell which aims to determine the cumulative amount of aceclofenac permeated over a certain time. The membrane in this study used cellulose acetate with pores measuring 0.45 µm with a diffusion surface area of 1.910376 cm^2. Before testing, the membrane was first hydrated in a phosphate buffer solution of pH 7.4 which is considered to have similarities with the pH of human biological fluids. The temperature on the instrument is set to 37°C±0.5 which is considered to be the temperatureof the human body. Samples taken after 6 hours will then be tested to determine their levels with a UV-Vis spectrophotometer.

The results of the membrane release test showed the cumulative amount of aceclofenac in liquid crystal cream and non-liquid crystal cream (vanishing cream) released per membrane area (Q) at 6 hours which can be seen in Table 3. Based on the test results, it can be seen that the liquid crystal cream has a better release rate than the non-liquid crystal preparation (vanishing cream). This is due to the formation of liquid crystals using amphiphilic compounds, so that an increase in the permeability of the stratum corneum is achieved. The results of the statistical analysis with the independent sample T-test using SPSS 29 obtained a p value <0.005 (0.001) which means that it indicates a significant difference in the permeation of the cumulative amounts of substances permeated per unit surface area of the membrane used.

Aceclofenac liquid crystal cream as a transdermal drug needs to be tested for permeation to determine the drug's ability to cross the skin, especially in the stratum corneum. This test is carried out in vitro using a Franz diffusion cell which aims to determine the cumulative amount of aceclofenac permeated over a certain time. The membrane in this study used a snake skin release (*Python reticulatus*) with a diffusion area surface area of 1.910376 cm^2.

The settings and testing methods are the same as those used in the drug release test, with the only difference being the membrane used.

In general, liquid crystal cream has better aceclofenac permeation than vanishing cream. This is evidenced by the high average Q (cumulative amounts of active substances permeated per unit area of membrane) in liquid crystal cream compared to vanishing cream which can be seen in Table 4. The results of statistical analysis with an independent sample T-test using SPSS 29 obtained a value of p <0.005 (0.001) which indicates a significant difference in the permeation of the cumulative amounts of substances permeated per unit area of membrane used.

Increased permeability in the stratum corneum can be achieved through the use of liquid crystals. This liquid crystal system shows good permeation due to the low surface tension of oil/water. High diffusion of active substances is also influenced because liquid crystals have a structure that shows similarities to the lipid membrane

Table 4. Permeation test result data.

Sample	Average concentration (µg/mL)	Average amount of substance (µg)	Average Q (µg/cm²) ± SD	Average J (µg/cm² hour ± SD
Aceclofenac liquid crystal cream	2.985	40.296	21.093 ± 0.5761	3.516 ± 0.096
Aceclofenac vanishing cream	1.928	26.032	13.627 ± 0.6532	2.271 ± 0.1089

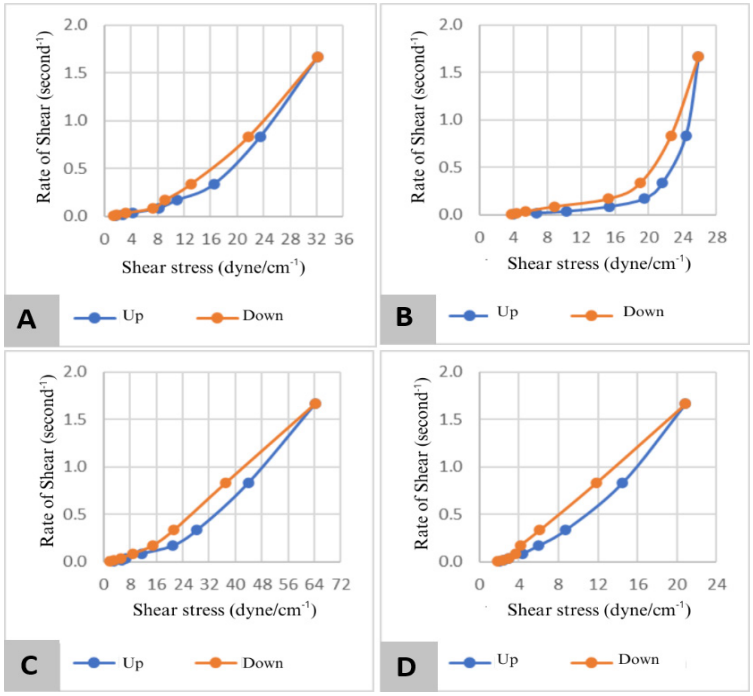

Figure 5. Flow properties of (A) liquid crystal cream, (B) liquid crystal cream of aceclofenac, (C) vanishing cream, and (D) vanishing cream of aceclofenac.

between cells in the skin, thus allowing increased partitioning of the drug to the stratum corneum [17].

Determination of viscosity is carried out using a Brookfield viscometer. The value of viscosity indicates the resistance of the liquid to flow, the higher the viscosity or the thicker the preparation, the more difficult the liquid is to flow. Viscosity can be influenced by the composition of the preparation. The flow properties of liquid crystal cream and vanishing cream can be seen in Figure 5.

The flow property curve formed in the liquid crystal cream sample, aceclofenac liquid crystal cream, vanishing cream, and aceclofenac vanishing cream show thixotropic flow properties. This is indicated by the decreasing curve being to the left of the increasing curve, which means that the preparation has a lower viscosity at one shear rate on the decreasing curve when compared to the increasing curve. In thixotropic flow, the structure of the material is damaged due to the shear rate and recovers upon standing. This flow property is a desired property in pharmaceutical preparations, because pharmaceutical preparations should ideally have high viscosity in the container but can be easily poured or spread during use [18].

Zeta potential measurement provides a precise analysis of the electronic state of the nanoparticle surface, and the data obtained can be used to predict the stability of formulations containing these nanoparticles. Zeta potential testing needs to be done to assess the stability of products containing nanoparticles such as liquid crystals. Stable conditions are at values greater than +30 mV and lower than -30 mV, while unstable conditions indicate that the system will easily flocculate at values between +30 mV and -30 mV [19]. The results of the zeta potential test of the liquid crystal cream showed a value of -50.8 ± 5.80747 mV which can be seen in Table 5. This value is above the

Table 5. Results of zeta potential testing of aceclofenac liquid crystal cream.

Replication	Zeta potential
1	-54.5
2	-42.6
3	-55.3
Average ± SD	**-50.8 ± 5.80747**

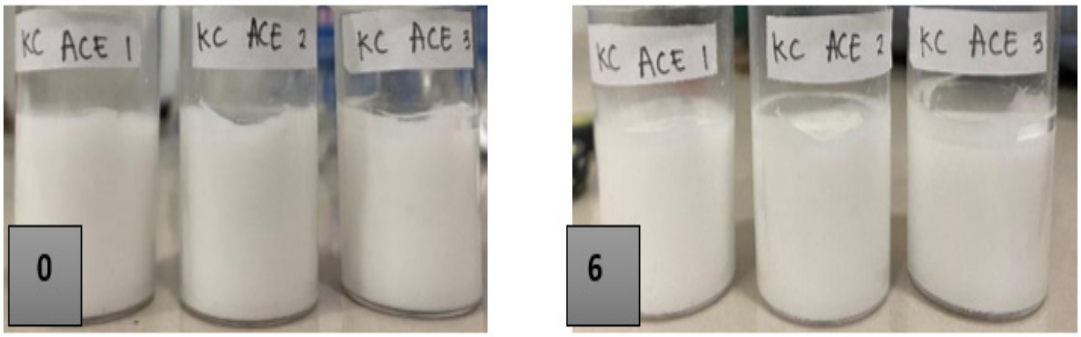

Figure 6. Observation results of stability tests of aceclofenac liquid crystal cream cycle 0 and cycle 6.

ideal value of -30 mV which means that the liquid crystal cream shows a stable condition.

Stability testing was carried out using the fr Horiba Scientific SZ-100eeze and thaw method which aims to see the physical stability of aceclofenac liquid crystal cream when faced with the influence of different temperature stress as indicated by the separation of the oil and water phases. Aceclofenac liquid crystal cream was placed at a temperature of 4°C for 24 hours and at a temperature of 40°C for 24 hours for 1 cycle and was carried out for 6 cycles.

The results of physical observations can be seen in Figure 6 which shows that the aceclofenac liquid crystal cream does not experience oil and water phase separation. The absence of cream phase separation in the freeze and thaw cycle depends on the cream's ability to recover from the crystal water pressure. At a temperature of 4°C the water phase freezes and tends to shrink, resulting in a narrowing of the water phase space and causing the oil globules to be close together, resulting in an increase in the viscosity of the preparation. In the thaw process or a temperature of 40°C, the crystals will melt and will spread back into the system. If the recovery rate of the cream is slow, instability can occur [20]. The results of observations in the form of zeta potential can be seen in Table 6. This value is above the ideal value of -30 mV which means that the liquid crystal cream shows a stable condition. Furthermore, from the polarization microscope analysis, it can be seen that the birefringence event still occurs after going through 6 freeze and thaw cycles as seen in Figure 7.

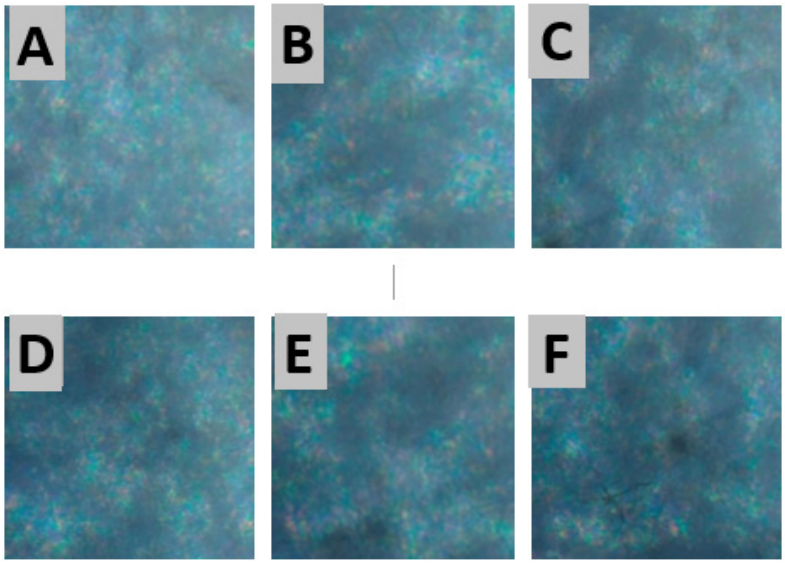

Figure 7. PLM observations of (A) cycle 0 replication 1, (B) cycle 0 replication 2, and (C) cycle 0 replication (D) after 6 freeze and thaw cycles replication 1, (E) after 6 freeze and thaw cycles replication 2, and (f) after 6 freeze and thaw cycles replication 3.

Table 6. Zeta potential test results after 6 freeze and thaw cycles.

Sample	Zeta potential
Aceclofenac liquid crystal cream replication 1	-47.5
Aceclofenac liquid crystal cream replication 2	-38
Aceclofenac liquid crystal cream replication 3	-55.2
Average ± SD	**-46.9 ± 7.03468**

Conclusion

The research findings demonstrate that aceclofenac can be formulated into a liquid crystal cream using glyceryl monostearate as a mesogen, exhibiting a birefringent lamellar phase texture. The aceclofenac liquid crystal cream possesses thixotropic flow properties, a zeta potential of -50.8 mV, and stability with no phase separation after six freeze-thaw cycles. Additionally, it enhances drug release through a cellulose acetate membrane (Q 27.849 ± 0.5479 μg/cm²) and increases permeation through a snake skin membrane (Q 21.093 ± 0.5761 μg/cm²), outperforming non-liquid crystal formulations like vanishing cream.

Conflict of Interest

The authors have no conflicts of interest regarding this investigation.

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