HYPOTHESIS: Multidisciplinary Journal Of Social Sciences
http://azramedia-indonesia.azramediaindonesia.com/index.php/hypothesis/index
DOI: https://doi.org/10.62668/hypothesis.v5i01.2500
Email : info@azramediaindonesia.com

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PHYSICOCHEMICAL CHARACTERIZATION AND STABILITY EVALUATION OF MEMBRANE-TYPE PATCH WITH CURCUMIN NANOEMULSION AS RESERVOIR

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Info Article
Received : 01 April 2026
Revised : 05 Mei 2026
Accepted : 01 Juni 2026
Publication : 30 Juni 2026

Keywords:
Curcumin, Nanoemulsion, HPMC Membrane-Type Patch

Kata Kunci:
Kurkumin, Nanoemulsi, Patch Tipe Membran HPMC.

Abstract: *Curcumin is a bioactive molecule derived from turmeric (Curcuma longa L.) that has pharmacological properties including antioxidant, anti-inflammatory, and anti-osteoarthritis actions. Howev er, curcumin has some limitations, including lower bioavailabi lity due to poor solubility and substantial first-pass metabolism. Curcumin can also be used in nanoemulsion systems. The nanoemulsion is combined with a membrane-type patch system to enhance and prolong curcumin's activity. The membrane-type patches were created using the solvent casting process with three different concentrations of HPMC as the polymer: F1 (6%), F2 (8%), and F3 (10%). The patches were evaluated for physicochemical parameters such as thickness, folding endurance, weight homogeneity, moisture content, pH, and active ingredient content, as well as stability using cycle tests. The results showed that different HPMC concentrations had a substantial effect on the patches' physicochemical properties. Higher HPMC concentrations resulted in increased folding endurance, weight, thickness, and active ingredient content, but moisture content and pH decreased. Stability tests revealed that the patches were stable in terms of folding endurance, weight homo geneity, & thickness, but unstable in terms of moisture content & pH*

Abstrak: Kurikumin merupakan senyawa bioaktif dari kunyit dengan aktifitas farmakologis seperti antioksidan, antiinflamasi, dan antiosteoart hritis. Namun kurkumin mempunyai keterbatasan seperti bioavailabilitas rendah akibat dari kelarutan yang rendah dan mengalami metabolisme lintas pertama. Sebagai alternatif, kurkumin dapat dimasukkan ke dalam sistem nanoemulsi. Namun, untuk mengoptimalkan dan memperpanjang aksi kurkumin, nanoemulsi dimasukkan ke dalam sistem patch tipe membrane. Preparasi patch tipe membran menggunakan metode solvent casting dengan perbedaan konsentrasi HPMC sebagai polimer yaitu F1 (6%), F2 (8%), dan F3 (10%). Evaluasi sediaan patch tipe membran meliputi karakteristik fisikokimia seperti ketebalan, ketahanan lipatan, keseragaman bobot, kelembapan, pH dan kandungan bahan aktif serta uji stabilitas dengan cycling test. Hasilnya bahwa perbedaan konsentrasi HPMC berpengaruh signifikan terhadap karakteristik fisikokimia patch. Semakin tinggi konsentrasi HPMC sebagai polimer maka semakin meni ngkat ketahanan lipatan, bobot, ketebalan dan kandungan bahan aktif. Sedangkan kelembaban dan pH cenderung menurun. Hasil uji stabilitas menunjukkan bahwa patch stabil pada ketahanan lipatan, keseragaman bobot serta ketebalan namun tidak stabil terhadap kelembaban dan pH

PENDAHULUAN

In the territory of Indonesia, turmeric can be found in almost all provinces. Traditionally, turmeric, especially the rhizome part, has been widely used by the surrounding community. Turmeric rhizomes contain two main bioactive compounds that are beneficial for health, namely curcuminoid groups (3-5%) and essential oils (2.5-6%) (Batubara & Prastya, 2020). The yellow color in turmeric is obtained from polyphenol pigments and fat-soluble substances referred to as curcuminoids. Curcuminoids are also the most active compounds in turmeric (Dutta et al., 2021).

Curcumin is a yellow hydrophobic polyphenolic compound extracted from the rhizome of turmeric (Curcuma longa L.) which is a family of Zingiberaceae, also known as diferuloylmethane (1E,6E)-1,7-bis(4-hydroxy-3-methoxypHenyl)-1,6-heptadiene-3,5-dione). Curcumin is composed of 77% Diferuloylmethane, 18% Demethoxycurcumin, and 5% Bisdemethoxycurcumin (Dutta et al., 2021). Curcumin has a promising pharmacological profile, but curcumin has some drawbacks that limit its therapeutic potential namely problematic drug delivery and poor bioavailability. Curcumin has a log P of 3.29 which indicates that it is almost insoluble in pure water (0.6 μg/ml) (Tabanelli et al., 2021). Curcumin has poor stability, which is rapidly degraded at pH 6 around 16% and at pH 6.5 around 23% within 2 hours at 37°C so it can lead to low systemic bioavailability of curcumin in the body (Kaluku et al., 2022).

Based on this, the development of potential applications of curcumin clinically can be used in nano-drug delivery systems. Nano-sized preparation delivery systems are useful for protecting, transporting and releasing bioactive compounds and serve to increase the bioavailability of lipophilic compounds in aqueous media (Larasati & Jusnita, 2020). Nano technology is an effective method for the release of active substances that are difficult to dissolve in water such as curcumin. One of the pharmaceutical preparations that can be used to overcome this problem is nanoemulsions (Sulastri, 2020). Nanoemulsions are a simple but highly effective delivery system that can be formulated from natural ingredients and can be designed to protect the functional ingredients in the product and control them once they enter the body. Nanoemulsions have kinetically stable properties, namely being able to maintain their properties in various chemical systems and thermodynamically stable, namely being able to be at low energy or in mechanical, thermal and chemical equilibrium (Sulastri, 2020).

Curcumin levels were found to be higher when formulated in the form of nanoemulsions compared to curcumin in the form of suspensions (Nirwan, 2020). Nanoemulsions can improve bioavailability as well as be thermodynamically stable in mixtures of water, oil, surfactants and cosurfactants. Nanoemulsions have a small particle size of about 10-500 nm, which causes them to have a large surface area and lower interface tension and are able to penetrate the skin more easily. Therefore, it is made in the form of transdermal preparations available on the market, one of which is transdermal patches (Kaluku et al., 2022). To optimize the route of administration and prolong the duration of action of curcumin, it is formulated in the form of a membrane-type patch preparation with curcumin nanoemulsion as a reservoir. This is to provide a gradual release of the active substance curcumin, avoid the first cross-metabolism in the liver, and can improve patient compliance. Nanoemulsions themselves, although thermodynamically stable and transparent, are uncomfortable and have low viscosity when used on the skin (Damayanti et al., 2019)

Transdermal patches are a delivery system using adhesives containing medicinal compounds by placing them through the surface of the skin to release active substances in certain doses into the bloodstream. While patches are preparations with a percutaneous route of administration intended for external use with a closed skin contact system. A physically good patch preparation should be homogeneous, smooth, thin, flexible, have low drying shrinkage and humidity (Fuziyanti et al., 2022). The quality of the patch preparation is judged not only from the physical parameters of the preparation but also the ability to release the active substance of the drug from the preparation. The effectiveness of the release of a drug from the patch is not only influenced by the physicochemical properties but also the additives (Palet et al., 2009). The type of transdermal patch used in this study is membrane-type patch. In membrane-type patches, a reservoir is embedded between the backing layer and a membrane layer. The membrane layer can be porous or non-porous (Lembang, 2021).

One of the components of a membrane-type patch is a reservoir. Drugs stored in reservoirs can be in the form of solutions, suspensions, gels, creams or dispersed in a solid polymer matrix and NLC (Nanostructured Lipid Carrier) system (Latifah & Rahman, 2024). The reservoir system has a separate drug layer, the drug layer in this system is a liquid compartment and is equipped with a backing layer (Lembang, 2021). In the manufacture of patches, an important component in the preparation is polymer (Putri, 2018). Polymers are the main constituent components that affect the physical characteristics of patches that have various functions such as film formers, drug release rate regulators, pressure-sensitive adhesives (Fuziyanti et al., 2022). In this study, hydroxypropyl methylcellulose (HPMC) polymer was used because HPMC is a good stabilizing agent, which can produce a strong, non-brittle, and flexible patch matrix (Fuziyanti et al., 2022). The method used in this study is the solvent casting method which consists of five stages, namely solution manufacturing, solution transfer into the mold, solution drying, preparation cutting and packaging (Fuziyanti et al., 2022). Based on the above background, research is needed that aims to formulate curcumin in the form of a membrane-type patch preparation with curcumin nanoemulsion as a reservoir. The patch formed is then characterized by physicochemical characterization such as fold resistance test, weight uniformity test, thickness test, humidity test, pH test and active ingredient content test. In addition, a stability test was also carried out on the preparation of membrane-type patches with curcumin nanoemulsion as a reservoir using the cycling test method.

METHOD

This research was conducted in a laboratory experiment, to make a formulation of membrane-type patch preparations with curcumin nanoemulsions as a reservoir formulated with various concentrations of polymers, namely F1 (6%), F2 (8%) and F3 (10%). Then a characteristic evaluation was carried out in the form of a thickness test, fold resistance test, weight uniformity test, humidity test, pH test, active ingredient content test and stability test using the cycling test method (freeze thaw). The results obtained were then analyzed if the normal distributed data was continued to the paired t-test and if the data was not normally distributed, the wilcoxon test was carried out. The tools used in this study include, glass tools (Pyrex), magnetic heater stirrer (Thermo Scientific), analytical scales (RADWAG), parchment paper, pipettes, pH meters (Trans Instruments), brookfield viscometer, UV-Vis spectrophotometry, particle size analyzer (PSA), dissolution tester (LORDERAN), petri dish (Iwaki), watch glass (Iwaki), stainless spoons, acid cabinets, ovens, desiccantizers, centrifugations, preparation glass, micrometers and climatic chambers, Homogenizer MHZ001 (Joan Lab). The ingredients used in this study are curcumin, HPMC (Hydroxypropylmethylcellulose) (Merck Germany), menthol, propylene glycol (Dow, Thailand), curcumin, tween 80 (Merck, Germany), span 80 (Merck, Germany), VCO, isopropyl mytrate, PEG 400, ethanol and aquades.

RESULT AND DISCUSSION

Result

The preparation of membrane-type patch preparations uses solvent casting techniques. This technique has the advantage of making the reservoir layer thinner and more evenly distributed (Fauzi, 2024). Solvent casting is a technique used for the manufacture of biodegradable films of polymers by dissolving the polymer in a suitable solvent. Where the solution is poured into the substrate and followed by evaporation of the solvent to produce a solid film (Hanifa et al., 2024). Curcumin nanoemulsion is poured on the top of the backing layer then leveled and dried under an acid cabinet for 48 hours. Furthermore, the pouring of the rate controlling membrane layer made of HPMC with different concentrations of 6%, 8% and 10%, propylene glycol and menthol.

This study uses HPMC because it is able to remove drugs from the matrix relatively quickly (Setyadi & Saryanti, 2022). HPMC is one of the polymers commonly used in topical drug delivery because it has non-toxic characteristics, does not cause irritation and is compatible with a wide range of drugs and additives. HPMC as a polymer can produce preparations with a good physical appearance, such as smooth texture, aeration and less wrinkle in patches (Syaputri et al., 2024). Propylene glycol was chosen because its use is safer, convenient, non-toxic and only mildly irritating when compared to glycerin (Misnamayanti et al., 2020). Propylene glycol functions as a plasticizer, the addition of plasticizer can provide elastic properties to the patch while increasing the flexibility of the transdermal patch, so that the resulting patch will have flexible and elastic properties that can be easy to use without causing trauma during replacement (Amalia, 2023). In addition, according to jagtap et al., 2017 who compared 3 plasticizers, namely glycerol, PEG 400 and propylene glycol, it was found that propylene glycol is better used as a plasticizer. Plasticizers are used to modify the physical characteristics of patches so that the resulting patches will be softer, more flexible and resistant to mechanical stress (Putri, 2018).

Meanwhile, menthol functions as an enhancer that has advantages such as being able to enlarge pores in the stratum corneum layer of the skin, so that it can increase the percutaneous transport of drugs and can also increase the release of drugs from preparations and be able to increase the solubility of medicinal ingredients (Setyawan et al., 2016). Menthol can increase drug partition into the stratum corneum and can reverse modify the arrangement of lipid membranes so that drugs can penetrate through the skin stratum corneum barrier more optimally (Maulina, 2022). Menthol has been researched as a skin penetration enhancer. When applied to the skin, menthol dilates blood vessels and can cause a cold sensation followed by an analgesic effect (Lembang, 2021). After the rate controlling membrane solution is evenly poured over the reservoir layer, it is dried again under the acid cabinet for 48 hours to remove the solvent.

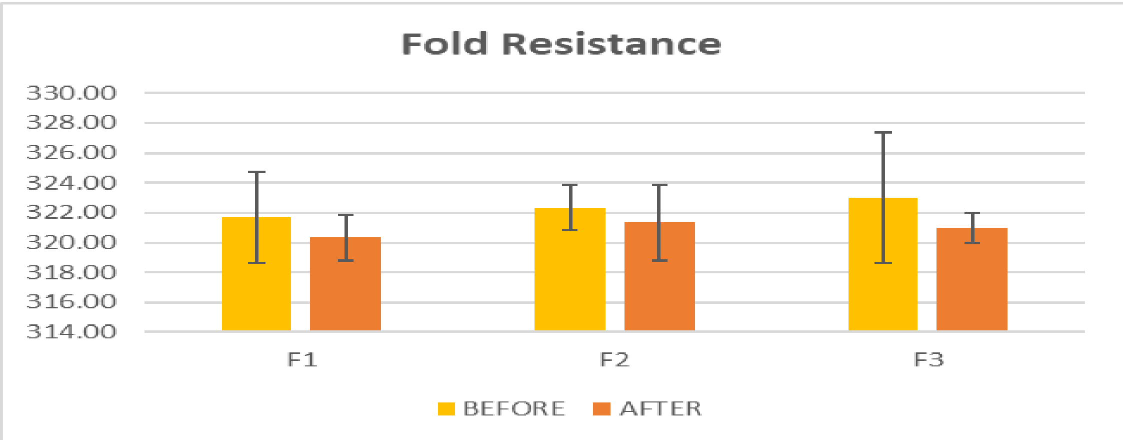
Fold Resistance Result

An evaluation of the resistance of the fold is carried out to determine the flexibility and elasticity of the patch after it is folded at the same angle so that it is not easily torn during use and storage.

Table 1. The results of the average evaluation of membrane-type patch fold resistance test with curcumin nanoemulsion as a reservoir.

Formula	Fold Resistance	
	Before	After
F1	321,67±3,06	320,33±1,53
F2	322,33±1,53	321,33±2,52
F3	323,00±4,36	321,00±1,00

Figure 1. Graphic of the average resistance of membrane-type patch folds with curcumin nanoemulsion as a reservoir.



Results of the evaluation of the average crease resistance obtained before and after the cycling test can be seen in table 1. Based on the results of the required fold resistance evaluation, it shows that F1, F2 and F3 have met the requirements. The fold resistance requirement according to previous research is >200 times (Fuziyanti et al., 2022). The results of this evaluation also showed that F1, F2 and F3 produced >200 folds without tearing. The high value of the crease resistance of a patch indicates that the patch has a good film shape so that it is not easily torn during use and storage (Fuziyanti et al., 2022). Elasticity can be affected by plasticizer factors that aim to increase flexibility (Simanullang et al., 2024). Plasticizers have the potential to increase the volume of cavities between polymer chains, allowing parts of the polymer molecular chain to move easily. Therefore, increased polymer movement has the potential to increase the flexibility and elasticity of the patch (Maddeppungeng et al., 2023). The use of propylene glycol as a plasticizer can increase the flexibility of the patch so that the patch does not break and tear easily (Wardani & Saryanti, 2021). In general, the more elastic a polymer is, the more malleable it is (Simanullang et al., 2024).

Based on statistical analysis using the *paired t-test*, a significance value of 0.300 ($P > 0.05$) was obtained. This shows that there is no significant difference between the folding resistance before and after the cycling test. This is because the average difference in fold resistance is not strong enough. The results of the paired t-test showed $p > 0.05$ so the difference was not statistically significant. However, if you observe the graph of the average durability of patch folds visually, you can see differences before and after the cycling test, especially in preparations with high HPMC concentrations. This is in accordance with the research of Syaputri et al., (2024) which states that there are differences before and after the cycling test (Syaputri et al., 2024). This happens due to a change in storage temperature in the patch which can reduce the water content in the patch preparation so that it becomes drier (Syaputri et al., 2024). If there is a decrease in the water content of the patch, it will cause the patch to become less elastic which can cause the resistance of the patch folds to decrease. This is in accordance with the statement of Setyadi & Saryanti in their research that the water content in a polymer will affect the elasticity properties of a polymer (Setyadi & Saryanti, 2022).

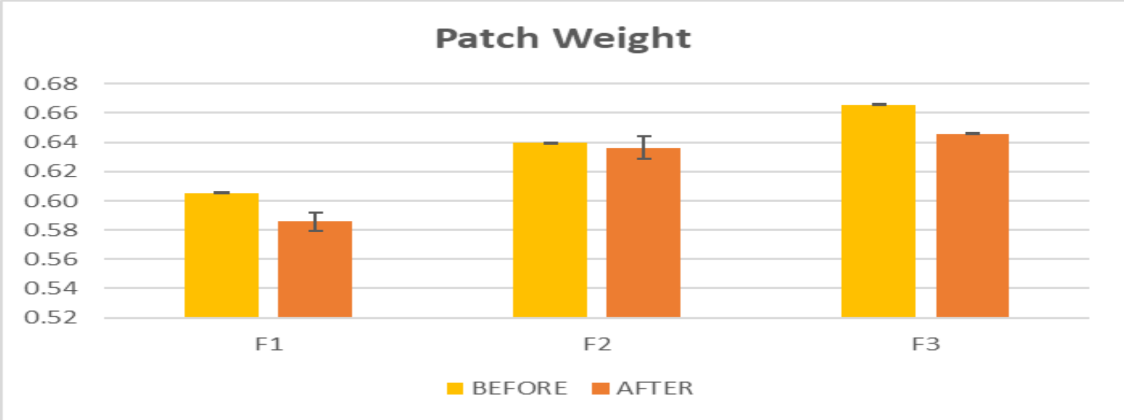
Weight Uniformity Result

Evaluate the uniformity of weights to assess the extent of consistency in the formulation process of the patch preparation. An effective formulation process will result in a patch with a relatively balanced weight, so that the dose of the drug in the patch can be guaranteed to be uniform.

Table 2. The results of the average evaluation of the uniformity test of the weight uniformity of membrane type patches with curcumin nanoemulsion as a reservoir.

Formula	Patch Weight (g)	
	Before	After
F1	0,60±0,00	0,59±0,01
F2	0,63±0,01	0,62±0,00
F3	0,64±0,00	0,63±0,00

Figure 2. Graphic of the average uniformity of weight of membrane-type patch preparations with curcumin nanoemulsions as reservoirs.



Weight and patch thickness have a significant relationship because the heavier the patch produced, the more it will affect the thickness of the patch (Maddeppungeng et al., 2023). The results of the weight uniformity evaluation can be seen in Table 2. has results that meet the standard deviation of <0.05%. Which indicates that the uniformity of the weight of the patch has been qualified and acceptable. This indicates that there is a uniformity of the content of active substances in the formula (Simanullang et al., 2024). Based on the statistical analysis of the wilcoxon test, a significance value of 0.515 ($P > 0.05$) was obtained, indicating that there was no significant difference in weight uniformity before and after the cycling test. In line with the research of Simanullang et al., (2024) which states that there is no significant difference in patch weight between before and after the stability period (cycling test) (Simanullang et al., 2024). In the graph of the average uniformity of the weight of the patch preparation, it can be seen visually that in each formula it shows that variations in the concentration of HPMC as a polymer can affect the weight of the patch preparation. The higher the concentration of HPMC used, the greater the weight produced (Wardani & Saryanti, 2021). An increase in patch weight can also be affected by a solvent that has not fully evaporated which can then result in an increase in the weight of the patch preparation (Mallaka et al., 2024). In F1, F2 and F3 experienced a decrease in value after the cycling test due to several factors such as uneven mixing of the mixture and solvents that did not evaporate all during the previous patch drying proce (Mallaka et al., 2024).

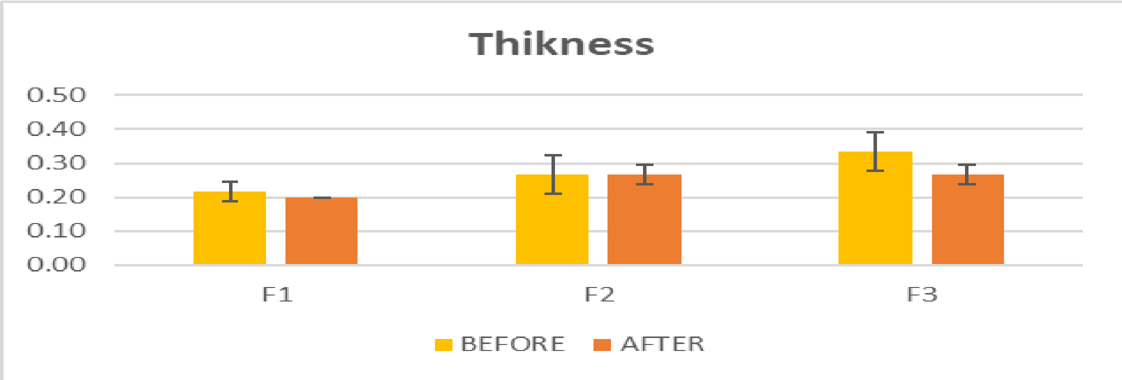
Thickness Patch Result

Thickness evaluation shows the uniformity of the thickness of the patch. The thickness obtained indicates the uniformity of the solution when poured into the mold (Wardani & Saryanti, 2021).

Table 3. The results of the average evaluation of the membrane-type patch thickness test with curcumin nanoemulsion as a reservoir.

Formulation	Thikness (mm)	
	Before	After
F1	0,22±0,03	0,20±0,00
F2	0,27±0,06	0,27±0,03
F3	0,33±0,06	0,27±0,03

Figure 3. Graph of the average thickness of membrane-type patch preparations with curcumin nanoemulsion as a reservoir.



The results of the evaluation of the average patch preparation thickness test before and after the cycling test can be seen in table 3. The results of this test meet the requirements for the thickness of the patch, which does not exceed 1 mm because the patch that is too thick will cause it to be difficult to remove the active substance from the preparation (Syaputri et al., 2024). Based on wardani & saryanti research, the increase in patch thickness is caused by variations in the concentration of HPMC as a polymer used in each formula. High concentrations of HPMC polymers can increase the thickness of the patch (Wardani & Saryanti, 2021). The thinner the patch produced, the better the penetration of the active substance into the skin. Where thin patches will be easier to accept in use (Maddeppungeng et al., 2023). Weight and patch thickness have a significant relationship because the heavier the patch produced, the more it will affect the thickness of the patch (Maddeppungeng et al., 2023). The thickness of the patch is affected by the concentration of the polymer and the level of solubility, When the solubility decreases and the concentration increases, the thickness of the patch will also increase (Simanullang et al., 2024).

Based on the results of statistical analysis with the Wilcoxon test, a significance value of 0.395 ($P > 0.05$) was obtained, indicating that there was no significant difference before and after the cycling test. This is in accordance with the research of Simanullang et al., (2024) which states that the patch does not experience significant changes in thickness during before and after the cycling test. Thus extreme temperature changes do not affect the thickness of patch preparations (Simanullang et al., 2024). In accordance with the research of Mallaka et al., 2024 which states that the patch does not show any change in thickness either at room temperature or cold temperature (Mallaka et al., 2024).

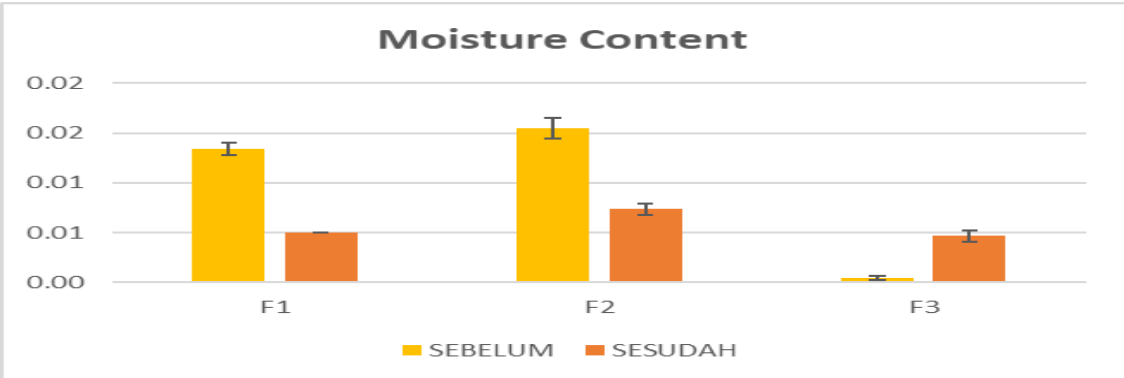
Moisture Content Result

Evaluate the moisture to determine the ability of the patch to absorb moisture. The value of low moisture ability can make the patch relatively stable and protected from microbial contamination (Maddeppungeng et al., 2023). Low moisture content is recommended to maximize stability, reduce brittleness, provide good compactness and reduce sensitivity to bacterial activity (Simanullang et al., 2024).

Table 4. The results of the average evaluation of the moisture test of membrane-type patch preparations with curcumin nanoemulsions as reservoirs.

Formula	Moisture (%)	
	Before	After
F1	0,01±0,00	0,01±0,00
F2	0,02±0,00	0,01±0,00
F3	0,00±0,00	0,00±0,00

Figure 4. Graph of the average moisture content of membrane-type patch preparations with curcumin nanoemulsions as reservoirs.



The results of the moisture evaluation of the patch preparation can be seen in Table 4. The moisture of the patch is declared to have met the requirements where the requirement for moisture is <10%. The results of this absorbency are in accordance with the research of Syaputri et al., 2024 which states that the higher the HPMC concentration, the lower the moisture of the patch, this is because HPMC has lipophilic properties so that the patch is composed of water-insoluble polymers which are finally able to maintain the moisture of the patch (Syapuri et al., 2024). Too low moisture content will cause patches to brittle easily but if the moisture content is too high, it will lead to bacterial growth (Setyadi & Saryanti, 2022). Based on the results of the statistical analysis of the wilcoxon test, a significance value of 0.021 ($P < 0.05$) was obtained, which shows that there is a significant difference before and after the cycling test. This shows that in F3 with a concentration of 10% HPMC it has good moisture. In accordance with the statement of Syaputri et al., (2024), in their research which stated that HPMC has an effect on moisture in patch preparations (Syaputri et al., 2024). The higher the HPMC concentration, the lower the moisture patch (Syaputri et al., 2024). This is due to the concentration of HPMC or polymers used. HPMC is known as a lipophilic polymer so that the entire patch is made of a polymer that is insoluble in water so that it affects the patch preparation (Syaputri et al., 2024).

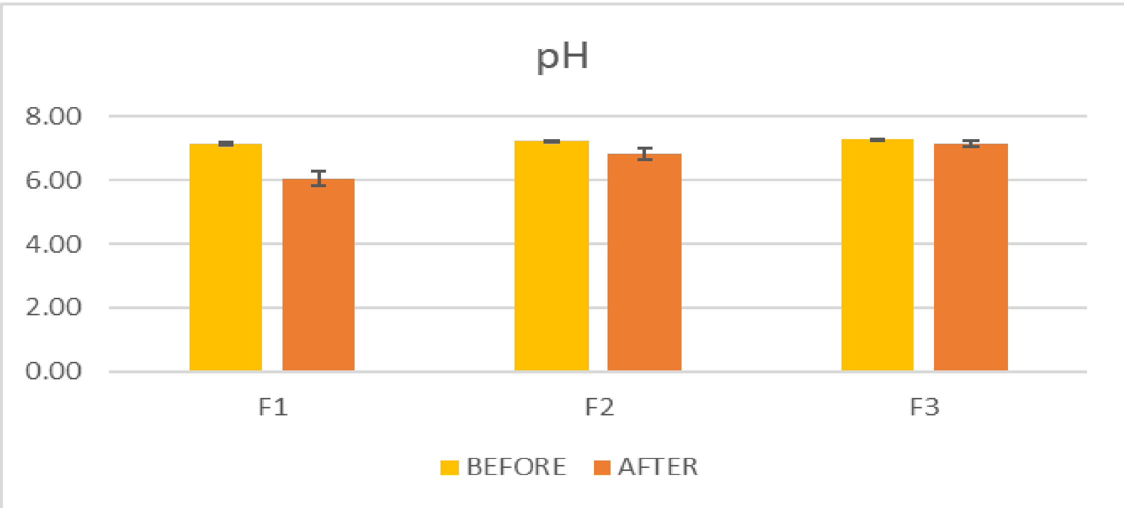
pH Result

The pH evaluation of the patch preparation aims to determine the safety of the preparation. The pH should not be too acidic as it can irritate the skin and also should not be too alkaline as it can cause scaly skin (Wardani & Saryanti, 2021). In addition, it can also affect the hydration level of polymers in the skin (Maddeppungeng et al., 2023). This pH test is to ensure that the transdermal patch containing curcumin nanoemulsion as a reservoir has a pH range that corresponds to the physiological pH of the human skin. The criteria for an acceptable pH range so as not to irritate the skin are 4-8 (Ermawati & Prilantari, 2019).

Table 5. The results of the average evaluation of the pH test of membrane-type patch preparations with curcumin nanoemulsions as reservoirs.

Formula	pH	
	Before	After
F1	7, 14±0,03	6,04±0,23
F2	7,22±0,01	6,84±0,17
F3	7,26±0,02	7,13±0,08

Figure 5. Graph of the average pH test of membrane-type patch preparations with curcumin nanoemulsion as a reservoir.



Based on the results of the evaluation of membrane-type patch preparations with curcumin nanoemulsion as a reservoir have met the criteria for the pH of the topical preparation, which does not exceed the pH that has been set. HPMC has a pH of 3-11 (Setyadi & Saryanti, 2022). A more dominant concentration of ingredients can affect the pH range (Setyadi & Saryanti, 2022). This suggests that higher the concentration of HPMC can increase the pH of the patch preparation. Based on the results of statistical analysis with the paired t-test, a significance value of 0.009 (P <0.05) was obtained, indicating that there was a significant difference before and after the cycling test. This is in accordance with research conducted by Simanullang et al., (2024) which states that there are significant differences before and after the cycling test. It shows that there is an effect of differences in the pH of patch preparations at extreme temperatures (Simanullang et al., 2024).

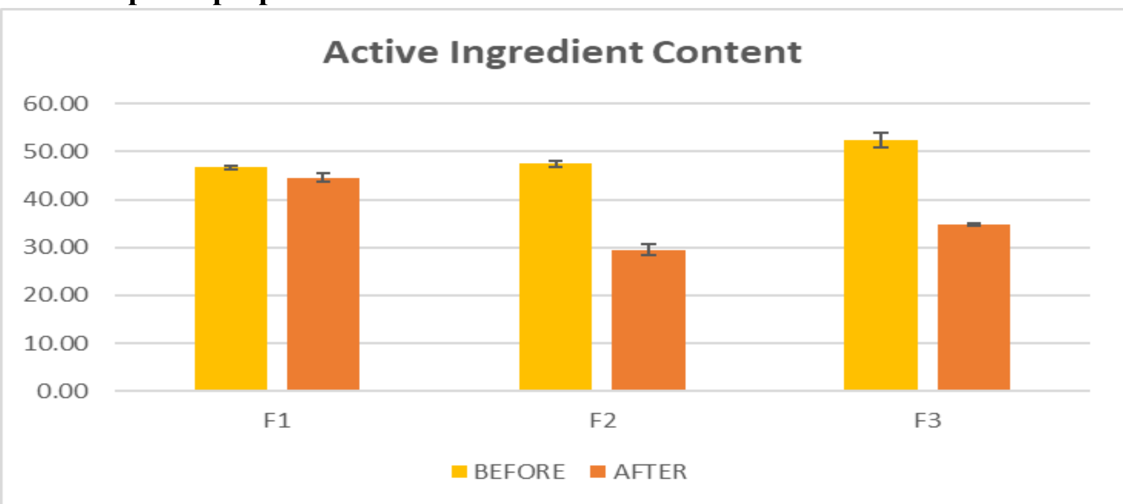
Drug Content Evaluation Result

Evaluation of the bioactive content in patch preparations aims to ensure proper and consistent dosage. Testing of the active ingredient is performed to ensure that each patch contains a uniform active ingredient. The inconsistency of the content of the active ingredient in each patch can affect the therapeutic effect produced (Latifah & Rahman, 2024).

Table 6. The results of the average evaluation test of the active ingredient content of membrane-type patch preparations with curcumin nanoemulsion as a reservoir.

Formula	Active Ingredient Content (%)	
	Before	After
F1	46,71±0,40	44,57±0,86
F2	47,44±0,55	29,53±1,06
F3	52,43±1,49	34,71±0,30

Figure 6. Average graph of the active ingredient content test of membrane-type patch preparations with curcumin nanoemulsion as a reservoir.



The results of the evaluation of the active ingredient content of the patch preparation can be seen in Table 6. and Figure 6. shows that the higher the concentration of HPMC as a polymer can form a denser and more homogeneous polymer network that can keep curcumin in the form of nanoemulsions protected and not evaporated or degraded during the drying process. So that the content of active ingredients in the patch increases along with the increase in the concentration of the polymer. However, after the cycling test, there was a decrease in the content of active ingredients caused by improper storage such as temperature changes, oxidation, exposure to light (Devi et al., 2025). Based on research by Syarifah et al., 2023 which states that there is a difference in curcumin levels in samples stored in storage facilities with temperatures of 37°C and 40°C. This happens because curcumin compounds are degraded into other compounds. And showed that curcumin compounds are degraded and unstable at 37°C and 40°C storage sites (Syarifah et al., 2023). So that it can accelerate the degradation process of the patch itself and can cause a change in pH. Based on the results of statistical analysis using the wilcoxon test, a significance result of 0.110 ($P > 0.05$) showed that there was a difference before and after the cycling test. Therefore, it can be concluded that membrane-type patch preparations with curcumin nanoemulsions as reservoirs degrade at extreme temperatures.

CONCLUSION

Based on the results and discussions that have been presented, it can be concluded that the higher the concentration of HPMC as a polymer can increase the folding density, weight, thickness and active ingredient content of membrane type patches. The lower the concentration of HPMC as a polymer can decrease the moisture value of the membrane-type sera pH patch. Statistical analysis showed that there was no significant difference in fold resistance, uniformity of the shape and thickness of the patch before and after the cycling test. And there were significant differences in pH, humidity and active ingredient content of membrane-type patch preparations before and after cycling tests.

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