Formulation and Physical Properties Testing of Spray Gel Preparation of Ethyl Acetate Extract of Ketapang (Terminalia atappa) Leaves

Maulita Indrisari[1], Nur Khairi[2]*

[1]Department Pharmocotherapy, Palangka Raya University, Palangka Raya, Central Kalimantan, Indonesia
[2] Department Pharmaceutical and Technology, Almarisah Madani University, Makassar, Indonesia

*Corresponding Author: nurkhairijalil@gmail.com

ABSTRACT

Bioactive compounds from plants have long been used in the development of pharmaceutical and cosmetic formulations, particularly for effective and stable topical applications. One plant that has great potential is ketapang (*Terminalia catappa*) leaves, which contain flavonoids, saponins, and tannins with broad pharmacological activities. This study aims to develop a spray gel formulation of ethyl acetate extract of ketapang leaves and evaluate its physical stability. Ethyl acetate extract of ketapang leaves was extracted using maceration method and used in three spray gel formulations with varying extract concentrations. Physical stability evaluation was conducted by measuring viscosity, pH, homogeneity, spray pattern, and temperature stability during accelerated storage using the cycling test method. The results showed that all spray gel formulas remained stable in terms of color, odor, texture, and homogeneity after storage. Viscosity decreased slightly in formulas I and III but remained within the acceptable range. The pH of the preparation was stable within the physiological range of 4.5-6.5, which is safe for the skin. The spray pattern remained optimal despite slight changes after storage. The stability test showed that the spray gel had good resistance to high temperature and other storage conditions. This study proves that ketapang leaf ethyl acetate extract spray gel has potential as a topical product that is stable, effective, and safe, and opens up opportunities for further research on its therapeutic effectiveness.

Keywords: ketapang leaf extract, spray gel, physical stability

INTRODUCTION

Bioactive compounds from plants have long been a concern in the development of pharmaceutical and cosmetic formulations, especially in effective and stable topical dosage forms. One plant that has great potential in this field is ketapang (Terminalia catappa) leaves, which are known to

contain various bioactive compounds with broad pharmacological activities. Several studies have reported that ethyl acetate extracts of ketapang leaves are rich in flavonoids, saponins, tannins, and glycosides, which contribute to various therapeutic benefits, including antioxidant and antimicrobial activities (Anarado et al., 2020; Araújo et al., 2023). Flavonoids in these extracts act as free radical scavengers that protect cells from oxidative stress (Milovanović, Živković and Vucelić-Radović, 2010), while saponins and tannins are known to inhibit the growth of pathogenic microorganisms through microbial cell membrane inhibition mechanisms (Khan et al., 2018).

In addition, the use of ethyl acetate extracts as active ingredients in topical formulations is growing, mainly due to their properties that favor the penetration of active compounds into the skin and their broad pharmacological effects. Studies show that this extract has antibacterial and antifungal activities capable of inhibiting various microbial strains (Adamu, Naidoo and Eloff, 2014; Sanan, Murti and Hertiani, 2024). The activity of this plant is largely due to the flavonoid content that can chelate metal ions essential for bacterial growth, as well as saponins that can damage the integrity of microbial cell membranes (Khan et al., 2018). In pharmaceutical applications, the ethyl acetate extract of ketapang leaves has great prospects for use in topical dosage formulations, especially in the form of spray gels, which offer ease of application as well as effectiveness in spreading active substances on the skin.

Spray gel preparations are an attractive option in pharmaceutical and cosmetic formulations due to their easy-to-apply properties and fast drying time. Spray gels combine the advantages of a gel, such as the ability to adhere to the skin and release active substances gradually, with the practicality of a spray form that allows even distribution over the application area. The main components in spray gel formulations include gelling agents, surfactants, preservatives, and humectants, each of which has a role in determining the physical stability of the product (Rizkiyan et al., 2022). For example, Carbopol 940 is often used as a gelling agent due to its ability to produce optimal viscosity and good stability under various storage conditions. Similarly, the use of humectants such as propylene glycol plays a role in maintaining moisture and preventing drying of the product during storage (Rizkiyan et al., 2022).

One of the main challenges in the development of plant extract-based spray gels is ensuring their physical stability during shelf life. The physical stability of the preparation includes parameters such as viscosity, pH, homogeneity, spreadability, dry time, and resistance to changes in temperature and humidity. Previous studies have shown that the stability of

topical preparations can be affected by interactions between additives and active compounds, which can cause changes in physical characteristics such as an increase or decrease in viscosity, discoloration, or even phase separation (Sugihartini and Wiradhika, 2017). Therefore, physical stability evaluation is an important aspect in spray gel formulation to ensure that the product remains effective and safe to use throughout its shelf life.

Previous studies have explored the formulation and stability of various herbal extract-based gel and spray preparations, but specific research on the physical stability of ketapang leaf ethyl acetate extract spray gel is still very limited. Several studies have demonstrated the effectiveness of ketapang extracts in various topical dosage forms, but not many have comprehensively evaluated the physical stability of spray gel formulations, including the influence of environmental factors on dosage characteristics (Ng and See, 2019). In addition, no study has specifically examined the best combination of additives to maintain the physical stability of spray gels containing this extract. The difference between this study and previous studies lies in the formulation of a spray gel based on ethyl acetate extract of ketapang leaves designed with optimal physical stability in mind. By exploring the appropriate combination of additives and evaluating the stability parameters thoroughly, this study is expected to contribute to the development of topical preparations based on natural ingredients that are more stable and effective. In addition, with the increasing demand for herbal preparations that have high efficacy and ease of use, the results of this study can benefit the pharmaceutical and cosmetic industries in producing innovative and evidence-based products.

METHODOLOGY

Research Tools and Materials

The tools and materials used in this study include digital scales, analytical scales (Kern), measuring cups, funnels, stirring rods, planel cloth, spatulas, viscometers, maceration containers, Ketapang leaves, carbopol, Trietanolamine (TEA) Propyl glycol, DMDM hydantoin, ethyl acetate, and aquadestillate.

Sample Processing

The samples used in this study were Ketapang leaves obtained from Biringkanaya District, Makassar City, South Sulawesi Province. The Ketapang leaves obtained were then collected and then wet sorted with the aim of separating impurities or other foreign materials by washing with running water. Then dried by aerating and avoiding direct sunlight. The sample is ready to be used as research material.

Extract Preparation

Ketapang symplisia that has been prepared is then extracted using the maceration method using ethyl acetate solvent for 3 times 24 hours while occasionally stirring, then the filtrate and residue are obtained and then macerated again 1 time 24 hours until the filtrate is obtained again with the residue, the filtrate obtained is combined and then evaporated by airing, until a thick extract is obtained.

Formulation

Table 1. Formula

Ingredients	Formula I (%)	Formula II (%)	Formula III (%)	Function
Ketapang Leaf Extract	1%	2%	3%	Active Substance
Carbopol	0,5	0,5	0,5	Viscosity Enhancer
Trietanolamine	0,5	0,5	0,5	Alkalizing Agent
Propilen Glikol	10%	10%	10 %	Penetration Enhancers
DMDM Hydantion	0,6 %	0,6 %	0,6 %	Preservative
Aquadestillata	Add 100	Add 100	Add 100	Solvent

The preparation of spray gel is done by first dispersing carbopol 940 which is dispersed with distilled water that has been heated in a mortar and then crushed until there is no collection and expands in the form of a gel. After that, triethanolamine was dripped into the mortar containing carbopol 940 and then crushed until homogeneous. then put propylenglycol and DMDM Hyndantion into the mortar, then crushed. After that, add ketapang leaf extract which was previously dissolved using distilled water and then homogenized, after homogeneous, the preparation was put into the prepared container and then evaluated.

Evaluation

Stability Test

The stability test was carried out with the cycling test method. The preparation was stored at 40°C for 24 hours. Testing was carried out for 6 cycles. Then it was seen whether there were any changes from the organoleptic test, pH test and viscosity test, spray pattern test and homogeneity test (Pleguezuelos-Beltrán et al., 2022).

Organoleptic Test

This test is carried out by observing the color, odor and texture of the preparation that has been made (Kuo, 2003).

Homogeneity Test

Spray gel preparation is applied to a piece of preparate glass (transparent). Then it is seen whether or not there are particles/substances that have not been mixed homogeneously (Yuliani Agung B., Marwati M & Candra K.,2020).

pH test

Measurement of the pH of the gel preparation was carried out using a pH meter. The pH of the preparation that meets the skin criteria is in the onyerval of 4.5-6.5. Tests were carried out on spray gel preparations (Yenigün et al., 2024).

Viscosity Test

Viscosity test is carried out by putting the preparation into a tube-shaped container and then installing a spindle 63. The spindle must be submerged in the test preparation. The viscometer is turned on and make sure the rotor can rotate, then observe the needle of the viscometer pointing to the number on the viscosity scale and then recorded (Qian, Lin and Bao, 2016).

Spraying Test

The spraying pattern was carried out by spraying the Ketapang leaf extract spray gel from the bottle with a distance of 5, 10, 15 cm on a sheet of paper. The test was observed through the amount of preparation that came out of the bottle per spray (Kuo, 2003).

Adhesion Test

This test is carried out on the skin on the upper arm and sprayed preparations from a distance of 30 mm or 3 cm. After spraying, 10 seconds are counted to see if any preparation sticks or droplets from the spray drip down (Yuliani Agung B., Marwati M & Candra K.,2020).

RESULTS AND DISCUSSION

Organoleptic evaluation aims to observe changes in color, odor, and texture of the spray gel preparation before and after accelerated storage. The results are presented in Table 2.

Table 2. Organoleptic Examination Results

Formula	Before Accelerated Storage			After Accelerated Storage		
	Color	Odor	Texture	Color	Odor	Texture
F1	Brownish green	Odorless	Thick liquid	Brownish green	Odorless	Thick liquid
F2	Brownish green	Odorless	Thick liquid	Brownish green	Odorless	Thick liquid
F3	Brownish green	Odorless	Thick liquid	Brownish green	Odorless	Thick liquid

Description:
F1 : Spray gel formula with 1% concentration of ketapang leaf extract
F2 : Spray gel formula with ketapang leaf extract concentration 1%
F3 : Spray gel formula with ketapang leaf extract concentration 1%

These results indicate that during accelerated storage, no changes occurred in the color, odor, and texture aspects of the three spray gel formulas tested. Good organoleptic stability can be attributed to the stability of the ethyl acetate extract of ketapang leaves, which has been known to contain flavonoid and saponin compounds that are relatively stable to certain environmental conditions (Araújo et al., 2023). In addition, the use of stabilizing agents such as Carbopol 940 can help maintain the gel texture during storage (Rizkiyan et al., 2022).

Table 3. Homogeneity Results

Formula	Homogeneity	
	Before Accelerated Storage	After Accelerated Storage
F1	Homogeneous	Homogeneous
F2	Homogeneous	Homogeneous
F3	Homogeneous	Homogeneous

Description:
F1 : Spray gel formula with 1% concentration of ketapang leaf extract
F2 : Spray gel formula with ketapang leaf extract concentration 1%
F3 : Spray gel formula with ketapang leaf extract concentration 1%

Homogeneity was tested to ensure that all ingredients in the formulation were evenly mixed.

All formulas remained homogeneous both before and after accelerated storage, indicating that the dispersion of extracts and additives in the spray gel was stable. This is in accordance with previous findings that the use of polymers such as Carbopol 940 and dispersant agents such as

Polysorbate 80 can improve the stability of the mixture in topical preparations (Dahlizar et al., 2018).

Table 4. Viscosity Measurement Results

Formula	Viscosity Value	
	Before Accelerated Storage	After Accelerated Storage
F1	36,67 ± 5,77	33,33 ± 5,77
F2	43,33 ± 5,77	43,33 ± 5,77
F3	46,67 ± 5,77	43,33 ± 5,77

Description:
F1 : Spray gel formula with 1% concentration of ketapang leaf extract
F2 : Spray gel formula with ketapang leaf extract concentration 1%
F3 : Spray gel formula with ketapang leaf extract concentration 1%

Viscosity is a key parameter in the physical stability of spray gels. A decrease in viscosity after storage was found in FI and FIII, but remained within the acceptable range. This is likely due to partial degradation of the gelling agent polymer or interaction with the bioactive extract, which has also been reported in studies on other herbal extract-based gel preparations (Sugihartini and Wiradhika, 2017). The better viscosity stability of FII can be attributed to the balance between the concentration of gelling agent and active substance. The results showed that the viscosity decreased slightly in FI and FIII after storage, but remained within acceptable limits.

This decrease in viscosity can be caused by the interaction between the gelling agent (Carbopol 940) with bioactive compounds in the extract, which can cause changes in the structure of the gel polymer network (Dahlizar et al., 2018). This is in line with the findings of other studies which state that herbal extract-based formulations tend to experience changes in viscosity in long-term storage, especially when the extract contains polyphenols that can interact with polymers in the gel matrix (Sugihartini and Wiradhika, 2017).

Despite the slight decrease in viscosity, the homogeneity test results showed that the spray gel remained stable without any phase separation, indicating that the selection of additives such as humectants (Propylene Glycol) has played a role in maintaining the stability of the gel matrix (Rizkiyan et al., 2022).

Table 5. Results of pH Measurement

Formula	pH Value	
	Before Accelerated Storage	After Accelerated Storage
F1	5.11 ± 0.10	5.14 ± 0.04
F2	5.36 ± 0.09	5.36 ± 0.09

F3	5.23 ± 0.07	5.23 ± 0.07

Description:
F1 : Spray gel formula with 1% concentration of ketapang leaf extract
F2 : Spray gel formula with ketapang leaf extract concentration 1%
F3 : Spray gel formula with ketapang leaf extract concentration 1%

The pH measurement was carried out to ensure the stability of the pH of the preparation in accordance with the pH of the skin (4.5 - 6.5).

The results showed that the pH of the preparation was relatively stable after storage. This stability is important to prevent skin irritation (Yenigün et al., 2024). The pH stability also indicates that the bioactive compounds in the ethyl acetate extract do not undergo significant degradation that affects the acidity of the medium (Ng and See, 2019). This study is in line with previous research which shows that pH stability in topical formulations is highly dependent on the selection of additives, such as buffering agents used to maintain pH stability during storage (Ng and See, 2019). In this formulation, sodium citrate was used as a pH balancing agent, which has been shown to be effective in maintaining the stability of plant extract-based formulations.

Table 6. Spraying Pattern

Formula	Spray Pattern	
	Before Accelerated Storage	**After Accelerated Storage**
F1	5.33 ± 0.58	6.33 ± 0.58
F2	6.67 ± 1.53	7.00 ± 1.00
F3	7.00 ± 1.00	7.67 ± 0.76

Description:
F1 : Spray gel formula with 1% concentration of ketapang leaf extract
F2 : Spray gel formula with ketapang leaf extract concentration 1%
F3 : Spray gel formula with ketapang leaf extract concentration 1%

Results showed a slight increase in spray pattern after storage. This can be attributed to the decrease in viscosity, which allows for a wider and better distributed spray. In another study, the use of surfactants such as Polysorbate 80 was also shown to improve spray power and stability of liquid preparations (Dahlizar et al., 2018).

The results showed that the ketapang leaf ethyl acetate extract spray gel had good physical stability, as evidenced by the parameters of viscosity, pH, homogeneity, spray pattern, and temperature stability tests. There were no significant changes in color, odor, or texture during accelerated storage, indicating that this formulation has high stability against environmental factors. This study is in line with previous studies which stated that ethyl

acetate extract has high stability due to its ability to dissolve bioactive compounds such as flavonoids and tannins, which have been shown to have strong antioxidant and antimicrobial activities (Araújo et al., 2023). These active compounds have also been reported to have an important role in increasing the stability of pharmaceutical preparations, especially in topical formulations such as gels and creams (Milovanović, Živković and Vucelić-Radović, 2010)

CONCLUSION

Based on the results obtained, it can be concluded that the spray gel based on ethyl acetate extract of ketapang leaves has good physical stability in various parameters tested, such as viscosity, pH, homogeneity, spray pattern, and temperature stability test. From the results of this study, it is recommended to use ketapang extract with a concentration of 2%.

REFERENCES

Adamu, M., Naidoo, V. and Eloff, J. (2014) 'The antibacterial activity, antioxidant activity and selectivity index of leaf extracts of thirteen South African tree species used in ethnoveterinary medicine to treat helminth infections', *BMC Veterinary Research*, 10(1). Available at: https://doi.org/10.1186/1746-6148-10-52.

Anarado, C. *et al.* (2020) 'Comparative phytochemical and anti-microbial studies of leaf, stem, root of Spathodea companulata', *Asian Journal of Applied Chemistry Research*, pp. 10–20. Available at: https://doi.org/10.9734/ajacr/2020/v6i130148.

Araújo, S. *et al.* (2023) 'In vitro antioxidant and antitrypanosomal activities of extract and fractions of Terminalia catappa', *Biology*, 12(7). Available at: https://doi.org/10.3390/biology12070895.

Dahlizar, S. *et al.* (2018) 'Design of a topically applied gel spray formulation with ivermectin using a novel low molecular weight gelling agent, palmitoyl-glycine-histidine, to treat scabies', *Chemical and Pharmaceutical Bulletin*, 66(3), pp. 327–333. Available at: https://doi.org/10.1248/cpb.c17-00965.

Khan, M. *et al.* (2018) 'Green tea seed isolated saponins exerts antibacterial effects against various strains of gram positive and gram negative bacteria, a comprehensive study in vitro and in vivo', *Evidence-Based Complementary and Alternative Medicine*, 2018(1). Available at: https://doi.org/10.1155/2018/3486106.

Kuo, J. (2003) 'The effect of protective agents on the stability of plasmid DNA by the process of spray-drying', *Journal of Pharmacy and Pharmacology*, 55(3), pp. 301–306. Available at: https://doi.org/10.1211/002235702702.

Milovanović, M., Živković, D. and Vucelić-Radović, B. (2010) 'Antioxidant effects of Glechoma hederacea as a food additive', *Natural Product Communications*, 5(1). Available at: https://doi.org/10.1177/1934578x1000500116.

Ng, Z. and See, A. (2019) 'Effect of in vitro digestion on the total polyphenol and flavonoid, antioxidant activity and carbohydrate hydrolyzing enzymes inhibitory potential of selected functional plant-based foods', *Journal of Food Processing and Preservation*, 43(4). Available at: https://doi.org/10.1111/jfpp.13903.

Pleguezuelos-Beltrán, P. *et al.* (2022) 'Advances in spray products for skin regeneration', *Bioactive Materials*, 16, pp. 187–203. Available at: https://doi.org/10.1016/j.bioactmat.2022.02.023.

Qian, L., Lin, J. and Bao, F. (2016) 'Numerical models for viscoelastic liquid atomization spray', *Energies*, 9(12), p. 1079. Available at: https://doi.org/10.3390/en9121079.

Rizkiyan, Y. *et al.* (2022) 'Nades extract of Gedong mango leaves and mulberry leaves in spray gel as a sunscreen', *International Journal of Applied Pharmaceutics*, pp. 121–125. Available at: https://doi.org/10.22159/ijap.2022.v14s4.pp29.

Sanan, A., Murti, Y. and Hertiani, T. (2024) 'Characterization of antibacterial bioactive compounds from Kusambi leaf extract (Schleichera oleosa (L) Oken)', *Journal of Pharmaceutical Science and Application*, 6(1), p. 21. Available at: https://doi.org/10.24843/jpsa.2024.v06.i01.p03.

Sugihartini, N. and Wiradhika, R. (2017) 'Gel formulation of ethanol extract of mangosteen peel (Garcinia mangostana L.) as a medication for burns in Wistar rats', *Jurnal Kedokteran Dan Kesehatan Indonesia*, 8(2), pp. 110–117. Available at: https://doi.org/10.20885/jkki.vol8.iss2.art6.

Yenigün, V. *et al.* (2024) 'Formulation of nasal analgesic sprays with diclofenac sodium, ibuprofen, paracetamol, and evaluation of in vitro toxicity', *Science Progress*, 107(4). Available at: https://doi.org/10.1177/00368504241304200.

Yuliani Agung B. Marwati M. & Candra K., Y. (2020) 'Physico-chemical characteristics of giant featherback (chitala lopis) and mackerel (scomberomorus commerson) bone gelatins and their potential as gelling agents in gel mixtures for roselle (hibiscus sabdariffa l.) soft jelly candies', *Walailak Journal of Science and Technology (Wjst)*, 17(7), pp. 678–685. Available at: https://doi.org/10.48048/wjst.2020.4559.