A COMPARATIVE STUDY OF THE PRODUCTION COSTS OF HYDROPHOBIC OINTMENTS, HYDROPHILIC OINTMENTS, AND GELS IN RELATION TO DRUG FORMULATION STABILITY

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Abstrak

Povidone – iodine memiliki sifat antiseptik untuk penyembuhan luka. Penelitian ini membuat sediaan antiseptik dalam bentuk sediaan semi solid dengan perbedaan basis yang digunakan. Penelitian ini bertujuan untuk mengetahui apakah perbedaan basis pada formula yang digunakan dapat mempengaruhi stabilitasnya dan berapa biaya yang digunakan untuk masing – masing formula. Formula 1 dengan basis hidrokarbon, formula 2 dengan basis hidrofilik, formula 3 gel basis Na-CMC. Ketiga formula diamati stabilitasnya menggunakan metode freeze – thaw dengan perbedaan suhu selama 18 hari penyimpanan dan diamati secara organoleptis, homogenitas, daya sebar, viskositas pH lalu diproses menggunakan one way ANOVA dan grafik kontrol I-MR. Hasil penelitian menunjukkan bahwa perbedaan basis pada formula berpengaruh signifikan terhadap nilai daya sebar, pH dan viskositas dengan nilai signifikan 0,000. Perbedaan formula juga mempengaruhi hasil organoleptis dan homogenitasnya. Formula 2 memiliki stabilitas paling baik berdasarkan hasil pengujian yang dilakukan. Dari segi biaya, formula 2 memiliki biaya bahan baku yang lebih besar dibandingkan dengan Formula 1 dan Formula 3.

Kata kunci: Antiseptik, stabilitas dan biaya.

Abstract

Povidone – iodine has antiseptic properties for wound healing. This research makes antiseptic preparations in semi-solid dosage form with different bases used. This research aims to find out whether the different bases in the formula used can affect its stability and how much it costs for each formula. Formula 1 with a hydrocarbon base, formula 2 with a hydrophilic base, formula 3 gel with a Na-CMC base. The stability of the three formulas was observed using the freeze - thaw method with different temperatures for 18 days of storage and observed organoleptically, homogeneity, spreadability, pH viscosity and then processed using one way ANOVA and I-MR control charts. The research results showed that the different bases in the formula had a significant effect on the spreadability, pH and viscosity values with a significant value of 0.000. Differences in formula also affect organoleptic results and homogeneity. Formula 2 has the best stability based on the results of the tests carried out. In terms of costs, Formula 2 has greater raw material costs compared to Formula 1 and Formula 3.

Keywords: Antiseptic, cost and stability**.**

1. INTRODUCTION

Health maintenance is important in increasing animal productivity. Animal productivity and reproductivity can be achieved optimally if the animals are in a healthy condition. (Taufan, 2011).

Ways that can be used to maintain animal health include providing disinfectants, antiseptics, providing feed supplements, vaccinations, antibiotics, deworming and providing quality feed. One example of hygiene is by administering antiseptics, compounds that are antiseptic include povidone - iodine (Resa, 2022).

Povidone – iodine is an iodine formulation that attacks key proteins, nucleotides and fatty acids in bacteria which ultimately causes cell death (Selvaggi et al, 2003).

Povidone – iodine has the function of accelerating the healing of lacerations in animals, the dose used is 10% because if in high concentrations it can cause skin irritation, in addition to that if in large quantities and excessively it can inhibit wound granulation, in wound care in general povidone – iodine used 10% (Irma, 2017).

Povidone – iodine has an oral LD_{50} toxicity value in mice and rats of 14,000 – 22,000 mg/kg, whereas at a dose of 2,000 mg/kg BW in male chickens it does not cause toxicity (D. Sani, 2021).

The antiseptics used are usually in liquid form, but this form evaporates more easily and is less attached to the therapeutic target, therefore it is necessary to develop antiseptics in the form of ointments or gels because they can form a protective layer on wounds so that they can speed up healing, in ointments and gel preparations. Care must be taken in selecting the base because the base used can affect the stability of the ointment and gel preparations. The base functions as a carrier, protector and softener. The base must release the drug optimally which must not damage or inhibit the therapeutic action, besides that the composition of the raw materials and the dosage form of the drug used can affect the price of the drug, due to differences in the formula and process of making the drug. (Sulaiman, 2008).

Control Charts use individual moving range charts (I-MR) because I-MR can be used to help to see whether a process is stable or not (Amanda S, 2023).

Therefore, research was carried out regarding stability comparisons and analysis of raw material cost calculations for hydrophilic base ointments, hydrophobic base ointments and gels with a Na CMC base.

2. RESEARCH METHOD

This research was conducted to see a comparison of the stability and price of each formula, including formula 1 with a hydrophobic ointment type using Vaseline Alba base, formula 2 with a hydrophilic ointment type using a PEG 400 base in combination with PEG 4000 and formula 3 gel using the gelling agent carboxymethyl cellulose. The tools used in this research are glassware, mortar, pestle, analytical balance, climatic chamber, petri dish, Brookfield viscometer, pH meter, digital caliper, refrigerator, dry cabinet, hot plate, weighing stone, clear glass plate . The ingredients used in this research were povidone–iodine, methyl paraben, propyl paraben, BHT, Vaseline Alba, PEG 400, PEG 4000, Na CMC and distilled water. The research process first carried out a preformulation study, then ointment and gel were made, then a freeze-thaw stability test was carried out for 6 cycles where in 1 cycle the samples were stored at temperatures of 4°C, 27°C and 40°C, then organoleptic observation evaluation was carried out homogeneity, spreadability, viscosity and pH. The data obtained for organoleptic results and homogeneity

were observed descriptively, while the results of spreadability, viscosity and pH were processed using control charts and statistical analysis using one way ANOVA, then the raw material costs for each formula were calculated.

Table 1 Formula of hydrophobic base, hydrophilic base and CMC Na

No.	Material	Concentration (%)			Function
		Formula 1 (Hydrophobic)	Formula 2 (Hydrophilic)	Formula 3 (Gel)	
1	Povidone Iodine	10%	10%	10%	Active pharmaceutical ingredient
2	Methyl Paraben	0.18%	0.18%	0.18%	Preservative
3	Propyl Paraben	0.02%	0.02%	0.02%	Preservative
4	BHT	0.05%	0.05%	0.05%	Antioxidant
5	Vaseline Alba	Ad 10 gr	-	-	Hydrophobic ointment base
6	PEG 400	-	71.27%	-	Hydrophilic ointment base
7	peg 4000	-	18.48%	-	Hydrophilic ointment base
8	Na CMC	-	-	2.5%	Gel base
9	Aquadest	-	-	Ad 10 gr	Gelling agent developer

Evaluation of Ointment and Gel Preparations

a. Organoleptic test
   Organoleptic evaluation by visually observing the ointment and gel preparations for the shape, color, odor and texture of each formula (Aristha, 2019).
b. Homogeneity Test
   A total of 0.5 grams of ointment and gel is smeared on a glass object, then rubbed and touched to see its homogeneity (Aristha, 2019).
c. Spreadability Test
   A total of 0.5 grams of ointment and gel was placed on a round glass, then another glass was placed on top, then a load of 100 grams was placed and left for 1 minute, then the diameter of the sample was measured (Olivia, 2013).
d. Viscosity Test
   This test uses a brookfield viscometer with adjusted RPM, time and spindle, then wait until the viscosity value appears on the tool (Adeltrudis, 2017).
e. Test pH
   A total of 0.5 grams of ointment is diluted with 50 ml of distilled water, then the pH meter is dipped until the number on the pH meter shows a stable number (Yetti, 2019).

3. RESULT AND DISCUSION

After going through the freeze – thaw stability test process for 6 cycles at temperatures of 4°C, 27 and 40°C, the following results were obtained :

a. Organoleptic test
   In this evaluation, the color, odor and texture were observed organoleptically after a freeze-thaw stability test was carried out. The results obtained by formula 1 showed no color change with a distinctive ointment odor and no rancidity, however the texture of the ointment was less smooth and oily. Formula 2 in terms of color has no color change with the result being a brown ointment, the odor has not changed, with a typical povidone - iodine smell and a soft and smooth texture. In terms of color, Formula 3 has no color change with the resulting gel being blackish brown, but from day 1 to day 18 there are air bubbles in it. The odor produced does not change where it smells typical of povidone – iodine and does not experience rancidity and has a soft and soft texture fine.

Table 2. Organoleptic test results for formula 1, formula 2 and formula 3

Days to	Temperature	Parameter	Cycle	Results		
				F1	F2	F3
1 - 18	4°C, 27°C, 40°C	Form	1 - 6	chocolate ointment	Chocolate ointment	The gel contains bubbles
		Smell		typical vaseline	typical of povidone	typical of povidone
		Texture		Bit rough	gentle	gentle

c. Homogeneity Test

Based on the results of observations during 6 storage cycles of the three formulas, it was found that formula 1 had poor homogeneity, while for formulas 2 and 3 the homogeneity results were good. Formula 1 contains small granules that are not yet homogeneous with the base so that when applied to the surface of the skin it feels a little rough.

Table 3. Homogeneity test results for formula 1, formula 2 and formula 3

Days to -	Temperature	Cycle	Results		
			F1	F2	F3
1, 2 and 3	4°C, 27°C and 40°C	1	0	+ 1	+ 1
4, 5 and 6	4°C, 27°C and 40°C	2	0	+ 1	+ 1
7, 8 and 9	4°C, 27°C and 40°C	3	0	+ 1	+ 1
10, 11 and 12	4°C, 27°C and 40°C	4	0	+ 1	+ 1
13, 14 and 15	4°C, 27°C and 40°C	5	0	+ 1	+ 1
16, 17 and 18	4°C, 27°C and 40°C	6	0	+ 1	+ 1

Information :
+ 1 : Homogeneous
0 : Less homogeneous
- 1 : Inhomogeneous

d. Spreadability Test

The spreadability test carried out for 6 cycles for formula 1, formula 2 and formula 3 had a spreadability ranging between 3 cm – 5 cm. Formula 3 has the highest spreadability compared to formulas 1 and 2. Formulas 1 and 2 have more or less relatively the same spreadability. The spread power results for formula 1, formula 2 and formula 3 have stable spread power values because they are in the UCL (Upper Control Limit) and LCL (Lower Control Limit) range using the I-MR control chart. The statistical test results have a significant p-value of 0.000, where the difference in base can affect the stability value of the spreadability of each formula because the p-value is < 0.05 (Yetti, 2019).

Table 4. Spreadability test results for formula 1, formula 2 and formula 3

Cycle	F1 (cm)	F2 (cm)	F3 (cm)
1	3.37	3.41	4.46
2	3.31	3.28	4.22
3	3.11	3.32	4.26
4	2.96	3.32	4.10
5	2.93	3.22	4.01
6	3.00	3.20	4.26
Average	3.11	3.29	4.21

e. Viscosity Test

Based on the results of observations made over 6 cycle with storage temperature different, we get differences in viscosity between formulas. Formula 1 with a base of alba vaseline has the highest viscosity, meanwhile formula 3 gel based on carboxymethyl cellulose has the lowest viscosity and formula 2 with a PEG base has a viscosity between the two. Viscosity observation results for formula 1, formula 2 and formula three using *control – charts* I-MR obtained that the viscosity value was at the UCL (Upper *Control Limits*)
and LCL (Lower Control Limit) which shows the stable viscosity value for each formula. The test results using analysis of variance show a p-value of 0.000 where the value is < 0.05 which shows that the basis influences the viscosity value of each formula. The table of analysis of variance test results for viscosity evaluation is in Appendix 15 (Yetti, 2019).

Table 5. Viscosity test results for formula 1, formula 2 and formula 3

Cycle	F1 (cps)	F2 (cps)	F3 (cps)
1	8523.67	8421.33	6502.23
2	8440	8222.33	6584
3	8577.33	8217.67	6550.33
4	8639	8133.67	6530
5	8663	8134.50	6374
6	8369.67	8181.67	6420.33
Average	8535.40	8094.50	6493.50

f. pH

Based on the results of observations made during 6 cycles at different storage temperatures, pH differences between formulas were obtained. The results of observations processed using the I-MR control chart from formula 1, formula 2 and formula 3 obtained good stability results because they were at the UCL (Upper Control Limit) and (Lower Control Limit) values. Testing using the analysis of variance method of the three formulas has a p-value of 0.000 where the difference in base affects the pH value of each formula because it has a p value-*value* < 0.05 (Yetti, 2019).

Table 6. pH test results for formula 1, formula 2 and formula 3

Cycle	F1	F2	F3
1	4.05	3.86	4.62
2	3.92	3.87	4.50
3	3.96	3.87	4.51
4	4.02	3.99	4.61
5	3.91	3.84	4.63
6	4.16	3.77	4.49
Average	4.03	3.87	4.56

g. Cost evaluation

The cost of raw materials used in this thesis is used as a metaphor, the possibility of price fluctuations can occur and there are price differences from each source and confidentiality from the company. This formula is made in preparations per 10 grams, as a benchmark, the maximum price used as a control and comparison is IDR – Z. The total price of each formula is compared with the control price to see the cost of each formula. The calculation results of formula 2 have the highest costs, while formula 3 has the lowest total price and formula 1 is between the two.

Discusions the results of observations using the freeze - thaw stability test method carried out in 6 cycles for 18 days with 3 different temperatures, namely at 4°C, 27°C and 40°C, were obtained for organoleptic tests for formula 1 hydrophobic base using Vaseline Alba and formula 2 hydrophilic bases using PEG 400 and PEG 4000 bases have good stability, indicated by the absence of physical changes, odor and texture of the ointment, but formula 3 gels with CMC Na base have poor organoleptic results, indicated by the presence of air bubbles in the gel. This is because this base produces a colloidal dispersion in the water which forms spots or bubbles in the gel (Ellsy, 2024).

Homogeneity observations for formulas 2 and 3 had good homogeneity and good stability because during the observation there were no coarse grains on the glass object. Formula 1 has poor stability as indicated by the presence of substances that do not mix with the base and is a little rough when applied, this is because the active ingredients are not dispersed into the base. A homogeneous ointment is characterized by the active substance being evenly dispersed in the base (Rina, 2014).

The results of observing the spreadability using the I-MR control chart for formula 1 obtained an average value of 3.11 cm, a UCL (Upper Control Limit) value of 3.38 cm and an LCL (Lower Control Limit) value of 2.84 so that the spreadability value was at the upper control limit and lower control limit. Formula 2 obtained an average value of 3.29 cm, the UCL (Upper Control Limit) value or upper control limit was 3.45 cm and the LCL (Lower Control Limit) value or lower control limit was 3.14 cm so that the results of the dispersion power There are no values that are outside the upper or lower control limits so that formula 2 has a stable spread power value. Formula 3

obtained an average value of 4.21 cm from 6 cycles, the UCL (Upper Control Limit) value or upper control limit was 4.63 cm and the LCL (Lower Control Limit) value or lower control limit was 3.80 cm so that from The spread power results for 6 observation cycles have no values that are outside the upper or lower control limits so that formula 3 has a stable spread power value. Observation of viscosity for 6 cyclesprocessed using the I-MR control chart for formula 1, the UCL (Upper Control Limit) or upper control limit value was obtained at 8854.6 cps and the LCL (Lower Control Limit) value or lower control limit was 8216.3 cps and the value an average of 8535.4 cps from 6 cycles for formula 1, there are no values outside the upper control limit and lower control limit, indicating that formula 1 has good viscosity stability values. Formula 2 obtained a value of UCL (Upper Control Limit) or upper control limit which obtained a value of 8293.4 cps and an LCL (Lower Control Limit) value or lower control limit obtained a value of 8094.5 cps and an average value of 8193.9 cps from 6 cycles For formula 2 there are no values outside the upper control limit and lower control limit, indicating that formula 2 has good viscosity stability values. Formula 3 obtained a value of UCL (Upper Control Limit) or upper control limit obtained a value of 6673.30 cps and an LCL value (Lower Control Limit) or lower control limit obtained a value of 6313.60 cps and an average value of 6493.50 cps from 6 cycles For formula 3 there are no values outside the upper control limit and lower control limit, indicating that formula 3 has good viscosity stability values. The results of pH observations during 6 storage cycles processed using the I-MR control chart for formula 1 obtained a UCL (Upper Control Limit) value or upper control limit of 4.31 and an LCL (Lower Control Limit) value or lower control limit of 3.69 and an average value of 4.03 from 6 cycles for formula 1, there are no values outside the upper control limit and lower control limit, indicating that formula 1 has a good pH stability value. For formula 2, the UCL (Upper Control Limit) or upper control limit value was 4.05 and the LCL (Lower Control Limit) or lower control limit value was 3.68 and the average value was 3.87 from 6 cycles for formula 2 There are no values outside the upper control limit and lower control limit, indicating that formula 2 has good pH stability values. Formula 3 obtained a UCL (Upper Control Limit) value or upper control limit value of 4.77 and an LCL (Lower Control Limit) value or lower control limit value of 4.35 and an average value of 4.56 from 6 cycles for formula 3 There are no values outside the upper control limit and lower control limit, indicating that formula 3 has good pH stability values. Statistical results using the one way ANOVA method from the results of the spreadability, viscosity and pH tests have a p-value of 0.000 where the different bases in the formula affect the resulting spreadability, viscosity and pH values because they have a p-value < 0.05 (Yetti , 2019).

Formula 2 is said to have good stability because the results of organoleptic observations, homogeneity, spreadability, viscosity and pH show good stability results, in contrast to formula 1 which has poor stability results and formula 3 has poor organoleptic results. In the cost evaluation, formula 2 has a higher cost than formula 1 and formula 3.

4. CONCLUSIONS AND SUGGESTIONS

From the results of research carried out, differences in base formulas influence the stability results (organoleptic, homogeneity, spreadability, viscosity and pH) of hydrophobic base ointments, hydrophilic base ointments and CMC Na base gels with the main substance povidone – iodine and of the three formulas observed, formula 2 has higher raw material costs and has better stability.

Suggestions for this research require further research regarding the optimization of formula 2 with different base concentrations on the resulting stability and

costs so that cost effectiveness can be obtained and in vitro and in vivo studies of formula 2 are needed to determine the antiseptic activity of the formula.

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