

EFFECT OF COMBINATION OF CARBOPOL-940 BASE AND HPMC GEL EXTRACT OF ALOE VERA FLESH ON PHYSICAL PROPERTIES AND ANTIBACTERIAL ACTIVITY OF PROPIONIBACTERIUM ACNES

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ABSTRACT

Aloe vera (*Aloe chinensis* Barker.) has been shown to be efficacious as an antibacterial which has the potential to treat acne caused by the bacteria *Propionibacterium acnes*. The use of this combination can increase the viscosity, dissolution, diffusion, and bioavailability of the preparation. This study aims to determine the effect of the combination of Carbopol base and HPMC as a gelling agent on the physical properties and antibacterial activity of aloe vera gel against *P. acnes* bacteria. Aloe vera flesh extract was obtained using 70% ethanol maceration method. The gel preparation has an active substance concentration of 0.50% using a combination base of Carbopol:HPMC with a ratio of 1.00:0.50; 0.75:0.75; and 0.50:1.00. The tests included tests of adhesion, dispersibility, and viscosity as well as measurement of antibacterial activity by measuring the diameter of the inhibition zone formed on the media. The resulting data from the physical properties of the gel were analyzed by linear regression correlation. While the data on the results of the antibacterial activity were analyzed by statistical tests using the ANOVA method. The results showed that with increasing concentration of HPMC, the adhesive power and viscosity decreased, but the dispersion power increased. The three gel formulations had different zones of inhibition due to differences in diffusion that occurred in the test medium.

Keywords: Aloe Vera, Gel, *Propionibacterium Acnes*.

PRELIMINARY

Aloe vera (*Aloe chinensis* Barker.) empirically has efficacy in skin care and cosmetics because aloe vera has antifungal, antiviral, and antibacterial activity so that it can treat skin infections such as acne, herpes, and scabies (Kumar et al., 2010; Bashir et al., 2011; Rajeswari et al., 2013; Chatterjee et al., 2019). Specific ingredients

that have antibacterial activity in aloe vera are anthraquinones and saponins (Arunkumar et al., 2009). Anthraquinone compounds are phenolic compounds found in the sap of aloe vera flesh (TBreathpathi et al., 2010; Thu et al., 2013). Research by Bashir et al., (2011) showed that aloe vera flesh was 100% effective against Gram-

negative bacteria and 75.3% against isolated Gram-positive bacteria (Bashir et al., 2011). This is confirmed by the research of Sawarkar et al., (2010) which stated that aloe vera meat inhibited the growth of *Propionibacterium acnes* by an average of 8.4 mm and the research of Tistripathi et al., could inhibit the growth of *Staphylococcus aureus* by 18 mm (Sawarkar et al., 2010; Tjiwapathi et al., 2010).

Based on the above, aloe vera has the potential to be formulated into topical preparations (Riddle, 2007). One of the effective dosage forms for topical application is gel with various combinations of Carbopol and HPMC bases. The Carbopol-HPMC comparison (2:1) gives a higher percentage of drug diffusion when compared to the Carbopol-HPMC formulation with a lower ratio or single use of both Carbopol and HPMC (Quinones & Ghaly, 2008). In addition, these two hydrogels are very suitable for topical preparations with excess sebaceous gland function (Voigt, 1984). Some of the advantages of Carbopol are that it is compatible with various active substances, is bioadhesive, has stability, organoleptic characteristics and good patient acceptance, while HPMC is inert, does not cause skin irritation, has good resistance to microbial attack, and provides film strength. which is good when it dries on the skin (Islam et al., 2004; Quinones & Ghaly, 2008; Panjaitan et al., 2012).

Based on the above reference, the next problem is how to realize herbal products in the form of gel preparations from aloe vera flesh extract which can be immediately used as an antibacterial with good effectiveness, safety, without significant side effects and

economical prices. This thought motivated and prompted researchers to conduct research on the effect of the combination of Carbopol and HPMC in aloe vera flesh extract gel on the physical properties and antibacterial activity of *Propionibacterium acnes*.

LITERATURE REVIEW

Acne is a skin disease that often occurs in adolescence to adulthood which is characterized by the presence of blackheads, papules, pustules, nodes, and cysts on the face, neck, upper arms, chest, and back. Acne can affect a person's quality of life by giving a bad psychological effect in the way a person assesses, perceives and responds to his condition and situation. In normal skin conditions, there is often a buildup of dirt and dead skin cells due to lack of care and maintenance, especially in skin that has a high rate of oil reproduction. As a result, the hair follicles become clogged, resulting in comedones (Ravisankar, et, all. 2015).

The dead skin cells and dirt that have accumulated are then exposed to acne bacteria, resulting in acne. Untreated acne will develop swelling (enlarged and reddish) called papules. When the inflammation gets worse, white blood cells begin to rise to the surface of the skin in the form of pus (pus), these pimples are called pustules. Inflammatory acne occurs because the follicles in the dermis expand because they contain solid fat, then rupture, causing an invasion of white blood cells to the sebaceous follicle area, resulting in an inflammatory reaction. Inflammatory acne has the characteristics of being red, rapidly growing, filled with pus and painful.

If the pustules are not maintained, the collagen network will be damaged to the dermis layer, so that the skin or face becomes scarred (Titik, H. 2018).

METHOD

Ingredients

Aloe vera (*Aloe chinensis* Barker.) was obtained from Parung, Bogor. Ingredients such as Carbopol 940 (Chemical Material), Hydroxypropyl Methylcellulose 606 (Chemical Material), 70% ethanol (brataco), and distilled water (brataco). Meanwhile, materials

with analytical quality were used from Merck such as ethyl acetate, methanol, and KOH. Media Nutrient agar (Oxoid®), silica gel 60 GF254 (Merck), and bacteria *Propionibacterium acnes* ATCC 11827 (Thermo Scientific).

Extract

Identification Identification was carried out to verify the extract used in various ways such as organoleptic testing, concentration of residual solvent, and qualitative thin layer chromatography, as well as the antibacterial activity of the extract.

Formula

Table 1. Formula aloe vera gel preparation

Ingredients	FI	FII	F III
Aloe vera extract (%)	0.50	0.50	0.50
HPMC (%)	0.50	0.75	1.00
Carbopol (%)	1.00	0.75	0.50
TEA (%)	1.00	1.00	1.00
Propylene glycol	10.00	10.00	10.00
Glycerin	10.00	10.00	10.00
Aquadest (mL) ad	100.00	100.00	100.00

Evaluation

Spreadability test

A sample of 1.00 g of gel is placed in the center between two round glass scales, where the glass at the top is loaded by placing weights in succession starting from 50 g, 100 g, 200 g, 300 g, 400 g, 500 g, and 1 kg for 1 minute each per weight. Measurements were carried out until the diameter of the gel spread was constant. Good

spreadability ensures even distribution of the gel when applied to the skin. This procedure was carried out in triples (Roudhatini, 2013).

Adhesion test

A total of 0.50 grams of gel is spread on one object glass and then covered with another object glass. At the top was given a load of 1 kg for 5 minutes. This pair of

object glasses is mounted on a stickiness tester, and simultaneously the time it takes for 2 glass objects to be separated or separated is recorded. This procedure was carried out in triples (Roudhatini, 2013).

Viscosity measurement

The preparation of aloe vera flesh extract was measured for viscosity using a Brookfield viscometer with a suitable spindle. Measurements were carried out 3 times for each gel preparation (Wathoni et al., 2009).

Antibacterial activity of the gel

The aloe vera flesh extract gel that had been prepared was tested for its activity in three replications. The turbidity level of the bacterial inoculum suspension aged 3x24 hours was measured according to the standard McFarland 0.50 (108CFU/mL). 200 L of bacterial suspension was planted on each 20 mL TSA medium in 3 petridisks. The surface of the media was made using the method of wells with a diameter of 8 mm as many as 5 holes with a minimum distance of 20 mm for each hole. 0.10 g of gel was added to each well made. Incubated for 3x24 hours in an incubator with the help of a catalyst and an indicator that makes the atmosphere anaerobic at 37oC, the inhibition of the gel can be calculated by looking at the inhibition zone formed.

Data Analysis

Obtained from the calculation of the physical properties of aloe vera gel were analyzed using linear regression correlation, namely by looking at the value of the standard curve equation that was formed.

Meanwhile, the data for the antibacterial activity test results of *Propionibacterium acnes* from aloe vera flesh extract gel were statistically tested using the one-way ANOVA method with confidence intervals 95%.

RESULT

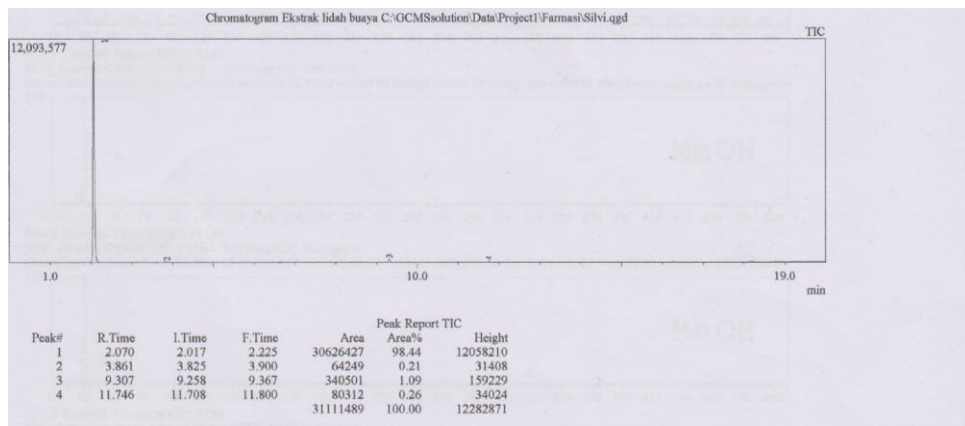
Extract Identification

Based on the research, it was found that the color of the extract was brown and had a distinctive smell of aloe vera flesh (Table 2). After testing the solvent concentration with GC-MS, it was found that the thick extract of aloe vera meat did not have ethanol as a solvent. This is evidenced by a peak that reads only methanol as the internal standard (appendix 1). And when tested with qualitative TLC, there were red violet spots after being sprayed with 5% KOH. The presence of red spots is possible in the results of aloe vera flesh extract containing anthraquinone compounds. This is also reinforced by Harborne (1987) that after spraying the plate using a KOH solution, the color which was originally yellow changes to red, purple, green or violet (Harborne, 1987). From the preliminary test of extract activity, it is known that the concentration of 12.50 mg/mL is the smallest concentration that gives a zone of inhibition. The amount of extract that was inserted into *the paper disk* was 20 L so that it could be seen that the concentration contained was 250 mg, this concentration could be known as *the minimum inhibitory concentration (MIC)*. The dose used is twice the MIC, so that in 100 g the preparation contains 500 mg of extract.

Table 2. Extract identification test data

Parameter	Description
Color	Brown
Odor	Characteristic of aloe vera flesh
Form	Thick liquid textured
Solvent concentration	No residual solvent
TLC test (qualitative)	Red Spots (after 5% KOH spray)
Antibacterial activity	MIC 250mg

Appendix 1. Results of Residual Solvent Levels



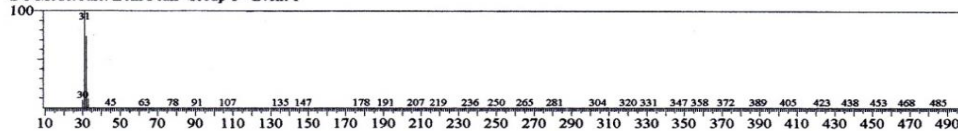
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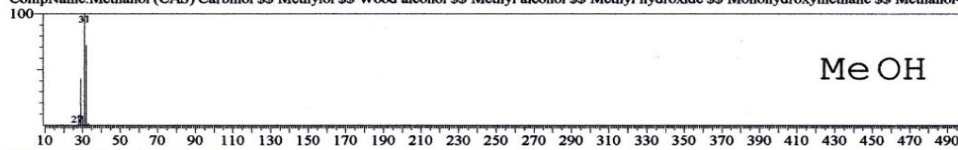
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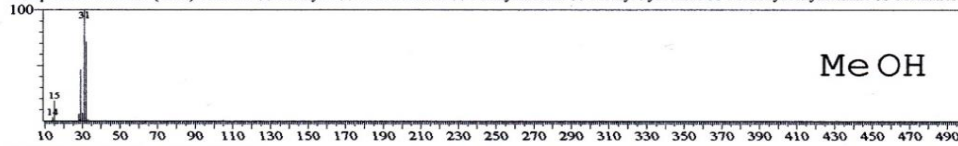
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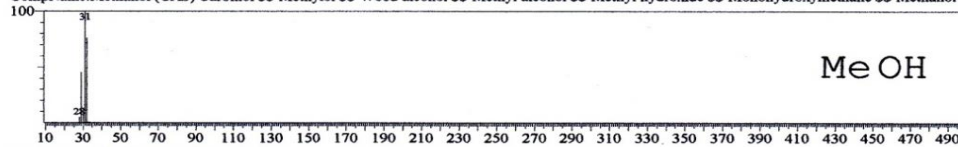
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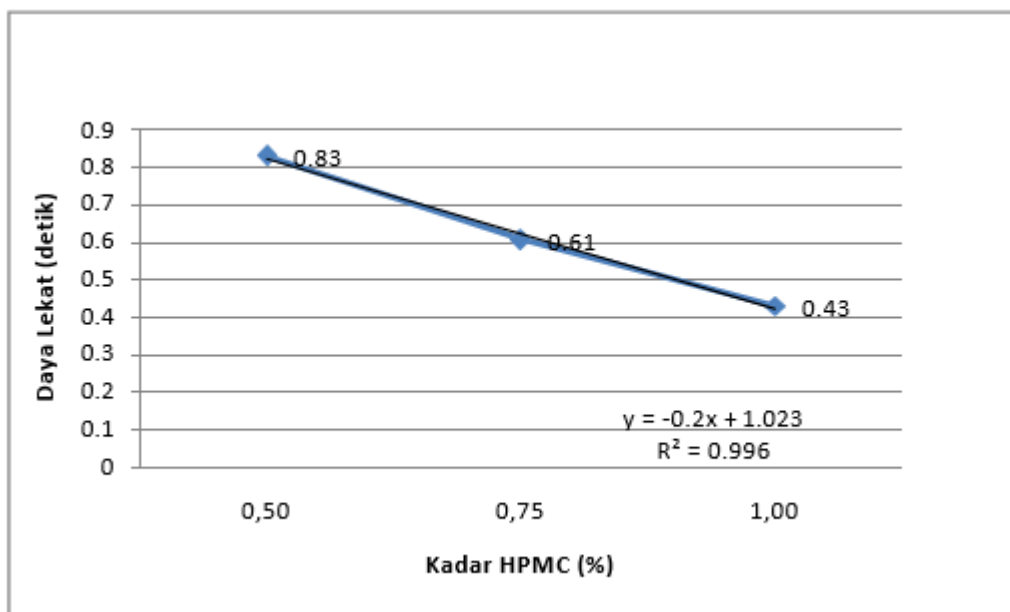
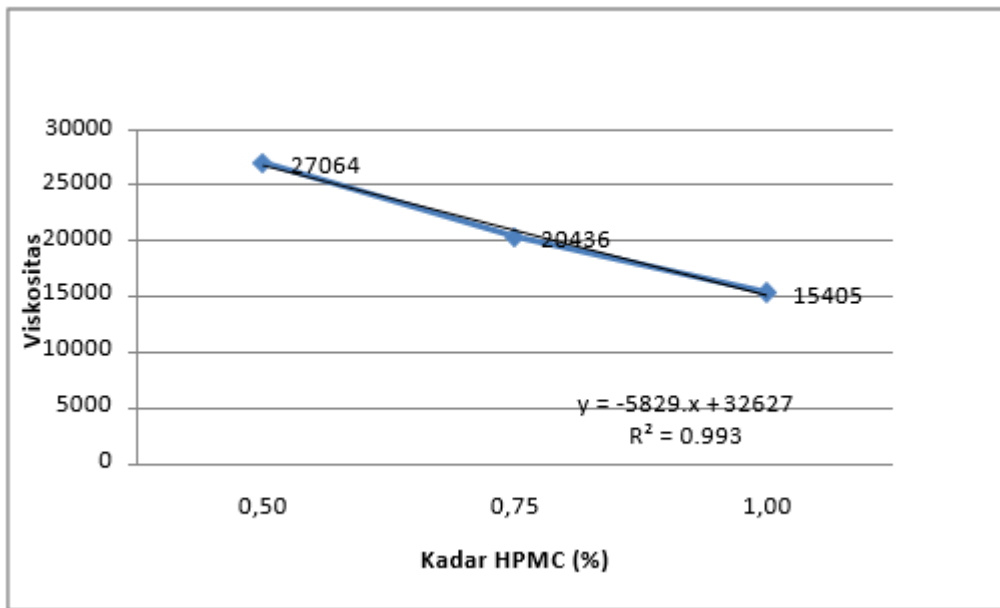
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SI:97 Formula:C H4 O CAS:67-56-1 MolWeight:32 RetIndex:0

CompName:Methanol (CAS) Carbinol \$\$ Methylol \$\$ Wood alcohol \$\$ Methyl alcohol \$\$ Methyl hydroxide \$\$ Monohydroxymethane \$\$ Methanol-w



Appendix 2. Equation of Evaluation Linear Regression



Appendix 3

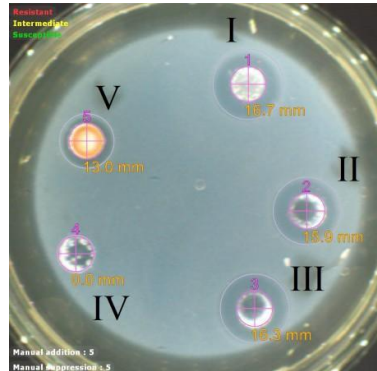


Figure 1. Diffusion test results of wellness of aloe vera gel

Remarks :

Hole 1: Carbopol:HPMC (1.00:0.50%)

Hole 2: Carbopol: HPMC (0.75:0.75%)

Hole 3: Carbopol:HPMC (0.50:1.00%)

Hole 4: No active substance Carbopol:HPMC (1.00:0.50%)

Hole 5: Control positive 2.50%

DISCUSSION

Testing Gel Preparations

Table 3. Gel Preparation Test Results

Gel	X±SD		
	Spreadability (cm)	Adhesiveness (seconds)	Viscosity (cPs)
F I	5.01±0.07	0.83±0.03	27064±329.09
F II	5.53±0.15	0.61±0.03	20436±159.79
F III	6.66±0.13	0.43±0.03	15405±194.85

Spreadability Test The

dispersion power is directly proportional to the speed of the gel to spread. Based on these results, it can be concluded that variations in the combination of Carbopol and HPMC bases affect the physical properties of the preparation. At F I (1.00; 0.50%) it has the lowest

dispersion of 5.01 cm and then there is an increase in dispersion in F II (0.75; 0.75%) by 5.53 cm and F III (0.50;1.00%) by 6.66 cm. Based on the results above, the dispersion of the gel can be said to be good because it is in the range of 5-7 cm (Garg *et al.*, 2002). Factors that

affect the spreadability of the gel is the amount and strength of the gel matrix. The more and stronger the gel matrix, the lower the dispersion of the gel. *The gelling agent* is responsible for the gel matrix. The increase in concentration will increase and strengthen the gel matrix. Therefore, the dominant factor that determines the dispersion response is the concentration of Carbopol in the base (Roudhatini, 2013). Linear regression correlation analysis obtained the equation $Y=0.825x+4.0833$ (appendix 2), where X is the basis for HPMC, Y is the dispersion, with a positive b value (0.825). So it can be concluded that the higher the concentration of HPMC, the higher the spreadability of the gel.

Adhesiveness

The test aims to determine the ability of the gel to adhere and coat the skin surface so that it can function optimally. The greater the value of adhesion, the greater the diffusion of the drug because the bond that occurs between the gel and the skin is getting longer, so that the gel can give the expected effect. In table 3 it can be seen that there is a decrease in gel adhesion. FI has a higher adhesion yield of 0.83 seconds compared to FII of 0.61 seconds, and FIII which is only 0.43 seconds. This could be due to the fact that FI is a formula that has

the highest Carbopol concentration of 1.00%, resulting in a thicker gel and resulting in higher adhesion than other formulas.

Linear regression correlation data showed that there was an effect of the combination of HPMC and Carbopol on the stickiness of aloe vera gel. It can be seen that the results of the linear regression equation are $Y=-0.2x+1.0233$, thus it can be said that with the increase in the concentration of HPMC base in aloe vera gel, there is a decrease in adhesion.

Viscosity

From the results of Table 3 shows that variations in base combinations can affect the viscosity of each formula. The viscosity values of aloe vera flesh extract gel FI, FII, and FIII were 27,064 cPs, 20,436 cPs, and 15,405 cPs. The results of the examination of the three formulations can be concluded that the more the amount of Carbopol used and the less HPMC added, the thicker the preparation will be and will have an impact on the higher the viscosity. The linear regression correlation data shows that there is an effect of HPMC as a basis with increasing gel viscosity. It can be seen that the linear regression equation is $Y=-5829.5x+32627$. The higher the HPMC concentration, the lower the viscosity (b=-5829.5).

Activity Test

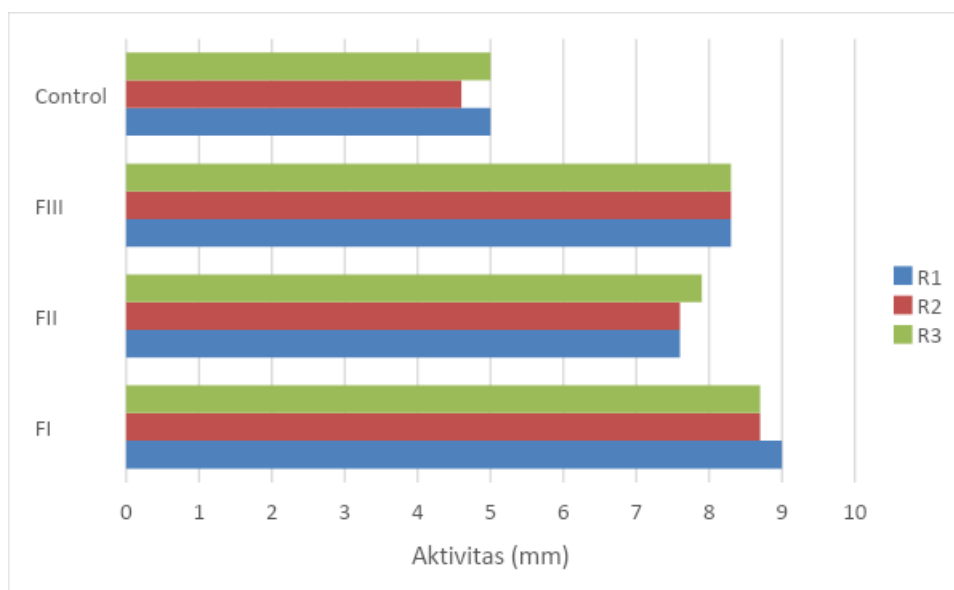


Figure 1. Gel Antibacterial Activity Test Results

Based on the results of statistical tests using the *one-way* ANOVA method, it showed a significance value of 0.003 ($p < 0.05$). This shows that there is a significant difference. Furthermore, the *Post hoc Tukey* which showed that the aloe vera extract gel with a combination of Carbopol and HPMC bases had significantly different antibacterial activity ($p < 0.05$) and was greater than that of the positive control. FI gave the

greatest activity with an inhibitory power of 8.80 ± 0.17 and was classified in the medium category, while the positive control was included in the weak category with an inhibitory power of 4.86 ± 0.23 (Davis & Stout, 1971). This is in accordance with the journal Quinones *et al.*, (2008) which states that the use of a combination of Carbopol: HPMC (2:1) will increase the dissolution and diffusion of the drug (Quinones *et al.*, 2008). *Propionibacterium acnes* ($p < 0.05$).

CONCLUSION

Variations in the combination of Carbopol and HPMC in the gel preparation of aloe vera flesh extract can affect the physical properties of the gel. The higher the concentration of HPMC used, the lower the viscosity and adhesion, while the spreading power increases. Gel preparations with variations in the combination of Carbopol and HPMC had activity with the positive control against

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