

POTENTIAL NANO GEL AVOCODO SEED EXTRACT AS AN ALTERNATIVE RELIEF IN WOUNDS AFTER REMOVAL OF WHITE RATS TOOTH

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Abstract. Inflammation, bleeding, swelling, pain, dry socket are common complications of tooth extraction. The inflammatory response is divided into two, including the administration of non-steroidal anti-inflammatory drugs (NSAIDs) and steroid anti-inflammatory drugs. Every use of chemical drugs has side effects. Herbal ingredients are needed, namely avocado seeds as an alternative treatment in preventing inflammation in wounds after tooth extraction. Avocado seeds contain polyphenols that play a role in inflammation in wounds, including flavonoids, alkaloids, tannins, and saponins. Experiment with randomized posttest design with control group design. Consisting of intervention group nano gel avocado seed extract 10%, positive control group povidone iodine 10% and aquadest. Observations were made for 7 days. The variables studied were inflammation of the wound after tooth extraction of rats and histopathological examination (Lymphocytes, Neocapillary and Fibroblasts). Based on the results of the unpaired test, the avocado and povidone groups were not significantly different ($p=0.143$), the avocado and aquadest groups had a significant difference ($p=0.001$) and the povidone and aquadest groups had a significant difference ($p=0.015$). The administration of nano gel of avocado seed extract with a concentration of 10% and 10% povidone iodine has the same ability in the process of wound regeneration and increases new blood vessels and can also reduce the number of lymphocyte inflammatory cells as evidenced by histological examination. The administration of nano gel of avocado seed extract is effective and can be applied as an alternative to prevent inflammation in wounds after tooth extraction in white rats.

Keywords: potential; nano gel avocado seed extract; inflammation wound extraction.

INTRODUCTION

Dental and oral health is one part of body health that cannot be separated from each other, because dental and oral health can affect overall body health.

The presence of dental and oral diseases can affect general health, although it does not cause death directly. Dental & oral health is generally not a priority for some people, and in fact teeth and mouth are the gateway for germs or bacteria to enter as a result can damage the health of other body organs ([Hasiru et al., 2019](#)); ([Laily et al., 2021](#)).

From Basic Health Research data in 2018 that the proportion of dental & oral health problems and getting services from medical personnel in Indonesia is 57.6%, ([Laily et al., 2021](#)) and the tooth extraction rate in Indonesia reaches 7.9%. Meanwhile, the tooth extraction rate in Central Java in 2018 reached 5.2%. ([Lumunon et al., 2019](#)) ([Kemenkes, 2018](#)).

Tooth extraction is a the process of removing a tooth from the alveolus, in which the tooth can no longer be treated and can no longer be maintained. In the act of tooth extraction complications can occur caused by local or systemic factors of the patient and ([Winiswara et al., 2021](#)); ([Lande et al., 2015](#)). Complications due to wounds after tooth extraction that are often found are classified as intraoperative, after extraction and long after extraction. Bleeding, swelling, pain, dry socket, fracture, and mandibular dislocation are complications that are commonly found due to tooth extraction. ([Lande et al., 2015](#)).

Post-extraction of teeth can not be

separated from the formation of a wound or hole called a socket. The basic response to damage or injury after tooth extraction is inflammation, which then proceeds in the process of tissue repair, namely the replacement of dead cells with living cells from fibrous tissue. The main cells involved in the wound healing process are fibrous. When the tissue becomes inflamed, fibroblasts immediately migrate to the wound area, multiply and produce a collagen matrix to repair damaged tissue ([Khairunnisa et al., 2018](#)).

Currently, research using herbal ingredients is the focus of researchers. c. Avocado plant (*Persea Americana mill*) is one of the most widespread plants in Indonesia. This study used avocado seeds (*Persea Americana mill*) as an alternative treatment to prevent inflammation in wounds after tooth extraction. Avocado seeds contain several polyphenols that play a role in the process of preventing inflammation in wounds, including flavonoids, alkaloids, tannins, and saponins ([Amelia et al., 2017](#)).

Research conducted by Asep, et al. The effectiveness test of avocado leaf extract with a concentration of 5% w/w showed the best effectiveness on wound healing after 5 days. (8) Research conducted by Sastya, et al. effectiveness of banana tree sap extract (*Musa paradisiaca*) whose content or compounds are the same as avocado seeds is effective and also effective and optimal in the process of accelerating the healing of socket wounds after tooth extraction. Research conducted by ([Lande et al., 2015](#)). The effect of avocado seed extract (*Persea Americana mill*) on bleeding time in cutting

the tail of mice (Strain Balb-c) has an effect on the acceleration of bleeding time, compared to negative controls ([Winiswara et al.](#), 2021).

Based on the above background, this study was conducted to prove the potential of avocado seed extract nano gel as an effort to prevent inflammation in wounds after tooth extraction and has great effectiveness as anti-inflammatory, antibacterial, antioxidant and antimicrobial.

Previous studies that have a similar discussion are research conducted by ([Bujung et al.](#), 2017) with the aim of knowing the inhibition of avocado seed extract (*Persea Americana mill*) on the growth of *Streptococcus mutans*. The results of the study stated that avocado seed extract had a very strong inhibitory effect on the growth of *Streptococcus mutans*.

Research conducted by ([Putri](#), 2017) aimed to determine the effectiveness of administration of avocado seed extract on the growth of *Streptococcus viridans* bacteria. The results showed that avocado seed extract had an antibiotic effect against *Streptococcus viridans* at a concentration of 50% with an inhibitory diameter of 19.49 mm, a concentration of 25% had an average diameter of 14.57 mm, a concentration of 12.5% had an average diameter of inhibition. an average of 13.03 mm, a concentration of 6.25% has an average inhibitory diameter of 11.25 mm.

Research conducted by ([Malangngi et al.](#), 2012) with the aim of determining the tannin content and testing the antioxidant activity of fresh and dried avocado seed extract. The results showed that the highest

antioxidant activity was shown by the extract of ordinary dried avocado seeds (93.045%), followed by dry butter avocado seeds (92.970%), fresh ordinary avocado seeds (85.870%) and fresh butter avocado seeds (67.645%). Avocado seeds have a high percentage of antioxidant activity so they can be considered as a source of natural antioxidants.

Other relevant research was conducted by ([Zakiah et al.](#), 2021) which aims to obtain a good formulation and physical stability, antioxidant power and the effect of different HPMC on antioxidants. The results of avocado seed extract research based on linear regression test using SPSS application showed that there was an effect of HPMC differences on viscosity and antioxidant power.

This research is a new innovation using nano avocado seed extract (*Persea Americana mill*) which is made into a gel preparation. The difference between this study and other studies is that the dependent variable only examines the effectiveness of avocado seed extract on the growth of streptococcus and also the anti-inflammatory activity contained in avocado seeds.

Based on the above background, this study was conducted to prove the potential of nano gel of avocado seed extract (*Persea Americana mill*) and can be applied as an alternative to prevent inflammation in wounds after tooth extraction of white rats (*Rattus Norvegicus wistar*), analyze the effectiveness of nano gel of fruit seed extract. avocado (*Persea Americana mill*) with 10% concentration and 10% povidone iodine on the prevention of wound

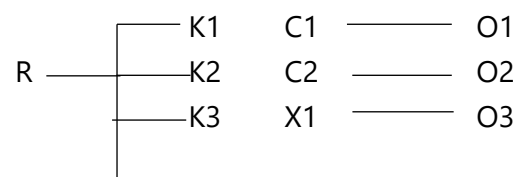
inflammation after tooth extraction of white rats (*Rattus Norvegicus wistar*) and knowing the histopathological description of gingival tissue between the use of nano gel of avocado seed extract with a concentration of 10% (*Persea Americana mill*) and 10% povidone iodine on days 3, 5 and 7 on wounds after tooth extraction of white rats (*Rattus Norvegicus wistar*).

METHODS

Research will be carried out in May 2022 at the UNDIP Integrated Laboratory (bioano), Experimental Animal Laboratory of UNDIP Medical Faculty, UNDIP Medical Faculty Central Laboratory, UNDIP Histology Preparation Laboratory, and Diponegoro National Hospital. This study consisted of independent variables, namely nano gel avocado seed extract (*Persea Americana mill*), the dependent variable was inflammation of the wound after tooth extraction and histopathology of the injured gingival tissue. The sample required in this study amounted to 30 samples. However, only 24 samples will be observed with the reason that 6 other samples were sacrificed for histopathological examination on days 3,5 and 7.

The sampling method in this study was based on the inclusion and exclusion criteria set by the researcher. The inclusion criteria that have been set by the researcher are the sample using the type of white rat (*Rattus Norvegicus wistar*), male sex, body weight between 180-250 grams and age of about 2-3 months (adults). And the

exclusion criteria were that there were abnormalities that appeared in the rats in the form of abnormalities in the teeth and rats that died during the adaptation period. The type of research used is laboratory and field experiments, pure experiments with randomized posttest with control group design. research True experimental with randomized posttest with control group design can be described as follows (Notoatmodjo, 2018).



Information :

R : Randomization

K1 and K2 : Control group

K3 : Intervention group

C1 : Negative control group giving aquades

C2 : Positive control group giving povidone iodine 10%

X1 : Intervention group giving nano gel extract Avocado seeds concentration 10%

O1 : Posttest administration of distilled water

O2 : Posttest administration of povidone iodine 10%

O3 : Posttest administration of nano gel of avocado seed extract 10% concentration

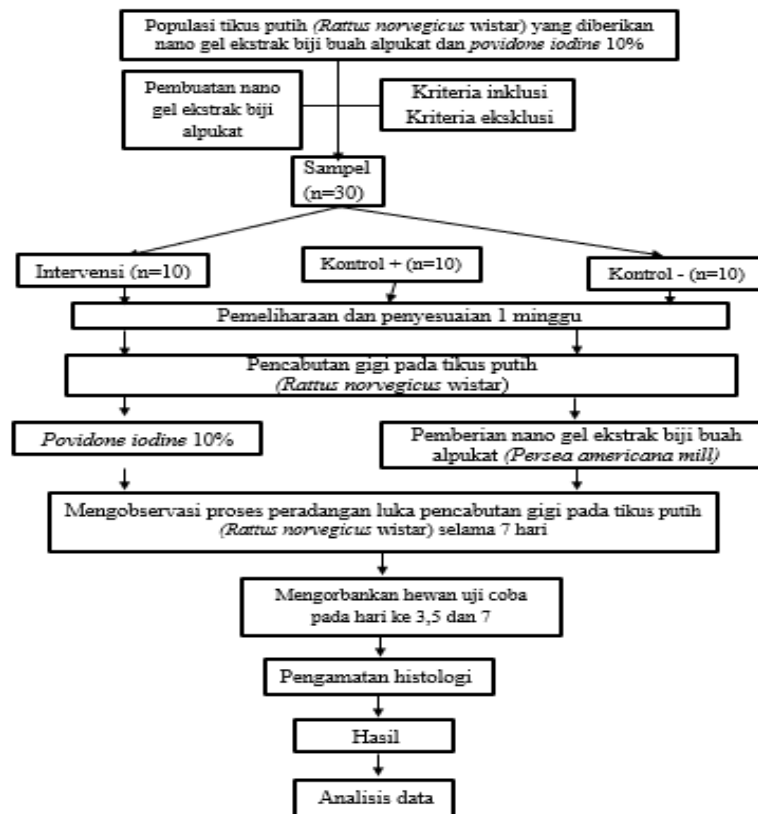


Figure 1. Research Flow Research

Results and Discussion

Reduction of inflammation in test animals seen from post-wound conditions tooth extraction according to a predetermined score, namely a score of 4 is severe inflammation, positive bleeding (not healed), a score of 3 is severe inflammation,

positive bleeding, a score of 2 is moderate inflammation, negative bleeding, a score of 1 is mild inflammation, negative bleeding and a score of 0 is negative inflammation (cured). Then these results were proven by histopathological examinations on days 3, 5 and 7.

1. Data Analysis Presentation Description

Table 1. Results of Observation of Inflammation in Wounds After Rat Teeth Extraction On K1 Nano Gel Avocado Seed Extract

Day	Intervention Group (K1)									
	K1	K2	K3	K4	K5	K6	K7	K8	K9	K10
1	4	4	4	4	4	4	4	4	4	4
2	3	3	3	3	3	2	2	3	3	3
3	2	2	2	2	1	2	2	2	2	2
4	1	2	1	1	1	1	1	-	1	2
5	1	1	1	1	1	1	1	-	1	1
6	0	0	0	1	0	0	0	-	-	1
7	0	0	0	0	0	0	0	-	-	0

Table 1 shows that the intervention group was treated with the application of nano gel avocado seed extract concentration of 10% on day 3 of observation there is a score of 2 (moderate

inflammation), on day 5 of observation there is a score of 1 which means (mild inflammation) and on day 7 the observation shows a score of 0 which means the wound has no inflammation.

Table 2. Results of Observation of Inflammation in Wounds After Teeth Extraction of Rats on C+ (Povidone iodine 10%)

Day-Contr ol	group +									
	C+ 1	C+ 2	C+ 3	C+ 4	C+ 5	C+ 6	C+ 7	C+ 8	C+ 9	C+ 10
1	4	4	4	4	4	4	4	4	4	4
2	3	4	4	3	4	3	3	3	3	4
3	3	3	3	3	3	3	2	3	3	3
4	2	3	3	3	3	2	2	-	2	3
5	1	2	2	3	2	1	1	-	2	2
6	1	1	1	2	1	1	1	-	-	1
7	0	0	1	1	0	0	0	-	-	0

Table 2 shows that the C+ control group was positive with 10% Povidone iodine application treatment on day 1 3 observations there is a score of 3 (severe inflammation) meaning there is positive

bleeding, on the 5th day of observation there is a score of 2 which means (moderate inflammation) and on day 7 the observation shows a score of 0 which means the wound has no inflammation.

Table 3. Results of Observation of Inflammation in Wounds After Teeth Extraction of Rats on C- (Aquadest)

Day C	Control Group -									
	- 1	C- 2	3	C- 4	C- 5	C- 6	C- 7	C- 8	C- 9	C- 10
1	4	4	4	4	4	4	4	4	4	4
2	4	4	3	4	3	3	4	4	4	4
3	4	3	3	4	3	3	3	3	3	4
4	3	3	3	3	3	3	3	-	3	3
5	2	3	2	3	2	2	3	-	3	3
6	2	2	1	2	2	2	2	-	-	2
7	1	1	0	1	1	1	1	-	-	1

Table 3 shows that the C- negative control group with Aquadest application treatment on the 3rd day of observation contained a score of 4 (severe inflammation) means there is positive bleeding, on day 5 of observation there is a

score of 3 which means (severe inflammation) and on day 7 the observation shows a score of 1 which means the wound still has mild inflammation.

Table 4. Results of Observation of Lymphocyte Inflammatory Cells in Wounds After Teeth Extraction Rats

Field of view	K1 3	K1 5	K1 7	C+ 3	C+ 5	C+ 7	C-3 C-	5	C- 7
I	+2	+1	+2	+1	+1	+2	+3	+2	+4
II	+2	+2	+1	+1	+1	+1	+2	+3	+2
III	+1	+1	+1	+1	+1	+1	+2	+3	+3

Table 5. Observations New Blood Vessels (Neocapillaryzation) In Wounds After Teeth Extraction Rats

Visual Field	K1 3	K1 5	K1 7	C- 3	C- 5	C- 7	C+3	C+ 5	C+ 7
I	1	1	1	2	1	2	1	0	1
II	1	0	0	2	1	2	1	1	1
III	1	1	0	1	2	1	0	1	1

Table 6. Observations of Connective Tissue (Fibroblasts) in Wounds After Teeth Extraction

Field of View	Rats									
	K1 3	K1 5	K1 7	3	C- 5	7	C +3	C+ 5	C+ 7	
I	3	3	2	1	2	1	3	2	2	
II	3	2	3	1	1	1	3	2	2	
III	2	2	2	2	1	2	2	2	3	

Based on tables 4,5 and 6 show the final results of inflammatory cell observations lymphocyte, that is, there is a picture of a difference in the number of inflammatory cells of lymphocytes in K1, C+ and C-, and there is a picture of an increase in neocapillaryization in K1, C+ and C and an increase in fibroblasts on day 7 which

means fibroblasts are aligned with the wound surface.

2. Presentation of Inferential Data Analysis

a. Normality Test

Table 7. Normality Test

Chi	-Square Sig.
Nano gel avocado seeds 10%	0.001
Povidone iodine 10%	0.000
Aquadest	0.000

Based on the normality test of the data using the *Chi-Square* it was found that the 7th day data for all groups had an abnormal distribution (*Chi-Square* $p < 0.05$) so that p rejected and it can be concluded that the variable data did not spread following a normal distribution so that the 7th day data calculation used the

Mann-Whitney nonparametric statistical test.

b. Non-parametric Mann-Whitney

Table 8. Test of different groups of Avocado Seeds and Povidone

Treatment	N	Mean ±SD	P- Value
Avocado Seed	8	0.3750±0.494	0.143
Povidone	8		

Table 9. Different test groups of Avocado Seeds and Aquadest

Treatment	N	Mean ±SD	P-Value of
Avocado Seeds	8	0.3750±0.494	0.001
Aquadest	8		

Table 10. Different test groups of Povidone and Aquadest

Treatment	N	Mean ±SD	P-Value of
Povidone	8	0.3750±0.494	0.015
Aquadest	8		

Based on the unpaired test, prevention of increased inflammation in Wounds after tooth extraction of *Rattus norvegicus* white rats on day 7 can be observed:

The group that was given nano gel of avocado seed extract (*Persea Americana mill*) in preventing increased inflammation after tooth extraction had the same ability as the group given 10% povidone iodine with p value =0.143.

The group that was given nano gel of avocado seed extract (*Persea Americana mill*) in preventing an increase in inflammation after tooth extraction had a significant difference with the group given aquadest with p value = 0.001.

The group that was given 10% povidone iodine in preventing the increase in inflammation after tooth extraction had a significant difference with the group given aquadest with p value = 0.015.

Several studies have shown that avocado seed extract can improve the prevention process and can also reduce the risk of high inflammation in wounds after tooth extraction. Avocado seeds are known to contain polyphenolic compounds, flavonoids, which are good in helping the

process of preventing wound inflammation after tooth extraction. Flavonoids have biological and pharmacological activities, among others, are anti-inflammatory and protect blood vessels. The use of flavonoids in the health sector has been widely used in the treatment of inflammatory diseases.

Wounds after tooth extraction of rats in the positive control group (C+) could completely heal from inflammation on day 7 and wounds after tooth extraction of rats and in the intervention group (K1) could completely heal from inflammation on day 6. These results can also confirm that the hypothesis in this study can be accepted, namely that there are differences in the process of preventing wound inflammation after tooth extraction of rats in the positive control group and the intervention group.

In this study, the Particle Size Analyzer (PSA) test was used to measure the particle size distribution using the Dynamic Light Scattering (DLS) method using the Non-Invasive Back Scatter (NIBS) technique. 151.8 nm (nanometer), in these results are included in the nano size requirements because the nanoparticle size ranges from (10-1000 nm). With a touch of nano technology, it is expected that the active

substances will be able to penetrate cell walls. In the provision and use of avocado seed extract nano gel which synergizes the wound healing effect and anti-inflammatory effect of avocado seed extract nano gel will provide a better inflammation prevention effect and change pharmacogenetic properties and its pharmacogenomics to be faster ([Marhamah et al., 2014](#)).

Observations of lymphocyte inflammatory cells in the avocado seed extract nano gel group (*Persea Americana mill*) obtained on the 3rd day were less than 50 cells per field of view, then continued to decrease on the 5th and 7th days, which may be due to the acute inflammatory process occurring more rapidly so that on day 1 the lymphocytes which are inflammatory cells infiltrate the wound area more rapidly. On the 3rd, 5th, and 7th days, the number of lymphocytes decreased, which indicated that the antigen was no longer present, the inflammatory phase had ended, and the wound had begun to enter the proliferative phase.

The most important component in the tissue healing process is the rearrangement of the collagen network which can affect the quality of the wound. The targets in the body's biological process to compensate for wounds are components that play a role in the stages of wound healing. Fibroblasts are one of the components of wound healing in the form of cells that are widely distributed in connective tissue, producing collagen precursor substances, elastic fibers, and reticular fibers. In the wound healing stage, fibroblasts play an important role in the process of fibroplasia.

Fibroplasia is a wound repair process that involves connective tissue which has four components, namely the formation of new blood vessels, migration and proliferation of fibroblasts, deposition of ECM (extracellular matrix), and maturation and organization of fibrous tissue (remodelling). In these four components, fibroblasts play a role in the fibrosis process involving two of the above components, namely fibroblast migration and proliferation and ECM deposition by fibroblasts ([Masir et al., 2012](#)). The results of this study are the same as the theory above, the results of histological examination of the wound after tooth extraction of white rats showed a score of +2 which means that the fibroblasts are parallel to the wound surface and have tissue thickness (fibroblasts), in the intervention group, the administration of nano gel of avocado seed extract was better because of the flavonoid content in the avocado seed which functions as an anti-inflammatory so that it can increase the inflammatory process of the wound after tooth extraction. In the negative control that was only given feed and aquadest, this was because it did not contain anything, so the wound healing process after tooth extraction continued to occur even though it took a long time, because of the inflammatory phase from within the body to the wound. This happens because there are still microbes and tissue damage that must be phagocytized by cells in the wound area, which are still much different from the active ingredients in the avocado seed extract nano gel.

And the neocapillary observation showed the final result on day 7 was a decrease in neocapillary formation because the wound had started to heal so it had started to stop the neocapillary formation process. This decrease indicates that the neocapillaries formed on days 3 and 5 are considered sufficient to perform the task as a blood supply containing nutrients and other factors that are useful for healing so that the wound begins to close. The results showed that the average number of neocapillaries in the treatment group was higher than the negative control group. The results also showed that distilled water did not have active ingredients so that the wound healing process took longer and had a low number of neocapillaries.

The use of herbal plants as an alternative in reducing inflammation has been carried out in several studies, but no one has researched on nano gel which is a novelty or latest innovation in this study. Research by Yani Corvianindya Rahayu used avocado seed powder with a concentration of 10% (*Persea Americana mill*) to reduce the number of PMN neutrophils in mice induced by E.Coli ,and on the third day there was a change and affect the number of PMN neutrophils ([Rahayu, 2009](#)). Another study used banana tree sap extract (*Musa paradisiaca*) in the healing of socket wounds after tooth extraction and the results showed that there was a reduction in the level of inflammation and bleeding from day 1 to day 7 during administration of ethanol extract of banana tree sap ([Khairunnisa et al., 2018](#)).

In this study, the wound after tooth extraction of white rats on day 6 in the

avocado seed extract nano gel group had no inflammation and in the avocado seed extract nano gel group the inflammation was faster than 10% povidone iodine and aquades. One theory states that the process of preventing inflammation in post-tooth extraction wounds occurs due to fibroblast activity which can increase collagen tissue in wounds so that inflammation prevention of post-tooth extraction wounds in mice can occur which is influenced by the application of herbal ingredients, namely nano gel avocado seed extract.

A journal review by Yani Corvianindya Rahayu mentioned the benefits of avocado seeds in reducing neutrophil PMN cells that cause inflammation in wounds after tooth extraction in mice induced by E. Coli. The results of this study are in line with the journal above, it is known that the application of nano gel of avocado seed extract has the same potential as 10% povidone iodine in preventing increased inflammation in post-extraction wounds with a p-value of 0.143. Nano gel of avocado seed extract can prevent inflammation in wounds after tooth extraction and the duration of inflammation is also shorter and can minimize the occurrence of infection or inflammation caused by the entry of microorganisms into the wound. Inflammation of post-extraction wounds is a common problem in the community and is recognized as a more common cause during treatment. This can be avoided by giving avocado seed extract nano gel but further research needs to be done in direct application to humans in order to avoid things that are not desirable.

CONCLUSIONS

Based on the analysis that has been carried out, several conclusions were obtained, namely the administration of nano gel of avocado seed extract (*Persea Americana mill*) with a concentration of 10% on the wound after tooth extraction of white rats (*Rattus Norvegicus wistar*) has potential and can be applied as an alternative herbal ingredient to prevent inflammation, administration of avocado seed extract nano gel (*Persea Americana mill*) with a concentration of 10% did not have a significant difference with the administration of 10% povidone iodine in preventing inflammation in post-tooth extraction wounds in mice and administration of avocado seed extract nano gel (*Persea Americana mill*) with a concentration of 10%. 10% and 10% povidone iodine, have the same ability in the process of wound regeneration, increase new blood vessels and reduce the number of lymphocyte inflammatory cells as evidenced by histological examination.

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