



HISTOPATHOLOGICAL TEST OF PLACENTAL TISSUE TO MEASURE THE EFFECTIVENESS OF MAHKOTA DEWA FRUIT (*PHALERIA MACROCARPA*) IN OVERCOMING PLACENTAL INFLAMMATION IN CASE OF PREECLAMPSIA

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ABSTRACT

Hypertension in pregnancy (HDK) is one of the main complications that contribute to maternal and infant morbidity and mortality. This study aims to analyze the placental profile in pregnancies with hypertension and its relationship with the condition of the newborn. This study used an observational analytical design with a case-control approach. The sample consisted of 60 respondents consisting of 30 mothers with HDK (case group) and 30 mothers without hypertension (control group), selected using consecutive sampling technique. Data analysis was performed using t-test, Chi-square, and logistic regression with a significance level of $p < 0.05$. There were significant differences in placental profiles between the case and control groups, where the HDK group had lower weight (420 ± 55 vs 510 ± 60 grams; $p = 0.001$), diameter (16.5 ± 1.8 vs 18.2 ± 1.5 cm; $p = 0.002$), and thickness (2.1 ± 0.4 vs 2.8 ± 0.5 cm; $p = 0.001$). The incidence of infarction (60.0% vs 20.0% ; $p = 0.002$) and calcification (66.7% vs 26.7% ; $p = 0.001$) was higher in the HDK group. The condition of newborns in the HDK group showed a higher incidence of LBW (50.0% vs. 20.0% ; $p = 0.015$), APGAR <7 (40.0% vs. 16.7% ; $p = 0.032$), and asphyxia (43.3% vs. 16.7% ; $p = 0.021$). Analysis showed that low placental weight (OR=3.8 ; $p = 0.008$), infarction (OR=4.5; $p = 0.004$), and calcification (OR=3.9; $p = 0.006$) were significantly associated with the condition of newborns. Placental profiles in hypertensive pregnancies experienced significant changes and were closely associated with the condition of newborns.

Keywords: histopathology; mahkota dewa; phaleria macrocarpa; inflammation placenta; preeclampsia

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INTRODUCTION

Preeclampsia is complications pregnancy with risk the biggest from all disturbance hypertension in pregnancy that occurs in 2–4% of all pregnancy (Raghu et al., 2023). In a way clinical preeclampsia marked by an increase pressure blood and proteinuria after age 20 weeks pregnant. However, behind manifestation clinical said, preeclampsia own base complex pathology, especially in the placental organ (Vlachodimitropoulou et al., 2024). One of factor main role in pathogenesis preeclampsia is inflammation chronic placenta consequence disturbance invasion trophoblast and spiral artery remodeling in the placenta (Hurrell et al., 2024; H. Tong et al., 2024; Zhang et al., 2024). Consequence occurrence inflammation placenta cause occurrence hypoxia placenta, increase stress oxidative, as well as release various inflammatory mediators to in circulation maternal, such as tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and C- reactive protein (CRP) (Simanjuntak & Rumahorbo, 2024; Danielli et al., 2022). These mediators then make things worse dysfunction endothelium, increasing permeability vascular, and worsen condition clinical preeclampsia. In general microscopic, inflammation placenta can observed through infiltration cell inflammation, necrosis network trophoblast, and disorders vascularization placenta (H. Tong et al., 2024; Simanjuntak & Rumahorbo, 2024; H. Tong et al., 2024).

Although has Lots put forward pathophysiology between preeclampsia with inflammation placenta , however until moment this not yet found therapy that is special targeting the inflammatory process

placenta in preeclampsia. Approach medical use only nature symptomatic, such as antihypertensive, anticonvulsant, and labor as solution definitive for save mother and fetus (Nakimuli et al., 2025; Bacmeister et al., 2025). Treatment in a way pharmacological also still own limitations, both from aspect effectiveness term long and potential effect side to mother and fetus (Bucher et al., 2024). On the other hand, herbal plants become increasingly alternative glanced at in the world of modern medicine, including for support health pregnancy. Innovation therapy that can help overcome pathology base preeclampsia, especially inflammation placenta is very necessary as effort prevention to complications advanced with still guard security for mother and fetus. One of them plants that have potential big is fruit crown god (*Phaleria macrocarpa*) (Simanjuntak & Rumahorbo, 2024).

Fruit Crown of God (*Phaleria macrocarpa*) is plant drug native Indonesian origin from Papua and has been used for a long time in treatment traditional. Fruit This contain various compound bioactive such as flavonoids, saponins, polyphenols, and tannins which are known own effect antioxidants and anti-inflammatory (Ahmad et al., 2023; Abdur Rashid Mia et al., 2023; Putri et al., n.d.). Some studies previously show that extract fruit The Crown of God is able lower TNF- α and IL-6 levels as well hinder activity enzyme proinflammatory such as COX-2. Effects This show that The Crown of God has potential as agent anti-inflammatory that can used For condition pathological like preeclampsia (Simanjuntak & Rumahorbo, 2024; Christina et al., 2022). However , until moment this research that evaluates effectiveness extract fruit Crown of the Gods in direct to inflammation placenta still limited, especially using animal models induced pregnancy preeclampsia. Examination histopathology placenta mouse pregnant is relevant and accurate approach for evaluate impact therapy to structure and level inflammation network placenta. With background behind said, research this aim for evaluate effectiveness extract fruit Crown of God (*Phaleria macrocarpa*) in reduce inflammation placenta based on inspection histopathology in mice induced pregnancy preeclampsia. The results of study This expected can become base scientific for development herbal based therapy plant more local safe and effective in handle preeclampsia and complications related to it.

METHOD

Study This is study experimental pure with use *post-test only control group design*. Subject study is mouse White (*Rattus Norvegicus*) Wistar strain female that was impregnated and used as a model for preeclampsia through induction *Monosodium Glutamate* (MSG) is made in form solution stock 8 mg/ mL. MSG is weighed as much as 800 mg, dissolved in distilled water as much as 100 mL, and shake until the MSG dissolves. Pour in the MSG to in a beaker glass and ready used for induce test animals. Twenty-five test animals were induced with 100 mg/ kgBW of MSG every day for 7 days for make hypertension test animals (Sukma, 2020). Study carried out in the laboratory Faculty Medicine, Cenderawasih University, Jayapura, during period April to month December 2025. Population in study this is mouse white female (*Rattus norvegicus*) Wistar strain which is currently pregnant. The sample used totaling 30 tails, divided in a way random into 6 groups based on study previously by (Simanjuntak & Rumahorbo, 2024; Mia et al., 2022):

Table 1.

Distribution Test Animal Group

Group Negative control (C-)	pregnant mice, without treatment .
Group Control positive (C+)	Pregnant rat with preeclampsia model No given treatment
Group Control (C1)	Pregnant rat with preeclampsia model given Nifedipine (10 mg/kg BW)
Group Treatment (T1)	Pregnant rat with preeclampsia model given extract Crown of Gods with dose 180 mg/kg BW
Group Treatment (T2)	Pregnant rat with preeclampsia model given extract Crown of Gods with dose 360 mg/kg BW
Group Treatment (T3)	Pregnant rat with preeclampsia model given extract Crown of Gods with dose 720 mg/kg BW

Extract fruit crown god given orally with dose in accordance group, for 10 days consecutive after induction preeclampsia started (day 18–27 of pregnancy). Extract made through the maceration

process use solvent 70% ethanol, then dried and adjusted the dosage for oral administration. Analysis Histopathological Placenta taken through Biopsy placenta with thickness full (minimum 3 biopsies/ placenta) taken with fast after giving birth, fixed in 10% formalin for 5–7 days, and immersed in paraffin. Slices five micrometers thick processed and colored with hematoxylin and eosin and evaluated by an expert pathology that is not know results pregnancy assessed. Data Analysis using the ANOVA statistical test to see difference between group, continued with Tukey's post-hoc test if there is difference significant. Significance value set at $p < 0.05$.

RESULT

Observation histopathology placenta use microscope light with 400x magnification. taking picture histopathology placenta use camera and displayed on the monitor layer. Observation histopathology observed placenta in the form of infiltration cell inflammation, edema, necrosis, degeneration, and cell structure .

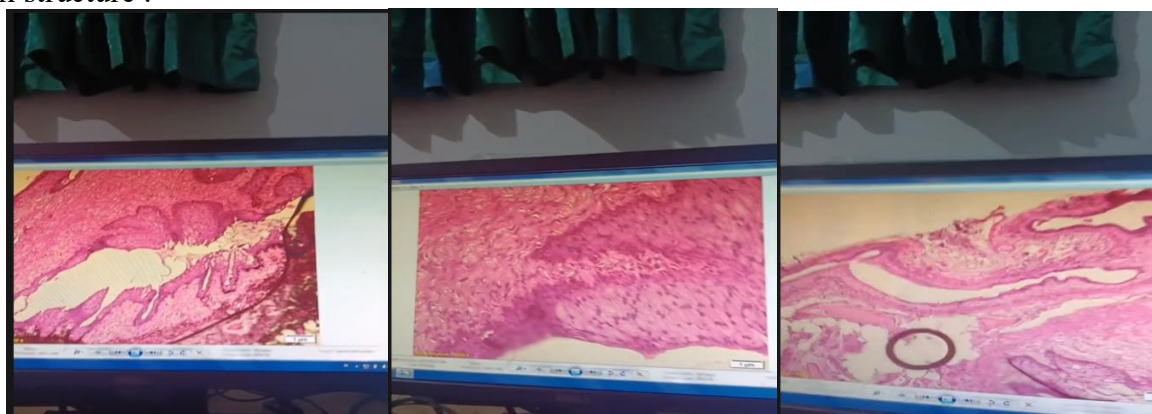


Figure 1. Observation Histopathology Network Placenta on Monitor Screen

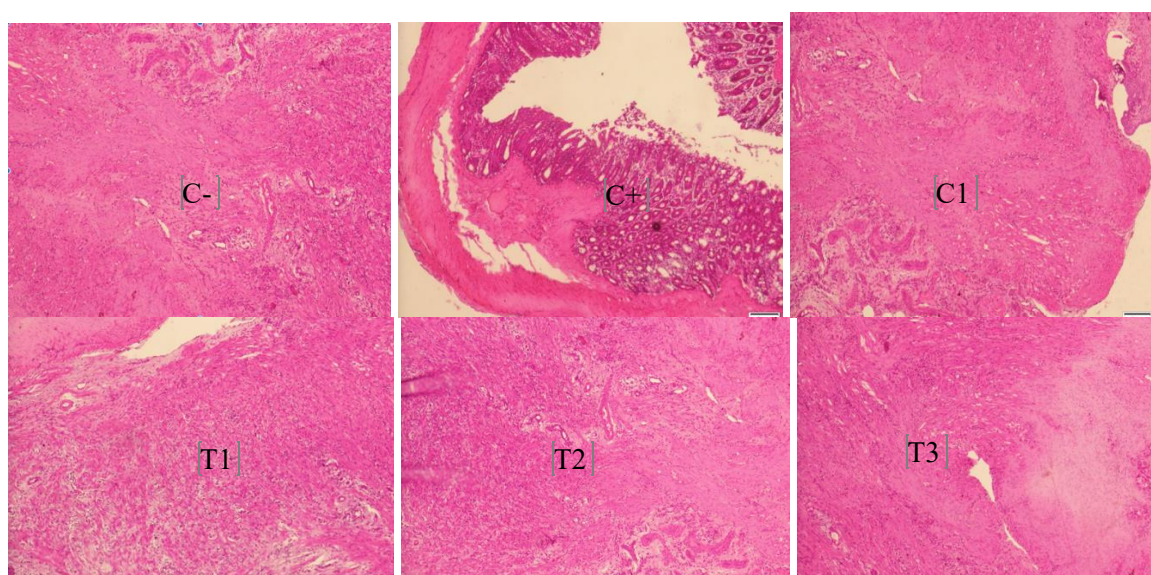


Figure 2. Observation Histopathology Network Placenta With 100x magnification

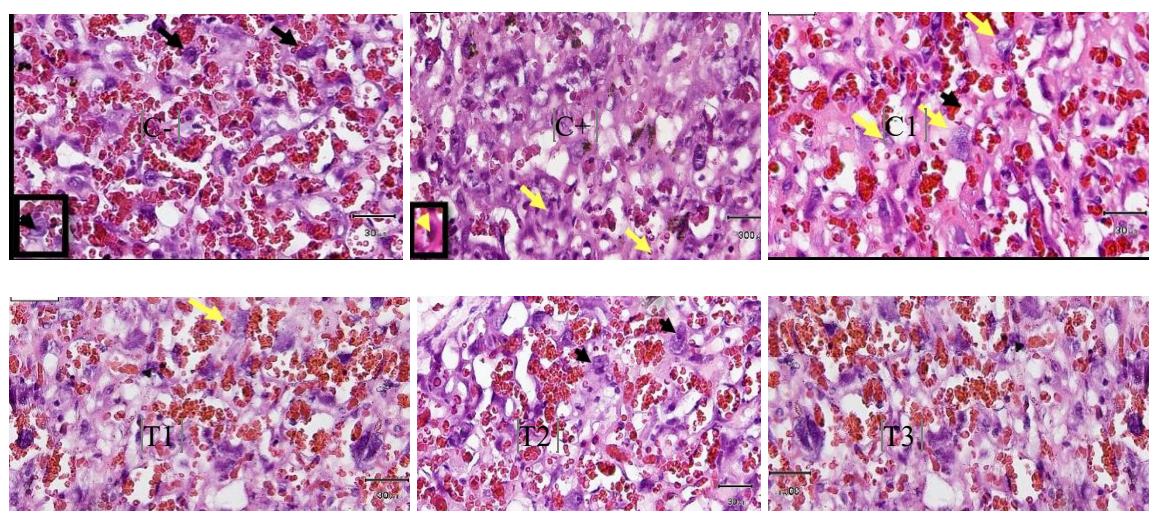


Figure 3. Observation Histopathology Network Placenta With 400x magnification

Placental Tissue Histopathology Scoring Results

The results of the histopathological examination of the placenta in all groups of test animals based on inflammatory cell infiltration, edema, necrosis, degeneration, and cell structure with use semi-quantitative scale 0-3 for each parameter is presented in table following This (Burton et al., 2025):

Table 2.

Placental Histopathology Examination Scoring Results Based on Group

Group	Scoring Results
C-	0, 2, 2, 1, 0
C+	15, 14, 10, 13, 14
C1	8, 8, 7, 9, 8
T1	8, 9, 8, 8, 7
T2	1, 3, 3, 2, 2
T3	6, 3, 2, 4, 5

Information scale :

Infiltration cell inflammation (0 = no there is ; 1 = light ; 2 = moderate ; 3 = heavy)

Edema intervillous (0 = no there is ; 1 = light ; 2 = moderate ; 3 = heavy)

Necrosis /fibrinoid (0 = no there is ; 1 = light ; 2 = moderate ; 3 = heavy)

Degeneration trophoblast (0 = no there is ; 1 = light ; 2 = moderate ; 3 = heavy)

Structure cells (0 = normal; 1 = slightly disturbed ; 2 = disturbed ; 3 = damaged heavy)

Data Analysis Results

Before the data was analyzed using a difference test, the data was tested for data normality using *Shapiro-Wilk* with results served in table following this:

Table 3.

Results of Data Normality Test Based on Group

Group	P Value	Information
C-	0.416	Normal
C+	0.327	Normal
C1	0.527	Normal
T1	0.614	Normal
T2	0.291	Normal
T3	0.472	Normal

Based on the table of data normality test results, it can be seen that all significance values are above 0.05, which means that the data is normally distributed. Therefore, the data analysis can be continued using the One-Way ANOVA test. The ANOVA test results obtained a P value of 0.001, so it can be concluded that there is a significant difference between groups in the total score of the placental tissue histopathology test results. Because the results of the difference test proved to have

a significant difference, it was continued with the Tukey post-hoc test to see which group has most significant difference . Post Hoc test results served in table following this:

Table 4.
Tukey's post-hoc test results

Comparison	P Value	Information
C- vs C+	0.000	Very significant
C+ vs C1	0.002	Significant
C+ vs T1	0.001	Significant
C+ vs T2	0.000	Very significant
C+ vs T3	0.004	Significant
C1 vs T2	0.003	Significant
T1 vs T2	0.002	Significant
T2 vs T3	0.011	Significant
C- vs T2	0.682	Not Significant

Interpretation of results:

- Group C+ (positive control) showed the highest total score (10–15), indicating the most severe level of placental inflammation due to the untreated preeclampsia model.
- Group C- (negative control) had a very low score (0–2) which described normal placental tissue without inflammation.
- Groups C1 (Nifedipine) and T1 (Mahkota Dewa 180 mg/kgBW) showed a decrease in inflammation scores, but were not yet equivalent to the negative control.
- Group T2 (Mahkota Dewa 360 mg/kgBW) showed the lowest score among the treatment groups (1–3) — approaching normal conditions.
- The T3 group (720 mg/kgBW) showed moderate scores (2–6), slightly higher than T2, possibly due to mild toxic effects at high doses.

DISCUSSION

Study This aim For evaluate effectiveness extract ethanol Fruit Crown of God (*Phaleria macrocarpa*) in overcome inflammation placenta in preeclampsia model through inspection histopathology network placenta. Research results show that induction preeclampsia using monosodium glutamate (MSG) is able to cause change histopathological significance in tissue placenta, which is characterized by an increase infiltration cell inflammation, edema intervillous, necrosis, degeneration trophoblast , as well as disturbance cell structure. Findings This confirm that the test animal model used succeed represent condition pathophysiology preeclampsia as reported in literature latest (Gatford et al., 2020; W. Tong et al., 2022).

Group control MSG- induced positive (C+) without therapy show score histopathology highest, depicting degrees inflammation heavy placenta. In biological, condition this related with stress oxidative and dysfunction endothelium that triggers release of inflammatory mediators overload on the network placenta. Preeclampsia known cause disturbance remodeling spiral arteries, hypoxia placenta, as well as activation response maternal immunity leading to damage placental tissue. Findings This in line with study previously reported that inflammation placenta is component central in pathogenesis preeclampsia (W. Tong et al., 2022). Group control negative (C-) indicates description histopathology relatively normal placenta with score inflammation is very low. This is confirm that change histologically that occurs in the group treatment especially caused by induction condition preeclampsia, not by factors physiological pregnancy solely. Condition normal placenta is characterized by a structure intact villi, minimal infiltration cell inflammation, as well as no found necrosis and degeneration trophoblast (Vornic et al., 2024). Administration of nifedipine to the group control comparator (C1) is proven lower score inflammation placenta compared to group control positive. Nifedipine as antagonist channel calcium known own effect vasodilation and is able to repair perfusion uteroplacental, so that in a way No direct lower degrees hypoxia and response inflammation network placenta (Obeagu & Obeagu, 2024; W. Tong et al., 2022). However Thus, the results histopathology show that improvements that occurred Not yet fully resemble

condition normal placenta , which indicates that therapy pharmacological conventional own limitations in suppress the inflammatory process placenta in a way comprehensive (Vornic et al., 2024).

Group treatment extract Fruit Mahkota Dewa dose 180 mg/ kgBW (T1) shows decline score inflammation comparable placenta with nifedipine group. Effects This allegedly related with content compound bioactive Mahkota Dewa such as flavonoids, saponins, and polyphenols which have activity anti - inflammatory and antioxidant compounds the play a role in hinder production cytokines proinflammatory as well as lower stress oxidative which contributes to damage network placenta (Fernenda et al., 2024; Putri et al., n.d.). Interestingly , the group treatment dose of 360 mg/ kgBW (T2) shows score histopathology lowest among all over group treatment and approach condition control negative. Findings This show that dose the is most effective dose in pressing inflammation placenta. In mechanistic, optimal dose of extract Crown of the Gods is suspected capable give effect anti-inflammatory maximum without cause effect toxic, so that the regeneration and repair process structure network placenta can ongoing more optimal. Some study experimental report that effect pharmacological herbal plants often follow pattern non-linear dose-response, where the dose medium give effect therapeutic best. On the other hand, the group treatment dose high 720 mg/ kgBW (T3) indicates score more inflammation tall compared to T2 group. Phenomenon this indicates existence possibility effect toxic light or stress cellular at a dose high, which is precisely can trigger response inflammation secondary. Some studies mention that giving dose tall compound phytochemicals certain can disrupt cell homeostasis and increase production radical free (Fernenda et al., 2024). Findings This confirm importance determination optimal dose in development therapy based material nature.

In a way overall, results study this show that extract Fruit The Crown of Gods has potential significant as agent anti-inflammatory in overcome inflammation placenta in cases preeclampsia. Effectiveness best obtained at a dose of 360 mg/ kgBW, which is capable of lower degrees damage histopathological placenta in a way meaningful. Findings this support development Crown of Gods as candidate phytopharmaceuticals adjuvan in handling preeclampsia, in particular for pressing inflammation placenta plays a role important in pathogenesis disease.

CONCLUSION

Fruit The Crown of God is proven effective lower degrees damage histopathological placenta in a way significant in the preeclampsia model.

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