

Effect of Young Papaya (*Carica papaya L.*) Fruit Extract on Infiltration of Endometrial Inflammatory Cells of Female Rats (*Rattus norvegicus*)

Cecen Suci Hakameri

Prodi S1 Kebidanan dan Profesi Bidan STIKes Hang Tuah Pekanbaru
Jl. Mustafa Sari No 5 Tangkerang Selatan Pekanbaru, Telp (0761) 33815 Fax (0761) 863646

ARTICLE INFO

Keywords:

Extract of young papaya (*Carica papaya L.*); Endometrial Infiltration of Inflammatory Cells

ABSTRACT

Young papaya fruit is a plant thought to have anti-fertility compounds. The active compounds in young papaya fruit are thought to be able to interfere with ovarian function so that it has an impact on the normal endometrial cycle. The endometrium is the innermost lining of the uterus which is the site of implantation and development of the embryo. The aim of this study was to examine the effect of young papaya extract on the infiltration of inflammatory cells of the endometrium of female rats (*Rattus norvegicus*). This study uses the Post Test Only Control Group method. Total samples were 24 rats (*Rattus norvegicus*), 2-3 months old and 200-300 grams in weight. Samples were taken randomly, divided into 4 groups. Group (K) without being given treatment. Group (P1) was given 200 mg / 200gr BW of young papaya extract. Group (P2) was given young papaya fruit extract 400 mg / 200gr BW. Group (P3) was given young papaya fruit extract 600 mg / 200gr BW. After 20 days of treatment, the endometrial inflammatory cell infiltration was calculated. The results showed that giving young papaya fruit extract (*Carica papaya L.*) reduced the infiltration of endometrial inflammatory cells. The results of statistical analysis using the one way ANOVA test showed the effect of giving papaya extract on endometrial inflammatory cell infiltration ($p = <0.001$). It can be concluded that there is an effect of giving young papaya (*Carica papaya L.*) fruit extract on the infiltration of inflammatory cells in the endometrium.

E-mail:

cecen.sh@gmail.com

Copyright © 2021 Science Midwifery.

1. Introduction

Indonesia is a country that is rich in medicinal plants, one of which is the papaya plant. Papaya plants are economically valuable plants that have many benefits, ranging from leaves, fruit to their roots that can be used in human life. (Walansendow, et al. 2016). In India, women and men use papaya fruit as a means of contraception. Women can use young papaya to avoid pregnancy. Green papaya is rich in enzymes that can be used to prevent pregnancy, besides men in Asia such as Sri Lanka, India and Pakistan often use papaya seeds as a natural contraceptive option and are used for the long term (Ram Dayal, 2017). Young papaya fruit contains several phytochemical substances such as saponins, alkaloids, tannins, flavonoids, triterpenoids, and quinones (Iwuagwu et al, 2013; Nadiyah et al, 2016). The active compounds in papaya are thought to work as anti-fertility compounds.

Basically, anti-fertility compounds work through two mechanisms, namely through cytotoxic effects and through hormonal effects (Hediningrat, 2002). The bioactive compounds contained in young papaya extract are thought to work through these two mechanisms. Alkaloids, saponins and triterpenoids work based on cytotoxic effects, which interfere with cell development, both ovum cells in the ovaries, so that the synthesis of progesterone and estrogen hormones will also be disrupted or the cells that make up the layers of the endometrium and myometrium (Rusmiati, 2011) Saponin compounds have a mechanism which damages the cell membrane by increasing the permeability resulting in cell leakage followed by the release of intracellular material. These compounds diffuse through the outer membrane and susceptible cell walls, then bind to the cytoplasmic membrane and interfere, thereby reducing cell stability, causing the cytoplasm to leak out of the cell resulting in cell death (Francisi et al, 2002).

The purpose of this study was to see the effect of young papaya fruit extract (*Carica papaya L.*) on the infiltration of inflammatory cells in the endometrium of female rats (*Rattus norvegicus*). This research is an experimental study with a Post Test Only Control Group design. The study used a sample of 24 female rats (*Rattus norvegicus*) aged 2-3 months with a body weight of 200-300 grams, which were divided into 4 groups, the control group without extracting, the treatment group 1 dose 200 mg / 200 gr BW, the treatment group 2 doses of 400 mg / 200 g BW, treatment group 3 doses of 600 mg / 200 g BW. The sample was taken by surgery. The dead female mouse was placed on the fixation board. Perform a laparotomy, identify and cut the uterus, then fix it in 10% BNF

Science Midwifery

Journal Homepage: www.midwifery.iocspublisher.org

solution for 24 - 48 hours. After fixation, it was continued with the paraffin method and observations were made with the field of view to determine the infiltration of inflammatory cells in the endometrium.

2. Method

This research is an experimental study with a post test only control group design carried out at the Natural Material Chemistry Laboratory, Faculty of Pharmacy, Andalas University, Biomedical Laboratory and Anatomical Pathology Laboratory, Faculty of Medicine, Andalas University. Data on the number of endometrial inflammatory cell infiltration were analyzed first by means of the normality test using the Shapiro Wilk test. The results of the normality test showed that the data were normally distributed ($p > 0.05$), then statistical analysis was carried out using the one way ANOVA test. The results of statistical tests using the one way ANOVA test showed the effect of giving young papaya extract (*Carica papaya* L.) on endometrial cell infiltration with a value ($p = <0.001$)

3. Result and Discussion

The results of the normality test of endometrial inflammatory cell infiltration using the Shapiro Wilk test obtained normal distribution data ($p > 0.05$), then statistical analysis was continued with one-way ANOVA test.

Table 1.

One way ANOVA test results Infiltration of Female Rat Endometrial Inflammatory Cells (*Rattus norvegicus*) in Control and Treatment Groups

Subject Group	n	Endometrial Inflammatory Cell Infiltration Average \pm SD	p
Control	6	73,57 \pm 16,72	<0,001
Treatment 1	6	77,87 \pm 9,20	
Treatment 2	6	51,60 \pm 7,75	
Treatment 3	6	42,53 \pm 8,48	

Description: Control, without treatment
 Treatment 1 (Dose 200mg / 200grBB)
 Treatment 2 (Dose 400mg / 200grBB)
 Treatment 3 (Dose 600mg / 200grBB)

Table 1 above shows the results of the one way ANOVA test which shows the mean endometrial inflammatory cell infiltration in the control group is 73.57 ± 16.72 , treatment group 1 is 77.87 ± 9.20 , treatment group 2 is 51.60 ± 7.75 , and treatment group 3 namely 42.53 ± 8.48 . There was a significant difference between the control group and the treatment group $p = <0.001$ ($p < 0.005$). To see the differences in each of these groups, a Bonferoni type Multiple Comparison test (post hoc test) was carried out as seen in Table 2.

Table 2.

Multiple Comparison test (post hoc test) of Bonferoni type on Infiltration of Female Rat Endometrial Inflammatory Cells (*Rattus norvegicus*) in Control and Treatment Groups

Group	Significance Level of Endometrial Inflammatory Cell Infiltration			
	Control	Treatment 1	Treatment 2	Treatment 3
Control	-	1,000	0,016	0,001*
Treatment 1	1,000	-	0,003*	0,000*
Treatment 2	0,016	0,003*	-	0,000*
Treatment 3	0,001*	0,000*	1,000	-

Table 2 .It can be seen that the results of the Multiple Comparison test (post hoc test) for the Bonferoni type, there were significant differences between the control group and treatment group 3 ($p = 0.001$), and there was a significant difference between treatment group 1 and treatment 2 ($p =$

0.003) and 3 ($p = 0.000$). There is also a significant difference between treatment group 2 and treatment 3 ($p = 0.000$).

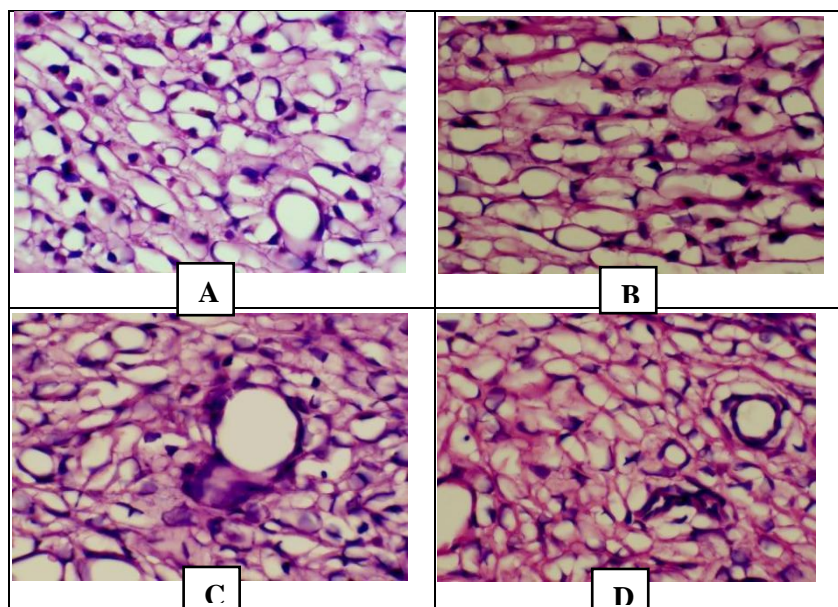


Fig 1 Microscopic Overview of Infiltration Histology of Endometrial Inflammatory Cells

Description: A: Control, without treatment
 B: Treatment 1 (Dose 200mg / 200grBB)
 C: Treatment 2 (Dose 400mg / 200grBB)
 D: Treatment 3 (Dose 600mg / 200grBB)

3.1 Discussion

After being analyzed based on the One Way Anova test, it was found that giving young papaya extract (*Carica papaya* L.) had a significant effect on the infiltration of inflammatory cells of female rats (*Rattus norvegicus*). In this study, there was a significant difference in the administration of young papaya (*Carica papaya* L.) fruit extract in each treatment. Significant differences were seen in the control group with treatment group 2 and treatment group 3. Then a significant difference was seen in treatment group 1 with treatment 3.

The decrease in the number of leukocytes seen in treatment groups 2 and 3, is thought to be caused because the endometrial cycle also affects the leukocyte cycle so that the number of leukocytes depends on the cycle that is occurring. This is evidenced by the slowdown in endometrial cell thickening and the most significant reduction in endometrial gland density in group 3 at a dose of 600 mg / kg BW, so that it is thought to have an effect on the number of leukocytes in the endometrium of rats.

The active compound in young papaya (*Carica papaya* L.) is thought to be able to disrupt the endometrial cycle. In this study, researchers suspect that the endometrium is in the early phase of proliferation. In the early phase of proliferation, it was found that there was a thin thickness of the endometrium, small glands and few leukocytes, so that the active compound was able to slow down the proliferation of the endometrium. Besides that, in general the active compounds in young papaya fruit also cause anti-inflammation, one of which is a flavonoid compound.

Flavonoids are compounds that have pharmacological activity as anti-inflammatory. The role of flavonoids as anti-inflammatory is by reducing the number of leukocytes and reducing complement activity, thereby reducing leukocyte adhesion to the endothelium and resulting in a decrease in the inflammatory response (Nijveldt et al, 2001). The mechanism of flavonoid compounds as anti-inflammatory compounds is through several pathways, such as through inhibition of neutrophil degranulation, inhibition of cyclooxygenase (COX) enzyme activity, and lipooxygenase so that prostaglandins are not formed which are inflammatory mediators.

Flavonoids are one of the secondary metabolic products found in young papaya extract. The content of flavonoids is thought to play a role in the anti-inflammatory process. According to the

Science Midwifery

Journal Homepage: www.midwifery.iocspublisher.org

research of Anaga et al (2010), the presence of alkaloid and flavanoid compounds in papaya seed extract has anti-inflammatory activity. The study suggests that the methanolic extract from papaya seeds exhibits moderate and acute anti-inflammatory effects, which may be responsible for its use in treating acidic skin and swollen wounds. The results showed the presence of a very strong bioactive compound which had to be taken in very low doses.

4. Conclusion

Based on the results of research on the effect of young papaya fruit extract (*Carica papaya* L.) on infiltration of endometrial inflammatory cells of female rats (*Rattus norvegicus*), it was concluded that there was an effect of giving young papaya fruit extract (*Carica papaya* L.) on the infiltration of endometrial inflammatory cells of female rats (*Rattus norvegicus*).

5. References

- [1] Anaga, AO. and Onehi, EV. (2010). Antinociceptive and anti-inflammatory effects of themethanol seed extract of *carica papaya* in mice andrats. *African Journal of Pharmacy and Pharmacology* Vol. 4, No. 4. pp. 140-144.
- [2] Francis, GZ. Kerem, HPS. Makar. K. Becker. (2002). The Biological Action of Saponins in Animal System: Review. *British Journal of Nutrition*. No. 88. pp. 587-605.
- [3] Hedinigrat, S. (2002). *Efek Pemberian Infusa Buah Manggis Muda (GarciniamangostanaLinn) Terhadap Spermatozoamencit (Musmusculus)*. Majalah Andrologi Indonesia. Vol. 10, No. 4. pp.130.
- [4] Iwuagwu, M. Chukwuks, KS. Uka, UN. (2013). Evaluation of Nutritional Components of *Carica papaya* L. at Different Stages Of Ripening. *Journal of Pharmaceutical and Biological Sciences*.Vol. 6. No. 4. pp.13-16
- [5] Nadiyah, LD. Kharisma, Y. Yuniarta. (2016). Penentuan Derajat Toksisitas Akut Ekstrak Air Buah Pepaya (*Caric papaya* L.) Muda Pada Mencit Menggunakan Purposed New Recommended Method. *Jurnal Jamu Indonesia*.Vol. 1, No. 2. pp.15-19
- [6] Nijveldt RJ, Nood EV, Hoorn DECV, Boelens PG, Norren KV, Leeuwen PAMV.(2001). Flavonoids: a review of probable mechanisme of action and potential applications. *American Journal of Clinical and Nutrition*.
- [7] Ram, D. (2017). *Papaya Seeds Have Been Used In Some Cultures as aContraceptive*. Diakses 26 Agustus 2019.
- [8] Rusmiati. (2011). Pengaruh Ekstrak Metanol Kulit Kayu Durian (*Durio zibethinus* Murr) Pada Struktur Mikroanatomi Ovarium da Uterus Mencit (*Mus musculus*). *Sains dan Terapan Kimia*, Vol. 4, No. 1. pp.29-37.
- [9] Walansendow, R., Janette M, R. dan Lydia, T. 2016. Pengaruh pemberian ekstrak biji pepaya (*Carica papaya* L.) terhadap kualitas spermatozoa tikus Wistar (*Rattus norvegicus*). *Jurnal e-Biomedik (eBm)*. 4(1): 1-4.