

**EVALUATION OF THE SECURITY OF THE USE OF GUAJAVA
PSIDIUM EXTRACT CAPSULE ON HEART FUNCTION IN
DENGUE FEVER AND DENGUE HEMORAGIC FEVER PATIENTS
IN TYPE C HOSPITAL**

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Abstract

There are 126,675 DHF sufferers in 34 provinces and 1,229 of them died, while the Incidence Rate (IR) in Central Java is 47.9 per 100,000 population. Based on the safety of Psidium guajava Linn on the liver by calculating the lethal dose average showed that there were no deaths from the two experimental models of Swiss mice and Wistar mice in the dose range up to 2,000 mg/kg BB. Safety tests in rats proved lethal dose 50 (LD50) of guava leaf extract more than 5 g/kg. This study aims to determine the effect of psidii capsules containing guava leaf extract (Psidium guajava Linn.) toward levels (SGOT and SGPT) of DF and DHF patients in PKU Muhammadiyah Wonosobo Hospital. This study belongs to perspective cohort analytic observational using blood plasma patients of PKU Muhammadiyah Wonosobo Hospital of 37 patients in the period of March to August 2018 which were divided into two groups, namely standard therapy + guava leaf extract capsules and the group receiving standard therapy only. Dosage of Psidium guajava 3x2 capsules for 3 to 4 days. Examination of SGOT and SGPT levels used UV-vis spectrophotometry. General linear model was used for analyzing the data. The average SGOT level after treatment was 64 U/L in DF and 99 at DHF while the SGPT levels were 30 U/L and 35 U/L. Average levels of SGOT and SGPT decreased. There were no differences in SGOT and SGPT mean of DF and DHF patients in the two groups after giving guava leaf extract capsules with $p > 0.05$. In SGOT mean, there was an increase in SGOT after giving guava leaf extract probably because there were patients who had chronic liver disorders.

Keywords: Dengue Fever, Dengue Hemorrhagic Fever, Guava extract capsule, SGOT SGPT

1. INTRODUCTION

DHF sufferers in 34 provinces are 126,675 and 1,229 of them died, while Incidence Rate (IR) in Central Java 47.9 per 100,000 population with Case Fatality Rate (CFR) of 1.6 (Depkes RI, 2004). Dengue infection, besides causing a decrease in platelets, leukopenia and an increase in hematocrit, can also cause liver dysfunction characterized by an increase in SGPT (Serum Glutamic Pyruvate Transaminase) and SGOT (Serum Glutamic Oxaloacetic Transaminase) (Smith & Khakpoor, 2009). Research conducted by Darmawan (2015) in 2015 at Dr. Soetomo Surabaya Hospital in 162 samples showed that the average value of SGPT and SGOT were 57.5 IU/L (34-103 IU/L); SGPT 49.25 IU/L (26-65 IU/L) Acute toxicity test in rats proved that lethal dose 50 (LD50) of guava leaf extract more than 5g/kg. Psidium guajava with a dose of 2000 mg/kg does not cause any mortality (Roy et al., 2006).

2. RESEARCH METHOD

This study used blood plasma in 37 patients at PKU Muhammadiyah Wonosobo Hospital in the March to August period. The inclusion criteria in this study were patients with diagnosis of DF and ICD A90 and A91 DHF, adults >18 years old and willing to be the subject of the study. Data recording used the Case Record Form sheet, SGOT and SGPT measurements used Uv-Vis Spectrophotometry, while the analysis used the General Linear Model. This study has received an ethical permit from the Ahamd Dahlan University Ethics Commission.

3. RESULT AND DISCUSSION

3.1. Result Research

Respondents who were willing and fulfilled the inclusion criteria were 37 subjects. Patients' characteristics (table 1) in this study had an average age of 42 years in the standard therapy group + extra leaves capsule and 37 years in the standard therapy group. Age 42.22 ± 14.83 in the treatment group and 37.53 ± 14.48 in the control group, initial temperature were 37.18 ± 0.72 and 37.63 ± 0.96 ; fever day 4.00 ± 0.90 and 3.68 ± 0.82 ; initial SGOT were 64.61 ± 36.68 and 70.21 ± 55.38 ; Initial SGPT were 44.88 ± 22.98 and 57.57 ± 55.87 ; early platelets were 109 ± 4.28 and 94.79 ± 3.77 ; perceived complaints of patients with fever, nausea, vomiting, headache, heartburn, joint pain, myalgia, weakness, bleeding, diarrhea, coughing, tingling, difficult BAK and tightness. SGOT and SGPT analysis in (table 2) mean SGOT levels of DF patients in the treatment group before therapy scored 53 U/L and after therapy 64 U/L while in the control group scored 71 U/L before therapy and 62 U/L after therapy while levels SGPT treatment group averaged levels before therapy scored 45 U/L and after therapy 30 U/L. In patients with DHF the SGOT level of the 102 U/L treatment group and after 99 U/L the control group before therapy was 67 U/L and after therapy 53 U/L while at the SGPT level the treatment group before therapy was 42 U/L and after therapy 35 U/L in the control group before therapy 52 U/L and after therapy 35 U/L. Based on the significance value in the two groups was not significantly different with $p=0.641$ at SGOT and 0.270 at SGPT DF patients, whereas at DHF the SGOT 0.233 and SGPT 0.90.

Table 1 Patients' Characteristics of DF and DHF at PKU Muhammadiyah Hospital Wonosobo in March to August.

Patients' Characteristics	Standard therapy+ guava leaves extract capsule (n=18)	Standard therapy (control) (n=19)	<i>p value</i>
Male (n,%)	10 (47.60)	11 (52.40)	1.000
Age (mean $\pm$ SD)	42.22 ± 14.83	37.53 ± 14.48	0.491
Temperature (mean $\pm$ SD)	37.18 ± 0.72	37.63 ± 0.96	0.125
Initial SGOT level	64.61 ± 36.68	70.21 ± 55.38	0.721
Initial SGPT level	44.88 ± 22.98	57.57 ± 55.87	0.377
Fever Day	4.00 ± 0.90	3.68 ± 0.82	0.274
Initial platelets	109 ± 4.28	94.79 ± 3.77	0.307

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Complaints			
Fever (n,%)	18 (100)	19 (100)	0.468
Nausea (n,%)	10 (55.55)	8 (42.11)	
Headache (n,%)	10 (55.55)	8 (42.11)	
Heartburn (n,%)	4 (22.22)	3 (15.79)	
Joint pain (n,%)	0 (0)	4 (21.05)	
Weakness (n,%)	5 (27.78)	6 (31.58)	
Bleeding (nosebleeds, gums, hematuria, melena)	0 (0)	1 (5.26)	
Diarrhea	1 (5.55)	2 (10.52)	
Cough	1 (5.55)	2 (10.52)	
Tingling	0 (0)	1 (5.26)	
Myalgia	1 (5.55)	3 (15.79)	
Difficult to urinating	0 (0)	1 (5.26)	
Tightness	1 (5.55)		

Table 2 Differences level of SGOT and SGPT among groups before and after giving guava leaf extract capsule

SGOT		Group 1 (mean±SD)	Group 2 (mean±SD)	<i>p value</i>
DF	Pre	53±(2.55)	71±(6.02)	0.641
	Post	64±(3.96)	62±(3.77)	
DHF	Pre	102±(4.88)	67±(4.46)	0.233
	Post	99±(4.33)	53±(3.01)	

Notes: Group 1= standard therapy + guava leaf capsule
Group 2= standard therapy + placebo (control)

SGPT		Group 1	Group 2	<i>p value</i>
DF	Pre	45±(2,56)	57±(5,63)	0,270
	Post	30±(2,79)	50±(5,45)	
DHF	Pre	42±(1,13)	52±(3,97)	0,909
	Post	35±(1,29)	35±(9,54)	

Notes: Group 1= standard therapy + guava leaf capsule
Group 2= standard therapy + placebo (control)

3.2. Discussion

It is known that male patients are more than females, namely 21 people (56.75%) while females are 16 people (43.24%) with $p > 0.05$. Research conducted at Dr. Soetomo Hospital

Surabaya, a patient diagnosed with DF and DHF as many as 162 patients, in *dengue fever* occurs mostly in men compared to women with a percentage of 68.30% for men and 31.70% of women as well as those with *dengue hemorrhagic fever* 67 (57.26%) men and 50 (42.74%) women (Darmawan, 2015).

The incidence of dengue fever is at most at the age of 11 to 30 years by 60%, aged 31 to 50 by 31.08% and the least at the age of 51 to 70 years by 8.10%. This is similar to this study, the least age also occurs at the age of 51 to 67 years at 27.02% (MEHBOOB et al., 2012). Based on the data (table 1) it can be seen from the complaints that most often occur in DF and DHF patients, namely 37 patients had fever (100%), nausea-vomiting (48.64%), headache (48.64%), heartburn (18.91%), joint pain (10.81%), weakness (29.72%), bleeding (nosebleeds, gums, hematuria, melena) 2.70%, diarrhea 8.10%, cough (8.10%), tingling (2.70%), fever (10.81%), difficulty in urinating and tightness (2.70%). WHO states that clinical symptoms in DF and DHF patients are fever, headache, hemorrhagic manifestations, heartburn, which can be associated with an increase in SGPT and nausea and vomiting (WHO & UNICEF, 2012).

Dengue fever is defined as an acute febrile illness followed by more than two symptoms such as headaches, muscle aches, joint pain, rash, and hemorrhagic manifestations. Based on the data (table 2), it was found that the average SGOT level of patients after giving guava leaf extract capsules increased in DF patients but SGOT and SGPT levels in DHF patients tended to fall. SGOT mean in DF patients after treatment has increased. This may be due to one subject experiencing chronic liver disorders with SGOT 238 levels but having decreased to 200 U/L. At the significance of SGOT and SGPT levels in DF and DHF patients between the treatment and control groups were not significantly different because the $p > 0.05$.

Dengue virus can cause enzyme transaminase activity to increase by 1-1.5 times with SGOT enzyme activity higher than SGPT (Lei et al., 2001). The study resulted in SGOT enzyme activity of patients with liver dysfunction having a significant increase in the fever phase <72 hours and when the temperature subsided with a value of $p = 0.05$. In the results of bivariate analysis, liver enlargement is more common in patients with liver dysfunction, but in multivariate analysis, it is explained that hepatomegaly is not an independent variable that can predict heart disfunction. In vitro study, Udem et al. (2011) used Psidium guajava Linn chloroform extract with a dose of 24.3 mg/ml in group 2 and 45.9 mg/ml in group 3 and group 1 as a control given orally for 28 days. The results of AST and ALT measurements increased AST levels in both treatment groups. The results of the analysis of this increase were not significant between groups 2 and group 3 while compared with controls had a value of $p < 0.05$.

The increase in AST activity in this study is due to a disturbance in the liver and possibly in other body tissues. SGPT levels after therapy in the standard group + guava leaf extract capsules were lower than before therapy as well as the standard therapy or control group. Case report research by Anggraini & Nasronudin (2013) on non-dengue SGOT and SGPT levels increased 1-3x normal value and in dengue positive fever SGOT levels increased 1-3 times the normal value, but at SGPT levels were still within normal limits with a value of $p = 0.022$. SGPT and bilirubin levels rarely increase in dengue fever patients compared to SGOT level.

Giving capsules of guava leaf extract as supportive therapy is carried out during the patient's hospitalization. Research by Tajul et al. (2011) on the evaluation of the activity of

guava leaf extract as hepatoprotector and antioxidant in rats induced by paracetamol that the hepatoprotector effect on guava leaf extract has a correlation to decreased serum enzyme activity and has antioxidant status at a dose of 500 mg/kg but the duration of administration for 10 days is different from this research which is given only for 3 to 4 days. *Psidium guajava* Linn besides being safe, cheap can be used as an alternative chemopreventive treatment and protection in the management of liver disease (Gutiérrez et al., 2008). Another study in India in mice induced using CCl₄, *Psidium Guajava* showed hepatoprotector activity with a duration of 9 days (Roy et al., 2006). In the *Psidium guajava* toxicity study by calculating lethal dose averages in Swiss rats and in Wistar rats concluded that there were no deaths from the two experimental models in the dose range up to 2 g/kg body weight. Acute toxicity test in rats proves lethal dose 50 (LD₅₀) of guava leaf extract more than 5 g/kg (Indonesian Ministry of Health, 2010).

4. CONCLUSION

There were no differences in SGOT and SGPT levels in the standard therapy group + guava leaf extract capsules with standard therapy (control) with a value of $p > 0.05$. Based on the safety of guava leaf extract capsules, it is safe and does not significantly increase SGOT and SGPT levels.

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