

# The Effect of Poguntano Leaf Extract (*Curanga feel-terrae* Merr.) on Procalcitonin Levels in Acute Bacterial Rhinosinusitis Rat Model

Andrina Yunita Murni Rambe<sup>1\*</sup>, Delfitri Munir<sup>1</sup>, Rosita Juwita Sembiring<sup>2</sup>, Syafruddin Ilyas<sup>3</sup>

<sup>1</sup>Otolaryngology-Head and Neck Surgery Department, Faculty of Medicine, Universitas Sumatera Utara, Indonesia

<sup>2</sup>Clinical Pathology Department, Faculty of Medicine, Universitas Sumatera Utara, Indonesia

<sup>3</sup>Biology Department, Faculty of Mathematics and Natural Sciences, Universitas Sumatera Utara, Indonesia

**Keywords:** Poguntano Leaf Extract, Procalcitonin, Acute Bacterial Rhinosinusitis

**Abstract:** Background: Acute rhinosinusitis is a common condition caused by a viral and bacterial infection. Procalcitonin (PCT) has been proofed as a biomarker for bacterial infections. PCT levels increase to higher levels in bacterial infection. The extract of Poguntano leaf contains phytochemicals namely flavonoids, saponins, tannins, glycosides, terpenoids, and steroids. Objective : This study aimed to determine the effect of Poguntano leaf extract on Procalcitonin level expression in acute bacterial rhinosinusitis rats model Methods : Twenty-four female Wistar rats were divided randomly into three groups, negative control (group A), positive control (group B), group obtaining Poguntano extract 10mg/kg/day orally for 5 days at the 10<sup>th</sup> day after induction (group C). Rhinosinusitis was induced by the insertion of sponge impregnated with a solution containing *Staphylococcus aureus* into nasal cavities of study group B and C. The groups were euthanized within 1 day (group A), 10 days (group B), and 15 days (group C). Procalcitonin blood level was measured by ELISA. Results: there was a significant reduction of Procalcitonin levels in the treatment group than in the control group. Conclusion: this study suggests that Poguntano leaf can reduce procalcitonin levels in a rat model of acute bacterial rhinosinusitis.

## 1 INTRODUCTION

Acute rhinosinusitis (ARS) is a common upper respiratory tract disorder that involves inflammation of the nasal and paranasal sinus mucosa. It is often caused by a viral infection of which only 0,5 to 2% of cases are complicated by a bacterial infection. However, the efficacy of antibiotics is limited or controversial. There is significant overuse of antibiotics due to uncertainty to differentiate bacterial from viral rhinosinusitis on the basis of clinical judgment alone.

Compared with non-bacterial ARS, bacterial ARS encompassed a more powerful local and systemic inflammatory reaction. These responses were strongest at the beginning of respiratory symptoms, indicates that bacterial ARS starts to develop during an early phase of symptoms. In theory, biomarkers that parallel the local and systemic inflammatory reaction could shed light on the pathophysiology and development of bacterial ARS. (Autio, 2017).

Procalcitonin (PCT), a proinflammatory biomarker, has been proposed as a pertinent marker of bacterial infection. It is released ubiquitously in response to bacterial toxins and bacterial-specific proinflammatory mediators (Schuetz, 2013; Autio, 2017). Circulating levels of PCT are elevated in bacterial infections but remain relatively low in viral infections (Kofteridis, 2009).

Despite the development of new antibiotics and advances in sinus surgery over the past few decades, rhinosinusitis is still an enigmatic process.

Herbal medicines have been used for generations to treat bacterial ARS, and there has been an increasing interest in herbal medicine both in the USA and in Europe (Bachert, 2009). Herbal medicine is a promising alternative in the treatment of ARS (Koch, 2016).

Poguntano is abundantly growing in Indonesia and traditionally has been used as stimulant, diuretic, malaria and recently is used for the treatment of Diabetes Mellitus (Sitorus, 2014). The extract of Poguntano leaf contains chemical compounds such

as flavonoids, saponins, tannins, glycosides, steroids, and triterpenoids (Patilaya, 2015).

## 2 MATERIALS AND METHODS

### 2.1 Preparation of Extract

Poguntano leaves were collected from Pancur Batu, Deli Serdang District, North Sumatera and identification of the leaves were performed at Department of Pharmacology Pharmacy, Faculty of Pharmacy, University of Sumatera Utara, Indonesia.

### 2.2 Rats and Groups

Twenty four female Wistar rats aged 6-8 weeks and weighing 180-200 grams were used. They were housed in pathogen-free conditions in the Animal Laboratory of Biology Department, Faculty of Mathematics and Natural Sciences, University of Sumatera Utara, Indonesia, and the rats were given food and water at all times. All animals were kept under standard conditions for a period of seven days prior to study initiation. The study was approved by the Ethics Committee, Medical Faculty, University of Sumatera Utara.

Rats were randomly divided into three groups of 8. Table 1 shows the interventions for each group. The rats in group A were sacrificed on the 1<sup>st</sup> day without given induction or tested extract (negative control). The rats in group B were sacrificed 10 days after the experiment induction (Cheng, 2009; Ozcan, 2011) without given tested extract (positive control) and the rats in group C were sacrificed 15 days after the experiment induction with a given extract of Poguntano leaves 10 mg/BB/day for 5 days orally (Juwita, 2009) started at the 10<sup>th</sup> days after induction. The animals were sacrificed by cervix dislocation.

Table 1: Group of treatments

Group	Treatment
A	Animals were given standard food and water ad libitum without induction and tested extract (negative control)
B	Animals were given standard food and

	water ad libitum with induction but without tested extract (positive control)
C	Animals were given standard food and water ad libitum with induction and extract of Poguntano leaves 10 mg/BB/day for 5 days orally at the 10 <sup>th</sup> day after induction

### 2.3 Preparation of Bacterial Suspension and Induction of Rhinosinusitis

Strain ATCC 25923 of *S aureus* was suspended to reach a concentration of  $900 \times 10^6$  cells/ml using a McFarland Nephelometer Standard III at the Department of Microbiology, University of Sumatera Utara Hospital. After the administration of sedative, the right nasal cavities of the animals were filled with the sponge for indirect obstruction of the maxillary sinus ostium (Figure 1).

The sponges were soaked in 1.0 ml solution containing bacteria. No procedure was performed in the left nasal cavity.



Figure 1. Insertion sponge into the right nasal cavity

### 2.4 Procalcitonin Determination

PCT levels were measured in sera using Rat Procalcitonin (PCT) ELISA kit by Cusabio (CSB-E13419r) according to the manufacturer's instruction with detection range 31.25-2000 pg/ml.

### 2.5 Data Analysis

All data are expressed as group mean  $\pm$  SD and analyzed using SPSS. Kolmogorov-Smirnov test was applied for the analysis of data distribution. The parametric test of analysis of variance (ANOVA) was used to analyze the data. The effects of treatment were examined using two-way analysis of

variance, with a Bonferroni correction for post-hoc pairwise comparisons. A critical value for significance of  $p < 0.05$  was used throughout the study.

### 3 RESULTS

The results of the phytochemical screening are presented in Table 2. As can be seen in Table 2, it is shown that the chemical compounds contained in Poguntano leave consisted of tannins, saponins, triterpenoids/steroids, flavonoids, and glycosides.

Table 2: The result of phytochemical screening

No	Screening	Results
1	Alkaloids	Negative
2	Tannins	Positive
3	Saponins	Positive
4	Triterpenoids/ Steroids	Positive
5	Flavonoids	Positive
6	Glycosides	Positive

Table 3 : Procalcitonin levels

Group	Procalcitonin levels, Mean (SD), pg/ml	<i>p</i>	B	C
A	287,5 (120,62)	<0,001	<0,001	1,000
B	699,38 (214,17)			<0,001
C	191,13 (51,75)			

The lowest level of procalcitonin was found in group C with an average of 191.13 pg/ml (SD = 51.75 pg/ml). While the highest PCT levels were found in group B (positive control) with an average value of 699.38 pg/ml (SD = 214.17 pg/ml).

Using the ANOVA test showed that there were significant differences in the mean PCT in the 3 study groups. From the results of the Post Hoc test with the Bonferroni test showed that there were significant differences between groups A and B ( $p < 0.001$ ) and group B and C ( $p < 0.001$ ). There was no difference in mean PCT levels between group A and C ( $p = 1,000$ ).

### 4 DISCUSSION

In this study, the highest increase in procalcitonin (PCT) levels occurred in the ARS-induced group without given poguntano extract (group B) with an average value of 699.38 pg/ml (SD = 214.17 pg/ml). This is in accordance with the statement of Autio (2017) which states that biomarkers that are compatible with both local and systemic inflammatory reactions can show pathophysiological and bacterial development in ARS, where PCT is one of the proinflammatory markers that can be associated with bacterial infections.

PCT is considered the most promising marker in the assessment of upper respiratory tract infections to distinguish etiologies from bacterial and non-bacterial (Kofteridis, et al., 2009). PCT release is mediated by cytokines which are increased due to the response of bacterial infections, such as tumor necrosis factor  $\alpha$  and interleukin  $1\beta$ , while PCT is retained by the release of interferon due to its response to viral infection (Dilger, et al., 2019).

The increase in PCT in this study is in accordance with a series of clinical studies documenting an increase in PCT levels in shock septic patients due to bacteremia (Gilbert, 2011). A cohort study in Wegener granulomatosis also showed an increase in PCT levels in patients suffering from bacterial infections, but PCT levels appear normal in patients with active autoimmune (Limper, et al., 2010).

Based on the ANOVA test, there was a significant difference between the groups that were only induced by ARS (group B) and the group given poguntano extract (group C).

If assessed from the average, in this study it was also seen that the lowest PCT levels were found in the group given poguntano leaf extract ten days after induction, in group C. Decreased PCT levels after

being given this poguntano extract in reducing inflammatory reaction due to ARS induction according to the statement Auliafendri, et al. (2019) which states that modern pharmacological investigations have indicated that poguntano extract has an anti-inflammatory, antipyretic, analgesic, antioxidant, diuretic, antidiabetic, hepatoprotective, and antihelminthic effect. This is in accordance with Sibagariang (2017) who concluded from some of the results of previous studies that poguntano contains chemical compounds in the class of glycosides, flavonoids, saponins, tannins and steroids/triterpenoids. Tannin is considered to have an anti-inflammatory and anti-diabetes effect. The activity of tannin as an anti-inflammatory has been widely investigated (Park, et al, 2013).

In addition, flavonoids (also called bioflavonoids), are one of the natural ingredients that can be found in plants, have been considered to have an anti-inflammatory function both in vitro and in vivo. Various studies have shown that flavonoids react through a variety of mechanisms to prevent the occurrence of inflammatory responses and also areas cardioprotective, neuroprotective and chemopreventive agents (Hassan, et al., 2012).

The inflammatory response occurs through three important phases where each phase is mediated by a different mechanism, where the acute phase is characterized by local vasodilation and increased capillary permeability, the subacute phase is characterized by infiltration of leukocytes and phagocytic cells, whereas in the chronic proliferative phase is indicated by tissue degeneration and fibrosis (Yassine, et al., 2016).

Yassine, et al., (2016) in his study has demonstrated the role of flavonoids in the anti-inflammatory process. In the initial phase where histamine and serotonin release is followed by edema due to the production of bradykinin and prostaglandin (this phase is known to be sensitive to both steroid and non-steroidal anti-inflammatory agents), flavonoids are seen to inhibit important enzymes that play a role in biosynthesis of tissue activator production, especially prostaglandins and nitric oxide. Flavonoids are also seen to be effective in inhibiting arachidonic acid metabolism which mediates prostaglandin biosynthesis through inhibition of cyclooxygenase 1 (COX-) and cyclooxygenase 2 (COX-2) enzyme gene expression. The active ingredient of flavonoids is also considered capable of being an effective scavenger of reactive oxygen species due to the presence of phenolic hydroxyl groups so that it is also considered a strong antioxidant (Satria, et al., 2017).

## 5 CONCLUSION

According to our study, it can be concluded that the extract of Poguntano leaf can reduce procalcitonin levels in a rat model of acute bacterial rhinosinusitis. Further investigation is needed to isolate and identify the compounds present in the extract, which are responsible for this activity.

## REFERENCES

- Auliafendri, N., Rosidah, Yuandani, Suryani, S., Satria, D. 2019. The Immunomodulatory Activities of *Picasia Fel-Terrae* Lour Herbs towards RAW 264.7 Cells. *MJMS*.7(1): 24-28.
- Autio, T.J., Koskenkorva, T., Leino, T.K., Koivunen, P., and Alho, O.P. 2017. Longitudinal Analysis of Inflammatory Biomarkers During Acute Rhinosinusitis. *The Laryngoscope*. 127: E55-61.
- Bachert, C., Schapowal, A., Funk, P. and Kieser, M. 2009. Treatment of Acute Rhinosinusitis with the Preparation from *Pelargonium sidoides* EPs 7630: A Randomized, Double-blind, Placebo-controlled Trial. *Rhinology*. 47: 51-58.
- Cheng, Y., Wei, H., Li, Z., Xue, F., Jiang, M., Chen, W., et al. 2009. Effects of Intranasal Corticosteroids in the Treatment of Experimental Acute Bacterial Maxillary Sinusitis in Rabbits. *ORL*. 71: 57-65.
- Hassan, M.M., Daula, A.F.M.S.U., Jahan, I.A., Nimmi, I., Adnan, T., Al Mansur, A., Hossain, H. 2012. Anti-inflammatory Activity, Total Flavonoids and Tannin Content from the Ethanolic Extract of *Ageratum conyzoides* Linn. Leaf. *Int. J. Pharm Psychopharmacol Res*. 1(5): 234-241.
- Juwita, N.A. 2009. Karakteristik Simplisia dan Uji Efek Antiinflamasi Ekstrak Etanol Daun Poguntanoh (*Curanga fel-terrae* Merr.) terhadap Mencit Jantan [Skripsi]. Medan: Universitas Sumatera Utara, Program Studi Sarjana Farmasi.
- Kim, D.H., Jeon, E., Park, S.N., Park, K.H., Park, Y.S. and Yeo, S.W. 2011. Effects of a Tumor Necrosis Factor- $\alpha$  Antagonist on Experimentally Induced Rhinosinusitis. *Journal of Biomedicine and Biotechnology* 2011: 1-9.
- Koch, A.K., Klose, P., Lauche, R., Cramer, H., Baasch, J., Dobos, G.J., et al. 2016. A Systematic Review of Phytotherapy for Acute Rhinosinusitis. *Forsch Komplementmed* 23: 165-169.
- Kofteridis, D.P., Samonis, G., Karatzanis, A.D., Fragiadakis, G.M., Bourliaris, C. A., Maraki, S., et al. 2009. C-Reactive Protein and Serum Procalcitonin Levels as Markers of Bacterial Upper Respiratory Tract Infections. *Am. J. Infect. Dis*. 5(4): 282-287.
- Ozcan, K.M., Ozcan, I., Selcuk, A., Akdogan, O., Gurgun, S.G., Deren, T., et al. 2011. Comparison of Histopathological and CT Findings in Experimental Rabbit Sinusitis. *Indian J Otolaryngol Head Neck Surg*. 63(1): 56-59.

- Park, M., Cho, H., Jung, H., Lee, H., Hwang, K.T. 2013. Antioxidant and Anti-inflammatory Activities of Tannin Fraction of the Extract from Black Raspberry Seeds Compared to Grape Seeds. *Journal of Food Biochemistry*: 1-12.
- Patilaya, P. dan Husori, D.I. 2015. Karakteristik Ekstrak Air Daun Poguntano (*Curanga fel-terrae* Lour/Merr) yang Berpotensi Sebagai Antelmintik. *Jurnal Ilmiah Manuntung* 1(1): 90-93.
- Satria, D., Silalahi, J., Haro, G., Ilyas, S. and Hasibuan, P.A.Z. 2017. Antioxidant and Antiproliferative Activities of an Ethylacetate Fraction of *Picria Fel-Terrae* Lour.Herbs. *Asian Pac J Cancer Prev*. 18(2): 399-403.
- Schuetz, P., Briel, M. and Mueller, B. 2013. Clinical Outcomes Associated with Procalcitonin Algorithms to Guide Antibiotic Therapy in Respiratory Tract Infections. *JAMA*. 309(7): 717-718.
- Sitorus, P., Harahap, U., Pandapotan, M. and Barus, T. 2014. Isolation of  $\beta$ -sitosterol from n-Hexane Extract of *Picria feel-terrae* Lour. Leave and Study of Its Antidiabetic Effect in Alloxan-Induced Diabetic Mice. *Int J Pharm Tech Res*. 6(1): 137-141.
- Yassine, E.Z., Dalila, B., Latifa, E.M., Smahan, B., Lebtar, S., Achour, S., Abdellah, F. 2016. Phytochemical Screening, Anti-inflammatory Activity and Acute Toxicity of Hydro-ethanolic, Flavonoid, Tannin and Mucilage Extracts of *Lavandula stoechas* L.from Morocco. *IJPPR*. 8(1) : 31-37.

SCITEPRESS  
SCIENCE AND TECHNOLOGY PUBLICATIONS