



RESEARCH ARTICLE

Antiasthmatic effect of *Curcuma aeruginosa* extract on isolated organ of the trachea [version 1; referees: awaiting peer review]

Swandari Paramita ^{1,2}, Emil Bachtiar Moerad³, Sjarif Ismail^{2,4}, Eva Marlina⁵

¹Laboratory of Community Medicine, Faculty of Medicine, Mulawarman University, Samarinda, East Kalimantan, 75119, Indonesia

²Center for Medicine and Public Health Research, Institute for Research and Community Services, Mulawarman University, Samarinda, East Kalimantan, 75119, Indonesia

³Department of Internal Medicine, Faculty of Medicine, Mulawarman University, Samarinda, East Kalimantan, 75119, Indonesia

⁴Laboratory of Pharmacology, Faculty of Medicine, Mulawarman University, Samarinda, East Kalimantan, 75119, Indonesia

⁵Laboratory of Organic Chemistry, Department of Chemistry, Faculty of Mathematics and Natural Sciences, Mulawarman University, Samarinda, East Kalimantan, 75119, Indonesia

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Abstract

Background: Asthma is a major health problem worldwide. Antiasthma drugs have side effects and can be expensive. It is important to develop antiasthma drugs from medicinal plants that have fewer side effects and are cheaper. One of the medicinal plants used for antiasthma treatment comes from *Curcuma aeruginosa* (*Zingiberaceae* family). The aim of the research is to examine spasmolytic activity of ethanol extract of *C. aeruginosa* on isolated guinea pig tracheas to determine the antiasthma effects.

Methods: The spasmolytic activity of *C. aeruginosa* extracts was tested in separated organs of guinea pig trachea. Guinea pig was sacrificed and its trachea rings were suspended in L-shaped wire loops in organ baths containing the Krebs solution aerated with carbogen. Isometric contractions of tracheal rings were measured by the transducer coupled to the amplifier. The trachea rings were exposed to DMSO as negative control, aminophylline as positive control and *C. aeruginosa* extracts. The single concentration-relaxation curve was obtained in every preparation.

Results: The result showed that the decrease of the spasmolytic activity in the guinea pig tracheal tone due to *C. aeruginosa* extract was significantly better ($p=0.022$) when compared to the negative control. Meanwhile, the EC_{50} value of aminophylline (0.019 ± 0.05) was not significantly different ($p=0.454$) with *C. aeruginosa* (0.024 ± 0.05).

Conclusion: It could be concluded that *C. aeruginosa* extracts have the potency to be further developed as a new natural source of the antiasthma agents.

Keywords

antiasthma, *Curcuma aeruginosa*, spasmolytic

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REVIEW

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Corresponding author: Swandari Paramita (swandariparamita@gmail.com)

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Introduction

Asthma is an inflammatory airway disease characterized by the occurrence of a respiratory airway hyper response and reversible narrowing of the airway¹. Asthma is one of the major non-communicable diseases in the world. About 235 million people worldwide suffer from asthma, particularly children. The strongest risk factors for developing asthma are a combination of genetic susceptibility to certain inhalable allergens and environmental exposure to them². Asthma medications are given to manage asthma sufferers³. Herbal preparations are one of the most popular complementary treatments used by asthmatic patients. Many important asthma drugs such as B2-agonists, anticholinergics, methylxanthines, and cromones have herbal origins⁴. Some medicinal plants have the effect of reducing smooth muscle stiffness, similar to the mechanism of asthma drugs, especially the anticholinergic drugs⁵. Research has also shown that some medicinal plants have the anti-inflammatory effects, following the same mechanism of corticosteroid drug used in asthma treatment⁶.

The genus *Curcuma* (family *Zingiberaceae*) consisting of more than 100 species is used widely as food and in traditional medicines⁷. Indonesia is home to many species of *Curcuma*. The various species of *Curcuma* often used are *C. longa* (turmeric), *C. xanthorrhiza*, *C. heyneana*, *C. aeruginosa*, *C. mangga*, and *C. zedoaria*. Turmeric is the most frequently used plant for traditional medicine in Indonesia. *C. aeruginosa* considered as indigenous *Curcuma* species in Indonesia are currently not extensively studied, yet⁸.

Important medicinal plants from the genus *Curcuma* with anti-asthmatic potential include *C. longa*⁹. Other rhizomes of *Curcuma* species are traditionally used in the treatment of asthma, i.e. *C. aeruginosa*¹⁰, *C. mangga*¹¹, *C. caesia*¹², and *C. zedoaria*¹³. The antiasthma effects of *C. aeruginosa* are currently known, therefore, the objective of this study was to establish the tracheospasmodic activity of *C. aeruginosa* applied on isolated tracheas of guinea pigs.

Method

Plant materials

The sampling of medicinal plants was conducted in Kutai Kartanegara District, East Kalimantan (0°59'51.1"S 116°58'33.1"E). Plants were then identified in the Faculty of Mathematics and Natural Sciences, Mulawarman University by comparing to the university herbarium collection.

Plant extractions

The rhizomes of *C. aeruginosa* were sliced and dried at room temperature for 3 days, crushed and transferred into a glass container. Approximately 1 kg of crushed rhizomes was soaked in 1 L of absolute ethanol (9401-03 Alcohol, Anhydrous, Reagent, J.T. Baker) for 5 days. The mixture was shaken occasionally with a shaker (3525 Incubator Orbital Shaker, Lab-Line, US). After 5 days, the materials were filtered (Whatman Filter Paper 11µm, Sigma-Aldrich) and evaporated using a rotary evaporator (RV06-ML Rotary Evaporator, IKA, Germany). The dried extracts were obtained and stored at 4°C in a dark bottle until use.

Experimental model

One male guinea pig (*Cavia porcellus*) (6 months old, 485 g) was obtained from Animal House Faculty of Medicine (Mulawarman University). They were treated in a controlled room temperature of 25°C, with a 12-hour light/dark cycle, and access to food pellets and filtered water *ad libitum*. The guinea pig was anesthetized intraperitoneally with a ketamine injection (Hameln Pharmaceuticals, Germany) at a dose of 60 mg/kg before the trachea was taken. After anesthetized, animals were euthanized by cervical dislocation. The trachea was quickly dissected by adhering fat and connective tissue of guinea pig.

Spasmolytic activity

The trachea rings were suspended in L-shaped wire loops in 10 ml organ baths (PL3508B6 Panlab Organ Bath System, ADInstruments), containing the Krebs solution (K3753 Krebs-Henseleit Buffer, Sigma-Aldrich) aerated with carbogen by maintaining the temperature at 37°C. Isometric contractions of tracheal rings were measured by the transducer (7004 Isometric Force Transducers, Ugo Basile) coupled to the amplifier (FE 221 BridgeAmp, ADInstruments) connected to PC running **LabChart V5** software. An equilibration period of 90 minutes was done in Krebs solution. At the end of the equilibration period, the tracheal rings were stimulated with histamine in order to establish viability. After equilibration, the tracheal rings were exposed to DMSO (W387520 Methyl sulfoxide, Sigma-Aldrich) as the negative control, aminophylline (A1755 Aminophylline, Sigma-Aldrich) as positive control drugs and extract of *C. aeruginosa* according to the experimental protocol by Janbaz *et al.*¹⁴. The dosage for DMSO, aminophylline and plant extract were 0.0001, 0.0003, 0.001, 0.003, 0.01, and 0.03 mg/ml given 700, 750, 800, 850, 900, and 950 seconds after equilibration on the organ baths. The dose-response curve for trachea relaxation activity was obtained in every preparation.

Data analysis

Trachea relaxation activity is tabulated in the mean \pm SD curve of the dose-response curve. The value of EC₅₀ was calculated with Microsoft Excel 2016 as shown in **Dataset 1**. Data were analyzed using the Mann-Whitney because not normally distributed. All statistical analysis was performed using **SPSS** version 16.0 for Windows. A p-value of ≤ 0.05 was considered to be significant.

Ethical considerations

All protocols used in this experiment received approval from the Ethical Animal Care from the Medical and Health Research Ethics Commission, Faculty of Medicine, Mulawarman University No. 72/KEPK-FK/V/2018. All efforts were made to ameliorate any suffering of animals used in this research.

Results

The results of trachea relaxation between negative control, aminophylline, and *C. aeruginosa* extract presented in **Figure 1**. The result showed that the decrease of spasmolytic activity of *C. aeruginosa* extract was significantly better ($p=0.000$) than that in negative control. Meanwhile, the EC₅₀ value of aminophylline (0.019 ± 0.05) was not significantly different ($p=0.454$) with *C. aeruginosa* (0.024 ± 0.05), as shown in **Figure 2**.

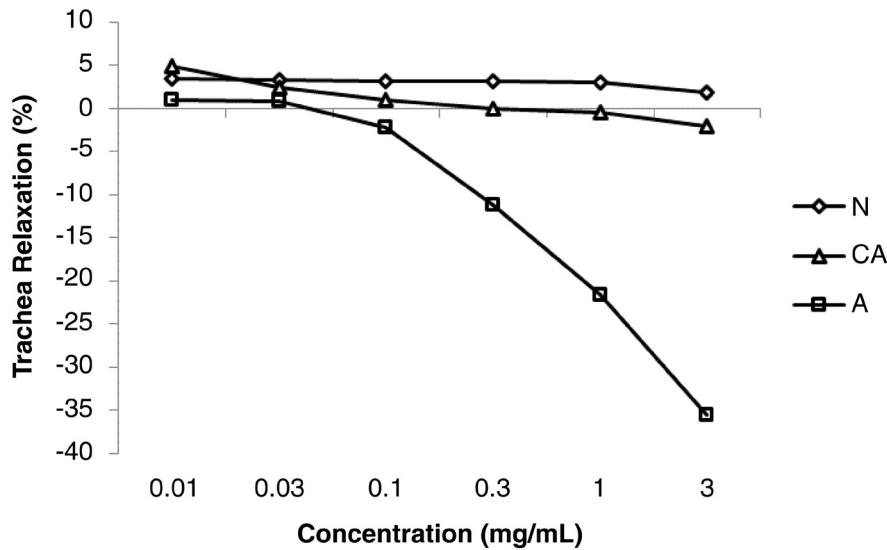


Figure 1. Graph of trachea relaxation differences between *C. aeruginosa* (CA), aminophylline (A) as the positive control and negative control (N) in isolated trachea of guinea pig.

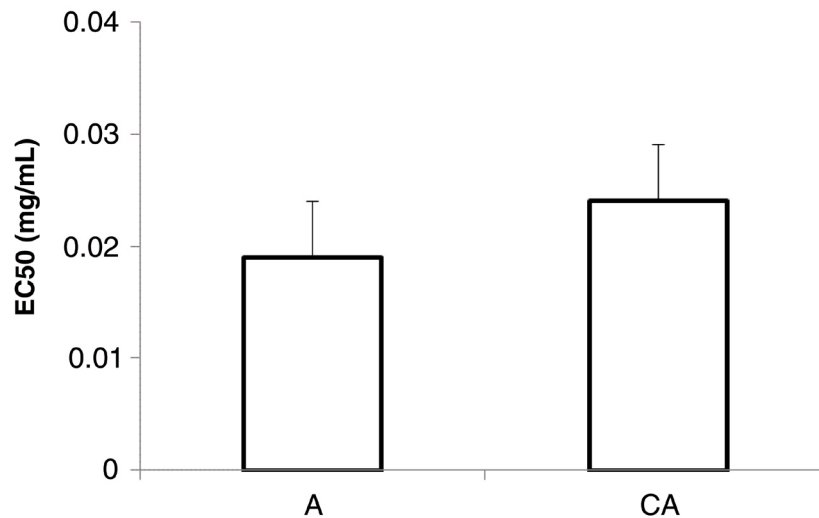


Figure 2. The EC₅₀ result on trachea relaxation between *C. aeruginosa* (CA) and aminophylline (A) as a positive control.

Dataset 1. Trachea relaxation between *C. aeruginosa* (CA), aminophylline (A) and negative control (N) and EC₅₀ result on trachea relaxation between *C. aeruginosa* (CA) and aminophylline (A)

<https://dx.doi.org/10.5256/f1000research.16416.d221690>

Discussion

C. aeruginosa (Supplementary File 1) is known in Indonesia as *temu ireng* or “pink and blue ginger” in English¹⁵. The color of fresh the rhizome can be yellows or greenish blue in color and mildly aromatic with a ginger-like aroma¹⁶. *C. aeruginosa*

has been used as a traditional medicine in South and Southeast Asia¹⁷. The rhizomes have been used for gastrointestinal and uterine disorders, as well as parasitic and fungal infection¹⁸.

Other pharmacological activities of *C. aeruginosa* that have been reported include inhibition of HIV, anti-cancer activity, hepatoprotective, antiandrogenic, estrogenic properties, antimicrobial, antioxidant, antiplatelet-activating factor-like, antipyretic, antinociceptive, and anti-inflammatory¹⁹. Germacrone, zedoarone, dehydrocurdione, curcumenol, zedoarondiol, and isocurcumenol were chemical constituents from sesquiterpenes isolated from rhizomes of *C. aeruginosa*²⁰. In this study, the examination of

antiasthma effects of *C. aeruginosa* has been reported. Further research is needed to identify the chemical compounds from *C. aeruginosa* that could convey antiasthma activity.

Conclusion

The results of this study indicate that ethanol extract of *C. aeruginosa* has an antiasthma effect based on the tracheospasmodic activity. Therefore, *C. aeruginosa* can be developed as a possible source of new antiasthma drugs.

Data availability

F1000Research: Dataset 1. Trachea relaxation between *C. aeruginosa* (CA), aminophylline (A) and negative control (N) and

EC50 result on trachea relaxation between *C. aeruginosa* (CA) and aminophylline (A)., [10.5256/f1000research.16416.d221690](https://doi.org/10.5256/f1000research.16416.d221690)²¹

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The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Supplementary material

Supplementary File 1: Picture of rhizome of *Curcuma aeruginosa* Roxb.

[Click here to access the data](#)

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