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EDITORIAL WORDS

apt. Mohammad Rizki Fadhil Pratama, S.Farm., M.Si.

Editor in Chief
Borneo J Pharm

Assalamu'alaikum Wr. Wb.

Alhamdulillahirabbil 'alamin. The next edition of **Borneo Journal of Pharmacy** (*Borneo J Pharm*), has been published at August 2020. Starting from this edition, *Borneo J Pharm* increases the frequency of publishing four times a year. This change aims to improve circulation of the best articles published by *Borneo J Pharm*. Also, starting from this edition, *Borneo J Pharm* applying the publish-as-you-go issue to present the title of the article that has been received as early as possible in order to increase the chances of readability and quotation of articles in *Borneo J Pharm*.

Starting in the 2019 edition, *Borneo J Pharm* has been accepted for indexing in **EMBASE** by Elsevier. This is an acknowledgment of the quality of the publications presented by *Borneo J Pharm*. In addition, *Borneo J Pharm* has also been accredited at **SINTA** in rank **3**. In the future, *Borneo J Pharm* will try to improve the accreditation to rank 2, and register with other indexers such as ESCI by Web of Sciences and ASEAN Citation Index. We will ensure this achievement as a start and will continue to improve the quality of *Borneo J Pharm*.

This edition contains six articles consisting of Pharmacology-Toxicology, Pharmacognosy-Phytochemistry, Microbiology Pharmacy, Natural Product Development, and Clinical-Community Pharmacy. This edition includes writings from five countries including Indonesia, India, Libya, Nigeria, and Russian Federation. The authors come from several institutions, including Sekolah Tinggi Ilmu Kesehatan Senior Medan, University of Tripoli, National Centre for Diabetes and Endocrinology of Libya, Pyatigorsk Medical and Pharmaceutical Institute, Kebbi State University of Science and Technology of Aliero, Federal Medical Centre of Birnin-Kebbi, Shri Gopichand College of Pharmacy, Meerut Institute of Engineering and Technology, NKBR College of Pharmacy and Research Centre, Universitas 17 Agustus 1945 Jakarta, and Universitas Esa Unggul.

Editorial boards are fully aware that there are still room for improvement in this edition, hence with all humility willing to accept constructive suggestions and feedback for improvements to the publication for the next editions. The editorial board would like to thank all editors and reviewers, and contributors of the scientific articles who have provided the repetoire in this issue. We hope that all parties, especially the contributors of the articles, could re-participate for the the publication in the next edition on November 2020.

Wassalamu'alaikum Wr. Wb.

Palangka Raya, August 2020

Editor-in-Chief

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Author Guidelines

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1. Writing is the result of research or review of critical analysis study in the field but not limited to Pharmacology-Toxicology, Pharmacognosy-Phytochemistry, Pharmaceutical, Analytical Pharmacy-Medicinal Chemistry, Natural Product Development, Clinical-Community Pharmacy, Management Pharmacy, and other Pharmacy aspects which have never been published in other scientific publication media.
2. Manuscripts that have been published in the form of a preprint on several platforms such as arXiv, INA-RXiv, SSRN, and ResearchGate are welcome to publish.
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   d. Introduction, contain background, reasons for the importance of underlying research or hypotheses, general approaches and objectives of the research and relevant literature review. The number of paragraphs not restricted but the contents must include background, objectives, positions on previous research, as well as the novelty of the research. The little theoretical basis which indirectly related to the contents of the article could be included without sub-chapters required. Citation is written in the form of the last name followed by the year of publication. If the author numbered two people, the last names of the two writers were written separated by the "&". Citation of more than one author written in "et al".
   e. Methodology, Research method consists of 2 sub-chapters including materials and methods. If data analysis is specific, or the way of analysis is novel, then data analysis subchapter could be added. The sub-chapters are written without numbering or bullet.
   f. Results and Discussion, at least contain three subjects (1) description of results, (2) interpretation or explanation of results, and (3) comparative of results with previous studies results. If the subchapters very length could be made sub-sub-chapters with Arabic numbering. Description of the results can be in the form of tables and figures with a serial number (Table uses a sequence of Roman numerals and placed at the top, while figures using Arabic numeric sequence and placed in the below).
   g. Conclusion, made in a single paragraph without the citation contains the final conclusion and suggestions for advanced research.
   h. References, a list of recently selected topics is published last five years (minimum 75% of at least 10 references). The bibliography is written in alphabetical order chronologically without the serial number (Harvard System) with modified APA style (Do not use parentheses for years and use periods instead of commas) and suggested using a reference management application such as EndNote, Mendeley, Zotero, and other applications.
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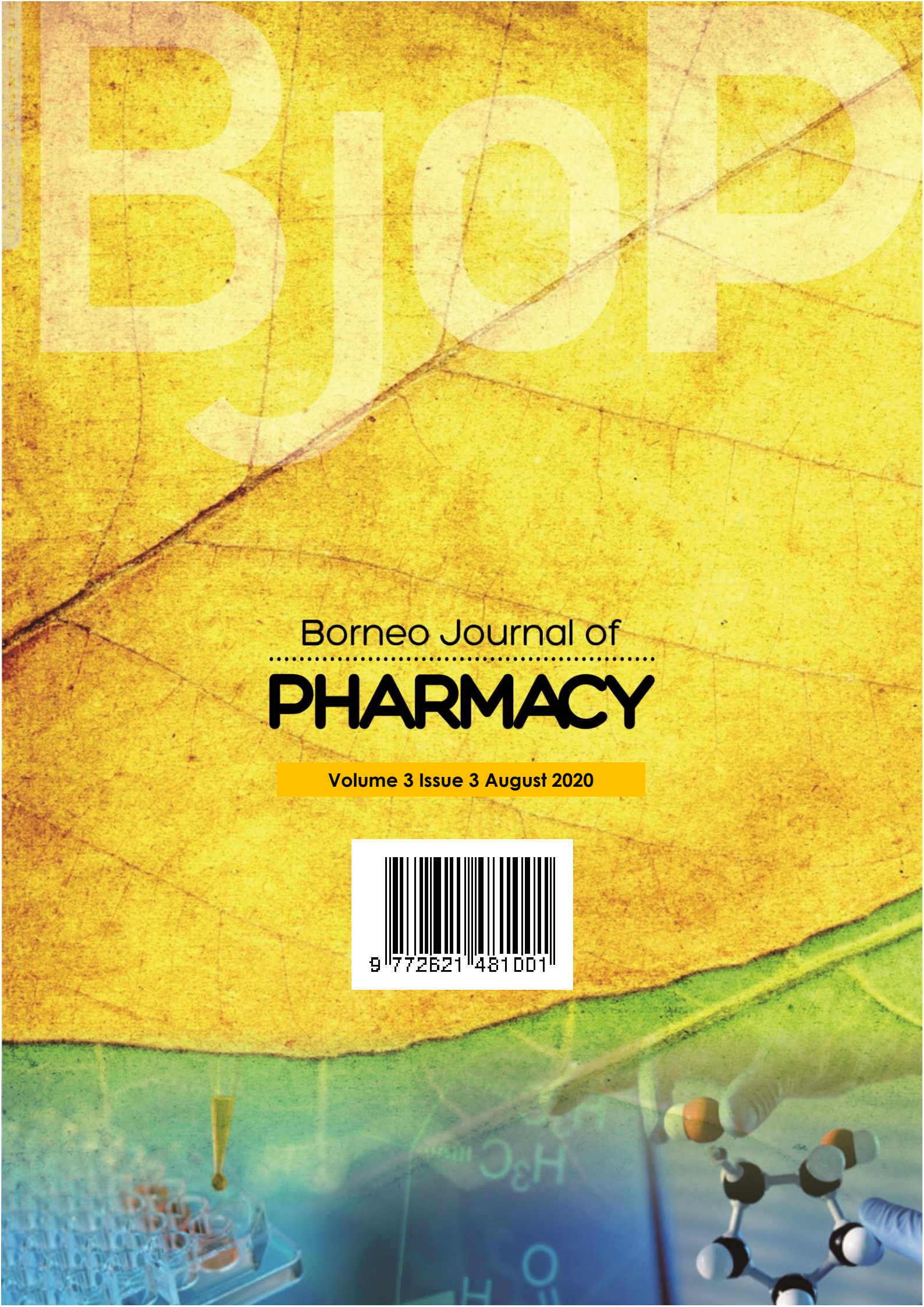
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Research Article

Antibacterial Activity of Bandotan (*Ageratum conyzoides* L) Leaves Extracts Against Methicillin-Resistant *Staphylococcus aureus*

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Keywords:
Ageratum conyzoides
Antibacterial
MRSA

Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of nosocomial infections throughout the world and can be life-threatening as well. This study aimed to determine the antibacterial activity of Bandotan (*Ageratum conyzoides* L) leaves ethanolic extract against MRSA's growth. *Ageratum conyzoides* leaves were extracted by ethanol and screened for their phytochemical constituent. Ethanolic extracts of *A. conyzoides* leaves were evaluated for their potential antibacterial activity using disc diffusion assay. The minimum inhibitory concentration (MIC) value was determined using the agar dilution method. Phytochemical screening shows that the extracts contain alkaloids, flavonoids, saponins, tannins, and steroids or triterpenoids. *Ageratum conyzoides* leaves extract shows a 25.1 mm inhibitory zone at 12.5% extract concentration with MIC value equivalents to 4.46 x 10^{-6} g of gentamicin. This study concludes that *A. conyzoides* leaves ethanolic extracts have potential antibacterial activity against MRSA.

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INTRODUCTION

Antibiotic resistance is one of the biggest threats to global health. It is rising to dangerously high levels in all parts of the world (Aslam *et al.*, 2018). Methicillin-resistance *Staphylococcus aureus* (MRSA) is a common cause of severe nosocomial infections (Choo & Hambers, 2016). It has developed resistance to numerous antibiotics caused by the misuse and overuse of antibiotics. The MRSA can hydrolyze almost any type of lactams, and its strains spread quickly, leading to a high mortality rate (Hu *et al.*, 2019). World Health Organization (WHO)'s first global report on antibiotic resistance reveals that more than one-quarter of *S. aureus* infections in the south-east Asia region are reported to be MRSA, which is home to a quarter of the world's population (Prestinaci *et al.*, 2015). Therefore, alternatives antibacterial against MRSA infections is still sought-after investigation.

Many antibacterial drugs were firstly isolated from natural sources (Rossiter *et al.*, 2017). Many studies revealed that medicinal plants provide antibacterial compounds from its secondary metabolites (Gorlenko *et al.*, 2020; Othman *et al.*, 2019; Voravuthikunchai & Kitpipit, 2005). Indonesia is a rich archipelago with an abundance of natural plants to explore. One of them is bandotan (*Ageratum conyzoides* L.) plants, which grow in many Indonesian regions and are classified as tropical weeds (Kotta *et al.*, 2020; Atisha & Mita, 2018). It is easy to find the weeds because it thrives in any garden and agricultural soils. It is also ubiquitous in disturbed sites and degraded areas (Marks & Nwachuku, 1986). The weeds are also noxiously regarded as harmful for crops,

but on the contrary, *A. conyzoides* have been known since ancient times for their therapeutic benefits (Garg *et al.*, 2015). The weed is traditionally used to treat new wounds, bleeding wounds, ulcers, eczema, bacterial infection diseases, arthrosis, headaches, pneumonia, analgesic, antispasmodic, anti-inflammatory, leprosy, and other skin diseases (Kamboj & Saluja, 2008; Achmad *et al.*, 2020). Recent studies have shown that bandotan leaves have antibacterial activity against *Staphylococcus aureus*, *Porphyromonas gingivalis*, *Streptococcus mutans*, and *Escherichia coli* (Mentari *et al.*, 2020; Achmad *et al.*, 2020; Sugara *et al.*, 2016).

Many research shows that *A. conyzoides* have various health benefits. However, there is still limited research on *A. conyzoides* leaves antibacterial activity specifically towards MRSA. Therefore, this study focused on assessing the antibacterial activity of *A. conyzoides* leaves extract towards MRSA.

MATERIALS AND METHODS

Plant material

Ageratum conyzoides plants were collected from the rice field at Limbangan, Garut, West Java, Indonesia. The plants were authenticated and determined at the Herbarium Unit, Department of Biology, Universitas Padjadjaran, Indonesia.

Extract preparation

Ageratum conyzoides leaves were washed and dried for ten days at 40°C. Dried leaves were grinded into powder and evaluated by the distillation method to analyze the moisture content. Extraction was performed by the maceration method. As much as 250 g of *A. conyzoides* leaves were extracted by ethanol 96% at room temperature. The solvent was replaced three times with fresh solvent every 24 hours. After filtration of total extracts, *A. conyzoides* leaves extract were evaporated by rotary evaporator until it dry and were weighed to determine the yield.

Phytochemical screening

The extract was subjected to various phytochemical screening to identify its chemical constituents, including alkaloids, flavonoids, saponins, tannins, quinones, steroids, or triterpenoids. The procedures for detecting those secondary metabolites are referred to Materia Medika Indonesia volume IV (1980).

Bacterial culture

Methicillin-resistance *Staphylococcus aureus* ATCC 43300 isolates were obtained from the Department of Pharmacy, Universitas Padjadjaran, Indonesia. The bacteria were maintained on Nutrient Agar (NA) slope and then subcultured on NA at 37°C for 18-24 hours.

Antibacterial activity

Antibacterial activity of *A. conyzoides* leaves extract was evaluated by disc diffusion method. Extract was diluted on dimethyl sulfoxide (DMSO) solution to yield 5%, 7.5%, 10% and 12.5% concentration. Bacteria inoculum was introduced onto the sterile NA plates' surface using a sterile loop and spread over the media for even distribution. The plates were divided into five sections: four sections for extract and one section for gentamicin. Blank sterile paper discs were placed on the NA surface and impregnated with 15 mL of the extracts. The plates were incubated at 37°C for 18-24 hours. The antibacterial activity was expressed as clear inhibition zones produced by the extracts. The test was repeated three times.

The minimum inhibitory concentration (MIC) was investigated using the agar dilution method. As much as 1 mL of *A. conyzoides* leaves extracts with various concentration (1%, 2%, 3%, 4%, and 5%) were added into 10 mL NA. Bacterial suspensions were inoculated onto each plate with a sterile loop, and the presence or absence of bacteria growth is recorded after suitable incubation. Incubation lasted for 18-24 hours at 37°C. The MIC was

determined as the lowest concentration of *A. conyzoides* leaves extracts, which completely inhibited bacterial growth. Furthermore, the MIC was converted by regression linear equation into its antibiotic dose.

RESULTS AND DISCUSSION

This study is experimental laboratory research. The moisture content of *A. conyzoides* L. leaves was 5%, which less than 10%. The yields extract obtained with maceration was 17.16 g from 250 g simplicia. The phytochemical screening showed that *A. conyzoides* leaves contained various secondary metabolites, such as alkaloids, flavonoids, saponins, tannins, steroids, or triterpenoids as shown in **Table I**. These results agree with the previous study of phytochemical screening of *A. conyzoides* leaves. It shows alkaloids, saponins, flavonoids, polyphenols, tannins, glycosides, resins, phenols, and essential oils (Achmad *et al*., 2020; Chew *et al*., 2018; Amadi *et al*., 2012). Plants synthesized the secondary metabolites to protect them from predators such as herbivores, insects, and microorganisms. It could kill or inhibit microorganism growth via different mechanisms (Chew *et al*., 2018).

Table I. Phytochemical screening of *A. conyzoides* leaves

Phytochemical	Simplisia	Extract
Alkaloids	+	+
Flavonoids	+	+
Saponins	+	+
Tannins	+	+
Quinones	-	-
Steroids/Triterpenoids	+	+

(+) : presence; (-) : absence of phytochemicals

The results of the antibacterial activity were revealed using the disc diffusion method. This is a standard qualitative assay to evaluate the antimicrobial activity of extracts or phytochemicals. *Ageratum conyzoides* leaves ethanolic extracts have demonstrated antibacterial activity against MRSA isolate. From **Figure 1**, it can be seen that the higher extract concentration produced a more expansive inhibition zone. The inhibition zone at 5% concentration of *A. conyzoides* leaves extract had the lowest average inhibition zone of 15.47 mm, while 12.5% had the largest average inhibition zone of 25.1 mm. *Ageratum conyzoides* leaves extract with 12.5% concentration, giving almost similar results compared to gentamicin, which was used as a comparative antibiotic. This activity may be attributed to the rich tannins and flavonoid contents of *A. conyzoides* leaves. Flavonoids and tannins have been reported to possess antimicrobial activity due to their ability to complex with the bacteria cell wall and inactivate enzymes, microbial adhesion, and cell envelops proteins (Cowan, 1999). These results confirmed the evidence in previous studies that reported that the extract of *A. conyzoides* has potential antibacterial activity against *S. aureus* (Garg *et al*., 2015; Sugara *et al*., 2016).

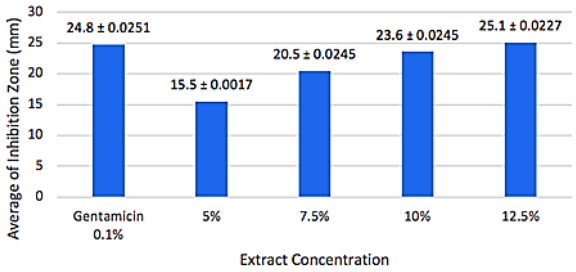

Figure 1. Antibacterial activity of *A. conyzoides* leaves extract against MRSA

The quantitative analysis using the agar dilution method showed that at a concentration of 1%, 2%, and 3% of *A. conyzoides* leaves extract still observed MRSA growth; meanwhile, the absence of MRSA growth can be seen at a concentration of 4% and 5% as shown in **Table II**. It was indicated that extract of *A. conyzoides* leaves active exhibiting the highest potency with MIC of 4%. Previously, the plant has been reported to have good antibacterial activity towards *S. aureus* with the MIC value of 2% (Budiman & Aulifa, 2020). According to research conducted by Astuti (2015), ethanolic extract of *A. conyzoides* leaves had the MIC value of 12.5 mg/mL against *S. aureus*. The MRSA was more challenging to

treat than most *S. aureus* because it is resistant to some commonly used antibiotics. Therefore, the MIC value for MRSA was higher than *S. aureus*.

Table II. Minimum inhibitory concentration of *A. conyzoides* leaves extract

Extract concentration (%)	Bacterial growth
1	+
2	+
3	+
4	-
5	-

(+) : growth of bacteria; (-) : no growth of bacteria

The MIC value of *A. conyzoides* leaves extracts then converted into equivalency of antibiotic dose. The concentration of 4% *A. conyzoides* leaves extract concentration was analyzed to determine its antibiotic dosage equivalency using the agar diffusion method as shown in **Figure 2**. Gentamicin was used as a reference standard antibiotic. Gentamicin is an aminoglycoside that inhibits bacterial protein synthesis by binding to its ribosomes (Krause *et al.*, 2016). The standard dose of gentamicin is 3-6 mg/kg/day divided every eight hours to treat MRSA prosthetic valve endocarditis. Gentamicin is regularly added with rifampin for the first two weeks of treatment (Galar *et al.*, 2019).

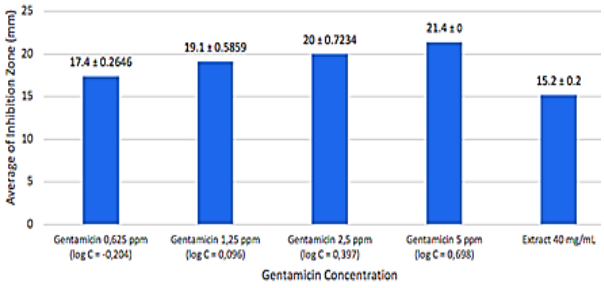

Figure 2. Inhibition zone of *A. conyzoides* leaves extract compared with gentamicin

Furthermore, the data was calculated by linear regression, as seen in **Figure 3**. The obtained equation concluded that 4% of *A. conyzoides* leaves extract was equivalent to 4.46 x 10^{-6} g of gentamicin. This concentration could be considered when designing the next potential drug to treat nosocomial infection caused by MRSA.

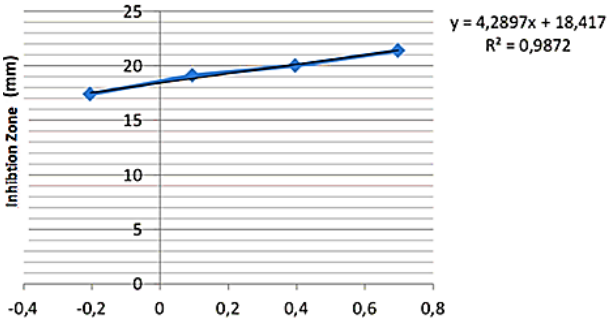

Figure 3. Linear regression graphic and equation of gentamicin inhibition zone

CONCLUSION

Ethanolic extracts of *A. conyzoides* leaves have potential antibacterial activity against MRSA. Further identification of the active constituents is needed to evaluate its efficacy and safety against MRSA.

ACKNOWLEDGMENT

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