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## Systematic Review: Potential of Garlic Extract (*Allium Sativum*) as a Treatment for Diarrhea (*E. Coli*)

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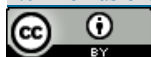
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### ABSTRACT

Diarrheal disease continues to be one of the major public health problems worldwide, with more than 1.5 million deaths each year and most of them in children under 5 years of age. The incidence of diarrheal diseases averages 2-3 episodes per child per year. Excessive use of antibiotics as antidiarrheals is associated with an increase in bacterial resistance to antibiotics, medical costs, and the incidence of side effects. In past research, it has been found that garlic has a wide antimicrobial spectrum so that it can kill gram-negative and gram-positive bacteria, so it can be used as an alternative treatment for diarrhea. The purpose of carrying out this study was to describe the potential for garlic extract that have an effect on gram-negative bacteria that cause diarrhea, this natural ingredient can be used as a safe alternative treatment to treat infectious diseases that cause gram-negative bacterial diarrhea. This research method is Narrative review (Literature review). In a journal that discusses the effectiveness of garlic as an antimicrobial regarding the antibacterial activity of thiosulfinates using the petri plate diffusion test, the efficacy of the substances cannot be compared with each other because the assumed diffusion rates are different. In the journal on Comparison of the antibacterial activity of thiosulfinates using the petri plate diffusion test, the efficacy of the substances cannot be compared with each other because the assumed diffusion rates are different. The results showed that the MIC and MBC results of each bacteria given garlic extract were different, even though they were both gram-negative bacteria. Garlic extract has the highest effectiveness on *E. coli* bacteria based on in vitro studies conducted, compared to *Salmonella*, *Shigella*, *V. cholerae* bacteria according to the characteristics of these bacteria

## INTRODUCTION

Diarrheal disease continues to be a major public health problem worldwide, with more than 1.5 million deaths each year, mostly in children under 5 years of age. The incidence of diarrheal disease averages 2-3 episodes per child per year (Qu et al., 2016). Diarrhea is a condition in which a person has bowel movements with a soft or liquid consistency, it can even be just water with a more frequent frequency in one day (Meckling, 1976). In Africa, around 3.6 million child deaths in 2010, 12% were caused by diarrheal diseases (Langendorf et al., 2015). In developed countries it is estimated that the incidence is around 0.5 – 2 episodes/person/year while in developing countries it is more than that (Zein, 2004). Diarrheal disease is still a public health problem in developing countries such as Indonesia, because of its high morbidity and mortality (Kemenkes RI, 2011). The prevalence rate of diarrhea in Indonesia fluctuates, based on data from the 2018 Health Research and Development Agency (Ministry of Health Research and Development), the highest prevalence of diarrhea is in East Java (48.48%) and the lowest is in D.I. Yogyakarta (40%), apart from that in East Java there was an outbreak of diarrhea with a total of 1,637,708 people. The 2013 & 2018 SKRT surveys showed a case fatality rate of 1.08% for toddlers. Cases of diarrhea that have been reported as many as 10,980 and 277 deaths. The prevalence of diarrhea caused by gram-negative bacteria is 45% (range: 40% - 50%) (Health Research and Development Agency, 2018). One that has the potential to cause diarrhea infection is caused by microorganisms that are not sterile, where germs enter to cause diarrhea (Marhamah, 2013).

Treatment of diarrhea caused by gram-negative bacteria uses a combination of antibiotics and PPI (Proton Pump Inhibitor) (Ana, et al. 2019). In addition, probiotic bacteria are also used by the general public for the treatment of diarrhea, although only limited to characterizing, purifying and multiplying isolates (Safrida et al., 2012). Medicines to treat bacterial infections are antibiotics (Nurmala et al., 2015). Antibiotics are chemical substances produced by organisms such as bacteria and fungi, which can interfere with other microorganisms (Sudigdoadi, 2001). Overuse of antibiotics is associated with an increase in antibiotic-resistant bacteria, treatment costs, and the incidence of side effects (Guarino et al., 2018). The emergence of

pathogenic germs that are resistant to one (antimicrobial resistance) or certain types of antibiotics (multiple drug resistance) greatly complicates the treatment process (Utami, 2012). The incidence of resistance due to antibiotics is Sulfoxazole 55%, Ampicillin 46.8%, Streptomycin 44%, Tetracycline 22.4%, Chloramphenicol 16.5% (Qu et al., 2016). Therefore, the treatment of diarrhea uses natural ingredients such as garlic extract which does not cause excessive side effects and resistance. Garlic extract contains antimicrobial ingredients, namely Allicin, which is effective for the treatment of gram-positive and negative bacteria (Choules et al., 2016).

Allicin which is a compound from garlic is able to inhibit gram positive and negative bacteria by inhibiting RNA production and lipid synthesis. This inhibition causes amino acids and proteins not to be produced and the bilayer of the cell wall is not formed so that bacterial growth and development does not occur (Saravanan, et al. 2010). Allicin has the capability to interact with unattached thiol groups by exchanging thiol disulfides present in glutathione and proteins (Lind et al., 1991). Garlic's antibacterial power against gram-negative bacteria is more complex, because it has an antimicrobial penetration sheath (Salima, 2015). Generally, bacteria are 1-cell or single-cell or unicellular, some gram-negative bacteria that are pathogenic, are inhibited by their DNA and RNA growth (صديقي، يسيلن مظهر، n.d.).

In studies conducted in the past it has been found that garlic has a wide antimicrobial spectrum so it can kill gram-negative and gram-positive bacteria (Salima, 2015) beberapa jenis bakterinya antara lain : *several types of bacteria include: Staphylococcus aureus, Klebsiella pneumoniae, Citrobacter, Enterobacter, etc.* (Moulia et al., 2018). The research focused on research on garlic extract which has a more potent effect on gram-positive bacteria, in research conducted on Staphylococcus aureus bacteria, it was found that Allicin had inhibited the growth of these bacterial cells through Dyallilsulfida or ajoene which had been processed, the study used a discussion of the advantages of the extract. and Allicin as a potent extract on only one type of gram bacteria. The effect of Allicin as an antidiarrheal for gram-negative bacteria is still not widely discussed, therefore it is necessary to do research based on a literature review on the potential

of garlic extract to have an effect on gram-negative bacteria that cause diarrhea.

The purpose of this study, to describe the potential of garlic extract against gram-negative bacteria that cause diarrhea, these natural ingredients can be used as a safe alternative medicine to treat infectious diseases that cause diarrhea-causing gram-negative bacteria. The main antimicrobial effect of garlic is due to the presence of diallyl sulfide and allicin which are the most abundant sulfoxide molecules in garlic extract which are responsible for and have therapeutic potential including bactericidal activity. The antimicrobial effect is more effective than the use of antibiotics in tackling gram negative bacteria.

## **METHODS**

This research method is Narrative review (Literature review). Research journals were obtained based on the criteria of Scimagojr, namely Q1 and Q2, and Q3. The target journal used is at least 100 journals in this study. The journal used is an average of the last 10 years of use. SCOPUS, PUBMED, COCHRANE, GOOGLE SCHOLAR, JAMA, UNIWEB are some of the references used as research methods.

This paper uses a qualitative descriptive method with a type of research in the form of library research, namely collecting information or scientific papers related to literature review which is literature. This research was conducted by combining descriptive and qualitative research. This study also presents data without any manipulation and other additional treatments. The main source of this research is previous scientific papers that are closely related to literature reviews, such as research method books, journal articles, internet articles, and other writings that are still related.

## **RESULTS AND DISCUSSION**

Garlic is a plant that is spread evenly in Central Asia, Siberia, and the western Himalayas that has grown in England before 1540 (Labu, 2015). Garlic (*Allium sativum*) has been known for a long time to be used as a spice in cooking and medicine (Prihandani, 2015). This plant is used as an antiseptic, anti-inflammatory, as well as other antimicrobial purposes. Allicin is one of the most important components in garlic's antibacterial

composition (Cai et al., 2007). this main component is responsible for other therapeutic potencies as it includes Diallyl sulfide or ajoene (Salima, 2015). Another benefit of garlic is that it can reduce the number of aerobic bacteria, so that ingredients added to garlic last longer (Hendra, 2017). Garlic (*Allium sativum*) was known as a medicinal plant around 300 BC by the Chinese and Central Asian tribes (Sutiyono et al., 2019).

The toxicity effects of most root canal drugs on the market currently lead to biological extract drugs from natural plants to reduce various toxic activities of chemicals. (Emilda et al., 2014). Garlic (*Allium sativum* L.) has several antibacterial components that affect the death of gram-negative bacteria. Antibacterial components of garlic are Allicin, ACSOs, Flavonoids, SAC, Lipids. Allicin, ACSOs, Flavonoids, and SAC work with DNA and RNA targets (Moulija et al., 2018). The target mechanism for these bacteria is to partially inhibit the synthesis of DNA and RNA and bacterial protein. The inhibition of nucleic acids, especially RNA from these bacteria causes inhibition of bacterial growth (Sutiyono et al., 2019). Flavonoid component, SAC is the main component in the destruction of bacterial cell membranes. In addition, these two components also affect the DNA and RNA damage of gram-positive and negative bacteria such as *E. coli*, *Salmonella*, *Shigella*, *V. cholerae* (Ankri & Mirelman, 1999). When these two components affect the bacterial cell membrane, the permeability of the bacteria is disrupted and causes leakage of molecules and ions, resulting in protein denaturation (Moulija et al., 2018). Chemical denaturation of proteins with Bovine Serum Albumin (BSA), this occurs because the flavonoid component dissolves substances in the cell walls with fat which results in inhibition of the transport of the intended bacterial substance. When the transport of substances is inhibited, these three components produce reactive allyl sulfonic acid, ammonia and pyruvic acid for destruction of the bacterial cell wall and as an antibacterial mechanism itself (Salehi et al., 2019). There are 2 effects of disrupting the transport of substances, namely causing the death of the bacterial cells or disrupting

the growth of bacterial cells which causes the death of gram-negative bacteria (Upa et al., 2017).

Antibacterial power Garlic (*Allium sativum*) on *Escherichia coli* (*E. coli*) bacteria has the ability to inhibit bacterial cell growth because Allicin increases the permeability of the bacterial wall which causes the SH groups (sulphihydril and disulfide) in the amino acids cystine and cysteine to disintegrate, so that they do not occur. proliferation in bacteria. This can cause bacteria to not divide and their growth

is stunted (Purwantiningsih et al., 2019). In *Salmonella* sp. and *Shigella* sp. it was found that pure garlic extract (*Allium sativum*) did not have good antibacterial activity. 2017) this correlates with the presence of the allicin component, if during extraction the inhibition occurs or is removed, the antibacterial effect is lost (Upa et al., 2017).

Based on a review of various literature, the in vitro results of garlic extract against these bacteria are in accordance with table 1

Table 1. Onion Extract Research on Several Bacteria

NO	Bacteria	Method	Result of KHM / KBM (mm)	Information
1.	<i>E. coli</i>	Disk diffusion	Concentration : 20% = 10.27 40% = 17.25 60% = 28.57 80% = 32.12 100% = 38.60 + = 29.27 - = 0 The most effective concentration is 100% concentration with KBM 38.60	Hardana Utama Salim Day, 2017
2.	<i>Salmonella</i>	Dilution test	Concentration: 6.25% = 0 12.5% = 0 25% = 2.25 50% = 2.75 100% = 5.75 + = 25 - = 0 The most effective concentration is the MIC concentration of 5.75 mm	Iesha Kinanti Adhuri, et al. 2018
3.	<i>Shigella</i>	Disk diffusion	Concentration : 100% = 0 + = 0 - = 0  In this study, the results showed that garlic extract was not able to inhibit <i>Shigella</i> bacteria	Gydian upa, dkk. 2017
4.	<i>V. cholerae</i>	1. Kirby-Bauer disc diffusion 2. Agar well diffusion and broth micro-dilution	Konsentrasi : Chinese Garlic Aqueous Extract : 133 mg/mL = $32.14 \pm 0.12$ 66.5 mg/mL = $25.71 \pm 0.09$	Original Article. Bilal Muhammad, et al. 2016. In Vitro Antimicrobial Activity of Garlic

using two-fold serial dilutions	33.25 mg/mL = 23.78 ± 0.07	(Allium Sativum) Against Clinical Isolates of Vibrio Cholerae. Departement Patologi dan biokimia dan molekuler Universitas Gujrat.	
	16.62 mg/mL = 20.56 ± 0.15		
	8.31 mg/mL = 18.17 ± 0.17		
	4.15 mg/mL = 14.57 ± 0.11		
	2.75 mg/mL = 0 ± 0		
	1.37 mg/mL = 0 ± 0		
	Pakistani Garlic Aqueous Extract:		Kumar, et al. 2016.
	133 mg/mL = 28.12 ± 0.05		Bactericidal Efficacy of <i>Allium sativum</i> (garlic)
	66.5 mg/mL = 24.43 ± 0.11		Against Multidrug resistant <i>Vibrio cholerae</i>
	33.25 mg/mL = 22.50 ± 0.06		of Epidemic Strains.
16.62 mg/mL = 19.56 ± 0.12	Jawaharlal Nehru		
8.31 mg/mL = 16.54 ± 0.13	University India.		
4.15 mg/mL = 12.15 ± 0.06			
2.75 mg/mL = 0 ± 0			
1.37 mg/mL = 0 ± 0			
Phenol 6% : 34.12 ± 0.13			
Normal Saline : 0 ± 0			

1. In this study, the results showed that the garlic extract that was able to inhibit the growth of bacteria was most effective in Chinese Garlic Aqueous Extract.
2. In this study, the results showed that garlic extract was able to inhibit the growth of *V. cholerae* bacteria at a concentration of 8 mg/m.

In the journal regarding Comparison of thiosulfinate antibacterial activity using the petri plate diffusion test, the efficacy of the substances cannot be compared with each other because the assumed diffusion rates are different. In the results of the study it was found that the results of the MIC and KBM of each bacteria given garlic extract were different, even though they were both gram-negative bacteria. This group of bacteria only has a thin peptidoglycan layer (5-10nm) with the main composition: Lipoprotein, outer membrane, and lipopolysaccharide (Hanif, 2009). The characteristics of *E. coli* bacteria are producing acid and gas, oxidase negative, indole and methyl red positive (Mancia et al., 2007). In addition, what distinguishes it from other gram-negative bacteria is

the IMVIC ++- test for each of these tests (Ijong & Dien, 2011). *E. coli* has a reduction rate of Allicin of 83.3% and a small portion has the ability to fail to reduce this compound (Ijong & Dien, 2011). *Salmonella* and *Shigella* are the same as *E. coli*, these two bacteria have cell walls and high lipid content (11-22 percent) and the cell wall structure is multilayered which makes it difficult for antibacterial substances to penetrate the target bacteria (Moulija et al., 2018). This is why sometimes there is no inhibition zone or minimal kill zone for the two bacteria. *V. cholerae* bacteria produce enterotoxin which has a function as extracellular protection for the bacteria and breaks the transport chain of antibacterial substances that will enter (Maheshwari et al., 2011). This is what causes these

bacteria to have varied results when tested for different MIC and KBM.

## CONCLUSION

According to many previous studies, garlic has a substance called Allicin which can inhibit the growth of gram-negative bacteria by inhibiting RNA production and lipid synthesis. In theory, the Allicin substance contained in garlic can be used as an anti-diarrhea drug. After conducting various studies using garlic extract on various types of bacteria that cause diarrhea, it was found that the effectiveness of garlic is relatively high due to the nature of garlic which has a digestive system. better resistance of the ability of bacteria. Garlic extract has the highest effectiveness against *E. coli* bacteria based on in vitro studies conducted, compared to *Salmonella*, *Shigella*, *V. cholerae* bacteria according to the characteristics of these bacteria.

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