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Antibacterial activity of cassava leaves (*Manihot esculenta crantz*)

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Abstract
Cassava (*Manihot esculenta Crantz*) is one of the plants that has been widely cultivated in Indonesia. Cassava consists of leaves, stems, roots, bark, and flowers. Cassava leaves which are greenish in color and compound leaf bones fingered with elliptical-shaped leaves with pointed tips, have antibacterial content. Antibacterial compounds are the result of secondary metabolites of cassava. Antibacterial compounds in cassava leaves work together by disrupting the permeability of cell membranes, cell proteins, and the balance of water and ions in bacterial cells. The method used in this review uses literature studies using Google Scholar in the form of national and international journals for the last 7 years. Based on the results of the literature obtained there are six types of antibacterial compounds contained in Cassava Leaves, namely cyanogenic glycoside compounds, Alkaloids, Flavonoids, Saponins, Tannins, Terpenoids, and Phenols. The type of bacteria will greatly affect the antibacterial effectiveness of Cassava Leaves.

Keywords: cassava leaf, antibacterial

Introduction
Cassava (Manihot *utilissima* or *Manihot esculenta Crantz*) is one of the plants that has been widely cultivated in various countries in the world and is widespread in Indonesia. [1] Cassava plants are one of the main types of agricultural plants in Indonesia. Cassava can is a food that is preferred by the community because it is one of the food sources of carbohydrates. [2] The taxonomy of cassava is:

Kingdom	: Plantae
Divisi	: Spermatophyta
Subdivisi	: Angiospermae
Kelas	: Dicotyledoneae
Ordo	: Euphorbiales
Famili	: Euphorbiaceae
Genus	: Manihot
Spesies	: *Manihot utilissima Pohl.; Manihot esculenta Crantz*

Cassava consists of leaves, stems, roots, bark, and flowers. Cassava leaves grow along the stem with long peduncles. Cassava leaves are greenish in color and compound leaf bones are fingered with elliptical leaves with pointed tips. The color of young leaves (shoots) is yellowish green or purplish green while adult leaves are dark gree). [3]

Cassava leaves (*Manihot esculenta Cranz*) are known to contain flavonoids, saponins, and tannins. These compounds are known to have antibacterial activity. [4] Flavonoids can form complex compounds with extracellular proteins so that the cell wall layer is not formed intact. This can cause changes in cell membrane permeability to inhibit the work of intracellular enzymes and water entering the cell uncontrollably. [5]

Saponins can bind to the cytoplasm by diffusing through the membrane, disrupting and destabilizing the membrane, and causing cytoplasm to leak out of the cell. This can eventually lead to bacterial death. [6] Tannins can inactivate bacterial adhesion, inhibit the work of enzymes, and inhibit protein transport on cell membranes by damaging cell membranes due to tannin toxicity to form complex bonds of metal ions that disrupt various bacterial functions. [7]

The ability of three compounds contained in Cassava leaves has been carried out in varying studies to be developed and analyzed. Based on the statement above, this study aims to analyze the content of antibacterial compounds in Cassava leaves. This literature study is a literature review related to antibacterial compounds in Cassava leaves (*Manihot esculenta* Cranz) taken from various sources, including research journals related to antibacterial compounds in Cassava leaves.

Method
The method used in this review is a literature *review* of ten journals based on relevant theories using Google Scholar in the form of national and international journals for the last 7 years (201: 6 - 202, 2) with keywords used, namely antibacterial in Cassava Leaves, and *Manihot esculenta Extracts on Antibiotic*.

Results and discussion

Table 1: Results of Previous Research

No.	Title	Results
1.	Antibacterial test of cassava leaf extract (*Manihot esculenta Crantz)* against *Fusobacterium nucleatum* and *Aggregatibacter actinomycetemcomitans*.	Based on the observations, the inhibitory power of cassava leaf extract against *F. nucleatum* and *A. actinomycetemcomitans* was only seen at doses of 200 µg / mL of 9.77±0.13 mm and 9.93±0.07 mm. Metronidazole analogs can inhibit *F. nucleatum* and *A. actinomycetemcomitans* by forming inhibitory zones of 15.08±0.12 mm and 15.10±0.21 mm, respectively. [8]

2.	Test of antibacterial activity of cassava leaf ethanol extract (*Manihot esculenta Crantz*) against the inhibitory power of *Escherichia coli* bacteria.	Phytochemical testing showed positive (+) results for flavonoids, saponins, and tannins. Different concentrations still produce excellent inhibitory zone criteria where a concentration of 20% has an inhibitory zone of 19 mm (strong) while concentrations of 40% - 60% have an inhibitory zone of 25 mm - 29 mm (very strong). The positive control used is that chloramphenicol can inhibit bacteria with a diameter of 32 mm (Very Strong). [9]
3.	Test of Antibacterial Activity of Cassava Leaves (*Manihot esculenta*) on *Staphylococcus aureus* and *Eschrichia coli* Bacteria.	Phytochemical testing showed positive (+) results for alkaloids, flavonoids, saponins, and tannins. A negative result (-) was tested on Triterpenoid compounds. In the antibacterial activity test, cassava leaf extract was able to inhibit the growth of *S. aureus* and *E. coli*. The highest bland zone in *S.aureus* was 11.1 mm and in *E.coli* by 5.2 cm at a cassava leaf extract concentration of 150.000 ppm. [10]
4.	Test of the inhibitory power of cassava leaf ethanol extract (*Manihot utilissima pohl*) originating from Pangkajene Sidrap Regency against bacterial growth.	The measurement of the inhibitory power of cassava leaf ethanol extract against *Staphylococcus aureus* was carried out using a caliper, where the average diameter at a concentration of 20% was 11.33 mm, a concentration of 30% was 12.66 mm, a concentration of 40% was 15.33 mm, while in the positive control, it was 21 mm and the negative control did not see an obstacle zone. [11]
5.	Test of antibacterial activity of cassava leaf ethanol extract (*Manihot esculenta*) against the growth of *Staphylococcus aureus* and *Escherichia coli*.	Cassava leaf ethanol extract screening results showed positive results (+) for alkaloids, flavonoids, tannins, terpenoids, and phenol compounds. The measurement results showed that the ethanol extract concentration of 80% with an inhibitory zone of 5.59 mm and 4.93 mm (medium) had the highest average inhibitory zone against *Staphylococcus aureus* and *Escherichia coli.* While the lowest average value was in the 75% concentration group with values of 4.12 mm and 4.07 mm. [12]
6.	Antibacterial activity test of extracts and fractions of cassava leaves (*Manihot esculenta Crantz*) against clinical isolates of *Staphylococcus epidermidis* and *Propionibacterium acnes* causing acne.	Cassava leaf ethanol extract has antibacterial activity against *S. epidermidis* and *P. acnes* with ethyl acetate fraction being the most active fraction. MIC value of ethyl acetate fraction against isolates of *S. epidermidis* in the concentration range of 2.5%-5% (w/v) and 1.25%-2.5% (w/v). The MBC value of ethyl acetate fraction against clinical isolates of *S. epidermidis* was at a concentration of 5% (w/v), while clinical isolates of *P. acnes* at a concentration of 2.5% (w/v). [13]
7.	Optimization of routine antibacterial activity of cassava leaves (*Manihot esculenta Crantz*)-gentamicin sulfate against *Staphylococcus aureus* bacteria.	A routine isolate of cassava leaves at a concentration of 1; 0,5; 0,1; 0,05; 0.01 mg/mL produces 11.3 consecutive inhibitory zones; 10,66; 9,18; and 6.15 mm. The inhibitory zone was not seen at a concentration of 0.01 mg / mL so the MIC value of routine isolate of cassava leaves against *S. aureus* was found at a concentration of 0.05 mg/mL. MIC routine isolates tested at concentrations of 0.05 mg/mL are included in the moderate category of *Staphylococcus aureus* according to the inhibitory zone category table by David Stout. [14]
8.	Effect of *Tamarindus indica L.* and *Manihot esculenta* extracts on antibiotic-resistant bacteria.	Based on MIC calculations, the highest number of M. *esculenta* is obtained at concentrations of 1000 (μg/mL) against *S. aureus* 33591 and *P. aeruginosa* 27853, namely 33 and 100. [15]
9.	A purely green synthesis of silver nanoparticles using *Carica papaya*, *Manihot esculenta*, and *Morinda citrifolia*: Synthesis and antibacterial evaluations.	Inhibition zone testing on cassava leaf extract (*M. esculante*) showed the highest results with the addition of AgNO3 in leaf extract (5: 3) against *E. coli* and *B. cereus* by 2 cm. [16]
10.	Antibacterial Activity of Cassava Leaf Extract (*Manihot esculenta Crantz*) against Shigella sp.	In the linear regression test, the significance value is <p-value (0.05) which means that Cassava leaf extract affects the growth of *Shigella sp*. The R[2] value of 0.933 or 93.3% (close to 100%) shows that statistically, the two variables are related, meaning that an increase in the concentration of cassava leaf extract affects the increase in the diameter of the inhibition zone formed. [4]

Antibacterial compounds are chemical or biological compounds both natural and synthetic that can inhibit bacterial growth and activity. [17] Antibacterial activity can be studied using several methods, namely the dilution method, agar diffusion method, and dilution diffusion method. The diffusion method is a frequently used method for the analysis of antibacterial activity. The working principle of the diffusion method is the diffusion of antibacterial compounds into solid media where test microbes have been inoculated. The results obtained are in the form of the presence or absence of clear areas formed around the disc paper which shows the inhibition zone in bacterial growth. [18]

Based on the results of the literature, several compounds can be ascertained contained in Cassava leaves with phytochemical testing, namely alkaloids, flavonoids, saponins, tannins, terpenoids, and phenols. These compounds will greatly affect antibacterial activity. The presence of antibacterial compounds is the result of secondary metabolites from plants. Plants have two types of metabolite compounds, namely primary and secondary metabolites. Primary metabolites are used by plants for growth, while secondary metabolites do not play a direct role in plant growth. Secondary metabolites are produced by plants in certain amounts under suffocation conditions. [19]

Flavonoid compounds as antibacterials damage energy metabolism, inhibit nucleic acid synthesis, and damage the cytoplasmic membrane because flavonoid compounds form complex compounds with extracellular proteins and can be followed by the exit of intracellular compounds so that flavonoids are considered constitutive antibacterial substances. [20, 21] Kusumawati (2015) reported that saponins work as antimicrobials by disrupting the stability of bacterial cell membranes, causing cell bacteriolysis. This causes the cytoplasm to leak so that intracellular compounds exit the cell resulting in cell death. [22]

Alkaloid compounds have antibacterial abilities by disrupting the constituent components of peptidoglycan in bacteria so that the cell wall layer is not formed intact and then causes cell death. [23] Tannins can inactivate bacterial adhesin, inhibit the work of enzymes, and inhibit protein transport on cell membranes by damaging cell membranes due to tannin toxicity forming metal ion complex bonds that disrupt various bacterial functions. [7] The mechanism of action of terpenoid compounds as antibacterial substances involves membrane damage by lipophilic compounds by binding to strong polymers and damaging porins, reducing the permeability of bacterial cell walls so that bacterial cells lack nutrients, stunted bacterial growth or die. [24] The mechanism of action of phenol as an antibacterial is by denaturing cell proteins so that the protein structure will be damaged and cause disruption of the balance of macromolecules and ions in the cell so that the cell becomes lysis. [6]

The presence of antibacterial compounds will greatly affect the inhibitory zone which indicates the suppression of bacterial growth. This is in line with the research of Pratiwi (2016), the R[2] value of 0.933 or 93.3% (close to 100%) shows that statistically, the two variables are related, meaning that an increase in the concentration of cassava leaf extract affects the increase in the diameter of the inhibitory zone formed. [4] The choice of dose and concentration of the extract is very influential on its antibacterial activity.

Based on the results of the literature, the inhibitory power of Cassava leaves (*Manihot esculenta Crantz*) is classified from mild to very strong. The greatest inhibitory power was found in 2 cm in *E. coli* and *B. cereus* bacteria with the addition of AgNO3 in Cassava leaf extract (*Manihot esculenta Crantz*). [16] The largest concentration that has been used is 80% in Sahreni research (2020). [12] However, the results obtained are only moderate. The greatest inhibitory power in mm units is in Potti's (2022) research of 25-29 mm and is classified as very strong. [9] The highest dose was carried out in the Lima study (2017), namely the extract concentration of 1000 (µg / mL). [15] However, differences in bacteria will greatly affect the difference in the value of the inhibitory zone significantly due to differences in bacterial cell wall thickness. An extract can kill microbes by entering through the cell wall and damaging its components. Gram-positive bacteria have cell walls that contain a lot of peptidoglycan and few lipids. While Gram-negative bacteria have a relatively complex cell wall and an outer membrane that protects peptidoglycan and contains many lipids (Hidayati, 2017). [25]

Conclusion

Cassava leaves (*Manihot esculenta Crantz*) have antibacterial activity because they contain antibacterial compounds in the form of alkaloids, flavonoids, saponins, tannins, terpenoids, and phenols. In addition, the concentration of Cassava Leaf Extract also has an inverse relationship to bacterial growth. The more concentrated the extract, the stronger the antibacterial compounds contained in it so the wider the zone of inhibition of bacterial growth. The type of bacteria will greatly affect the antibacterial effectiveness of Cassava leaves.

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