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Ajwa Date as Antibacterial Agent Against Salmonella Typhi

Andi Sitti Fahirah Arsal[1], Andi Alamanda Irwan[2], Hasta Handayani Idrus[3], Marzelina Karim[4], Nadila Ardyani Nahardi[5]

[1,2]*Department of Pharmacology Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia*
[3,4]Department of Microbiology Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia
[5]*Medical Student of the Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia*

ABSTRACT
Background: Salmonella typhi is the bacteria that causes typhoid fever. Salmonella typhi infection in the world there are around 11-20 million cases and causes 128,000-161,000 deaths per year. Antibiotics as a therapy for typhoid fever are currently a concern because of the discovery of strains that are resistant to these drugs. The use of plants by the community as a treatment has been carried out for generations. This is due to the assumption that herbal medicines have fewer side effects. Dates have many bioactive phytochemicals such as phenols, carotenoids, flavonoids, anthocyanins, and dietary fiber that have various curative potentials such as antioxidant, anti-inflammatory, anticancer, and antimicrobial properties.
Objective : This study aims to determine the potential of ajwa date extract as an antibacterial agent against Salmonella typhi.
Method : This research uses a literature review with a narrative review design. Researcher reviewed international journals and national journals retrieved from Google Scholar, Elsevier, PubMed, then then screening is carried out so that researchers review journals that are in accordance with this study.
Result : Ajwa dates have antibacterial activity against *Salmonella typhi*. The use of methanol in the extraction process showed higher antibacterial activity. The high bioactive compounds in ajwa dates such as phenolic content and antioxidant properties are factors that increase the antibacterial effect of ajwa dates.

Keywords : *Ajwa Date, Antibacterial Activity, Salmonella typhi*

I. INTRODUCTION

Salmonella typhi is the bacteria that causes typhoid fever. These bacteria include gram-negative bacteria that are motile, have flagella, do not form spores and are not encapsulated. Fever caused by Salmonella typhi is an acute infectious disease in the form of bleeding, damage to the liver, spinal cord, meningitis. During infection, these bacteria multiply in mononuclear phagocytic cells and are continuously released into the bloodstream.

Based on WHO data in 2018 it was estimated that global typhoid fever was 11-20 million cases per year, resulting in around 128,000-161,000 deaths per year.2 The incidence rate in Indonesia is still high, namely 358 per 100,000 rural population and 810 per 100,000.

100,000 urban population per year with an average of cases per year 600,000 – 1,500,000 sufferers. The mortality rate for typhoid fever in Indonesia is still high with a CFR of 10%

Based on research conducted by Santriani Hadi et al, it was found that the number of cases of typhoid fever in Makassar, especially at Ibnu Sina Hospital in 2016, was found to be 176 cases where the highest number was in April as many as 26 people and the lowest number in July was 6 people.

Based on the Decree of the Minister of Health of the Republic of Indonesia number 364/MENKES/2006 concerning the Control of Typhoid Fever, one of the treatments given to patients with typhoid fever is anti-microbial (antibiotics).5

Research conducted by Ismail Rahman in Makassar on Antibiotic Resistance to Salmonella Typhi in Typhoid Fever can be concluded that the sulfamethoxazole antibiotic showed resistance above 50% of the total number of samples and other types of antibiotics such as amoxicillin, tetracycline and chloramphenicol had a sensitivity above 50%. .6

The use of plants by the community as a treatment has been carried out for generations. This is due to the assumption that herbal medicines have fewer side effects. Many types of plants have been studied to determine their antibacterial effectiveness against Salmonella typhi bacteria, such as Lime peel (Citrus Aurantifolia), Salak fruit (Salacca Zalacca) which resulted in both fruits having antibacterial activity against Salmonella typhi.7,8 Al-Daihan and Bhat (2012) has conducted an in vitro study on the benefits of ajwa dates (Phoenix dactylifera L.) and the results showed that the content of ajwa dates, namely flavonoids, is effective as an antibacterial.9,10. Research conducted by Abdullah, showed that the extract of Ajwa dates tested on Salmonella typhi bacteria had an inhibition zone of 28.67 mm11, while Khalas Dates had an inhibition zone of 28.67 mm. has an inhibition zone of 19 mm and Sukkari dates have an inhibition zone of 20 mm.

Based on the description above, researchers are interested in examining the potential of Ajwa Dates Extract as an Antibacterial Agent against Salmonella Typhi bacteria so that it can be seen whether Ajwa Dates has the potential as an alternative in case of resistance cases in Salmonella typhi.

Salmonella Typhi

Salmonella enterica serotype typhi is a gram-negative, rod-shaped, flagellated bacterium whose only reservoir is the human body:[13]

Resistance of Salmonella typhi

Germs grow in aerobic and facultative anaerobic conditions, at a temperature of 15°C - 41°C (optimum growth temperature of 37.5°C) and a growth pH of 6-8. Germs die at a temperature of 56 ° C also in a dry state. In water can last for 4 weeks. It thrives in a medium containing bile salts, is resistant to brilliant green dyes and sodium tetrathionate compounds, and sodium deoxycholate. These compounds inhibit the growth of coliform bacteria so that these compounds can used in media for the isolation of Salmonella bacteria from feces.

Antigen Structure

1. The O antigen is the outermost part of the cell wall lipopolysaccharide and consists of repeating polysaccharide units. Some O-specific polysaccharides contain unique sugars. O antigens are resistant to heat and alcohol and are usually detected by bacterial agglutination. Antibodies to O antigens are mainly IgM

2. The K antigen in Salmonella typhi is called the Vi antigen which is located outside the O antigen. This antigen can interfere with agglutination with O antiserum, and can be associated with virulence.15

3. The H antigen is present in the flagella and is denatured or destroyed by heat or alcohol. The H antigen on the bacterial surface can interfere with agglutination with anti-O.[15] . antibodies

Ajwa Dates

Phoenix dactylifera L. commonly known as date palm is a monocot woody perennial plant belonging to the Arecaceae family. This plant is also known as the “Tree of Life” due to its high nutritional value and long life. Phoenix dactylifera L. comes from the Greek "Phoenix" which means date palm and "dactylifera" or "daktulos" which means finger.[17]

Ajwa dates are often called Prophet dates, because the tree only exists in Medina and the person who first introduced it was the Prophet Muhammad, who was narrated in a hadith from Sa'ad bin Abi Waqqash, from the Prophet sallallaahu 'alaihi wa sallam, that he once said: "Whoever consumes seven Ajwah dates in the morning, then on that day he will not be exposed to poison or magic" (HR Al-Bukhari (no. 5025). [18]

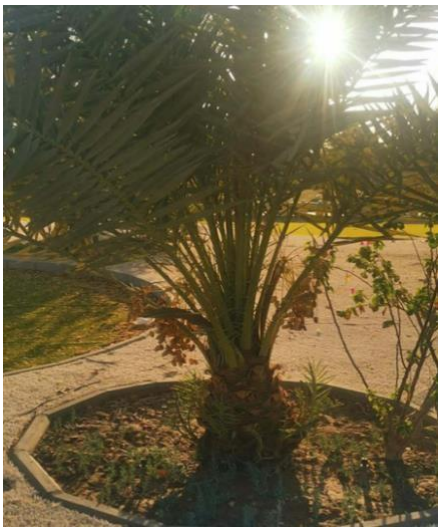

Figure 2.1 Ajwa Date Tree [21]

Figure 2.2 Ajwa Dates[22]

Taxonomy of Ajwa Dates

According to the United States of Agriculture (USDA), the taxonomy of the date palm (Phoenix dactylifera L.) is as follows[23]

Content of Ajwa Dates

Dates have high antioxidant activity because they are rich in phenolic compounds and flavonoids with free radical scavengers. The bioactive components detected in ajwa date extract were phenols, alkaloids, flavonoids, tannins, and carbohydrates.[24]

The unique nutritional composition of dates can serve as an important food in the human diet and play a major role in human nutrition and health providing part of the required daily recommended allowance. Dates also have many bioactive phytochemicals such as phenols, carotenoids, flavonoids, anthocyanins, and dietary fiber that have various curative potentials such as antioxidants, anti-inflammatory, anticancer, and antimicrobial properties. The positive effect of dates on human health is suggested for further research on the identification and isolation of bioactive compounds that help in the treatment of various diseases such as nerves, stomach, and heart. Thus, an affordable, safe and effective approach can be achieved to control disease, progression, and progression in contrast to expensive synthetic drugs, exhibiting side effects, and altering metabolic and genetic pathways.22

Bioactive compounds are biologically active substances derived from plants. These bioactive compounds have various structures ranging from simple molecules to polymers. Among the most important bioactive components in dates with potential to act as nutraceutical agents are phenolic acids, flavonoids, carotenoids, procyanidins, tocopherols and tocotrienols and sterols. These bioactive compounds can be found in both the pulp and seeds of dates

1. Phenolic Acids and Flavonoids

Hamad et al noted a high total phenolic content, in the range of 10.47 to 22.11 mg/100 g FW. In detail, Ajwa Al Madinah had the highest content (22.11 mg/100 g DW), followed by Nabt Saif (22 mg/100 g DW), while Khla Al Qassim had the lowest content (10.47 mg/100 g DW).

In this study, gallic acid, p-coumaric acid, and ferulic acid derivatives were each the most dominant phenolic compounds. In addition, different classes of flavonoids were identified in the varieties tested; quercetin, luteolin, apigenin, isoquercetrin, and rutin. The total flavonoid content was in the range of 1.22 and 2.82 mg/100 g DW, of which Saffawy had the highest content (2.82 mg/100 g DW), followed by Ajwa Al Madinah (2.78 mg/100 g DW).), and Al Qassim has the lowest content of 1.22 mg/100 g DW.[26]

2. Carotenoids

Carotenoids are chemical compounds synthesized mainly by higher plants and by some algae. In dates, the type and concentration of carotenoids varies greatly. In general, the main carotenoids found in dates are lutein and b-carotene; however, as is the case with all phytochemicals, their type and concentration depend on several factors, including location, cultivar and stage of ripening.25

The main source of carotenoids is the flesh of dates. The main carotenoids found in date pulp were lutein (1.08 g/100 g), a-carotene (0.30 g/100 g sample), b-carotene (0.22 g/100 g sample). sample) and b-cryptoxanthin (0.1 mg/100 g sample). It is also possible to find carotenoids in the seeds, but in lower concentrations than in the pulp

3. Phytosterols

Plant sterols are important components of cell membranes and are present in all plants. They are structurally comparable to cholesterol, with a difference in the lateral chains attached to the steroid ring. These compounds represent another group of fat-soluble phytochemicals present in dates. The edible parts of the fruit contain a lot of phytosterols, although the main sources of phytosterols are seeds and pollen. Phytosterol concentrations vary by cultivar and stage of maturation25. b-sitosterol, b-sitosteryl-3-O-β-glucoside, and b-sitosteryl-3-β-glucopyranoside-6′-O-palmitate are sterols reported in Ajwa dates.[22]

4. Tocopherols and tocotrienols

Tocopherols and tocotrienols are compounds that are important for human health because of their antioxidant capacity, especially their lipoperoxyl radical scavenging activity. They are known as highly efficient natural antioxidants, which protect the components of biological membranes. Therefore, the oil extracted from date palm seeds can be considered as a good source of tocopherols and tocotrienols.

Antibacterial Activity of Chemical Content of Dates

Various antibacterial properties have been reported from the pulp and seeds of dates with different cultivars in in vitro studies. This antimicrobial property can be attributed to the high content of polyphenolic compounds, including phenolic acids and flavonoids, as well as condensed tannins found in its composition. However, the exact mechanism behind the antibacterial activity of fruit and seed extracts obtained from dates has not been fully elucidated, which requires further study. However, it must be taken into account that antimicrobial activity will depend on many factors such as the cultivar used, maturity level, origin, environmental conditions, etc.25

Phytochemically, dates contain carbohydrates, phenolic compounds, alkaloids, flavonoids, vitamins and tannins. According to research by Al-Daihan and Shafi Bhat9, phenolic compounds can cause microbial inhibition. Compounds such as alkaloids, flavonoids and tannins have also been reported to inhibit bacterial growth and protect certain plants from bacterial infection. Until now, dates are the only food containing flavonol glycosides in sulfate form and are not detected in other vegetables and fruits.[22]

Alkaloids have antibacterial abilities because they have a quaternary aromatic group capable of intercalating with DNA, In addition, alkaloids are also able to disrupt the integrity of the peptidoglycan constituent components in bacterial cells. Peptidoglycan is a component of the bacterial cell wall so that the presence of such interference will cause the cell wall layer to not be fully formed and cause cell death.

The antibacterial action mechanism of saponins is by increasing the permeability of the cell membrane so that the membrane becomes unstable and results in cell hemolysis

Flavonoid compounds are antibacterial through 3 mechanisms, namely: inhibiting nucleic acid synthesis, inhibiting cell membrane function and inhibiting energy metabolism. The mechanism of action of flavonoids in inhibiting nucleic acid synthesis is carried out through ring B on flavonoids which have an important role in the intercalation process or hydrogen bonding by accumulating nucleic acid bases that inhibit DNA and RNA synthesis. Flavonoids inhibit the function of bacterial cell membranes through complex binding with soluble extracellular proteins that can disrupt the integrity of the bacterial cell membrane. Any disturbance in the permeability of the cell membrane will affect the electrochemical gradient of protons that pass through the membrane. The electrochemical gradient of protons across the membrane is very important for bacteria in ATP synthesis, membrane transport and bacterial movement, so the presence of favonoid compounds will cause disruption of the proton motive force which results in disruption of ATP synthesis, membrane transport and bacterial movement27. Some of the flavonoids contained in ajwa dates include quercetin, luteolin, apigenin, isoquercetrin, and rutin. This content can function as an antibacterial agent. Of these components there are several mechanisms in inhibiting the growth of bacteria. Quercetin, apigenin, and luteolin play a role in inhibiting bacterial nucleic acid synthesis. Quercetin and apigenin also work by disrupting membranes in which bacterial membranes have important roles such as respiration, osmoregulation, cellular transport processes, peptidoglycan biosynthesis and peptidoglycan cross-linking. If it can interfere with the fluidity and permeability of the bacterial plasma cell, it will directly or indirectly cause metabolic dysfunction and possibly drive the bacteria to its death.[10]

Abdullah examined the zone of inhibition, minimum inhibitory concentration, and minimum killing concentration of ajwa dates against Salmonella typhi bacteria, from this study it can be concluded that there is antibacterial activity of ajwa dates[11].

Inhibition Zone of Ajwa Dates on Bacteria Salmonella typhi[11] .

Consentration(mg/mL)	Inhibition Zone (mm)	
	Hot Water	Methanol
500	28,67 (±0.58)	29 (±0)
400	25,67 (±0.58)	25,33 (±0.58)
300	20 (±0.58)	21,33 (±1.15)
200	16,33 (±0.58)	15,33 (±0.58)

100	-	-

Table 2.2 KHM dan KBM Ajwa Dates on Bacteria *Salmonella typhi*[11]

	Hot Water	Methanol
Minimum Inhibitory Concentration	500 mg/mL	500 mg/Ml
Minimum Kill Concentration	500 mg/mL	500 mg/Ml

NARRATIVE REVIEW METHOD

This research is a literature study that collects a series of articles in the form of research articles and review articles relating to Phoenix Dactilyfera L and Salmonella typhi. Then proceed to review the articles so that a narrative review will be produced.

The strategy used in the literature search is to use keyword searches to get articles to be reviewed, the keywords are Phoenix Dactilyfera L (Ajwa Dates), Antibacterial Effects of Ajwa Dates on Salmonella tpyhi bacteria. Articles or journals were selected according to inclusion criteria and exclusion criteria with further analysis.

Search literature using an electronic based that is accredited/indexed by sinta such as google scholar, elsevier/clinical key, pubmed.

Reference Criteria

1. The reference discusses the potential of Ajwa Date Extract as an Antibacterial Agent against Salmonella typhi Bacteria.

2. References published from 2019-2022 (If there are no new references then the year may be pushed back)

Exclusion Criteria

1. References are not fully accessible.

2. Research articles whose publications are not in health journals.

II. Results

Based on the search results obtained as many as 83 journals from the keyword search "Antibacterial Effect of Ajwa Date Palm on Salmonella typhi". All journals with these keywords were included in the search and filtering. Then the researchers screened the titles and abstracts of the articles, at this screening stage, as many as 68 were excluded on the grounds that they did not match the inclusion criteria, did not fit the title and abstract, and were not fully accessible. In the end, there were 2 articles that matched the inclusion criteria, which will then be used in this literature review.

No	Journal Name	Title	Method	Writer	Results	Conclusion

	(year of publication)					
	International Journal Of Pharmaceu Tical Sciences And Research (2020)	In-Vitro Antibacteri al Activities Of Ajwa Date Fruit (Phoenix Dactylifera L.) Extract Against Selected Gram-Negative Bacteria Causing Gastroente Ritis	Experimental	N. Abdullah, N. F. Mohd. Ishak and W. S. Wan Shahida	This research use two extraction method that is with methanol and water hot. Activity antibacterial rated with diffusion test method well on medium Mueller-Hinton agar. At concentration 100 mg/mL no found antibacterial activity of both methods extraction. Lowest concentration which can inhibit bacteria Salmonella typhi which is 200 mg/mL. Based on zone diameter inhibit,extract methanol higher than hot water extract.	Second extraction methanol and hot water show existence potency activity antibacterial from bacteria gram negative To bacteria reason Gastroenteritis Second Extract that too have function bactericidal and bacteriostatic.
					In the methanol extract, the concentration of 200 mg/mL 15.33 mm,	

					concentration 300 mg/mL 21.33 mm, concentration 400 mg/mL 25.33 mm, and concentration 500 mg/mL 29mm. Hot water extract concentration 200 mg/mL 16.33 mm, concentration 300 mg/mL 20mm, concentration 400 mg/mL 25.67 mm, and concentration 500 mg/mL 28.67 mm. The positive control used is Ampicillin with a concentration of 1 mg/mL with zone of inhibition	
2	Journal of Infection and Public Health (2021)	Antimicrobial and anti-biofilm activities of polyphenols extracted from different Saudi Arabian date cultivars against human	Experimental	Al-Tamimi, Amal Alfarhan, Ahmed Rajago pal, Rajakrishnan	Antibacterial potential analyzed by zone block the formed in disc diffusion method on Mueller Hinton So that. Four kinds of varieties used on this research, among others are Ajwa, Safavid,	By whole, this research concluden that date cultivar Saudi Arabia is source that rich in nutraceuticals phenolic. They proven hinder growth microbes (bacteria and mushrooms) and hinderformation biofilm. Therefore, incorporating

		pathogens			Khalas, and Sukkari. The result, found the inhibition zone formed from dates ajwa (17.5 mm) more taller than 3 other types of dates (Safavid 17.2 mm, Khalas 13.6 mm, and Sukkari 15.5 mm). The minimum inhibitory concentration of Ajwa Dates was 80.4 mg/mL while that of Safawi Dates was 98.5 mg/mL, Khalas Dates and Sukkari Dates >100 mg/mL. Furthermore, a trial was conducted to see the ability of Ajwa dates and Safawi dates to inhibit the formation of biofilms, the results were that Ajwa dates were more active and caused a more significant reduction of 54.19% in Salmonella strain bacteria using MIC.[28]	dates into the diet, especially the Ajwa variety, can be useful in preventing various diseases caused by bacteria and viruses. fungi in humans.

III. Discussion

Based on the 2 reviewed journals, it was generally found that Ajwa Dates (Phoenix Dactylifera L.) have potential as antibacterial agents against Salmonella typhi bacteria. These results are in accordance with research conducted by Al-Daihan which states that date extracts from either the fruit or the leaves have antibacterial activity. Among other parts of ajwa dates, fruit extract showed the highest antibacterial activity. In the same study, Al-Daihan conducted a qualitative experiment to look at the phytochemicals contained in the leaves, fruit, seeds, and bark of the Ajwa Dates, the results found that various constituents in the fruit such as carbohydrates, alkaloids, steroids, saponins, flavonoids, and tannins9. This is thought to be the cause of the high antibacterial activity of the Ajwa Dates fruit extract.

In the journal Antimicrobial and anti-biofilm activities of polyphenols extracted from different Saudi Arabian date cultivars against human pathogens, it was found that Ajwa dates have the highest total flavonoids and total phenolics compared to other date varieties29. This is related to the journal Biological, Nutritive, Functional and Healthy Potential of Date Palm (Phoenix dactylifera L.): Current Research and Future Prospects which states the high phenolic compounds in P. dactylifera so that it can have a broad spectrum of antibacterial activity. which phenolic compounds produce hydrogen peroxide which inhibits bacterial growth[25.]

Toxicity test was carried out using the Bhrine Shrimp Lethality Test method, based on the Meyer toxicity index, Ajwa date palm seed extract was found to be toxic (active) because the LC50 value was 391,918 which was below 1000 g/ml. Median Lethal Concentration (LC50) showed a high content of bioactive compounds in Ajwa date palm seeds at a concentration of 100 g/ml because the mortality rate of nauplii was 50% which was the highest. This is due to the presence of phenolic compounds in Ajwa date seeds such as oleic acid and gallic acid. The bioactive compounds present in the seeds of Ajwa dates indicate that it has the potential to fight bacterial skin infections. Previous studies have proven that the bioactive compounds present in ajwa dates are known to be very rich in phenolic content and antioxidant properties and these properties are factors that enhance the antibacterial effect of ajwa dates. This condition proves that ajwa dates are toxic and can trigger penetration into bacterial cell walls so as to reduce bacterial growth[30.]

Research on the antibacterial activity of Ajwa Dates against Salmonella typhi is currently very limited, but there have been several studies conducted on other Gram negative bacteria. In a study conducted by Halabi et al (2022) on several gram-negative bacteria, including Klebsiella pneumoniae and Escherichia coli, the results showed that Ajwa dates had antibacterial activity against the tested Gram negative bacteria31. The same results were also found by Anwar et al (2022) who investigated the antibacterial activity of Ajwa Dates against several Gram negative bacteria[32.]

In research conducted by Abdullah et al. (2020) using 2 extraction methods, namely, with methanol and hot water. The result is that extraction with methanol shows higher antibacterial activity. In the study of Samad et al (2016) who compared the extraction method of methanol and acetone to see which method could best extract the phenolic content contained in dates. As a result, methanol which has a higher viscosity and is relatively more polar than acetone can extract phenolic compounds from dates better than acetone33. Other studies have shown that methanol is also efficient in extracting certain compounds such as catechins, epicatechins and epigallocatechin25.

The dose of using ajwa dates as therapy for Salmonella typhi infection has not been found, but in the study of Al Jouni et al (2018) which examined the effect of consumption of ajwa dates on infection rates in cancer patients, patients were given one ajwa date each breakfast as a trial dose per breakfast. days, if the patient does not show an allergic reaction, then the patient is given three ajwa dates per day, the dates are consumed along with their breakfast during the treatment care. The results found that there was a decrease in the infection rate in patients who consumed ajwa dates compared to patients who did not consume ajwa dates. Dates can be considered as an adjunct treatment to reduce microbial infections, which may result in better outcomes with conventional

treatment in pediatric patients undergoing cancer treatment34. The results obtained in this study are related to the Hadith Sahih Al-Bukhari no. 5326 which reads "Whoever eats a few 'ajwah dates every day in the morning, it will not harm him either poison or magic that day until the evening. And another said seven dates."

From the 2 journals reviewed, the results found were qualitatively found, namely Ajwa Dates had antibacterial activity seen from the presence of an inhibition zone formed, but quantitatively there were variations in the results of the inhibition zone, MIC and KBM. This can be caused by differences in sample preparation methods, extraction methods, and the level of maturity of the dates used so that it can affect the results of the study.

IV. Conclusion

Ajwa dates have the potential as an antibacterial agent that can inhibit and kill Salmonella typhi bacteria.
2. Ajwa dates contain the highest phenolic and flavonoid compounds among other varieties which act as a source of antibacterial.
3. The recommended dose of ajwa dates that need to be consumed to cause antibacterial effects on Salmonella typhi bacteria has not been studied.

References

[1] Ajmera, A. & Shabbir, N. Salmonella. StatPears (2022).

[2] World Health Organization (WHO). 2018. Typhoid. https://www.who.int/news-room/fact sheets/detail/typhoid.
[3] Kasim, V. N. A. ROLE OF IMMUNITY IN Salmonella Typhi INFECTION. (2020).
[4] Santriani Hadi, Ilma Khaerina Amaliyah, Z. Characteristics of Typhoid Fever Patients in the Hospital. Ibnu Sina Makassar City 2016 - 2017. (2020).
[5] Decree of the Minister of Health of the Republic of Indonesia number 364/MENKES/2006 concerning Typhoid Fever Control.
[6] Rahman, I. ANTIBIOTIC RESISTANCE AGAINST Salmonella typhi ON TYFOID FEVER DISEASE IN MAKASSAR CITY Antibiotic resistance to salmonella typhi on typhoid fever In Makassar. vol. 1 https://ejournal.unkhair.ac.id/index.php/kmj (2019).
[7] Setiyabudi, L. et al. PROFILE OF ANTIBACTERIAL ACTIVITY OF SALAK SKIN EXTRACT ON THE GROWTH OF THE BACTERIA OF Salmonella typhi. Jophus Scientific Journal: Journal of Pharmacy UMUS 2, 41–49 (2021).
[8] Pratiwi, D., Suswati, I. & Abdullah, M. ANTI-BACTERIAL EFFECTS OF LIME SKIN EXTRACT (CITRUS AURANTIFOLIA) ON SALMONELLA TYPHI IN VITRO. (2013).
[9] Sooad Al-Daihan. Antibacterial activities of extracts of leaf, fruit, seed and bark of Phoenix dactylifera. Afr J Biotechnol 11, (2012).
[10] Biharee, A., Sharma, A., Kumar, A. & Jaitak, V. Antimicrobial flavonoids as a potential substitute for overcoming antimicrobial resistance. Phytotherapy vol. 146 Preprint at https://doi.org/10.1016/j.fitote.2020.104720 (2020).
[11] Abdullah, N., Ishak, N. F. M. & Shahida, W. S. W. IN-VITRO ANTIBACTERIAL ACTIVITIES OF AJWA DATE FRUIT (PHOENIX DACTYLIFERA L.) EXTRACT AGAINST SELECTED GRAM-NEGATIVE BACTERIA CAUSING GASTROENTERITIS. Int J Pharm Sci Res 10, 2951 (2019).
[12] Abuelgassim, A. O., Eltayeb, M. A. & Ataya, F. S. Palm date (Phoenix dactylifera) seeds: A rich source of antioxidant and antibacterial activities. Czech Journal of Food Sciences 38, 171–178 (2020).
[13] Ashurst, J. v., Truong, J. & Woodbury, B. Salmonella Typhi. (2022).

[14] IDFKUI. Textbook of Medical Microbiology. Revised Edition. Jakarta: Literature Binarupa. 186 (2010).
[15] Brooks, G. F., Jawetz, E., Melnick, J. L., & Adelberg, E. A. (2012). Jawetz, Melnick, & Adelberg's Medical Microbiology 26th ed. New York: McGraw Hill Medical. 20 (2012).
[16] Ramasamy, R. & Mandal, B. K. Salmonella typhi. Trop Doct 25, 42 (2019).

[17] Wadhawan, N. & Rythm Bansal, R. B. A Study on Microbial Characteristics of Food Products Developed from Dates (Phoenix dactylifera L.). Int J Curr Microbiol Appl Sci 7, 441–451 (2018).
[18] Sahih Al-Bukhari Hadith No. 5025 - The Book of Food.

[19] Echegaray, N. et al. Phoenix dactylifera products in human health – A review. Trends in Food Science and Technology vol. 105 238–250 Preprint at https://doi.org/10.1016/j.tifs.2020.09.017 (2020).
[20] Munawwarah, H. al. RELATIONSHIP OF ADMINISTRATION OF DATE (Phoenix dactylifera L) VARIETY OF AJWA ON TOTAL BLOOD CHOLESTEROL LEVELS. (2015).
[21] Mohamed, S. et al. The Preventive and Therapeutic Effects of Ajwa Date Fruit Extract Against Acute Diclofenac Toxicity-Induced Colopathy: An Experimental Study. Drug Des Devel Ther 2022, 16–2601 (2022).
[22] Mirza MB, Syed FQ, Khan F, Elkady AI, Al-Attar AM, Hakeem KR. Ajwa Dates: A Highly Nutritive Fruit with the Impending Therapeutic Application. InPlant and Human Health, Volume 3 2019 (pp. 209-230). Springer, Cham.
[23] United States Department of Agriculture. 2016. Plants database. https://plants.usda.gov/home/plantProfile?symbol=PHDA4.
[24] Proceedings of the Second International Conference on the Future of ASEAN (ICoFA) 2017 – Volume 2. Proceedings of the Second International Conference on the Future of ASEAN (ICoFA) 2017 – Volume 2 (Springer Singapore, 2018). doi:10.1007/978-981-10-8471-3.
[25] Fernández-López, J., Viuda-Martos, M., Sayas-Barberá, E., Navarro- Rodríguez De Vera, C. & ngel Pérez-Álvarez, J. Biological, Nutritive, Functional and Healthy Potential of Date Palm Fruit (Phoenix dactylifera L.): Current Research and Future Prospects. Agronomy 12, (2022).
[26] Hamad, I. et al. Metabolic analysis of various date palm fruit (Phoenix dactylifera L.) cultivars from Saudi Arabia to assess their nutritional quality. Molecules 20, 13620–13641 (2015).
[27] Rahman, F. A., Haniastuti, T. & Utami, T. W. Screening of phytochemicals and antibacterial activity of ethanolic extract of soursop leaf (Annona muricata L.) on Streptococcus mutans ATCC 35668. Indonesian Dentistry Magazine 3, 1 (2017).
[28] Al-Tamimi, A., Alfarhan, A. & Rajagopal, R. Antimicrobial and anti-biofilm activities of polyphenols extracted from different Saudi Arabian date cultivars against human pathogens. J Infect Public Health 14, 1783–1787 (2021).
[29] Al-Tamimi, A., Alfarhan, A. & Rajagopal, R. Antimicrobial and anti-biofilm activities of polyphenols extracted from different Saudi Arabian date cultivars against human pathogens. J Infect Public Health 14, 1783–1787 (2021).
[30] Charting the Sustainable Future of ASEAN in Science and Technology. Charting the Sustainable Future of ASEAN in Science and Technology vol. 2 (Springer Singapore, 2020).
[31] Halabi, A. A., Elvice, B. H., Hagar, M. & Olama, Z. A. Date Fruit (Phoenix dactylifera L.) Cultivar Extracts: Nanoparticle Synthesis, Antimicrobial and Antioxidant Activities. Molecules 27, 5165 (2022).
[32] Anwar, S. et al. Role of Ajwa Date Fruit Pulp and Seed in the Management of Diseases through In Vitro and In Silico Analysis. Biology (Basel) 2022, 78 (2022).
[33] Samad, M. A., Hashim, S. H., Simarani, K. & Yaacob, J. S. Antibacterial properties and effects of fruit chilling and extract storage on antioxidant activity, total phenolic and anthocyanin content of four date palm (Phoenix dactylifera) cultivars. Molecules 21, (2016).
[34] al Jaouni, S. K. et al. Effects of Phoenix dactylifera Ajwa on Infection, Hospitalization, and Survival Among Pediatric Cancer Patients in a University Hospital: A Nonrandomized Controlled Trial. Integr Cancer Ther 18, 153473541982883 (2019).