ARTICLE REVIEW: POTENTIAL PHARMACOLOGICAL ACTIVITY OF LOBI-LOBI FRUIT (*Flacourtia inermis, Roxb*)

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ABSTRACT

The Lobi-lobi fruit is a tropical plant that is rich in secondary metabolites. Many studies have discussed the usefulness of secondary metabolites in this fruit. This study aimed to explore the secondary metabolites and pharmacological activities of lobi-lobi fruit (*Flacourtia inermis, Roxb*). The methods used included a literature review of various scientific journals discussing the health potential of fruits. The results showed that the lobi-lobi fruit extract had significant antioxidant activity with an IC_{50} value of 104.223 µg/mL, and showed potential as an antidiabetic and antibacterial agent. This discussion highlights the importance of bioactive components, such as phenolics, for providing therapeutic effects. The conclusion shows that this fruit has potential as a source of natural medicine and requires further research.

Keywords: secondary metabolites, *flacourtia inermis*, pharmacological activity

INTRODUCTION

Tropical fruit genetic resources (SDGs) in Indonesia are diverse and include various species. Indonesia has approximately 400 varieties of edible fruit plants. Unfortunately, the information currently available to the public is very limited because most of the SDGs in Indonesia have not been classified or properly inventoried. Tropical fruits are among the possible sources of natural antioxidants (Astari *et al*., 2024). Lobi-lobi fruit (*Flacourtia inermis, Roxb*) is rich in anthocyanins, which cause a red-purple color. Owing to their chemical composition, anthocyanins have pharmacological properties that include anti-inflammatory properties. They can also be used to absorb free radicals, which help prevent degenerative diseases, cancer, and aging. In addition, anthocyanins have anticarcinogenic, antihypertensive, antidiabetic, and liver function disease prevention properties (Jacob *et al*., 2022). In addition, Sri Lanka is home to the large *Flacourtia inermis Roxb*. (*Flacourtiaceae*) tree, which is also found in Malaysia, Indonesia, South India, Philippines, and parts of Africa. When ripe, the round, cherry-sized fruit, known as Lovi in Sri Lanka and the Batoko plum in English, turns deep red. The fruit can be sweet, although it is usually astringent and sour (A. G. A. W. Alakolanga *et al*., 2015).

The purpose of this article is to compare the pharmacological potential and secondary metabolite compounds of the *Flacourtia inermis, Roxb* plant, based on scientific article publications so that it can be a useful source of information for future research.

RESEARCH METHOD

This narrative review was based on pharmacological activity studies of lobi lobi fruit (*Flacourtia inermis, Roxb*) in the last decade. The authors used all original research published from January 2014 to October 2024 regarding the keyword: *Flacourtia inermis Roxb* activity, *Flacourtia inermis Roxb*, Antioxidant, Antidiabetes, Antiobesity, and Antibacterial. After the total number of article results according to the keywords appeared, they were summed up on each database website. Then, the articles that have been obtained

with titles and results that match the keywords, and then search and count the number of duplicate articles on each data website to be excluded, and then count the number of articles after screening articles from duplicate articles to be analyzed.

For the tools and databases, we searched for research articles using Google Scholar, Research Gate, and Science Direct. In addition, the software or tools we used were Mendeley, Duplichecker, and Grammarly. to paraphrase each explanation of the research article.

Article Selection Criteria

For inclusion criteria that the author makes reference to are articles that discuss all parts of the lobi-lobi fruit (*Flacourtia inermis, Roxb*) in the form of extracts, extract fractions, and secondary metabolite content of extract fractions that have been tested for pharmacological activity, while exclusion articles are: *Flacortia spp* research articles that do not discuss *Flacourtia inermis, Roxb* and duplicate articles that appear on each database website.

Research Procedure

The number of journals we obtained was 14. In addition, the method flow that we used refers to a previous study. Similar to the method described below (Vitamia *et al*., 2024):

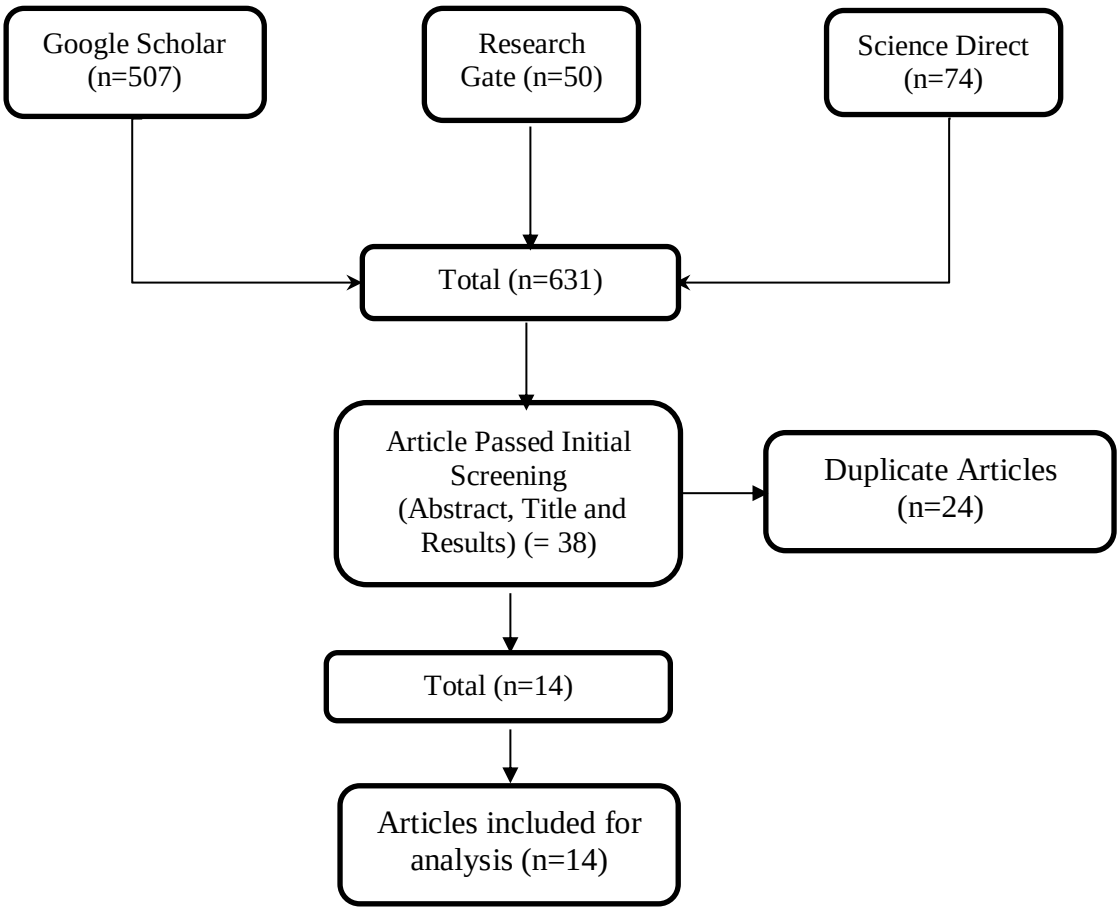

Figure 1. Search flow and identification of articles through databases

RESULTS AND DISCUSSION

Table I. Result Of Pharmacological Activity

Secondary Metabolite Compounds	Pharmacology Activity	Method	Results	Reference
Anthocyanin, Phenolic	Antioxidant Activity	DPPH	IC_{50}: 104.223 µg/mL	(Astari *et al*., 2024)
		DPPH	IC_{50} : 66.2 ppm	(A. G. A. W. Alakolanga *et al*., 2015)
		DPPH	Concentration 1000 mg/L : 81.752% IC_{50} : 10.94 mg/L	(Salmiyah and Bahruddin *dkk*. 2018)
		DPPH	IC_{50} : 50.011 g/L	(Yasin *et al*., 2022)
		pH Differential	26.56 ± 0.28 mg / 100 g (in wet weight) or 103.89 ± 1.08 mg / 100 g (in dry weight).	(Fitriyani *et al*., 2018)
		Maceration	10.35 mg/100 g and UV absorption 0.7553	(Rakhman *et al*., 2020)
		DPPH and ORAC	DPPH > 256, ORAC : 236.6 ± 14.6, TPC : 25.6 ± 1.0	(Rondevaldova *et al*., 2024)
Phenolic, Triterpenoid, Saponin, Tannin, Alkaloid, Flavonoid, Polyphenol.	Anti Diabetes Activity	Diabetic Induced By Alloxan	Dosage 150 mg/kgBW : 68.35%	(Jacob *et al*., 2022)
		High Fat Diet Induction	Dosage 27.95 mg/kgbb : 20.001 ± 1592	(Muninggar and Lestario, 2019)
		Inhibition of α-Glucosidase and α-Amylase enzymes	Extract MeOH : 710.69 ± 1.08 And 1948.39 ± 11.81 Total polyphenol content : 1.28 g per 100 g	(A. Alakolanga *et al*., 2015)
Flavonoid, Quinic Acid, Gibberellin A3	Anti Obesity Activity	In Vitro Inhibition	IC_{50} : 377.15 µg/ml	(Baby *et al*., 2023)
		High Fat Diet Induction	Doses of 200 mg/kg and 400 mg/kg demonstrated noteworthy decreases in body weight.	(Anbiah *et al*., 2024)
2,3-dihydroxybenzoic acid, Flavonoid, Tannin, Phenolic	Anti Bacterial Activity	Disc Diffusion	Inhibition zone with 20 mm on Staphylococcus aureus and Serratia marcescens bacteria with HCl substance	(George *et al*., 2015)
		Disc Diffusion	Has a very strong inhibitory power category in Staphylococcus aureus bacteria of 39 mm	(Nendissa *et al*., 2023)

Antioxidant Activity

The DPPH assay assesses antioxidant effectiveness based on the underlying mechanisms through which antioxidants mitigate lipid peroxidation, ultimately resulting in the neutralization of DPPH free radicals and, as a result, determines the potential for free radical scavenging (Baliyan *et al*., 2022).

Astari *et al*., (2024) stated that the 2,2-diphenyl-1-picrylhydrazyl (DPPH) technique was used in the antioxidant capacity test. The IC_{50} of Lobi-lobi fruit extract, 104.223 µg/mL, was determined by calculating the results of the antioxidant capacity test. The IC_{50} of 235.7 µg/mL was reported in this study, which is consistent with the study of Dwi Ratna Sari *et al*., and can be categorized as a possible source of natural antioxidants (Astari *et al*., 2024).

A. G. A. W. Alakolanga *et al*., (2015) reported that *F. inermis* fruit extract had good results in terms of antioxidant activity, as well as the inhibition of α-amylase, α-glucosidase, and lipase enzymes. The extract also contained significant amounts of anthocyanins and phenols. The total phenolic content (TPC) of fresh inermis fruit was determined to be 1.28 g GA equivalent/100 g fresh fruit. Additionally, by scavenging radicals, EtOAc and MeOH extracts demonstrated potent antioxidant activity against DPPH free radicals. The EtOAc extract exhibited the highest activity (IC_{50} 66.2 ppm) and was similar to the antioxidant activity of various red fruits, as measured by the DPPH method.

Salmiyah and Bahruddin (2018) reported that the optimal DPPH radical antioxidant activity was observed at a concentration of 1000 mg/L, resulting in an efficacy of 81.752%, whereas minimal activity occurred at a concentration of 100 mg/L, with a result of 62.895%. The findings regarding the efficacy of DPPH antioxidants in Lobi-lobi fruit showed that increasing the concentration of the test solution correlated with an increase in DPPH antioxidant activity, which exceeded 50% on average.

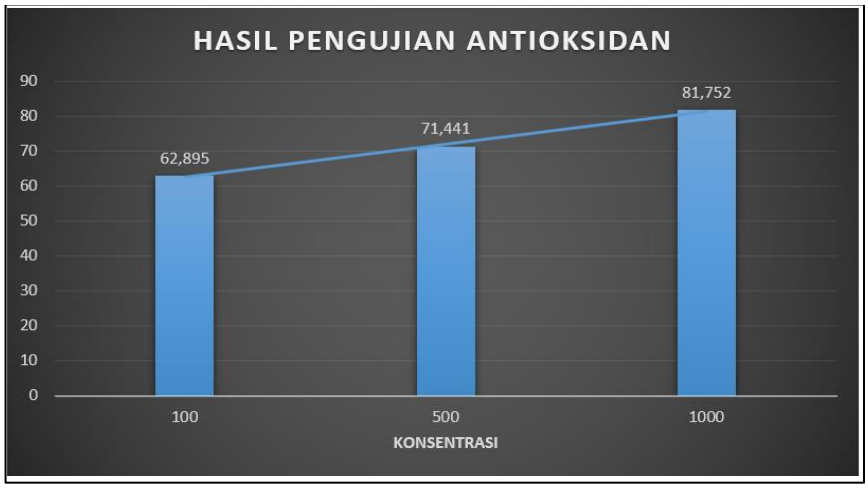

Figure 2. ***The antioxidant testing results (Salmiyah and Bahruddin dkk. 2018).***

Based on the results of Yasin *et al*. (2022), the lower the IC_{50} value, the more pronounced is the antioxidant activity. Specifically, the compound showed strong antioxidant activity when the IC_{50} was 50 ppm; it was classified as strong in the range of 50-100 ppm, moderate in 101-150 ppm, and weak if the antioxidant concentration exceeded 150 ppm. The concentration variations were analyzed at 3, 5, 7, and 10 ppm. Each concentration produced a different percentage of inhibition; for the lobi compound alone, the inhibition values were 82.919%, 84.061%, 85.088%, and 85.773%, respectively. The regression equation for the lobi extract was $y = 0.958x + 82.06$, with an R^2 value of 0.988, leading to an IC_{50} value of 50.011 g/L.

By the findings presented Fitriyani *et al*., (2018), the quantification of total anthocyanin content utilizing the pH differential method for tomi-tomi fruit yielded a value of 26.56 ± 0.28 mg/100 g (wet weight) or 103.89 ± 1.08 mg/100 g (dry weight). The anthocyanin concentration observed in this study was relatively lower compared to that reported by other research, which showed a total of 26.56 ± 0.28 mg/100 g (wet weight). This difference may be due to differences in geographical location; previous research has examined Lobi-lobi fruit cultivated in Maluku, whereas the current study focused on tomi-tomi fruit grown in Salatiga.

Based on the results of the DPPH and ORAC assays, in conjunction with TPC evaluations, various antioxidant characteristics of the investigated plant unterstreichen the disparities in antioxidant efficacy among the edible non-urban species (NUS) of trees in the Philippines while simultaneously offering a visual elucidation of their potential health advantages. *Flacourtia inermis Roxb* typically demonstrates an insignificant antioxidant capacity, as evidenced by its markedly low TPC levels. In contrast to these observations, previous research has indicated that *F. inermis* possesses antioxidant properties. Specifically, Alakolanga *et al*. (2015) reported a moderate level of antioxidant activity in *F. inermis* as determined by the DPPH assay, delineated by an IC_{50} value of 66.2 µg/mL. Mature fruits of *F. inermis* have been previously acknowledged as significant reservoirs of phenolic antioxidants, including quercetin, rutin, and esculin. Nevertheless, this investigation revealed an absence of antioxidant activity for these species in the DPPH assay, only minimal activity for ORAC, and relatively low total phenolic content. Such discrepancies may be ascribed to variations in the methodologies employed for processing the plant material (fresh fruit versus extract derived from dried plant material) or to the diverse extraction solvents utilized (ethanol versus methanol) (Rondevaldova *et al*., 2024).

To ascertain the presence of anthocyanins, a differentiation pH methodology was employed, with a pH range extending from 1 to 4.5. The absorbance of the solution was quantified using a UV-visible spectrophotometer at 520 and 700 nm. Furthermore, the anthocyanin concentration in the peel of *Flacourtia inermis* was found to be inferior to that of mangosteen (59.3 mg/100 g) and red dragon fruit (28.11 mg/100 g). The total anthocyanin content in the peel of *Flacourtia inermis* was derived from anthocyanidin-3-glycosides, while a UV absorption erythema transmission percentage of 0.7553 was obtained at a concentration of 1000 ppm (Rakhman *et al*., 2020). This is likely because mangosteen and red dragon fruits may have a more active anthocyanin biosynthesis pathway or higher enzyme expression, resulting in a greater anthocyanin content than *Flacourtia inermis Roxb.*

Anti Diabetes Activity

The following results were reported by Jacob *et al*., (2022), who used white rats as test subjects for antidiabetic experiments and obtained the following data: Blood glucose levels in the negative group receiving alloxan treatment were 394 ± 168.31 on day 1, increased to 402.8 ± 154.21 on day 7, and then increased to 428.8 ± 153.85 on day 14. The positive group receiving glibenclamide and alloxan treatment showed a decrease in blood glucose levels starting on day 1 by 430.6 ± 140.62, which decreased to 288 ± 150.41 on day 7, and then to 98.8 ± 19.16 on day 14. In addition, at a dose of 150 mg/kgBW, the percentage of blood glucose reduction on the 7th day decreased by 35.79% and on the 14th day by 68.35%, whereas at a dose of 300 mg/kgBW, the percentage of blood glucose reduction showed that on the 7th day, there was a decrease of 42.08% and on the 14th day by 66.03%.

In the experimental cohort, the ethanolic extract derived from Lobi-lobi fruit showed a decrease in glycemic levels from day 7 to 14, although it did not reach the normative glucose concentration state. However, the glycemic metrics for the groups administered doses of 150 mg/kg body weight (BW) and 300 mg/kgBW showed comparable effects to those observed in the positive control group.

The observed decrease in glycemic levels caused by the administration of the ethanolic extract of lobi fruit at a dose of 150 mg/kg BW was determined to be more efficacious than the 300 mg/kg BW group because it produced a more significant percentage decrease in glycemic levels. The underlying mechanism of the hypoglycemic effect in the rat model may be associated with the presence of bioactive chemical constituents, particularly alkaloids, flavonoids, phenolic compounds, triterpenoids, saponins, and tannins.

Using the results of Muninggar and Lestario (2019), this study attempted to investigate the effect of administering anthocyanins from Lobi-lobi fruit on the heart circumference of dyslipidemic mice. The findings showed that the most effective dose was identified at the second dose of 27.95 mg/kgbb, which resulted in an optimal increase in the maximum heart circumference structure in dyslipidemic mice when compared to the cohort

receiving Simvastatin 10 mg, which is recognized as a standard therapeutic intervention for dyslipidemia. Spearman's Correlation Test revealed a moderate relationship between anthocyanin dose and heart circumference, with a p value of 0.162 and a correlation coefficient of r = 0.412.

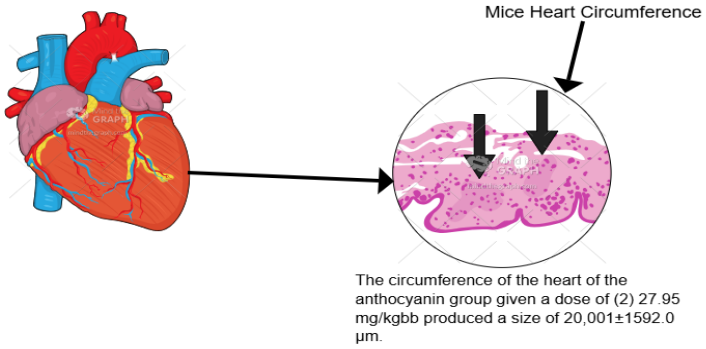

Figure 3. ***Mouse heart circumference*** ***(Muninggar & Lestario, 2019).***

From the results reported by A. Alakolanga *et al*., (2015), the main objective was to identify natural alternatives that have the capacity to inhibit the function of digestive enzymes and help in the regulation of blood glucose levels. It was determined that the total phenolic content present in the fruits of *F. Inermis* was measured, revealing a measurement of 1.28 grams of gallic acid equivalents per 100 grams of fresh fruit. This phenolic concentration is significant as it contributes to the potential antidiabetic properties of the extract, furthermore, the ethyl acetate (EtOAc) extract showed an IC_{50} value of 549.13 ± 3.47 ppm regarding the inhibition of α-glucosidase, while the methanol (MeOH) extract showed an IC_{50} value of 710.69 ± 1.08 ppm, and the n-butanol (N-BuOH) extract showed an IC_{50} value of 661.86 ± 4.33 ppm. In contrast, the positive control, Acarbose, revealed a much lower IC_{50} value of 13.83 ± 1.27 ppm for α-glucosidase inhibition.

Anti Obesity Activity

Results from the study conducted by Baby *et al*. (2023) detected various phytoconstituents within this particular plant using an array of analytical methodologies. The inhibitory activity on pancreatic lipase (PL) was noted in the extracts in a manner that was contingent upon dosage. In the implementation of the pancreatic lipase inhibition assay, it was ascertained that the ethanol fruit extracts displayed notable lipase inhibitory activity, with an IC_{50} value determined to be 377.15 µg/ml. The HPTLC fingerprinting of the ethanol extract indicated the presence of several bioactive compounds. High-Resolution Liquid Chromatography-Mass Spectrometry (HR-LC/MS) analysis of the most efficacious ethanol extract underscored the detection of a variety of phytochemicals, including phenolic compounds and flavonoids. Purification of the ethanolic fruit extract of FI (FF2) through column chromatography, followed by structural elucidation utilizing diverse spectroscopic techniques, substantiated the identification of two distinct compounds, specifically myricetin and quinic acid.

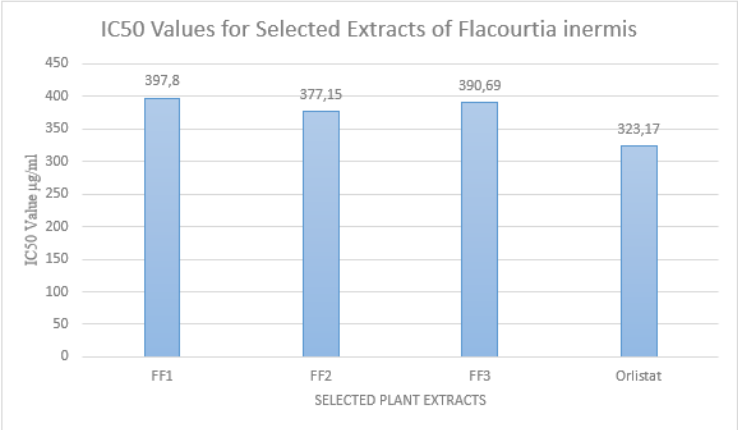

Figure 4. ***Comparison of FF1, FF2, and FF3 IC_{50} values with those of orlistat (Baby et al., 2023).***

Analysis showed that *F. inermis* fruits exhibited significant antiobesity properties, with FF2 administration (at doses of 200 mg/kg and 400 mg/kg) markedly reducing body weight gain and body mass index (BMI) relative to the high-fat diet (HFD) group. The incorporation of FF2 in conjunction with HFD resulted in reduced body weight gain, decreased glucose concentrations, and changes in serum lipid profiles. Both doses of FF2 reduced the detrimental effects associated with HFD, characterized by reduced triglyceride (TG), total cholesterol, and low-density lipoprotein (LDL) cholesterol levels, as well as increased high-density lipoprotein (HDL) cholesterol levels in the experimental group compared to the positive control. Furthermore, FF2 extract showed dose-dependent improvements in serum lipid and glucose concentrations, in addition to improvements in liver parameters, as evidenced by decreased levels of aspartate aminotransferase (AST), alkaline phosphatase (ALP), and alanine aminotransferase (ALT), thereby indicating potential therapeutic benefits in addressing dyslipidemia, hyperglycemia, and liver health associated with obesity. Histological analysis of white adipose tissue further corroborated the observed antiobesity effects (Anbiah *et al*., 2024).

Anti Bacterial Activity

Among the two experimental specimens, designated as A and B, specimen B, which encompasses 2,3-Dihydroxybenzaldehyde (DHB) in a sodium hydroxide solution (NaOH) (pH 10), demonstrated no effectiveness in inhibiting the proliferation of the assessed microbial strains. This finding unequivocally suggests that the antibacterial characteristics of 2,3-DHB are significantly diminished in an alkaline milieu. Conversely, the implications of 2,3-DHB in hydrochloric acid (HCl) (specimen A) were remarkable. Instead of displaying reduced activity in an acidic environment, its antibacterial effectiveness was noted to improve against all examined strains compared to that of 2,3-DHB in isolation. The inhibition zones recorded from the administration of 2,3-DHB in an acidic context ranged from 14 mm to 20 mm, in stark contrast to the inhibition zones of 8 mm to 12 mm observed with 2,3-DHB alone. Among the microbial strains assessed, Staphylococcus aureus, Pseudomonas aeruginosa, and Serratia marcescens were recognized as the most susceptible organisms to the combination of 2,3-DHB and hydrochloric acid (George *et al*., 2015).

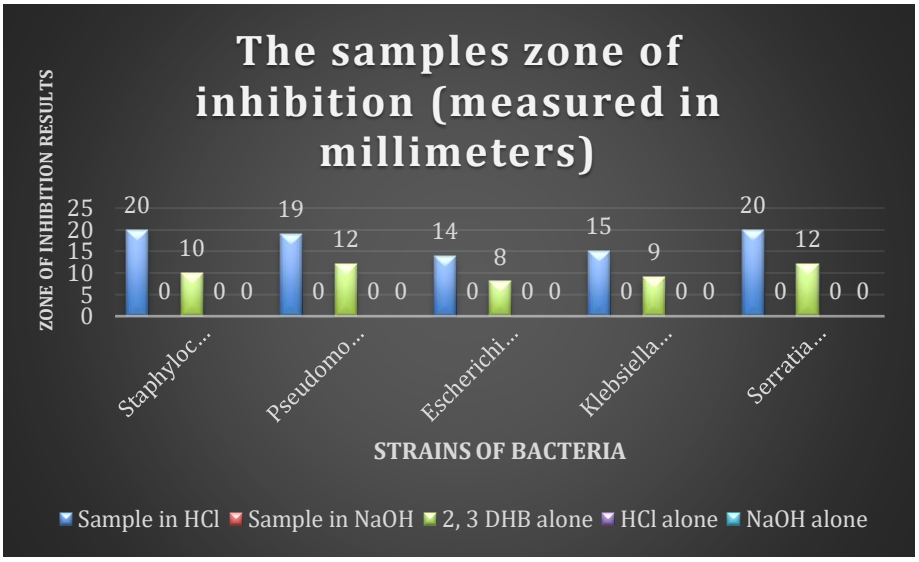

Figure 5. ***The effect of pH on 2,3 DHB activity to inhibit the growth of common bacterial strains (George et al. 2015).***

The measurement of the inhibitory zone diameter for 75% concentration was 39 mm, for 50% concentration was 30 mm, and for 25% concentration was 23.8 mm. It is evident that an increase in the concentration of the extract positively correlates with the magnitude of the inhibitory zone established against Staphylococcus aureus. The extensive diameter of the observed inhibitory zone can be attributed to the elevated levels of antibacterial agents present at higher concentrations. The presence of a zone indicating bacterial growth inhibition provides evidence that the extract contains active antibacterial compounds (Nendissa *et al*., 2023).

CONCLUSION

The results of a review of several articles indicate that lobi-lobi fruit (*Flacourtia inermis, Roxb*) can be used as a source of natural medicine. Extracts from this fruit show diverse pharmacological activities, including antioxidant, antidiabetic, antiobesity, and antibacterial activities. Bioactive components such as phenolics contribute to the observed therapeutic effects. These results indicate the importance of further exploration of secondary metabolites in fruits for the development of more effective health products. Further studies are needed to identify the mechanisms of action and the active components responsible for these pharmacological activities, as well as to explore their potential clinical applications.

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