



RESEARCH ARTICLE

Soursop (*Annona muricata* L.) in Indonesia: Biological evaluation, student perspective and internet trends

I Nyoman Jirna^{1*}, I Gede Sudarmanto¹, I Nyoman Purna¹, Nyoman Mastra¹, Cokorda Dewi Widhya Hana Sundari¹, I Nyoman Gede Suyasa¹, I Putu Gede P. Damayanto² & Muhammad Azli Ritonga³

¹Poltekkes Kemenkes Denpasar. Jl. Sanitasi no. 1, Sidakarya, Denpasar Selatan, Denpasar, 80114, Bali, Indonesia

²Herbarium Bogoriense, Research Center for Biosystematics and Evolution, National Research and Innovation Agency (BRIN). Jl. Raya Jakarta-Bogor, km 46, Cibinong, Bogor, 16911, West Java, Indonesia

³Doctoral Program, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Andalas. Kampus Limau Manis, Padang, 25163, West Sumatra, Indonesia

*Email: nyomanjirna@gmail.com



ARTICLE HISTORY

Received: 23 October 2023

Accepted: 17 July 2024

Available online

Version 1.0 : 22 October 2024



Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

Copyright: © The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited (<https://creativecommons.org/licenses/by/4.0/>)

CITE THIS ARTICLE

Jirna I N, Sudarmanto I G, Purna I N, Mastra N, Sundari C D W H, Suyasa I N G, Damayanto I P G P, Ritonga M A. Soursop (*Annona muricata* L.) in Indonesia: Biological evaluation, student perspective and internet trends. Plant Science Today (Early Access). <https://doi.org/10.14719/pst.3035>

Abstract

The study provided an overview of soursop (*Annona muricata* L.) in Indonesia, covering taxonomy, phytochemicals, antimicrobial tests, college student perspectives, and internet trends. Taxonomy details were sourced from literature, and herbarium specimens were deposited in the herbaria. Phytochemical compounds were identified using a UV-Vis spectrophotometer, while antimicrobial activity was assessed through disc diffusion. Student perspectives were collected via questionnaires, and internet trends were tracked with Google Trends. Data on taxonomy, student perspectives, and internet trends were analyzed descriptively, while experimental data underwent Kruskal-Wallis testing. Soursop, originally from tropical America, was likely introduced to Indonesia before 1884 and is now widespread. Soursop leaf extract exhibited phenol (2554.22 mg/100g), flavonoid (5263.43 mg/100g), and tannin (1469.77 mg/100g) presence. The study demonstrated its potent antimicrobial properties at concentrations of 25%, 40%, 55%, and 70%, with a 6 mm growth inhibition zone. College students at Health Polytechnic of Denpasar identified 42 treatable diseases with soursop, with fidelity levels (FL) ranging from 2.7% to 48.65%. The highest FL was observed for gout. Leaf and fruit parts of soursop are commonly used in traditional medicine. The trend of internet searches regarding the utilization of soursop (January 2011–September 2023) peaked in January 2012 and then declined until 2023, with the majority of searches occurring in central-western Indonesia.

Keywords

Annona muricata; antibacterial; internet trends; student perspectives; taxonomy

Introduction

The soursop (*Annona muricata* L., locally known as *sirsak* in Indonesia) thrives in the diverse landscape of Indonesia. This tropical fruit tree, belonging to the family Annonaceae, has garnered significant attention for its remarkable attributes. Soursop is a well-known plant deeply rooted in traditional medicine (1), owing to its rich composition of active substances renowned for their antibacterial properties (2). Surprisingly, information pertaining to the taxonomy of soursop in Indonesia has been overlooked, leaving a gap in our understanding. The lack of comprehensive taxonomy information for widely planted plants arises from a historical emphasis on docu-

menting and categorizing wild species. Moreover, there is a shortage of taxonomists with specialized expertise in cultivated plants, resulting in a dearth of research in this area. A detailed study of its taxonomy can provide accurate identification and classification information, and contribute to the broader understanding and conservation of Indonesia's rich plant biodiversity and the ecosystems it supports.

Even though there is a dearth of taxonomy data, as previously noted, soursop is a widely recognized plant with a strong presence in traditional medicine (1). This is attributed to its abundant array of active compounds, which are well-known for their antibacterial attributes (2), for example, against *Staphylococcus aureus* (3). *Staphylococcus aureus*, a gram-positive pathogenic bacterium, naturally inhabits the skin, mouth, and upper respiratory tract as part of the body's normal flora (4, 5). This particular bacterium has the ability to induce various health conditions, such as pneumonia, meningitis, endocarditis, and skin infections (6–8), posing a significant threat to individuals affected by its pathogenic nature. Fortunately, the infectious potential of *S. aureus* is limited to individuals with compromised immune systems (9), offering some respite for those with robust defense mechanisms. Notably, this bacterium does not possess the ability to attack and invade healthy tissues (10), ensuring the preservation of well-being in individuals with unimpaired immunity. However, *S. aureus* reportedly exhibits a robust resistance to a wide array of antibiotics (11), showcasing its ability to withstand the effects of multiple antimicrobial treatments.

As the resistance of *S. aureus* to a multitude of antibiotics continues to escalate, the efficacy of chemical-based treatments, especially antibiotics, in combating infectious diseases caused by this bacterium becomes increasingly limited. Utilizing medicinal plants as an alternative, such as soursop plants, can play a crucial role in prevention. Soursop leaf reportedly contains chemical compounds, such as anticancer, antiulcer, antidiabetic, anti-protozoal, antidiarrhea, antiviral, antihypertensive, and antibacterial properties (2). The presence of flavonoids, saponins, and tannins in soursop leaves (12, 13) is considered responsible for their antibacterial properties. The alkaloid group found in soursop consists of compounds such as lirioidine, which exhibits anti-tumor, antibacterial, and antifungal properties (14). Additionally, the methanol extract of the soursop leaf showed an inhibition zone of 12.1 mm against *S. aureus* (3). Unfortunately, the concentration of the extract utilized in their research was not clearly stated.

In addition to taxonomic studies and empirical research on the phytochemical and active antibacterial compounds in soursop, understanding the perspective of the public on the traditional medicinal use of soursop is also important. Public understanding, especially among college students, of the potential of soursop leaves in alternative medicine may vary. College students, especially at health campuses, however, are a crucial part of the future healthcare system. They are the prospective healthcare professionals who will provide healthcare services to the

community. Therefore, their understanding of traditional treatments, such as using soursop extract, and their attitudes towards it can influence how this alternative treatment is integrated into future healthcare practices. On the other hand, understanding the trend of online searches related to the use of soursop in the health sector is equally significant. Studying the trend of soursop utilization in health on the internet provides crucial insights into the level of interest and demand for soursop in the context of health use. This information can be used to guide strategic decisions in the health sector, including the development of products or therapies involving soursop, planning health campaigns, understanding consumer preferences and needs, and monitoring changes in the pattern of soursop use for health purposes. Based on the aspects mentioned above, research was conducted to provide a comprehensive overview of soursop in Indonesia. This research encompassed taxonomy information, analysis of phytochemical compounds, testing antimicrobial properties, presenting college student perspectives, and understanding internet trends regarding soursop in Indonesia.

Materials and Methods

Study period and area

The study was conducted from March 2019 to October 2019. Soursop leaves were harvested in Batubulan, Gianyar Regency, Bali, Indonesia. The quantitative phytochemical test of active antimicrobial substances from soursop was conducted at the Integrated Analytical Laboratory, University of Udayana, Indonesia, while the qualitative phytochemical test was conducted at the Laboratory of Department of Health Analysis, Health Polytechnic of Denpasar, Indonesia. The antimicrobial activity test was conducted at the Laboratory of Microbiology, University of Udayana, Indonesia. Taxonomy information was obtained by checking the herbarium specimen at the Herbarium Bogoriense (BO), National Research and Innovation Agency (BRIN) of Indonesia. The distribution of semi-structured questionnaires was carried out among students at the Health Polytechnic of Denpasar, Indonesia.

Taxonomy of soursop

Taxonomy information on soursop in Indonesia was obtained by studying literature (19, 21), as well as examining specimens from the Herbarium Bogoriense (BO) and living plant collection. Additionally, high-resolution images of specimens collected from Indonesia were also examined on several online database portals. Spatial data was extracted and collected from the Global Biodiversity Information Facility (GBIF) database available at <http://www.gbif.org>, as well as through literature study.

Phytochemical of soursop leaf extract

Soursop leaves (2.5 kg) were ground and extracted using the maceration method. The moisture-dried powder was determined by calculating the weight difference before and after oven drying (50°C, 12 hours). The extract was evaporated and concentrated by heating it at 40°C. The pure extract was diluted with 96% ethanol to obtain 25%,

40%, 55%, and 70% concentrations. A stock solution of 1 mg/mL was prepared by dissolving 0.01 g of the purified extract in 10 mL of distilled water for the quantitative determination of phenolics, flavonoids, and tannins. Total phenols were quantified using a modified Folin-Ciocalteu reagent method (15). A 0.4 mL aliquot of the dissolved extract was mixed with 0.4 mL of Folin-Ciocalteu reagent and 4.2 mL of 10% Na₂CO₃. The mixture was incubated for 90 minutes and then measured using a UV-Vis spectrophotometer at 760 nm. Flavonoids were determined using a modified method of (16). A 1 mL aliquot of the dissolved extract was added to 4 mL of distilled water, 0.3 mL of 10% AlCl₃, and 0.3 mL of 10% NaNO₂. The mixture was incubated for 30 minutes and measured using a UV-Vis spectrophotometer at 435 nm. Tannins were determined using a modified method of (16). A 0.5 mL aliquot of the dissolved extract was mixed with 0.5 mL of Folin-Denis reagent and 8.5 mL of 10% Na₂CO₃. The mixture was incubated for 60 minutes and then measured using a UV-Vis spectrophotometer at 725 nm.

Antimicrobial activity test of soursop leaf extract

This true experimental research used a post-test-only control group design with two randomly selected groups: a treatment group and a control group. The treatment groups had four extract concentrations (25%, 40%, 55%, and 70%), with 96% ethanol as the negative control and Ciprofloxacin as the positive control, each with four replicates. Colonies of *S. aureus* were suspended in a tube containing 5 mL of 0.85% physiological NaCl solution. The suspension was compared to a 0.5% McFarland standard. Sterile cotton swabs were immersed in the bacterial suspension and streaked on the Petri dishes with Mueller-Hinton media. The diffusion test was performed using a modified disc method (17). Discs were soaked in various extract concentrations, with 0.5% carboxy methyl cellulose for the negative control and 5 µg/mL Ciprofloxacin for the positive control. The discs were placed on Mueller-Hinton media 15 mm apart and incubated at 37°C for 24 hours in an inverted position.

College student perspectives of soursop benefits

The college student perspective was explored through questionnaire surveys. The respondents consisted of college students from the Health Polytechnic of Denpasar, Indonesia. The distribution of the questionnaire sheets was carried out randomly among college students.

Internet search trends regarding soursop benefits

The study used Google Trends (<https://trends.google.com>) to gather data from January 2011 to September 2023. This timeframe was chosen because Google Trends' algorithm has been refined since January 2011, providing an overview of its users' geographic area. Data was collected from the Indonesian region, covering all search categories related to various Indonesian keywords: "khasiat buah sirsak", "khasiat daun sirsak", "manfaat buah sirsak", and "manfaat daun sirsak" (daun = leaf, buah = fruit, sirsak = soursop). We used two synonymous keywords, "khasiat" and "manfaat", both meaning "benefits" and "advantages". This information was extracted and saved in a CSV file.

Data analysis

Taxonomy information was analyzed descriptively. Herbarium abbreviations followed the New York Botanical Garden's Index Herbariorum (<https://sweetgum.nybg.org/science/ih>). Soursop's spatial distribution in Indonesia was mapped using SimpleMappr (<https://www.simplemappr.net>). Phytochemical data were analyzed descriptively. Antimicrobial activity data were analyzed using the Kolmogorov-Smirnov test and then the Kruskal-Wallis test to compare soursop leaf extract's antimicrobial activity at different concentrations. Results were compared with the NCCLS table to identify the most effective concentration. The Least Significant Difference (LSD) test determined the variation in the inhibition zone between soursop leaf extract concentrations. College students' interview data was analyzed descriptively. Fidelity level (FL) was evaluated using Eqn. 1 (18). Internet search trend data was descriptively analyzed using Excel and presented in graphs and maps.

$$FL (\%) = (N_p/N) \times 100 \dots\dots\dots(\text{Eqn. 1})$$

N_p = the number of respondents reporting the utilization of a medicinal plant for a specific disease, and N = the total number of respondents mentioning the same plant for each disease (18).

Results

Taxonomy account of soursop

Annona muricata L., Sp. Pl. 1: 536. 1753. Type: Sloane, Voy. Jamaica 2: 166, t. 225. 1725. Lectotype designated by Khattoon S. 1985. Annonaceae. In: Nasir E, Ali SI (eds). Flora of Pakistan 167. Karachi: Department of Botany, University of Karachi (Fig. 1).

Synonym

Annona bonplandiana Kunth in F.W.H.von Humboldt, A.J.A. Bonpland & C.S. Kunth, Nov. Gen. Sp. 5: 58. 1821. *Annona cearaensis* Barb. Rodr. in Pl. Jard. Rio de Janeiro 6: 3. 1898. *Annona muricata* var. *borinquensis* Morales in Fl. Arbor. Cuba: 60. 1887. *Annona muricata* f. *mirabilis* R.E. Fr. in Ark. Bot. 21A(9): 11. 1927.

Description

Trees about 3–8 m high, evergreen. Stems cylindrical, bark rugose with numerous whitish lenticels, young branches hairy. Leaf blade ovate-elliptic to obovate-oblong, 6–18 × 2.5–7 cm, chartaceous to coriaceous, adaxially green and shiny, abaxially greenish and glabrous, apex acute to obtuse, base broadly cuneate to rounded, margins entire and slightly revolute, petioles 0.5–1 cm long and slightly swollen and glabrous. The inflorescence is axillary, 1- or 2(-3)-flowered. Flowers 3–4 cm in diameter, 3–5 cm long. Peduncle 2–5 mm long, pedicel 0.5–2.5 cm and pubescent to glabrous. Sepals are ovate-elliptic to triangular, 3.5–5 mm long, green. Outer petals are broadly triangular or cordate, 2.5–5 × 2.5–4 cm, thick, apex acute to obtuse, green, later yellowish, inside basally without a red spot; inner petals ovate-elliptic, 3–4 × 2–3.5 cm, slightly thin than outer



Fig 1. Lectotype of *Annona muricata* based on Sloane, Voy. Jamaica 2: 166, t. 225. 1725 (BM, code BM000594140). (Source: <https://data.nhm.ac.uk/media/b943af33-7bda-4573-a5df-9630e9ea1758>).

petals, imbricate, base clawed, apex obtuse, green, later yellowish. Stamens 4–4.5 mm; filaments fleshy; connectives apically dilated. Style short, stigma truncate. Fruit green to dark green, fleshy, edible, aromatic, oval, and often oblique or curved, 10–30 × 7–15 cm, covered with spine-like projections, base impressed, apex rounded; pulp white and tart. Seeds brownish yellow to dark brown, smooth, numerous, reniform, c. 2 × 1 cm. Fig. 2.

Distribution

This species can be found elsewhere in Indonesia, particularly in Sumatra, Java, Bali, Lombok, Sumbawa, Sumba, Flores, Timor, Kalimantan, Sulawesi, Maluku, and Papua (Fig. 3).

Uses

The fruit's flesh comprises a white pulp that is both edible

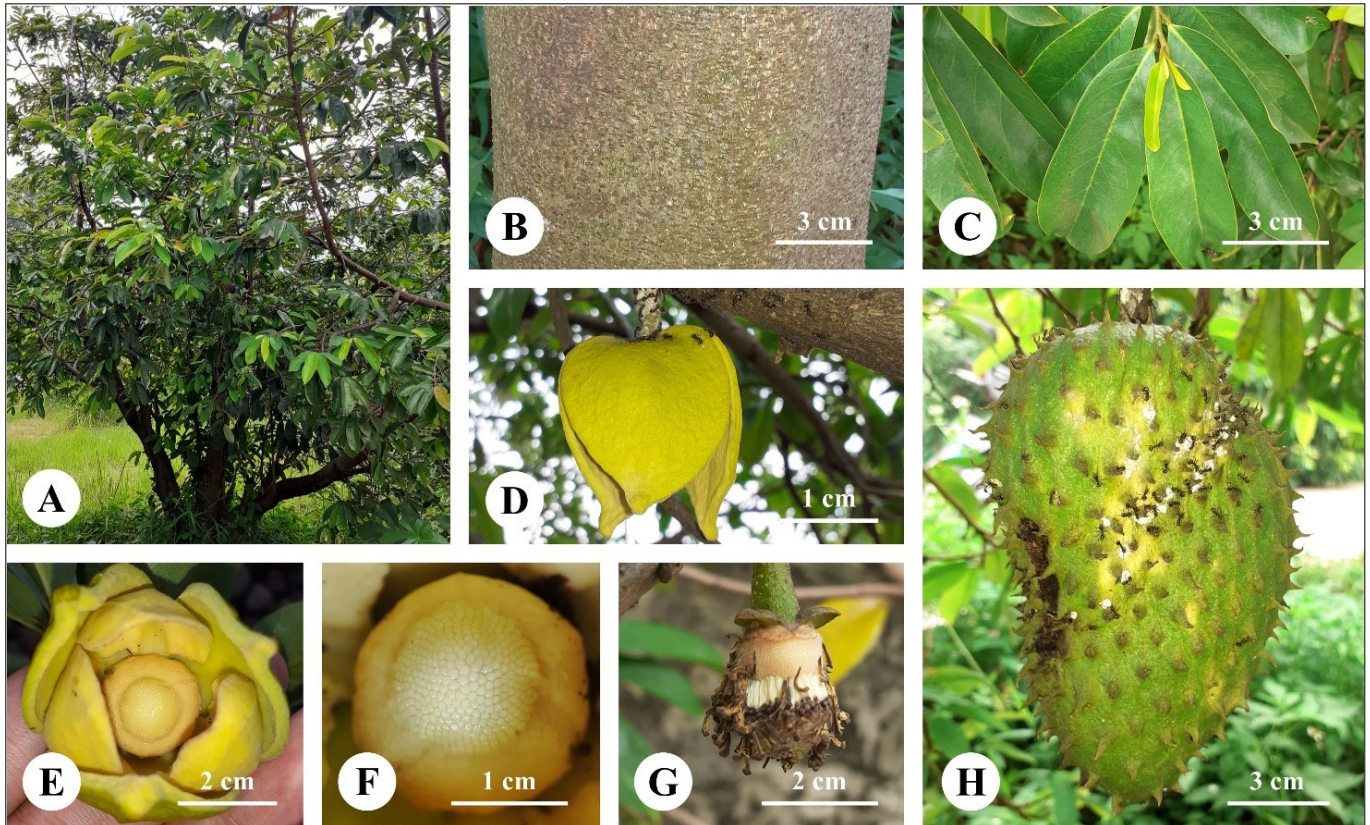


Fig. 2. *Annona muricata*: A. habit; B. stem; C. leaves; D. side view of flower; E. front view of flower; F. detail of stamens and stigmas; G. post-anthesis stage of flower; H. fruit. (Photos: I Putu Gede P. Damayanto).

Habitat and ecology

This species is cultivated around settlements in gardens, villages, cities, and mixed Dipterocarp lowland forests at an altitude of 4–1568 m.

and used in the production of fruit juice drinks and flavorings. Additionally, the fruit can be transformed into *dodol*, a sweet treat created by boiling the soursop pulp with water and sugar until it caramelizes and solidifies. Soursop leaves are commonly consumed as herbal medicine and are typically boiled to produce tea. Recently, the leaf extract of soursop has been used as a traditional scrub.

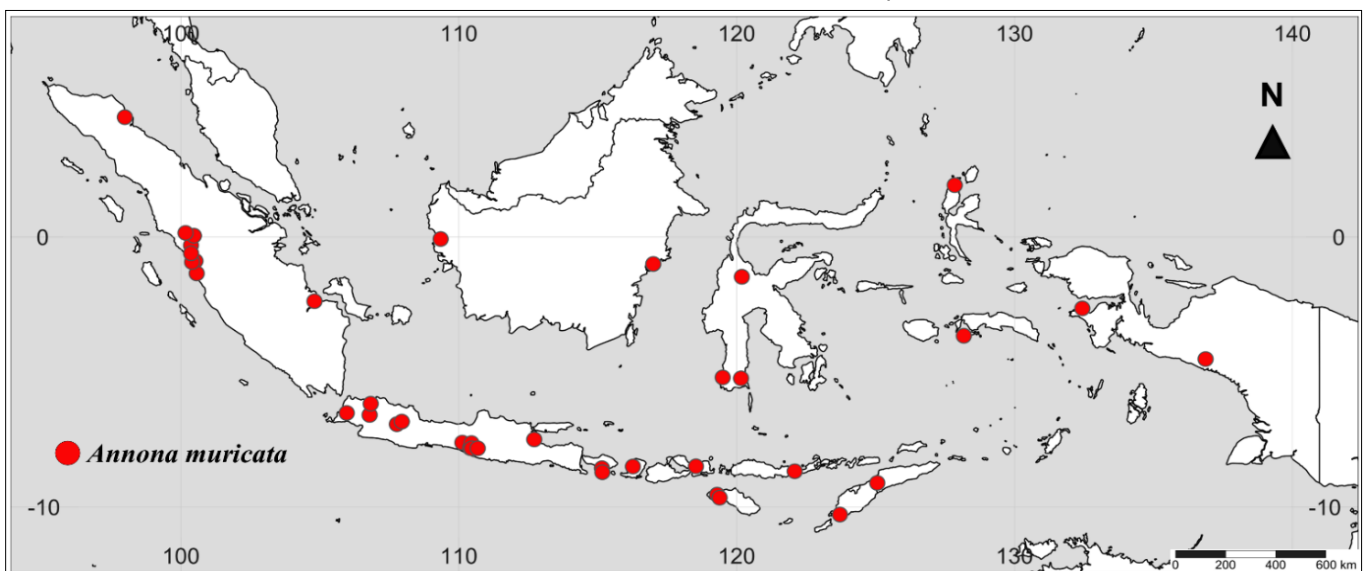


Fig. 3. Distribution of *Annona muricata* in Indonesia. (Source: data research).

Local names

Sirsak (Indonesia), *durian balando* (West Sumatra), *buah nona* (West Sumatra), *durian belanda* (North Sumatra), *nangka walanda* (West Java), *nangka bolanda* (Central Java), *sirsat* (Central Java), *silik* (Bali), *srikaye* (Lombok), *garoso jawa* (Sumbawa), *kalangga* (Sumba), *ro'o lukuta* (Sumba), *hau maninu* (Flores), *nangka belanda hutan* (Flores), *sarikaja* (South Sulawesi), and *nangka blanda* (Maluku).

Conservation status

Based on the International Union for Conservation of Nature (IUCN) Red List (<https://www.iucnredlist.org/species/143323191/143323193>), soursop is categorized as 'least concern' (LC). The LC category indicates that a species is evaluated as having a low risk of extinction in the wild.

Specimens examined

Indonesia: South Sumatra, Banyu Asin Regency, Banyuasin II, Sungsang IV, SH Dalimunthe et al. SHD87 (BO); West Sumatra, Kelumbuk No. 5, Kecamatan Kuranci, about 7 km east from Padang City, 4–10 m asl, Mardiah 1 (ANDA); West Sumatra, Kab. Pesisir Selatan, Kec. Empat Jurai, Tambang Village, 35–180 m asl, Anjas et al. 13 (ANDA); West Sumatra, Kab. Pesisir Selatan, Kec. Empat Jurai, Tambang Village, 35–180 m asl, Agung et al. 14 (ANDA); West Sumatra, Kab. Pesisir Selatan, Kec. Empat Jurai, Tambang Village, 35–180 m asl, Rahman et al. 15 (ANDA); West Sumatra, Sipisang Kayu Tanam Village, 150–250 m asl, Vivi et al. 08 (ANDA); Kalimantan, Kalimantan Timur, Wanariset research area, 50 m asl, Ambri & Arifin W322 (L); Java, DA Powell & HK Chey 721 (L); Java, West Java, Bogor Botanical Garden, WA van Heel XX.D. 83 (L); Java, West Java, Bogor Botanical Garden, Djoemadi ND XX.D. 72 a (L); Java, West Java, Boeahbatoeh [Buahbatu], 700 m asl, SM Popta 640/139 (L); Java, Soerabaja [Surabaya], JD Dorgelo 1921 (L); West Java, Bogor, Cibinong, ex Research Center for Biotechnology-BRIN, IPGPD Damayanto 1830 (BO); Maluku, North Halmahera, Limau Galela District, S Yushita 2489 (L); Maluku, Ambon, B Robinson 1782 (L, US); Flores, JAJ Verheijen 2273 (L); Timor, Ren Lakaan, 1568 m asl, PE Schmutz 2284 (L); Sumba, Southwest Sumba, Gollu Sapi Village, 501.7 m asl, Chors C/GS/09/0908/H-5 (BO).

Phytochemical of soursop leaf extract

Approximately 2.5 kg of soursop leaf was dried and ground into powder, resulting in 275 grams of crude powder. The moisture content of the dried soursop leaf powder was found to be 13.16%. The results of the quantitative test of the soursop leaf extract revealed the presence of three compounds: alkaloid, saponin, and phenol. Meanwhile, the test results for quinone compounds showed a negative value. The quantitative test of the soursop leaf extract showed the presence of phenol content of 2554.22 mg GAE/100g, flavonoid content of 5263.43 mg/100g, and tannin content of 1469.77 mg TAE/100g.

Antimicrobial activity of soursop leaf extract

The average diameter of the inhibition zone at various concentrations of soursop leaf extract against the growth of

S. aureus was consistently measured at 6 mm (Table 1, Fig. 4). When comparing these measurement results with the diameter of the inhibition zone of Ciprofloxacin antibiotics in the NCCLS table; they fall within the resistant category (≤ 21 mm). The positive control, represented by the antibiotic disk containing Ciprofloxacin, consistently exhibited inhibition zones across all replications. There were no significant differences in the diameter values of the inhibition zones, which were around 25.75 mm. The negative control, which was 96% ethanol, did not produce any inhibition zone.

Table 1. Zone of inhibition of soursop leaf extracts at various concentrations on the growth of *S. aureus* and category of National Committee for Clinical Laboratory Standards (NCCLS).

Repetition	Inhibition zone at concentrations				Standard deviation	Category of NCCLS
	25 %	40 %	55 %	70 %		
1	6	6	6	6	0.0	Resistant
2	6	6	6	6	0.0	Resistant
3	6	6	6	6	0.0	Resistant
4	6	6	6	6	0.0	Resistant
5	6	6	6	6	0.0	Resistant
6	6	6	6	6	0.0	Resistant
7	6	6	6	6	0.0	Resistant
8	6	6	6	6	0.0	Resistant
9	6	6	6	6	0.0	Resistant
10	6	6	6	6	0.0	Resistant
11	6	6	6	6	0.0	Resistant
12	6	6	6	6	0.0	Resistant
Average	6	6	6	6	0.0	Resistant

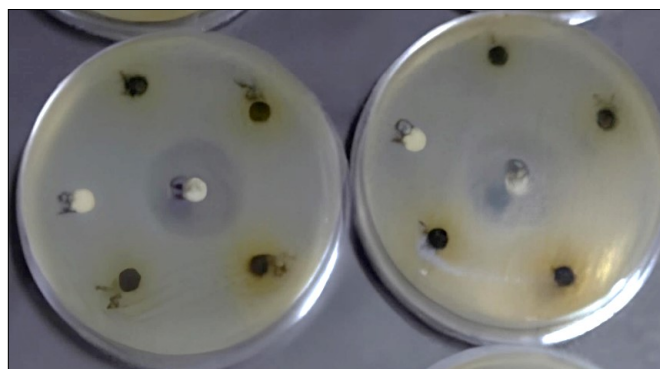


Fig. 4. Zone of inhibition (disk of the center part) of soursop leaf extracts on the growth of *S. aureus*. (Photo: I Nyoman Jirna).

The results of the Kolmogorov-Smirnov test yielded a p-value of 0.000 (<0.05), indicating that the data was not normally distributed. This was followed by the Kruskal-Wallis test, which also obtained a significant value (0.000), smaller than the predetermined α value (0.05). Significant differences were observed in the zone of inhibition of *S. aureus* growth between the soursop leaf extract concentration group and the control group. The differences in inhibitory activity among the various concentrations were further analyzed using the LSD test, which revealed a p-value of 0.000 ($p < \alpha$), indicating a significant difference between the extract concentration group and the control group.

College students' perspective on soursop benefits

A total of 46 college students at the Health Polytechnic of Denpasar were interviewed, with the majority being female (43 individuals) and only 3 males (Fig. 5A). Most respondents (31 individuals) were 19 years old, while others were 18 and 20 years old (Fig. 5B). College students of Health Polytechnic of Denpasar believed that there were

soursop plant commonly used in traditional medicine are the leaves (80.77%), fruits (17.31%), and all parts (1.92%).

Internet search trends on soursop benefits

A total of 155 sets of data were obtained in Google Trends for the keywords “ *khasiat buah sirsak* ” (benefits of soursop fruit), “ *khasiat daun sirsak* ” (benefits of soursop leaves), “ *manfaat buah sirsak* ” (advantages of soursop fruit), and

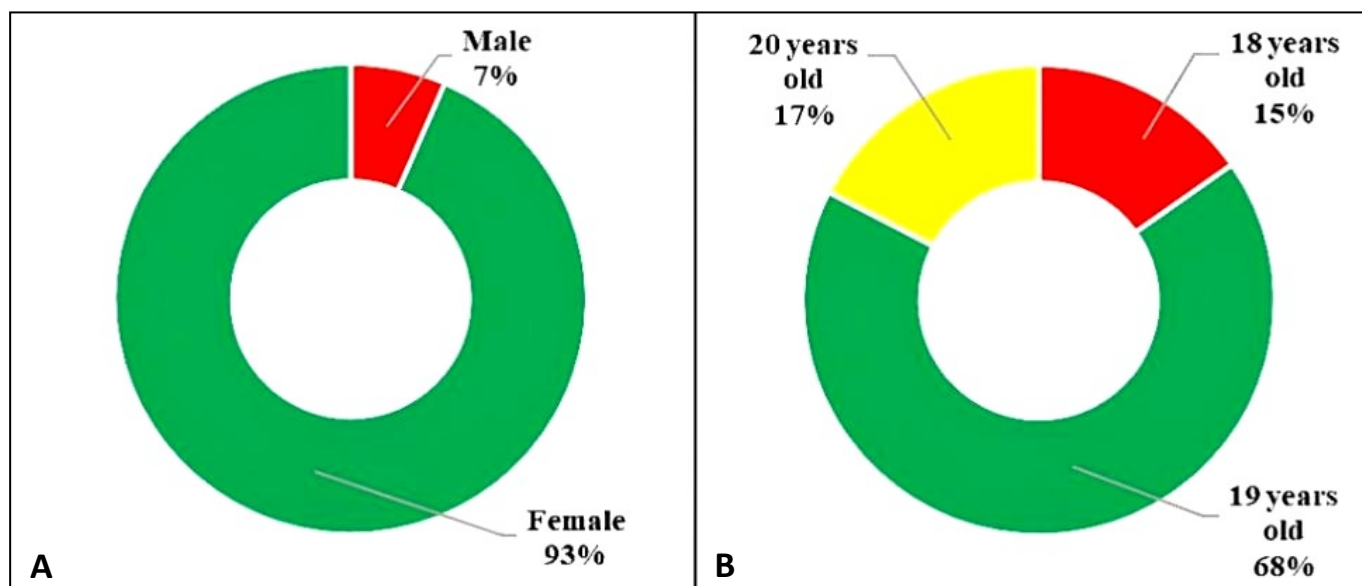


Fig. 5. Profile of respondents of college students at the Health Polytechnic of Denpasar: (A). gender ratio, (B). age status. (Source: data research).

42 types of diseases that could be traditionally treatable using soursop, with fidelity level (FL) values varying. The highest FL was observed for gout (48.65%), followed by cancer (43.24%), hypertension (43.24%), and diabetes (40.54%), while several diseases had the lowest fidelity levels, including anemia, arthritis, asthma, blood cancer, bowel cancer, breast cancer, cervical cancer, colon cancer, cough, diarrhea, diverticulitis, fever, heart cancer, hemorrhoids, herpes, influenza, liver diseases, lung cancer, oral cancer, ovarian cancer, prostate cancer, skin cancer, and sore throat (2.7% respectively) (Fig. 6). The parts of the

“ *manfaat daun sirsak* ” (advantages of soursop leaves) from January 2011 to September 2023. The highest average search inquiry on the internet was related to “ *manfaat daun sirsak* ” and the lowest was “ *khasiat buah sirsak* ” (Fig. 7). The trend of information searches regarding the utilization of soursop experienced an initial increase towards its peak in January 2012, and it gradually declined until 2023 (Fig. 8). Internet search activity using the keyword “ *manfaat daun sirsak* ” occurred in almost all regions of Indonesia (Fig. 9A), while searches using other keywords were mostly conducted in the central to the western areas of Indonesia (Fig. 9B-D).

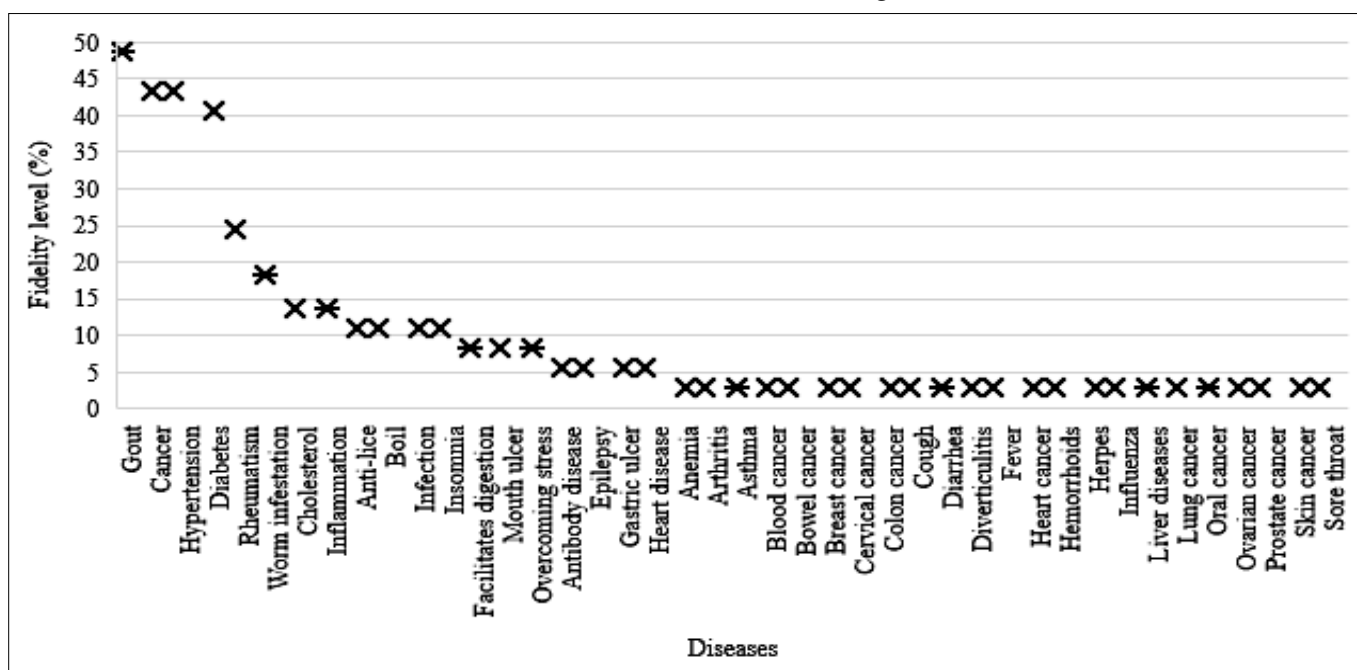


Fig. 6. Types of diseases reported to be traditionally treatable using soursop with their fidelity level. (Source: data research).

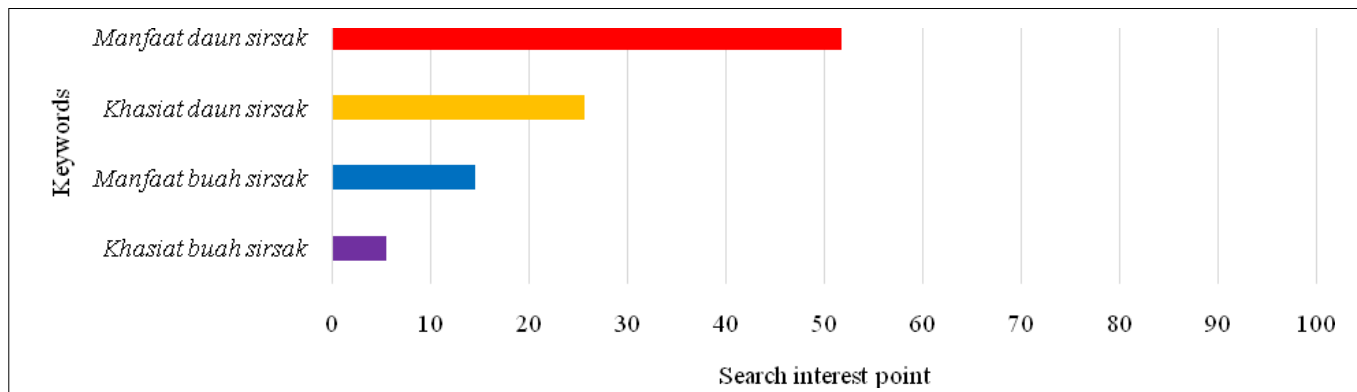


Fig. 7. Average internet searches in Indonesia using various keywords related to soursop from January 2011 to September 2023. The numbers represent search interest based on the highest point. A value of 100 indicates the keyword is at the peak of popularity, 50 signify half of that popularity, and a value of 0 indicates insufficient data availability. (Source: <https://trends.google.com/trends>).

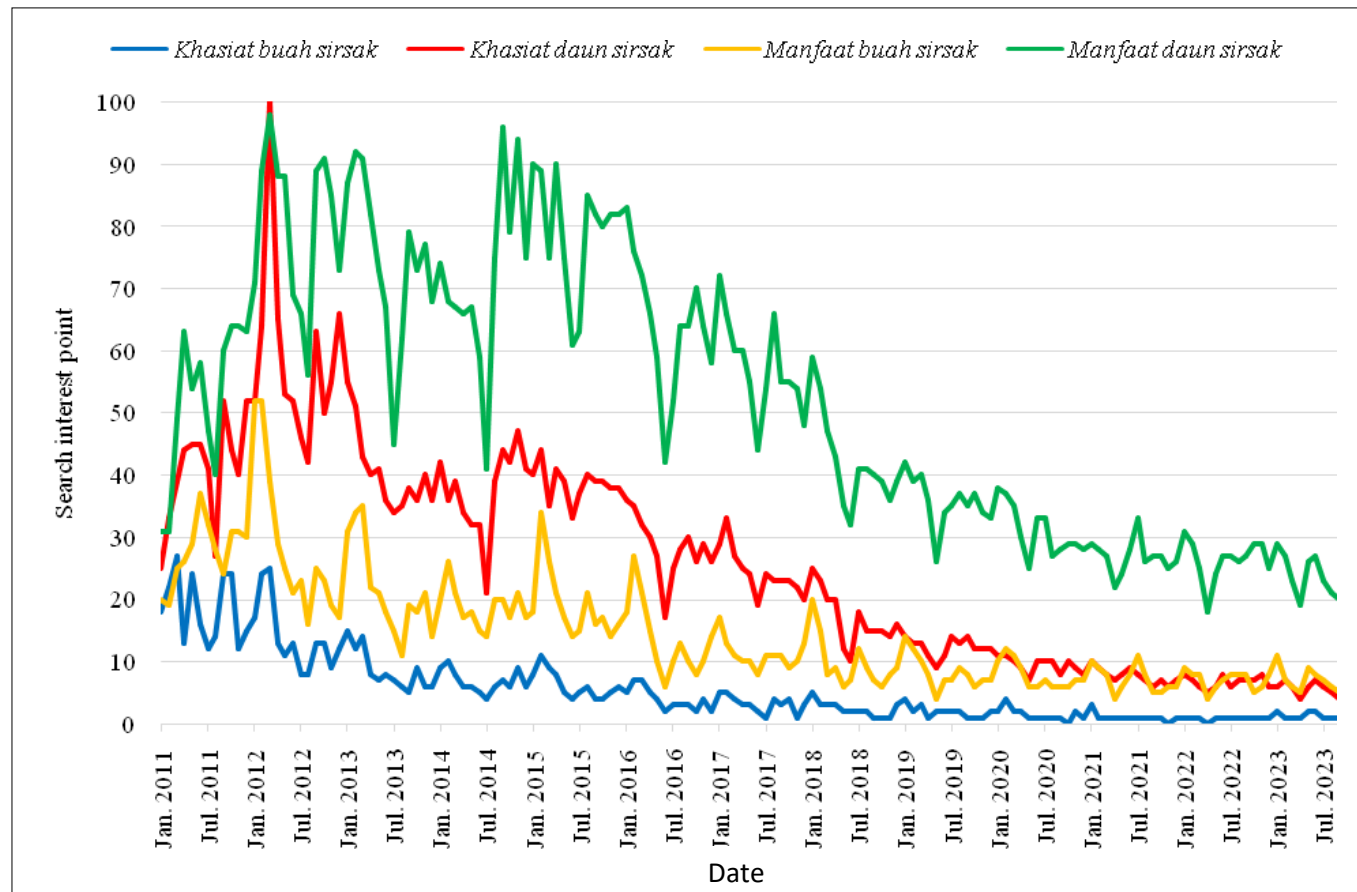


Fig. 8. Internet searches trends in Indonesia using various keywords related to soursop from January 2011 to September 2023. The numbers represent search interest based on the highest point. A value of 100 indicates the keyword is at the peak of popularity, 50 signify half of that popularity and a value of 0 indicates insufficient data availability. (Source: <https://trends.google.com/trends>).

Discussion

Taxonomy account of soursop

Soursop, or *A. muricata*, belongs to the family Annonaceae. This species was first described in Species Plantarum 1: 536 (1753) by Carl Linnaeus. The lectotype was designated in Flora of Pakistan 167 (1985) by Surayya Khatoon with the annotation ‘habitat in America calidiore, Sloane, Hist. Jam. 2: t. 225. 1725’. The lectotype is an illustration (code BM000594140) that is deposited in the Natural History Museum, London (BM) (Fig. 1). This lectotype was drawn by Everard Kickius and relates to the plant collected by Sloane [Sloane Mss.].

The soursop is a native of tropical America and the West Indies [subregion of North America, surrounded by

the North Atlantic Ocean and the Caribbean Sea]. It is an introduced species to Africa, Asia, and Australia. In Indonesia, this species is probably introduced during the Dutch colonial period. The evidence of this presumption can be observed through the plant’s local name, ‘durian belanda’ (Sumatra), which translates to ‘Dutch durian’ in English or ‘nangka walanda’ (West Java) or ‘nangka bolanda’ (Central Java), which translates to ‘Dutch jackfruit’ in English. These names refer to the fruit’s spines, which resemble those of the durian fruit (*Durio zibethinus* L., Malvaceae) or jackfruit (*Artocarpus heterophyllus* Lam., Moraceae). The introduction of soursop to Indonesia is thought to have taken a long time because various local names are already available in several regions in Indonesia. Even the Indonesian name itself, ‘sirsak’, is derived from Dutch ‘zuurzak’.

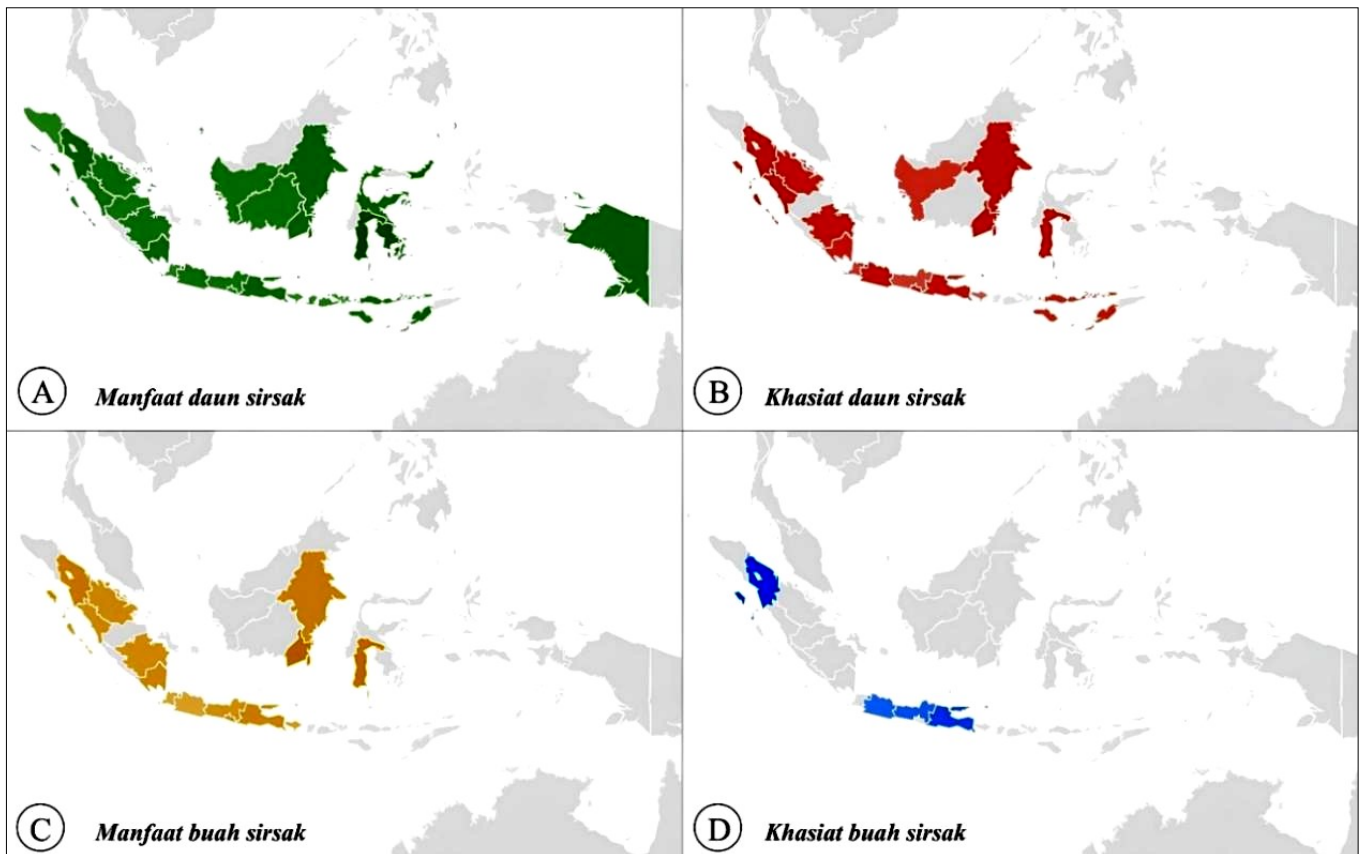


Fig. 9. Comparison of internet search activity using several keywords in Indonesia: color intensity indicates the percentage of searches. (Source: <https://trends.google.com/trends>).

The oldest known collection of soursop herbarium specimen from Indonesia is the specimen G. von Scheele s.n., collected from Lassem, Java [presumably Lasem, Central Java] in 1884 (<https://www.gbif.org/occurrence/351705441>). This specimen is stored at the Museum of Evolution, Uppsala University. Unfortunately, no online image of the specimen is available. Another specimen from Java (without specifying the exact location) is the collection by C. A. Backer s.n., collected in 1904 (<https://www.gbif.org/occurrence/2517344610>). In Sumatra (without specifying the specific location), the oldest known collection is the specimen R. M. P. Atmodjo 386, collected in 1904 (<https://www.gbif.org/occurrence/2514046067>). The specimen C. B. Robinson 1782 was collected from Ambon in 1913 (<https://www.gbif.org/occurrence/2514046851>). Meanwhile, the oldest specimen from Flores was collected by J. A. J. Verheijen 2273 in 1965 (<https://www.gbif.org/occurrence/2514045189>). Based on these records, we believe that soursop was introduced to Indonesia, particularly in Java, probably before 1884, and then to other areas in Indonesia. Soursop was among the initial fruit trees to be introduced to the Old World following Columbus' discovery of America (19). The Spanish brought it to the Philippines soon after, and it can now be found flourishing in numerous tropical nations.

In most cases, plants were introduced during the colonial period in Indonesia through the involvement of botanical gardens. Similar to the case of the invasive alien bamboo, *Chimonobambusa quadrangularis* (Franceschi) Makino (Poaceae) that was brought from Japan to the Cibodas Botanical Garden, West Java, around 1920 then escaped extensively in the nearby Mt. Gede-Pangrango

National Park, establishing itself as an invasive alien plant species (20). This species was also introduced to Sumatra, specifically in Sibolangit Tourist Park and Mt. Sibayak (20). It is possible that the same introduction method occurred with the soursop species, but it didn't become an invasive plant. Instead, people cultivate it extensively in various regions due to its delicious edible fruit. In the Bogor Botanical Gardens, West Java, the oldest collected specimen is Djumedi XX.D.72, collected in 1960 (<https://www.gbif.org/occurrence/2514047030>). Until 2019, soursop in the Bogor Botanical Gardens has been cultivated in block XXIV.B.131, which was collected from Central America (21). This confirms the assumption that soursop was introduced to Indonesia, particularly in Java, for the first time from Central America during the colonial period before 1884. The absence of well-defined ethnobotanical or folkloric beliefs surrounding soursop in Indonesia strongly suggests it is an introduced plant. In contrast, native Indonesian plants, like bamboo, are deeply woven into local myths, ethnobotanical knowledge, and folklore in Indonesia.

Phytochemical of soursop leaf extract

The dried soursop leaf powder in this study has a moisture content of 13.16%. Another research reported that the moisture content of soursop leaf powder fell within the range of 3 to 5% (22). A lower moisture content suggests better stability and longer shelf life for the powder. It helps to prevent microbial growth, minimize oxidation, maintain physical properties, and prevent undesirable chemical reactions. By reducing the water content, the concentration of active constituents, such as alkaloids, flavonoids, and tannins, increases in the final powdered form.

Three compounds were qualitatively detected in the soursop leaf: alkaloid, saponin, and phenol. These compounds play significant roles in the chemical composition of soursop leaves and may contribute to their potential benefits or properties. The quinone compounds showed a negative value, indicating that these compounds were either not found or present in very small amounts in the soursop leaf extract. Quinones are a class of organic compounds, and their absence or minimal presence suggests that they may not play a significant role in plants. Quinones have been identified as signaling agents in plants, although their role in plant signaling is not yet fully understood (23). However, several compounds classified as quinones have reportedly demonstrated potential antimicrobial properties against a broad range of bacteria, fungi, and parasites (24).

The present study conducted a quantitative test, which provided specific measurements of phenol, flavonoid, and tannin content in the soursop leaf extract. Similar results were also observed in a previous study. Soursop leaves were found to contain a variety of compounds, including alkaloids, coumarin, tannin, cardiac glycosides, flavonoids, carbohydrates, and phenols (25). Another study investigated the phytochemistry of soursop leaves and identified the presence of tannins, flavonoids, saponins, and terpenoids (12). Moreover, prior research emphasized the elevated concentrations of alkaloids, flavonoids, and phenols in the methanolic fractions of both soursop fruit and leaf (26).

In this study, flavonoid content has the highest value (5263.43 mg/100g), indicating a higher concentration of flavonoids in the soursop leaf extract. Phenol content follows with a slightly lower value (2554.22 mg GAE/100g), and tannin content has the lowest value (1469.77 mg TAE/100g). Another study discovered various phytochemicals in soursop leaf extract, including tannins (0.44 + 0.0013 mg/g), flavonoids (1.92+0.02 mg/g), phenolics (104.43+0.013 mg/g), carotenoids (0.302+0.001 mg/g), α -tocopherol (14.80+0.02 mg/g), reduced glutathione (7.4+0.01 mg/g), lycopene (0.34+0.01 mg/g), and vitamin C (1.98+0.011 mg/g) (27). The levels of phytochemical compounds found in leaves are reportedly affected by various factors such as quantity of leaf (28), harvest time, environmental conditions, soil type, solar exposure, and production location (29).

Antimicrobial activity of soursop leaf extract

Soursop leaf extract in various concentrations of this study did not exhibit significant sensitivity towards the growth of *S. aureus* compared to the NCCLS table. The inhibition zones formed at different concentrations of the tested soursop leaf extract consistently fell into the resistant category, with a uniform growth inhibition diameter of 6 mm. This lack of sensitivity can be attributed to the relatively low concentration of the active antibacterial compounds present in the soursop leaf extract, as well as the dilutions made during the testing process. Consequently, the extract's ability to inhibit bacterial growth is not fully maximized, and it fails to sensitively inhibit the growth of

S. aureus bacteria within the minimum range of 21 mm, as suggested in the NCCLS table.

Flavonoids have been identified as active compounds in soursop leaf extract and are known for their antibacterial properties (30). The reduced sensitivity observed in this study towards the growth of *S. aureus* can be attributed to the relatively low concentration of flavonoids. Young soursop leaf was selected as the material for this research, hypothesizing that their flavonoid content is lower compared to mature leaves due to the influence of photosynthesis on flavonoid synthesis. As secondary metabolites, young leaves naturally contain a lower concentration of flavonoids. A study reported a total flavonoid concentration of 410.833 mg/100g in young soursop leaf extract, whereas large (mature) soursop leaf extract samples contained 505.208 mg/100g (31). It is important to acknowledge that the flavonoid content in soursop leaves can vary depending on the plant's growth stage, environmental conditions, and extraction methods employed. Further research is necessary to fully comprehend the impact of these factors on the flavonoid content in soursop leaf.

The limited ability of soursop leaf extract to inhibit the growth of *S. aureus* bacteria in this study can be attributed to the initial preparation process, which involves direct heating under the sun. This process results in a decrease in flavonoid content and a water content of the extract that falls below the standard of 4.6% (32), reaching 10%. Water content in soursop leaf extract provides a favorable environment for bacterial growth. It has been reported that the moisture content of extract exceeding 10% will cause damage by microbes (22). The dilution of the extract is also believed to contribute to the reduced efficacy of antibacterial substances.

On the other hand, indirect drying methods such as sun drying or oven drying at temperatures below 50°C have been found to positively impact the phenol content (33). Phenols have also been identified as active compounds in soursop leaf extract known for their antibacterial properties (30). The evaporation process used in the study follows standard extract processing, employing a temperature of 50°C to evaporate ethanol while retaining water in the extract. Research suggests that a temperature of 45°C yields the optimal content of antimicrobial flavonoids (34).

In terms of the method chosen for testing the growth of *S. aureus*, the well diffusion method has been observed to result in larger inhibition zones compared to the disc diffusion method (35). This occurs because the osmolarity process takes place in the well method of extract concentration, which is higher than that of the disc diffusion method. In the well method, each hole is filled with extract concentration, making it more potent in inhibiting bacterial growth.

The results of this study do not align with previous studies on the bioactivity of methanol extract of young soursop leaf as an antibacterial against *S. aureus* and *Propionibacterium acnes* (now known as *Cutibacterium ac-*

nes) (36). The results of the study demonstrated the potential of soursop leaf extract to inhibit the growth of *S. aureus* and *C. acnes* (36). It should be noted that the use of methanol as a solvent may influence the antibacterial inhibition activity. There is no standardized method for the extraction of natural materials, resulting in potential variations in the results when extracts are produced in different laboratories. Some factors that affect the quality of the extract include chemical factors such as the type of antimicrobial and the amount of antimicrobial chemical compounds in the extract. Other factors that affect the quality of the extract are the extraction method and the solvent used. The ultrasonic extraction method produces the best extract quality (37). The use of ethanol solvent in the extraction process and concentration treatment produces a lower inhibition compared to using methanol solvent (36). In addition, other factors cannot be controlled, such as biological variations; for example, the place of origin of the soursop leaf used, which is influenced by the nutrient content of the different soil where the soursop plant grows, affects the amount of active ingredients present. Environmental factors such as air temperature, relative humidity, solar radiation, wind, plant temperature, water availability, and adequacy of light in the process of photosynthesis greatly affect the physiological function, anatomical form, and plant life cycle. These environmental factors may affect the secondary metabolites produced by the leaf (38).

College students' perspective on soursop benefits

The data presented provides valuable insights into the perspectives of college students at the Health Polytechnic of Denpasar regarding the benefits of soursop. A notable observation is the gender distribution among the participants, with a significant majority being female (93.5%) compared to only a small fraction of male respondents (6.5%). In general, college students at the Health Polytechnic of Denpasar are predominantly female, so it is not surprising to obtain imbalanced gender comparison data. The sample population for the study closely mirrored the overall demographic of Indonesian students, which was dominated by females (<https://pddikti.kemdikbud.go.id/mahasiswa>). Furthermore, the age distribution of the respondents shows that the majority of participants were 19 years old (67.4%), with a smaller portion being either 18 or 20 years old. This is common because the typical age range for undergraduate students in Indonesia falls between 18 and 22 years (39).

The belief among these college students that soursop can treat a wide range of diseases is noteworthy. They identified 42 types of diseases that can be traditionally treated using soursop, with varying levels of fidelity (Fig. 6). Fidelity level (FL) is a metric used to quantify the importance of a plant species in treating a particular ailment or health condition (18). It indicates the percentage of respondents within a group who exclusively use a particular plant species for a specific purpose (40). A higher FL suggests plant is highly valued and considered particularly effective for treating the specified condition. Based on Fig. 6, gout disease emerged with the highest FL (48.65%), indicating a strong belief in its effectiveness for treating

this condition. The college students' belief aligns with the findings reported that the coumarin fraction in soursop extract shows significant antioxidant and anti-uricemic properties, and it could be a potential treatment for gout, serving as an alternative to allopurinol with fewer side effects (41).

Apart from gout, there are three other diseases with high FL (ranging from 40.54% to 43.24%, Fig. 6), namely cancer, hypertension, and diabetes. Consistent with the research conducted by Mutakin et al. (2), it has been documented that soursop demonstrates effectiveness in acting as an anticancer, antihypertensive, and antidiabetic agent. Extracts from the fruit, stems, seeds, and twigs of soursop, when administered to fibrosarcoma cells, impeded the activity of matrix metalloproteinases, which are significant in the progression of cancer (42). Additionally, extracts from the leaves, twigs, and roots of soursop inhibited the proliferation of the human leukemia cell by disrupting matrix metalloproteinases, generating reactive oxygen species, and inducing G0/G1 cell cycle arrest, ultimately leading to the suppression of cancer cell growth (43). Furthermore, soursop leaf extract has demonstrated antihypertensive effects in normotensive rats by blocking calcium ion channels, resulting in reduced blood pressure (44). On the other hand, extracts derived from soursop fruit were found to demonstrate antioxidant and antidiabetic effects by inhibiting crucial enzymes associated with type 2 diabetes mellitus, including α -amylase and α -glucosidase, in vitro (45). Additionally, both the fruit pulp and leaf extract displayed significant capabilities in inhibiting α -amylase and α -glucosidase, as well as reducing the rate of glucose absorption into the bloodstream after ingestion, compared to the standard drug (46).

Regarding the parts of the soursop plant used in traditional medicine, the leaves were reported as the most commonly utilized component (80.77%). A smaller percentage of respondents mentioned using fruits (17.31%), while a very small proportion indicated using all parts of the plant (1.92%). Leaves and fruits are commonly utilized as sources for extracting phytochemical compounds essential for researching the potential medicinal properties of soursop (42–46). Additionally, less common parts like the seeds (41–42), roots (43), stems, and branches (42) have also been noted in studies.

The preference for herbal medicine as a treatment option was frequently attributed to discontentment with conventional therapies, positive past encounters, favorable attributes linked to herbal remedies, and adherence to familial customs (47). The belief among college students in the therapeutic potential of soursop for treating a wide range of diseases can be attributed to several factors. Firstly, traditional medicine practices and herbal remedies have deep historical roots in many cultures, including Indonesia. This cultural context likely contributes to the student's confidence in the efficacy of soursop. Additionally, the availability of anecdotal evidence or personal experiences, either from their own lives or from within their communities, may further reinforce these beliefs. In terms of

seeking information, self-directed research and family customs were considered equally or even more significant than seeking advice from healthcare professionals (47). Furthermore, there is significant backing in scientific literature affirming the potential health advantages of soursop, particularly facilitated by the enhanced accessibility of information through the growing presence of online resources. Studies have identified specific compounds within soursop that demonstrate antioxidant, anti-uricemic, anticancer, antihypertensive, and antidiabetic properties (2). These findings bridge the gap between traditional knowledge and empirical evidence, giving credence to the students' beliefs. Furthermore, the high FL associated with specific diseases, such as gout, cancer, hypertension, and diabetes, suggests a strong consensus within the community regarding soursop's effectiveness for these conditions. This collective belief may be influenced by word-of-mouth, shared experiences, or cultural traditions passed down over generations. The convergence of cultural beliefs, personal experiences, and scientific research provides a comprehensive foundation for college students' confidence in soursop's therapeutic potential. This multidimensional support system contributes to the widespread belief in soursop's ability to treat a variety of diseases.

Internet search trends on soursop benefits

Google Trends is a freely accessible tool created by Google, offering insights into the popularity of Google Search searches. These reports furnish time-series data, accessible for any chosen period from 2004 to the current date, and can be tailored to hone in on searches conducted in a particular language or originating from a specific location (48). Google Trends has found extensive applications in diverse research and case studies. The majority of these research endeavors utilizing Google Trends generate outcomes in the shape of predictions, preferences, and patterns.

The dataset in Fig. 7–9 offers a comprehensive overview of internet search trends regarding the benefits of soursop, encompassing both the fruit and its leaves, from January 2011 to September 2023. The dataset provides valuable insights into the popularity and geographic distribution of interest in soursop's potential advantages. Notably, searches pertaining to the benefits of soursop leaves garnered the highest average inquiries, suggesting a heightened curiosity or awareness surrounding the leaves compared to the fruit itself. The trend analysis reveals an initial surge in interest, peaking in January 2012, followed by a gradual decline over the subsequent years. This pattern indicates a temporary spike, possibly triggered by a specific event, publication, or health trend, which wasn't sustained over the long term. Speculatively, the increase in searches for the benefits of soursop in 2012 could be attributed to several factors. For example, during those years, there might have been publications or scientific research highlighting the health benefits of soursop. This information could have piqued public interest, leading them to seek further information on the internet. Moreover, in those years, the public may have experienced a

heightened awareness of the importance of health and a healthy lifestyle. This could have prompted them to seek information about foods or natural substances that could enhance their health. Additionally, there's a possibility that specific health events or epidemics that occurred during those years, are driving people to seek alternative solutions or treatments, including the benefits of soursop. However, it's important to remember that these factors are speculative, and further analysis is needed to understand the exact causes of the increased search for soursop's benefits during those years.

Geographically, searches for “*manfaat daun sirsak*” were widespread across Indonesia, indicating a broad interest in soursop leaves. Conversely, other keywords (“*khasiat buah sirsak*”, “*khasiat daun sirsak*”, and “*manfaat buah sirsak*”) were predominantly searched in the central to western regions of Indonesia. Several factors contribute to the higher prevalence of internet searches in central to western Indonesia. Firstly, this region, particularly Java and its surrounding islands, boasts superior information technology and communication infrastructure, resulting in faster, more stable internet access and a greater number of service providers (Fig. 10). Additionally, the higher population density in western Indonesia, particularly in Java and Sumatra (Statistik Indonesia 2023 at <https://www.bps.go.id>), leads to increased internet usage for various purposes (49), including seeking information on the benefits of soursop. Major economic and educational centers like Jakarta, Bogor, Bandung, and Surabaya further drive the demand for internet access, especially for health-related inquiries. Cultural and media influences also play a role, potentially making individuals in the Western region more inclined to search for health-related information. Overall, these intertwined factors collectively contribute to the elevated level of internet search activity in central-western Indonesia, particularly in the context of health-

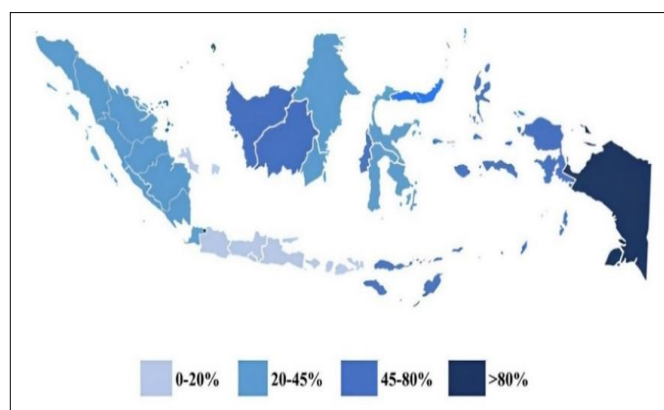


Fig. 10. Indonesian area with weak signal or no signal. (Source: <https://www.itu.int/en/ITU-D/Regional-Presence/AsiaPacific/Documents/Indonesia%20case%20study%5B1%5D.pdf>).

related topics such as the benefits of soursop.

The data highlights a greater interest in the benefits of soursop leaves compared to the fruit. This insight serves as a valuable cue for researchers and the food or health industries to channel marketing efforts or product development towards the benefits of soursop leaves. This information is crucial for stakeholders in devising effective mar-

keting strategies and health education initiatives for the future. Although internet searches for the benefits of soursop leaves appear to be consistently decreasing year by year in Indonesia, the opportunity to develop herbal medicine products from soursop leaf extracts remains quite open, especially for pre-packaged and ready-to-use herbal medicines. A prime illustration can be found in the outcomes of this research. The results of this study involve the use of soursop leaf extracts as a supplementary ingredient in the production of traditional scrubs, creating an innovative product known as “traditional soursop leaf extract scrub” (Fig. 11). This product aims to prevent infectious diseases caused by *S. aureus* bacteria, exhibiting antimicrobial inhibitory activity at a concentration of 25% with



Fig. 11. Author's research product “traditional soursop leaf extract scrub”. (Photo: I Nyoman Jirna).

an 8 mm inhibition zone (50).

Conclusion

Soursop is a native of tropical America and West Indies. It was introduced to Indonesia, probably before 1884, during the Dutch colonial period, from Central America. Currently, soursop is widely distributed and cultivated throughout Indonesia. Soursop leaf extract revealed the presence of phenols (2554.22 mg/100g), flavonoids (5263.43 mg/100g), and tannins (1469.77 mg/100g). The study indicated that soursop leaf extract contains active antimicrobial substances and exhibits antimicrobial potential in the resistant category at concentrations of 25%, 40%, 55%, and 70%, with a growth inhibition zone of 6 mm. College students of Health Polytechnic of Denpasar believed that 42 diseases could be traditionally treatable using soursop, with fidelity level values ranging from 2.7% to 48.65%. The four highest fidelity levels were observed for gout (48.65%), followed by cancer (43.24%), hypertension (43.24%), and diabetes (40.54%). The parts of the soursop plant commonly used in traditional medicine are the leaves (80.77%), followed by fruits (17.31%), and all parts (1.92%). The trend of information searches in Indonesia from January 2011 to September 2023 regarding the utilization of soursop experienced an initial increase, reaching its peak in January 2012 and gradually declining thereafter until 2023. Internet search activity regarding the utilization of soursop from January 2011 to September 2023 mostly occurred in the central to western regions of Indonesia.

Acknowledgements

We express our sincere thanks to Dr. Heru Santoso Wahito Nugroho for dedicating his valuable time to reviewing the manuscript in its early stages. We would like to acknowledge with gratitude the funding provided by Dana Penelitian POK Ditjen Tenaga Kesehatan Kementerian Kesehatan Indonesia for supporting this research. Our heartfelt appreciation goes to the Director of Scientific Collection Management (Herbarium Bogoriense), National Research and Innovation Agency (BRIN), for granting us access to the specimens and the Global Biodiversity Information Facility (GBIF) for the data provided. We would also like to extend our gratitude to the Integrated Analytical Laboratory and the Laboratory of Microbiology at the University of Udayana, as well as the Laboratory of the Department of Health Analysis at Health Polytechnic of Denpasar, for their warm hospitality during the research activities. Chors M. Bana (University of Nusa Cendana, Timor), Ridwan (Lombok), Susila (West Java), Kusuma Rahmawati (Central Java), Indira Riastiwi (Yogyakarta), Iksal Yanuarsyah (Sumbawa), Yasper Michael Mambrasar (Papua), college students of Health Polytechnic of Denpasar are acknowledged for generously providing the valuable information. We deeply appreciate the blind reviewers for their invaluable contributions in reviewing our research manuscript.

Authors' contributions

The research funding proposal was crafted by INJ. INJ and IPGPD collaborated on the research design. The data collection and interpretation involved INJ, IGS, INP, NM, CDWHS, and INGS. IPGPD played a role in creating and analyzing questionnaires and taxonomic data. IPGPD and MAR engaged in taxonomic studies, including the observation of herbarium specimens, analysis of questionnaires, and the provision of internet trend data. IPGPD was also responsible for processing and presenting graphical and visual materials. The drafting of the manuscript saw contributions from all authors, and the final version garnered unanimous approval.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None.

References

1. Moghadamtousi SZ, Fadaeinasab M, Nikzad S, Mohan G, Ali HM, Kadir HA. *Annona muricata* (Annonaceae): a review of its traditional uses, isolated acetogenins and biological activities. *Int J Molec Sci.* 2015;16(7):15625-58. <https://doi.org/10.3390/ijms160715625>
2. Mutakin M, Fauziati R, Fadhilah FN, Zuhrotun A, Amalia R, Hadisaputri YE. Pharmacological activities of soursop (*Annona muricata* Lin.). *Molecules.* 2022;27(1201):1-17. <https://doi.org/10.3390/molecules27041201>
3. Tuna MR, Kepel BJ, Leman MA. Uji daya hambat ekstrak daun sirsak (*Annona muricata* L.) terhadap pertumbuhan *Staphylo-*

- coccus aureus* secara *in vitro*, *Pharmakon*. 2015;4(4):65-70. <https://doi.org/10.35799/pha.4.2015.10194>
4. Kalgo ZM, Amin BM, Muhammed B, Saka HK. Prevalence and risk factors for lower respiratory tract infection: a multicenter study, at Kebbi State, Nigeria. *Int J Adv Health Sci Tech*. 2023;3(1):60-67. <https://doi.org/10.35882/ijahst.v3i1.170>
 5. Linz MS, Mattappallil A, Finkel D, Parker D. Clinical impact of *Staphylococcus aureus* skin and soft tissue infections. *Antibiotics*. 2023;12(557):1-27. <https://doi.org/10.3390/antibiotics12030557>
 6. Bassetti M, Labate L, Melchio M, Robba C, Battaglini D, Ball L, et al. Current pharmacotherapy for methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia. *Exp Opin Pharm*. 2022;23(3):361-75. <https://doi.org/10.1080/14656566.2021.2010706>
 7. Béraud G, Tubiana S, Erpelding ML, Moing VL, Chirouze C, Gorenne I, et al. Combined bacterial meningitis and infective endocarditis: when should we search for the other when either one is diagnosed? *Infect Diseases Ther*. 2022;11:1521-40. <https://doi.org/10.1007/s40121-022-00651-7>
 8. Leistner R, Hanitsch LG, Krüger R, Lindner AK, Stegemann MS, Nurjadi D. Skin infections due to panton-valentine leukocidin-producing *S. Aureus*. *Deutsc Arzt Int*. 2022;119(45):775-84. <https://doi.org/10.3238/arztebl.m2022.0308>
 9. Habib G, Mahmood K, Gul H, Tariq M, Ain QU, Hayat A, et al. Pathophysiology of methicillin-resistant *Staphylococcus aureus* superinfection in COVID-19 patients. *Pathophysiology*. 2022;29(3):405-13. <https://doi.org/10.3390/pathophysiology29030032>
 10. Nandhini P, Kumar P, Mickyamaray S, Alothaim AS, Somasundaram J, Rajan M. Recent developments in methicillin-resistant *Staphylococcus aureus* (MRSA) treatment: a review. *Antibiotics*. 2022;11(606):1-21. <https://doi.org/10.3390/antibiotics11050606>
 11. Lázár V, Snitser O, Barkan D, Kishony R. Antibiotic combinations reduce *Staphylococcus aureus* clearance. *Nature*. 2022;610:540-46. <https://doi.org/10.1038/s41586-022-05260-5>
 12. Agu KC, Okolie PN. Proximate composition, phytochemical analysis and *in vitro* antioxidant potentials of extracts of *Annona muricata* (soursop). *Food Sci Nutr*. 2017;5(5):1029-36. <https://doi.org/10.1002/fsn3.498>
 13. Hasan AEZ, Julistiono H, Bermawie N, Riyanti EI, Arifni FR. Soursop leaves (*Annona muricata* L.) endophytic fungi anticancer activity against HeLa cells. *Saudi J Bio Sci*. 2022;29(103354):1-9. <https://doi.org/10.1016/j.sjbs.2022.103354>
 14. Wullur AC, Schaduw J, Wardhani ANK. Identifikasi alkaloid pada daun sirsak (*Annona muricata* L.). *J Ilmiah Farm*. 2012;3(2):54-56.
 15. Cornelia M, Natania K, Cahyana H, Sutiyono E. Encapsulation of soursop (*Annona muricata* Linn.) leaf tea extract using natural mucilage. *Reaktor*. 2019;19(1):26-33. <https://doi.org/10.14710/reaktor.19.1.26-33>
 16. Ciupercă OT, Țebrencu CE, Volf I. Polyphenolic content evaluation in branches of *Rosa canina* L. and *Hippophae rhamnoides* L. species. *Bul Inst Polit Iași*. 2017;63(67):49-58.
 17. Khan ZA, Siddiqui MF, Park S. Current and emerging methods of antibiotic susceptibility testing. *Diagnostics*. 2019;9(49):1-17. <https://doi.org/10.3390/diagnostics9020049>
 18. Andriamparany JN, Brinkmann K, Jeannoda V, Buerkert A. Effects of socio-economic household characteristics on traditional knowledge and usage of wild yams and medicinal plants in the Mahafaly region of south-western Madagascar. *J Ethnobiol Ethnomed*. 2014;10(82):1-20. <https://doi.org/10.1186/1746-4269-10-82>
 19. Koesriharti. *Annona muricata* L. In: Verheij EWM, Coronel RE, editors. *Plant Resources of South-East Asia no 2: Edible Fruits and Nuts*. Bogor: PROSEA Foundation; 1991. p. 75-78.
 20. Damayanto IPGP, Muhaimin M. Notes on *Chimonobambusa quadrangularis* (Franceschi) Makino (Poaceae: Bambusoideae) as an invasive alien plant species in Indonesia. *Floribunda*. 2017;5(7):253-57. <https://doi.org/10.32556/floribunda.v5i7.2017.201>
 21. Ariati SR, Astuti RS, Supriyatna I, Yuswandi AY, Setiawan A, Saftaningsih D, et al. An alphabetical list of plant species cultivated in the Bogor Botanic Gardens. Bogor: Indonesian Institute of Sciences, Center for Plant Conservation, Bogor Botanic Gardens; 2019.
 22. Wulandari L, Dewi MKC, Kristiningrum N, Siswanti RAYN. Determination of total phenolic content and NIR-chemometrics classification model of queen and local varieties of soursop (*Annona muricata* L.) leaf powder. *Indon J Chem*. 2020;20(3):520-29. <https://doi.org/10.22146/ijc.43051>
 23. Laohavisit A, Wakatake T, Ishihama N, Mulvey H, Takizawa K, Suzuki T, et al. Quinone perception in plants via leucine-rich-repeat receptor-like kinases. *Nature*. 2020;587(7832):92-97. <https://doi.org/10.1038/s41586-020-2655-4>
 24. Goel S, Parihar PS, Meshram V. Plant-derived quinones as a source of antibacterial and anticancer agents. In: Singh J, Meshram V, Gupta M, editors. *Bioactive Natural Products in Drug Discovery*. Singapore: Springer; 2020. p. 245-79.
 25. Nguyen MT, Nguyen VT, Minh LV, Trieu LH, Cang MH, Bui LB, et al. Determination of the phytochemical screening, total polyphenols, flavonoids content and antioxidant activity of soursop leaves (*Annona muricata* Linn.). In: IOP Conf Ser Mat Sci Eng; 2020.736(062011):1-6. <https://doi.org/10.1088/1757-899X/736/6/062011>
 26. Agu KC, Okolie NP, Eze I, Anionye JC, Falodun A. Phytochemical analysis, toxicity profile, and hemomodulatory properties of *Annona muricata* (soursop). *Egypt J Haemat*. 2017;42(1):36-44. <https://doi.org/10.4103/1110-1067.206431>
 27. Muthu S, Durairaj B. Evaluation of antioxidant and free radical scavenging activity of *Annona muricata*. *Europ J Exp Biol*. 2015;5(3):39-45.
 28. Pérez-Burillo S, Giménez R, Rufián-Henares JA, Pastoriza S. Effect of brewing time and temperature on antioxidant capacity and phenols of white tea: relationship with sensory properties. *Food Chem*. 2018;248:111-18. <https://doi.org/10.1016/j.foodchem.2017.12.056>
 29. Guzmán-Maldonado SH, López-Manzano MJ, Madera-Santana TJ, Núñez-Colín CA, Grijalva-Verdugo CP, Villa-Lerma AG, et al. Nutritional characterization of *Moringa oleifera* leaves, seeds, husks and flowers from two regions of Mexico. *Agr Colomb*. 2020;38(2):287-97. <https://doi.org/10.15446/agron.colomb.v38n2.82644>
 30. Rarassari MA, Maftuch HN. Phytochemicals and antibacterial activities of soursop leaf (*Annona muricata*) against *Edwardsiella tarda* (*in vitro*). *J Life Sci Biomed*. 2016;6(1):6-9.
 31. Makuasa DAA, Ningsih P. The analysis of total flavonoid levels in young leaves and old soursop leaves (*Annona muricata* L.) using UV-vis spectrophotometry methods. *J App Sci Eng Tech Educ*. 2020;2(1):11-17. <https://doi.org/10.35877/454RI.asci2133>
 32. Febriani D, Mulyanti D, Rismawati E. Karakterisasi simplisia dan ekstrak etanol daun sirsak (*Annona muricata* Linn.). *Pr Farm Spesia*. 2015;1(2):475-80. <https://doi.org/10.29313/v0i0>
 33. Hermawan GP, Hendrawan L. Ekstrak daun sirsak (*Annona muricata* L) menggunakan pelarut etanol. *J Tekn Kimia Indust*. 2013;2(2):111-15.
 34. Yuliantari NWA, Widarta IWR, Permana IDGM. Pengaruh suhu dan waktu ekstraksi terhadap kandungan flavonoid dan aktivi-

- tas antioksidan daun sirsak (*Annona muricata* L.) menggunakan ultrasonik. Media Ilm Tekn Pangan. 2017;4(1):35-42.
35. Nurhayati LS, Yahdiyani N, Hidayatulloh A. Perbandingan pengujian aktivitas antibakteri starter yogurt dengan metode difusi sumuran dan metode difusi cakram. J Tekn Hasil Petern. 2020;1(2):41-46. <https://doi.org/10.24198/jthp.v1i2.27537>
 36. Rusmiyati I, Husain DR, Alam G. Bioaktivitas ekstrak metanol daun muda sirsak *Annona muricata* L. sebagai Antibakteri terhadap *Staphylococcus aureus* dan *Propionibacterium* [internet]. Makassar: Hasanuddin University; 2014 [cited 2023 Jul 25]. Available from: <https://core.ac.uk/download/pdf/25494099.pdf>
 37. Handayani H, Sriherfyna FH, Yunianta. Ekstraksi antioksidan daun sirsak metode *ultrasonic bath* (kajian rasio bahan: pelarut dan lama ekstraksi). J Pangan Agroind. 2016;4(1):262-72.
 38. Pramadya P, Hendrayana M. Efek ekstrak metanol daun sirsak (*Annona muricata*) dalam menghambat pertumbuhan bakteri *Salmonella typhi* secara *in vitro*. J Med Udayana. 2021;10(6):97-99. <https://doi.org/10.24843.MU.2021.V10.i6.P18>
 39. Kotera Y, Aledeh M, Barnes K, Rushforth A, Adam H, Riswani R. Academic motivation of Indonesian University students: relationship with self-compassion and resilience. Healthcare. 2022;10(2092):1-12. <https://doi.org/10.3390/healthcare10102092>
 40. Khan I, AbdElsalam NM, Fouad H, Tariq A, Ullah R, Adnan M. Application of ethnobotanical indices on the use of traditional medicines against common diseases. Evid Compl Altern Med. 2014;2014(635371):1-22. <https://doi.org/10.1155/2014/635371>
 41. Ewadh MJ, Smaism MF, Jawad AM, Mkhlof S, Aljubouri OM, Ewadh MM. Using soursop extracts for natural gout treatment. Amer J Biosci Bioeng. 2015;3(5):37-39. <https://doi.org/10.11648/j.bio.20150305.12>
 42. Drishya G, Nambiar J, Shaji SK, Vanuopadath M, Achuthan A, Kumar A, et al. RECK and TIMP-2 mediate inhibition of MMP-2 and MMP-9 by *Annona muricata*. J Biosci. 2020;45(89):1-11. <https://doi.org/10.1007/s12038-020-00056-z>
 43. Pieme CA, Kumar SG, Dongmo MS, Moukette BM, Boyoum FF, Ngogang JY, et al. Antiproliferative activity and induction of apoptosis by *Annona muricata* (Annonaceae) extract on human cancer cells. BMC Compl Altern Med. 2014;14(516):1-10. <https://doi.org/10.1186/1472-6882-14-516>
 44. Nwokocha CR, Owu DU, Gordon A, Thaxter K, McCalla G, Ozolua RI, et al. Possible mechanisms of action of the hypotensive effect of *Annona muricata* (soursop) in normotensive Sprague-Dawley rats. Pharm Biol. 2012;50(11):1436-41. <https://doi.org/10.3109/13880209.2012.684690>
 45. Adefegha SA, Oyeleye SI, Oboh, G. Distribution of phenolic contents, antidiabetic potentials, antihypertensive properties and antioxidative effects of soursop (*Annona muricata* L.) fruit parts *in vitro*. Biochem Res Int. 2015;2015(347673):1-8. <https://doi.org/10.1155/2015/347673>
 46. Agu KC, Eluehike N, Ofeimun RO, Abile D, Ideho G, Ogedengbe MO, et al. Possible anti-diabetic potentials of *Annona muricata* (soursop): inhibition of α -amylase and α -glucosidase activities. Clin Phytosci. 2019;5(21):1-13. <https://doi.org/10.1186/s40816-019-0116-0>
 47. Welz AN, Emberger-Klein A, Menrad K. Why people use herbal medicine: insights from a focus-group study in Germany. BMC Compl Altern Med. 2018;18(92):1-9. <https://doi.org/10.1186/s12906-018-2160-6>
 48. Cebrián E, Domenech J. Is google trends a quality data source? App Eco Lett. 2023;30(6):811-15. <https://doi.org/10.1080/13504851.2021.2023088>
 49. Kharisma B. Surfing alone? The internet and social capital: evidence from Indonesia. J Eco Struct. 2022;11(8):1-17. <https://doi.org/10.1186/s40008-022-00267-7>
 50. Sudarmanto IG, Jirna IN. Lulur tradisional daun sirsak menghambat pertumbuhan bakteri *Staphylococcus aureus*. Solok: Penerbit Mitra Cendekia Media; 2023.