



Ethno medical knowledge and traditional use of *Aristolochia bracteolata* Lam. for malaria among local communities in Jubek State of South Sudan: A cross-sectional survey

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ABSTRACT

Ethnopharmacological relevance: The recognized challenges to access conventional antimalarial medicines could have contributed to the extensive use of *Aristolochia bracteolata* Lam. (Aristolochiaceae) to manage malaria in South Sudan traditionally. However, the use and acquired experiences are not well documented.

Aim of the study: This study aimed to document the traditional use of *A. bracteolata* for malaria treatment and experiences among the local communities in Jubek State of South Sudan.

Methods: We performed a cross-sectional study in four counties in Jubek State and interviewed 396 community members, including traditional healers, using a semi-structured questionnaire. Four focused group discussions (FGDs) were also conducted using the interviewer guide. The inclusion criteria were; adults 18 years and older, men and women participants, at least one year residing in the study area before the study, and those with a history of medicinal plant use. Data were summarized and presented as proportions. Qualitative data were analyzed using a thematic content approach. The major themes that emerged were discussed. We applied the Pearson Chi-Square test at $\alpha = 0.05$ to test the study's significant differences in responses. The statistical package for social sciences version 21 software was used for data analysis.

Results: Women accounted for 208 (52.5%) of participants, with the majority 321 (81.1%) were between 18 and 45 years. Interestingly, most 312 (78.8%) had formal education. Moreover, about 208 (52.5%) participants collect the plant in their vicinity, where leaves were the most commonly used part 277 (46.4%), followed by the roots, seeds, and stems at 245 (41.0%), 71 (11.9%), and 4 (0.7%), respectively. Furthermore, about 63 (15.9%) of the participants experienced side effects, including early abortions, heartburns, sweating, and stomach discomforts. Conversely, a total of 387 (96.0%) reported getting cured of malaria. Generally, the quantity of medicine taken per day differs concerning parts of the plant, with leaves ranging from 1 to 10 pieces, roots at 0.4–1 g, and seeds at 0.1–0.5 g. The locals used these plant parts to prepare infusion and decoction traditional dosage forms for oral use.

Conclusion: The documented medicinal plant's therapeutic uses provided critical information on the traditional use of *A. bracteolata* by the community in Jubek state of South Sudan to treat malaria. Although most users reported getting cured of malaria, a notable proportion of them experienced side effects, including early-stage abortion and stomach discomforts. Thus, the use of *A. bracteolata* preparations, particularly in pregnant women, should be avoided. Finally, further studies are needed to devise a strategy to neutralize the toxic compounds and create community awareness on best practices to minimize side effects.

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1. Background

Malaria is a global health concern. In 2018, an estimated 228 million people had malaria, with African countries account for a significant share (WHO, 2018). For example, in South Sudan (SSD), more than 8.26 million individuals are at risk of malaria, and under-five children and pregnant women are particularly vulnerable (Africa et al., 2017). The recent statistics in SSD showed, in 2017 alone, at least 77,500 people were affected, claiming nearly 220 lives weekly (Africa et al., 2017; Sccse, 2015). Thus, malaria is now recognized as an important cause of increased morbidity and premature mortality.

South Sudan's current malaria treatment and control interventions involve using long-lasting insecticide-treated bed nets (LLINs), indoor residual spraying, and intermittent preventive treatment (IPTp) (Pasquale et al., 2013). In addition, early diagnosis and treatment with Artemisinin-based combination therapy (ACT) is the mainstay therapeutic strategy (Azairwe and Achan, 2011; Pasquale et al., 2013). These interventions have contributed significantly to the control of malaria and improved the health of the people. However, the continued political instability in SSD has hindered effective malaria control (Pasquale et al., 2013). Besides, increasing malaria parasite resistance to current anti-malarial drugs, emerging side effects such as vomiting, dizziness among others, and the high cost of these medicines contributed significantly to malaria treatment and control failure (Lee et al., 2017; Sinka et al., 2012).

These challenges are implicated in the increasing number of herbal medicines used to treat malaria in several local communities in SSD (Mathew, 2016). Jombo and colleagues reported a similar trend in Nigeria (Jombo et al., 2010). Local communities have been using several plant species, including; *Gardenia thunbergia* Thunb (Rubiaceae), *Cucumis dipsaceus* Ehrenb. Ex Spach (Cucurbitaceae), *Tamarindus indica* L. (Leguminosae), *Balanites aegyptiaca* (L.) Delile (Zygophyllaceae), and *Azadirachta indica* A. Juss (Meliaceae) (Mathew, 2016).

Aristolochia bracteolata Lam. (Aristolochiaceae) is one of the popular medicinal plants in SSD to treat malaria. It is commonly known as a worm killer, Dikeritimelo (South Sudan), and widely distributed and easily accessible in the communities (Abdalrahman, 2011; Mathew et al., 2020). The plant is also widely distributed throughout tropical Asia, Africa, and South America (Abdelgadir et al., 2011) and grows well on the river banks, bushlands, desert grassland, sandy, or lava soil (Kennedy and Wightman, 2011).

Traditionally, communities in Tamil Nadu, India, crush root part, soak in water for 8 h, and take orally as a gastric stimulant and treat cancer, lung inflammation, dysentery, and snakebite (Negi et al., 2003). Furthermore, local communities in India used root paste as a wound-healing agent. Usually, they take 100 g of fresh roots, grind to paste, mix with one spoonful of turmeric powder, warm, and apply on wounds (Bharath Kumar and Suryanarayana, 2014). Also, the fruits and the roots are used in Sudan to treat malaria and HIV-1 (Ali et al., 2002). On another occasion, Sudanese use roots to treat Scorpion stings and inflammation while leaves are for malaria treatment (Ahmed et al., 2010). Moreover, in South Sudan, the whole plant is used to treat malaria and other conditions, including fever, headache, general body pain, stomachache, diarrhea, and flu (Mathew, 2016).

Aristolochic acids (AAs) are the main phytochemicals isolated from *A. bracteolata* (Heinrich et al., 2009). These acids had nephrotoxicity, mutagenic and carcinogenic effects after prolonged use (Shoichi et al., 2003; Zhang et al., 2019). Furthermore, a recent meta-analysis confirms the increased risk of urinary tract cancers among individuals exposed to AAs (Kang et al., 2021). Considering the high use of *A. bracteolata* to treat malaria in SSD's local communities and the inadequate documented users' experience, this study's need was felt. Therefore, we documented the practices and experiences of using *A. bracteolata* to treat malaria among the local communities in Jubeck State of South Sudan. The study informed the local communities and policymakers on the need to devise strategies to prevent prolonged community exposure to this medicinal

plant to mitigate its unfavorable effects.

2. Methods

2.1. Study design and site

The cross-sectional survey was conducted in Jubeck state, located in the southern part of SSD (Fig. 1). Jubeck State is one of the 28 states of SSD located in the central part of the Equatorial region with 18,313.7 km². The State is bordering Imatong State to the east, Terekeka State to the North, Amadi State to the west, and Yei River State to the southeast. According to the census 2008, the State had an estimated population of 530,000 (Sccse, 2010, 2015). Jubeck state has fourteen counties; Dollo, Lyria Rokon, Oponi, Lobonok, Rejaf, Gondokoro, Mangala, Ganji Bungu, (Ganzi), Ladu, Wonduruba, and Luri. The inhabitants are mostly subsistence farmers (Ayach, 2016; Gudo et al., 2020).

2.2. Sample size and sampling technique

The sample size was calculated based on estimating proportion with a 95% confidence level. The percentage of plant use was estimated at 50%, with a margin of error of 0.05. Thus, the sample size calculated was 384. The calculated sample size was adjusted for a non-response rate of 4% to give the final sample size of 400. The qualitative part involved about 8–12 adults of both genders in focused group discussions (FGDs). The FGDs's participants were individuals identified from the general population who have ever used *A. bracheolata*. A total of 4 FGDs were conducted with one FGD from each county.

Initially, the Jubeck state was purposively selected from 28 states of SSD since it has a history of high use of malaria treatment plants (Mathew, 2016). For adequate representation, 10% (4) counties were randomly selected from the 14 counties within the Jubeck state (Turner, 2003). These counties were selected at random. Next, paper pieces with county names were placed in a basket, shuffled, and randomly picked four counties, each at a time without replacement (Sedgwick, 2015). Finally, Juba city County, Rajaf, Luri, and Jebel Ladu county were selected. The sample size drawn from each country was proportional to the population size of the county. In each selected county, study participants were conveniently selected for interview according to the following inclusion and exclusion criteria.

2.3. Inclusion and exclusion criteria

An adult 18 years or older who has ever used *A. bracheolata* to treat malaria, individuals reside in the study area for at least one year prior to the study, those who can understand English or Arabic language were included. On the other hand, individuals who were not at home at the time of the interview and those mentally impaired that compromised their ability to understand the questions were excluded.

2.4. Data collection

Semi-structured questionnaires were used to obtain information in an in-depth interview with study participants. The study tool was developed and pretested in the South Sudanese refugee community in Adjumani, West Nile district of Uganda. The pretest assessed the language clarity, its ability to capture intended information, and feasibility in terms of length. Data collected were demographic information of participants, *A. bracteolata* uses; the part(s) used, preparation method, dose, dosage forms, and experiences. In addition, four research assistants were trained on the proper use of questionnaires and ethical aspects in data collection before actual data collection.

The interviewer's guide was used in FGDs. This tool guided discussions concerning knowledge about malaria and the use of *A. bracteolata* at the community level. The FGDs took place in a quiet, open space under the shade. The discussions were conducted in Arabic, the SSD's

national language, and were tape-recorded. Each FGDs last for one and a half hour.

2.5. Data management and analysis

The qualitative data were transcribed verbatim into Arabic and then translated into English in MS word. Data were coded into major themes and sub-themes from readings of multiple scripts. Finally, quantitative data were entered into a statistical package for social science software (SPSS) ver. 21 (New York, USA) and analyzed. Initially, data were summarized into proportions. Then we applied the Pearson Chi-Square test at $\alpha = 0.05$ to test the association of *A. bracheolata* use and several independent variables.

2.6. Ethical considerations

The study protocol obtained ethical clearance from the Mbarara University of Science and Technology Research Ethical Committee (MUST-REC 26/11–18), Uganda. Also, we obtained permission to conduct the study in SSD from the Ministry of Health (MoH), the Republic of South Sudan, and Juba State and county authorities.

Written informed consent was obtained from each potential participant before data collection. In addition, we informed the participants that their participation in this study is entirely voluntary and that information will be kept confidential, and no personal identity will be collected, among others.

3. Results

3.1. Demographic characteristics of study participants (Table 1)

A total of 396 participants were interviewed. The majority (52.5%) were women, with the most participants (81.1%) were between 18 and 45 years old and (78.8%) had formal education. Furthermore, about 30.3% were unemployed, and the majority (78.5%) stayed in the study area for six years and above (Table 1).

3.2. Knowledge and traditional use of *A. bracteolata* for malaria

The FGDs indicated that participants had sufficient knowledge about malaria. The knowledge was assessed based on the understanding of the symptoms and causes of malaria. The typical quotes below illustrate.

When I start feeling feverish, headache, general body pain, I will know that I have malaria. Immediately, I will start to look for Dikeritimelo (A. bracteolata), either the leaves or root part. I will tell my wife to infuse for me, and I drink. (A man, Juba County).

I like using A. bracteolata for malaria treatment because it is very effective, including severe malaria conditions that arise at night. One day my three-month-old daughter was having a very high fever and vomiting at night; I knew it was malaria. Good enough I had this A. bracteolata dry root in the house; I just picked a little quantity and prepared it very fast, soak in water, and gave her to drink. Within a few minutes, I saw her sweating after 1 h. She became okay, and I continued giving her until she was fully recovered. Since that time, I keep the root part in the house, but I always use both leaves and roots. (A woman, Juba County).

I take this medicine (A. bracheolata) whenever I feel like having malaria; headache, feverish, stomach discomfort, nausea, and shivering. I used both leaves and roots parts I usually buy root from the market and keep in the house. I also give it to my children whenever they fall sick of malaria. (A woman, Rajaf County).

The quantitative findings showed that the plant parts were mainly collected from the surrounding environment (52.5%). Leaves were the most commonly used (46.4%), followed by the root part (41.0%). Other parts were less used (Table 2).

Regarding the plant collection mode, (32.3%) reported that they collect the plant by picking the aerial part and digging or uprooting the roots direct from their surrounding environment. The majority (68.2%) of participants do not have a specific time for collecting the plant. However, they collect this medicinal plant whenever they felt sick. The quotes below illustrate;

I collect this medicinal plant at any time I want, or I feel like collecting; I think collection time does not change anything in this medicine (A woman Juba and Luri county).

I can collect it at midday, even at night. It depends on what time I feel like having malaria's signs and symptoms (A man Juba and Luri county). These suggest that there is no such association between the efficacy of

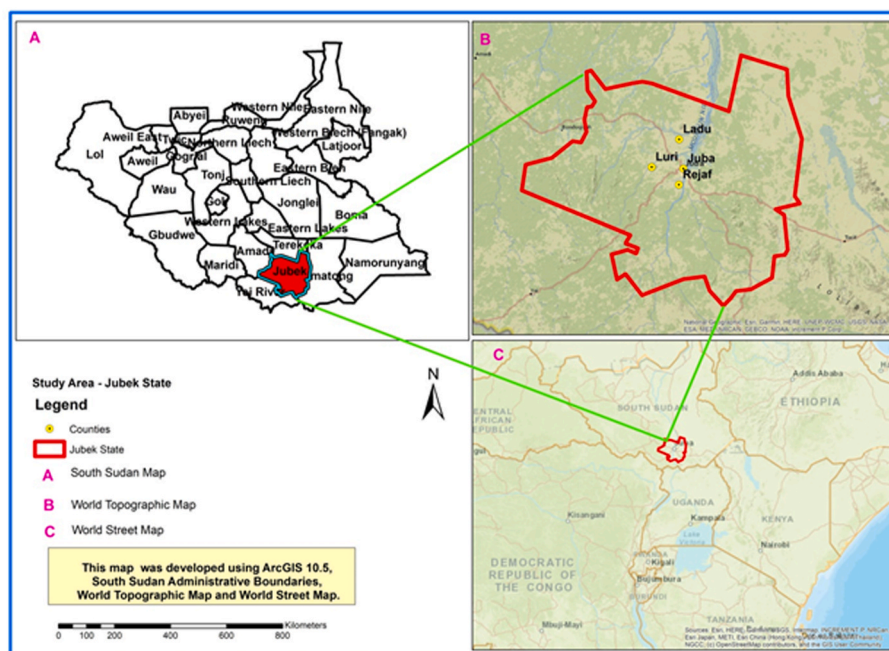


Fig. 1. A map of South Sudan showing the study area.

Table 1
Demographic characteristics of the participants.

Variables	Categories	N (%)
Age	18–30	133 (33.6)
	31–45	188 (47.5)
	46–60	40 (10.1)
	Above 60	35 (8.8)
Gender	Male	188 (47.5)
	Female	208 (52.5)
Marital Status	Single	97 (24.5)
	Married	242 (61.1)
	Divorced	23 (5.8)
	Widow/widower	34 (8.6)
Education	Primary (8 years of schooling)	107 (27.0)
	Secondary (12 years of schooling)	132 (33.3)
	Tertiary	73 (18.4)
	Not formally educated	84 (21.2)
Occupation	Civil servant	95 (24.0)
	Private sector employee	35 (8.8)
	Farmer	44 (11.1)
	Self-employed	102 (25.8)
	Un-employed	120 (30.3)
Residential area	Juba City Council	207 (25)
	Jebel Ladu County	60 (25)
	Luri County	77 (25)
	Rajaf County	53 (25)
Period lived in the area	Less than a year	5 (1.3)
	1–5 years	80 (20.2)
	6–10 years	115 (29.0)
	More than 10 years	196 (49.5)

medicine and the time of collection. Few informants (8.1%) collect the plant early in the morning, while only (1.3%) do it in the late evening (Table 2). The reason for collecting the herb from the early morning is to enable them to have enough quantity sufficient to take twice or three times a day. The following quotes illustrate;

I like collecting this medicinal plant early in the morning to start my treatment early in the morning hours. By the time it reaches afternoon when I am already feeling better, and I take another dose (A woman, Rajaf County).

I always collect this medicinal plant in the morning hours because it helps me very fast whenever I start taking it in the morning. (A man, Ladu County).

According to Table 2, communities prepared the leaves when fresh (21.2%) while roots when dry (27.0%). Community members dry the roots under the sunshine (20.7%) and (11.1%) under the shade or indoor. Conversely, the leaves were dried indoors/under the shade (2.8%) and sunshine (2.5%). There were slight differences in preparation methods per plant part. For example, for the preparation of roots, the majority (59.8%), first washed with clean water, pounded or crushed into powder, soaked in cold water for 30 min, then take a quarter glass orally. After that, water is added to re-soak for subsequent use. This addition of water continues until the extract is no longer having a bitter taste. Similarly, the leaves preparation indicated that most of the respondents (48.2%) picked the leaves from the surrounding, washed, pound, and soaked in cold water for 30 min to 1 h, then took a half glass of the extract orally.

On the other hand, the preparation of the seeds shown that (9.6%) of the respondents picked the few pieces of the plant seeds and swallowed them with water immediately. Several processes were noted, including pounded/crushed, soaked in cold/warm water, or boiled in hot water. The seeds can also be chewed or swallowed, and water is taken later. Moreover, seeds can be mixed with other herbs like Neem [*Azadirachta indica* A. Juss (Meliaceae)] and guava [*Psidium guajava* L. (Myrtaceae)] leaves to relieve pain, flu, and cough.

The local communities used all the plant parts of *A. bracheolata* to prepare herbal medicine to treat malaria orally (Table 3). Frequently, most participants (39.9%) take about 0.4 g–1 g of roots per day. On the other hand, the quantity of leaves taken by the communities (43.7%) ranges from 1 to 10 pieces per day.

Table 2
Plant collection and preparation.

Plant collection		N (%)
Area for plant collection	Surrounding	208 (52.5)
	Market	89 (22.5)
Plant part (s) used	Both surrounding and market	98 (25.0)
	Roots	245 (41.0)
	Stems	4 (0.7)
	Leaves	277 (46.4)
Mode of harvesting	Seeds	71 (11.9)
	Digging and uprooting the plant root	36 (9.1)
	Picking aerial plant part (s)	128 (32.3)
	Digging, uprooting, and picking the plant part (s)	143 (36.1)
Specific harvesting time	Yes	37 (9.3)
	No	270 (68.2)
If yes, time of collection	Early in the morning	32 (8.1)
	Late evening	5 (1.3)
Reasons for specific harvest time	To have adequate medicine to take twice or three times a day without going back for collection	19 (4.8)
	Believed medicine collected in morning has better ability to cure malaria quickly than other timing	18 (4.5)
Plant preparation		N (%)
Plant part prepared, fresh or dry	Dry roots part	107 (27.0)
	Fresh roots part	12 (3.0)
	Dry leaves part	1 (0.3)
	Fresh leaves part	84 (21.2)
	Fresh all parts	62 (15.7)
	Dry seeds part	5 (1.3)
	Fresh stems part	1 (0.3)
	Dry stems part	1 (0.3)
	All parts prepared either fresh and dry	123 (31.1)
Drying the roots	Indoor/under the shade	44 (11.1)
	Under the direct sunshine	82 (20.7)
Drying the stems	Indoor/under the shade	1 (0.3)
	Under the sunshine	4 (1.0)
Drying the leaves	Indoor/under the shade	11 (2.8)
	Under the sunshine	10 (2.5)
Drying the seeds	Indoor/under the shade	9 (2.3)
	Under the sunshine	12 (3.0)
Preparation from roots	By pounding the root part into powder, soak in water for 30 min and take a quarter tea glass	237 (59.8)
	By boiling the pounded roots for few minutes and take	12 (3.0)
	By Pounding the roots into powder, soak in water between 30mins and 1hr and take	14 (3.5)
	By breaking the roots into small pieces and swallow	16 (4.0)
	By chewing the root part	11 (2.8)
	By pounding the stem part into powder, soak in water for few minutes, and take	6 (1.5)
Preparation from stem	By the pound, the stem, boil in water for few minutes and take	4 (1.0)
	Skip (prepare other parts)	386 (97.5)
Preparation from leaves	By pounding the leaves, soak in water between 30 and 1hr and take	191 (48.2)
	By boiling leaves in water for few minutes and take	22 (5.6)
	By chewing the leaves	49 (12.4)

(continued on next page)

Table 2 (continued)

Plant collection	N (%)
By masking the dry leaves with Juice	1 (0.3)
Skip-(use other parts)	133 (33.6)
Preparation from seeds	38 (9.6)
By swallowing the seeds	25 (6.3)
By pounding the seeds, soak in water for few min. and drink the resultant juice	323 (81.6)
Skin (prepare other parts)	10 (2.5)
By chewing and swallowing the seeds as well	

Table:3

Doses, frequent, and duration.

Part and Dose	Quantity range	N (%)
Root dose	0.4–1.0 g	158 (39.9)
	1.1–1.7 g	100 (25.3)
	1.8–2.4 g	3 (0.8)
	2.5–3.1 g	10 (2.5)
	3.2–3.8 g	11 (2.8)
Stem dose	0.4–1.0 g	8 (2.0)
Leave dose	1–10 leaves	173 (43.7)
	11–20 leaves	78 (19.7)
	21–30 leaves	2 (0.5)
	Handful	7 (1.8)
Seed dose	0.1–0.5 g	58 (14.6)
	0.6–1.0 g	7 (1.8)
	1.1–1.5 g	7 (1.8)
	1.6–2.0 g	1 (0.3)
Frequent uptake per day	Once a day	48 (12.1)
	Twice a day	251 (63.4)
	Two - three times a day	7 (1.8)
	Three times a day	89 (22.5)
	Four times a day	1 (0.3)
Duration uptakes to get well	One day	56 (14.1)
	Two days	87 (22.0)
	Two-three days	18 (4.5)
	Three days	116 (29.3)
	Four -five days	84 (21.2)
	Six -Seven days	35 (8.8)
Frequent uptake per year	It depends on the frequency of the sickness	243 (61.4)
	Once a year	34 (8.6)
	Three times a year	33 (8.3)
	Four to ten times a year	52 (13.1)
	Eleven to sixteen times a year	31 (7.8)
	Twice a year	3 (0.8)
Period of used of this medicine	1–10 years	82 (20.7)
	11–20 years	89 (22.5)
	21–30 years	79 (19.9)
	31–40 years	46 (11.6)
	More than 40 years	100 (25.3)

Regarding the frequency and duration of use, the findings indicated that 63.4% of participants reported taking the herbal medicine twice a day, and about 29.3% of the participants reported taking this herbal medicine for three days for complete cure. Interestingly, the majority (61.4%) of participants used this medicine whenever they fall sick as their primary therapy. In addition, this study showed that 25.3% of the participants have been taking this medicine for more than 40 years.

3.3. Perceived efficacy of the plant

The majority (88.9%) of the participants had experienced sweating shortly after taking medicine. Also, 96.0% of the participants have admitted that this medicinal plant has never failed to cure malaria.

Conversely, 4.0% reported that the plant was not effective, and the failure of this herbal medicine was the reason to seek further medical attention to hospitals. Interestingly, about 97.5% of the informants do not combine this medicinal plant when treating malaria (Table 4).

3.4. Experiences of side effects

It was found that only 15.9% experienced the unwanted side effects, but the majority (84.1%) of the respondents had no unwanted effects. Some (12.4%) of the respondents experienced nausea, early-stage abortion, sweating, and gastrointestinal upset (Supplementary 1). Despite the side effects, about (13.4%) reported continued taking this herbal medicine. Intriguingly, 96.0% of the participants believed that this medicine has no harmful effect on humans. The results on overcoming the harm caused by this herbal medicine highlighted that some respondents believed avoiding using *A. bracteolata* preparations when pregnant or taking little quantity while others drink fresh eggs when feeling any harm to induce vomiting. There was no statistically significant difference ($p > 0.05$) between age categories and the perceived efficacy or the occurrence of side effects (Supplementary 2).

It is worth noting that some respondents mixed *A. bracteolata* with other herbs to treat malaria and other ailments. They believed that such a mixture enhances antimalarial efficacy and delay malaria recurrent. However, few respondents believed that the plant species works better than conventional medicine and helpful during emergencies. Pain killer is taken alongside *A. bracteolata* when the fever is very severe. Although most respondents indicated that the plant species is readily available and affordable, few expressed the need for standardized formulation (Supplementary 3).

3.5. Factors influence treatment outcome

There was a statistically significant difference between the duration of use (days) of the medicine and the quantity (dose) of roots taken per day, the quantity of leaves taken per day, the unwanted side effects after taking medicine, the knowledge of awareness whether this herb causes harm, the frequency of taking medicine per day, the days of taking medicine to get well and the frequency of taking medicine every year ($p < 0.05$) (Supplementary 4).

4. Discussion

Our findings showed that the plant leaves and roots were the most preferred to other plant parts. Individuals obtained the leaves mainly from the surrounding environment, while the roots from the market. As

Table 4

Perceived efficacy.

Themes	Perceived efficacy	N (%)
Feeling after taking the medicine	Feeling nauseous, like to vomit	8 (2.0)
	Sweating all over the body and feeling better	350 (88.9)
	Bitter taste and feel better	30 (7.6)
	Bitter taste, sweating, and a strong odor	1 (0.3)
	Bitter taste, shivering, and sweating	5 (1.3)
Has it ever failed to cure the disease	Yes	16 (4.0)
	No	380 (96.0)
When it failed to treat	I seek medical attention in the hospital	16 (4.0)
Do you combine it with other modern drugs?	Yes	10 (2.5)
	No	386 (97.5)
Reasons for combining herbal medicine with the modern drugs	To cure faster	10 (2.5)

expected, the liquid was the most common traditional dosage form prepared mainly by infusion and decoction methods. These local preparations were taken at varying doses, usually twice a day. The findings that the roots were highly used could mean the local communities in Jubek are not aware of the medicinal plant conservation strategies. This practice could likely increase the risk of extinction, as reported elsewhere (Asnake et al., 2016). On the other hand, the frequent use of fresh leaves and dried roots could indicate the availability and easy accessibility of this plant species in the community.

The use of *A. bracteolata* for the traditional management of malaria is well established. Individuals believed to have malaria perceived a feeling of recovery after taking the *A. bracteolata* decoction without mixing with other conventional medicines. It is remarkable to note that these traditional claims have been corroborated by the plant's pharmacological activities in animal studies (Ahmed et al., 2010; Tahir et al., 1999). Researchers attributed the antiparasmodial activities of the *A. bracteolata* to the presence of major phytochemical groups; alkaloids, terpenoids, and flavonoids (Prashant Tiwari et al., 2011).

The primary concern for using *A. bracteolata* has been its undesirable toxicity profile (Asase et al., 2010; Ishola et al., 2014). Its toxicity has been linked to Aristolochic acids (AAs) content (Heinrich et al., 2009; Kang et al., 2021). However, contrary to such findings, our study revealed that most local users had not experienced any harmful effects despite a long exposure. Nevertheless, a small number of respondents believed in taking little quantity or avoiding altogether using *A. bracteolata* preparations when pregnant because of its abortifacient effects on early pregnancy. The early-stage abortion reported in our findings is supported by the findings from another study that demonstrated AAs' abortifacient property (Nandhini et al., 2017). Furthermore, it should be noted that the lack of noticeable side effects among the majority of users does not necessarily mean the *A. bracteolata* local preparations are entirely safe. These scenarios could imply that the actual prevalence of side effect is underestimated among the local users due to unawareness of the signs and symptoms indicative of side effects linked to plant species, or it could also imply the AAs toxicity symptoms manifest at the terminal stage of its pathogenesis as reported in some studies (Jadot et al., 2017; Nortier et al., 2000). Another possible interpretation of these findings is based on previous study findings that demonstrated that water has low extraction efficiency of AAs due to its poor water solubility (Balachandran et al., 2005). Thus, the water extraction solvent used by the community for extraction does not efficiently extract the known toxic compounds (AAs), leaving the community protected against its effect. Moreover, preparation methods, doses used, and duration of use could also reduce the medicine's toxic content. However, such a claim warrants further investigations.

Interestingly, this plant was used for other common ailments, including cough, headache, acute stomach cramps, fever, common cold, general body pain, pneumonia, typhoid, joint pain, diarrhea, body fatigue, lower abdominal pain, scorpion bites, and snake bites. This could indicate that this plant has secondary metabolites that could respond to other diseases and malaria. The widespread use of the plant in the Jubek state community does not correlate with fear of the plant's reported potential toxicities.

5. Conclusion

The findings provide critical information on the traditional used of *A. bracteolata* by the community in Jubek state of South Sudan to treat malaria. Although most users reported getting cured of malaria, a notable proportion of them experienced side effects, including early-stage abortion and stomach discomforts. Thus, the use of *A. bracteolata* preparations, particularly in pregnant women, should be avoided. In addition, the antimalarial benefits reported in our findings point to the need for further research focused on strategies to neutralize the toxic compounds while retaining its antimalarial activity. Finally, community awareness of the potential toxicity effect of *A. bracteolata*

and best practices to minimize them is essential.

Authors' contribution

LSMA conceived and drafted an earlier version of the manuscript, collected data. PEO, ADL provided mentorship and supervision. ELP, PEO, ADL, AW, CUT revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Declaration of competing interest

Authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jep.2021.114314>.

Abbreviations

AAs	Aristolochic acids
ACT	Artemisinin-based combination therapy
IPTp	Indoor residual spraying and intermittent preventive treatment
FGDs	Focused group discussions
LLINS	Long-lasting insecticide-treated bed nets
SPSS	Statistical package for social science software

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