https://doi.org/10.48047/AFJBS.6.15.2024.14045-14065

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Research Landscape and Efficacy of *Zanthoxylum* Genus Against Malaria: A Global Review (2004-2023)

Lassané Ouédraogo [1,3*], Aminata P. Nacoulma[2,3], Moussa Compaoré[3], Raïnatou Boly[4], Martin Kiendrebeogo[3]

[1]Centre National de la Recherche Scientifique et Technologique (CNRST)/ Institut de l'Environnement et de Recherches Agricoles (INERA), Burkina Faso

[2]Laboratoire de Toxicologie, environnement et santé, Université Joseph Ki-Zerbo, Burkina Faso

[3]Laboratoire de Biochimie & Chimie Appliquées (LABIOCA), Université Joseph Ki-Zerbo

4 Centre National de la Recherche Scientifique et Technologique/ (CNRST) Institut de Recherche en Sciences de la santé (IRSS)

***Corresponding author**: lassanouedraogo@yahoo.fr

Volume 6, Issue 15, Oct 2024

Received: 15 Aug 2024

Accepted: 25 Sep 2024

Published: 21 Oct 2024

doi: 10.48047/AFJBS.6.15.2024.14045-14065

Abstract *Zanthoxylum* species are involved in traditional medicine in the treatment of malaria. This study aims to map the research landscape and identify networks of researchers working on the Zanthoxylum genus and malaria from 2004 to 2023. The literature review was conducted utilizing a variety of databases, including Google Scholar, ScienceDirect, and Dimensions. VOSviewer software version 1.16.20 was used for network mapping and an Excel 2019 spreadsheet for descriptive statistical analysis of the retrieved data. *Zanthoxylum* species identified as highly effective against Plasmodium falciparum were 12. The network of countries that participated in the research around *Zanthoxylum* species was about 28 countries, with Kenya receiving the most citations (41 total link strength), followed by France and the United State. The most used parts of the species are stem bark followed by root bark with respective values of 57% and 29%. The most commonly used solvent for extraction is methanol and then dichloromethane. The Plasmodium strains tested are about 9 with the D6 strain (32%) the most tested followed by the W2 strain (26%). The aqueous extract of *Zanthoxylum zanthoxyloides* root bark was the most effective against P. falciparum strain 3D7 and the dichloromethane/methanol extract of *Z. holstzianum* stem and root bark was most effective on the D6 and W2 strains. Fagaronine and nitidine are the most remarkable antiplasmodial compounds. Strengthening the network of researchers, especially in Africa, in the field of research related to *Zanthoxylum* species and especially on *Z. zanthoxyloides* and *Z. holstzianum* could open up better perspectives on promising molecules against Plasmodium strains.

Keywords: *Zanthoxylum species, network of researchers, stem bark, root bark, Plasmodium strains, antiplasmodial compound*

1. Introduction

Malaria affects several million people all over the world, and Africa is the region that pays the most for it. Malaria caused by Plasmodium species, remains a significant public health concern globally (Li et al., 2024), with the World Health Organization reporting that in 2022, approximately 94% of malaria cases occurred in the African region (Venkatesan, 2024). For example, malaria remains a significant public health challenge in Burkina Faso, a West African nation. In 2020, health authorities reported more than 11 million malaria case in the country (Bationo et al., 2023).

For many years in Africa, conventional and traditional medical approaches have been employed in efforts to control and reduce the impact of this widespread disease. There are indeed molecules in the form of medication that can treat the disease, but it continues to claim victims, sometimes because of forms of resistance and the context of poverty in Africa. The network of researchers continues their research on plants in order to identify active molecules capable of destroying all forms. Faced with this challenge related to plausibility, researchers are exploring the potential of various plant extracts against Plasmodium strains.

Let us take the case of the genus *Zanthoxylum*, which has several species that have been evaluated in the laboratory. The species of this genus, known for its diverse phytochemical composition, seem promising in traditional medicine in treating malaria and other diseases. It would therefore be interesting to deepen knowledge of this genus's species in relation to malaria. For example, *Zanthoxylum heitzii* Aubrév. & Pellegr.) P.G.Waterman has been shown to contain chemicals such as dihydronitidine, which is known to have strong anti-*Plasmodium falciparum* Welch activity even at low concentrations (Goodman et al., 2019). According to (Correa-barbosa et al., 2023). Additional species, such as *Zanthoxylum rhoifolium* (Lam.) and *Zanthoxylum chiloperone* Mart. ex (Engl) have also shown noteworthy anti-plasmodial activities, suggesting their potential as sources of novel antiplasmodial compounds.

Thus, it would be important to capitalize on the research already carried out on *Plasmodium* from species of the genus *Zanthoxylum* to control this disease through scientrometry through scientrometry better. It is very useful in guiding research efforts and improving the effectiveness of studies (Daradkeh et al., 2022). Indeed, the keywords employed, publication sources, and author affiliations form a comprehensive framework that broadens the understanding of specific plant species. This study aims to map the research landscape and identify networks of researchers working on the *Zanthoxylum* genus and malaria from 2004 to 2023.

2. Methodology

To conduct this study, databases were consulted, keywords were used and titles and abstracts were considered in Dimensions AI, Science Direct (ScienceDirect.com|) and google Scholar. The following criteria were therefore retained for this review: the date of the articles consulted on species of the genus *Zanthoxylum* and *Plasmodium* that should be comprised between 2004 to 2023; the keywords ("*Zanthoxylum* genus" AND "*Plasmodium* species"), (("*Zanthoxylum* genus" AND "malaria), ("*Zanthoxylum*" AND "*Plasmodium*") and(("*Zanthoxylum*" AND "malaria)" The data was collected from the Dimension database (n=35), Science Direct (n=21) and Google Scholar (n=7). The methodology involved a multi-source data extraction process to ensure comprehensive coverage of relevant literature. Data from Dimensions AI were exported as an Excel file, while articles from Science Direct and Google Scholar were systematically filtered and selected based on specific criteria. Notably, a significant portion of the articles retrieved from Science Direct and Google Scholar was also present in the Dimensions AI dataset, enhancing the reliability of the findings. The Excel data from Dimensions AI and data extract from articles was then utilized for descriptive analyses. Additionally, VOSviewer version 1.16.20 was employed to visualize the bibliometric networks, mapping relationships among researchers, countries, citations, co-authorships, and organizations, thereby providing insights into the research landscape (Kirby, 2023). The articles were filtered in Dimensions AI using indexing and abstracting services, namely the Norwegian Register for Scientific Journals (levels 1 and 2), ERA (Excellence in Research for Australia) for the years 2015 (n=32), 2018 (n=33), and 2023 (n=34), UGC-CARE Reference List (n=34), Directory of Open Access Journals (DOAJ) (n=11), PubMed (n=29), and the Flemish Academic Bibliographic Database for the Social Sciences and Humanities (VABB-SHW) (n=22). Thresholds were established based on the heading to highlight the most highly rated studies. The field citation ratio (FCR) and the relative citation (RCR) (Hutchins et al., 2016) were extracted by using Dimension for the most cited papers. The distribution of the species was retrieved on the Map of Life site (https://mol.org/species/) and was adapted.

3. Results and discussion

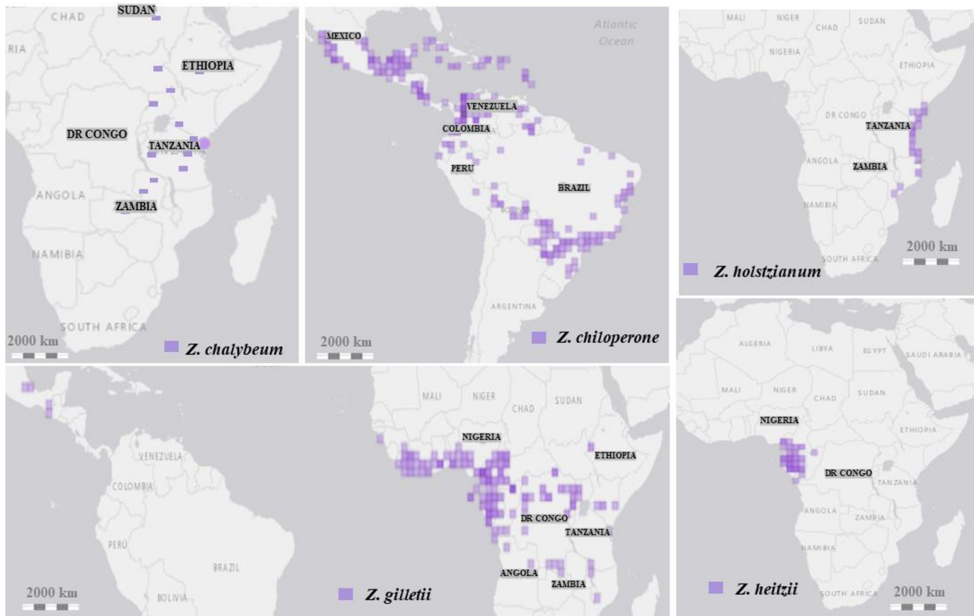
3.1. Antimalarial *Zanthoxylum* species Distribution

Species from *Zanthoxylum* genus identified for screening from 2004 to 2023 as antiplasmodial are pantropical and distributed in several parts of the world (Table 1 and Figure (1a/b/c)). Species from the *Zanthoxylum* genus, which are well-known for their role in malaria management, are largely found in Tropical Africa, where malaria remains a serious public health concern (Venkatesan, 2024), with far-reaching effects for society and a need for effective management approaches. In each region of the world, specific species of the *Zanthoxylum* genus are used in traditional medicine to treat malaria. In Western

Africa, *Z. zanthoxyloides*, *Z. gilletii*, *Z. leprieurii* and *Z. rhetsa* are the most predominant; in Central Africa, *Z. chalybeum*, Z. gilletii, *Z. heitzii*, Z. *leprieurii* and *Z. usambarense* are common; in East Africa, *Z. holtzianum* and *Z. gilletii* are prevalent; in Asia, *Z. rhetsa* is widely used; and in South America, *Z. gilletii*, *Z. chiloperone*, *Z. rhoifolium* and *Z. syncarpum* are notable. In each region of the world, specific species of the *Zanthoxylum* genus are used in traditional medicine to treat malaria. In Western Africa, *Z. zanthoxyloides*, *Z. gilletii*, *Z. leprieurii* and *Z. rhetsa* are the most predominant; in Central Africa, *Z. chalybeum*, *Z. gilletii*, *Z. heitzii*, *Z. leprieurii* and *Z. usambarense* are common; in East Africa, *Z. holtzianum* and *Z. gilletii* are prevalent; in Asia, *Z. rhetsa* is widely used; and in South America, *Z. gilletii*, *Z. chiloperone*, *Z. rhoifolium* and *Z. syncarpum* are notable.

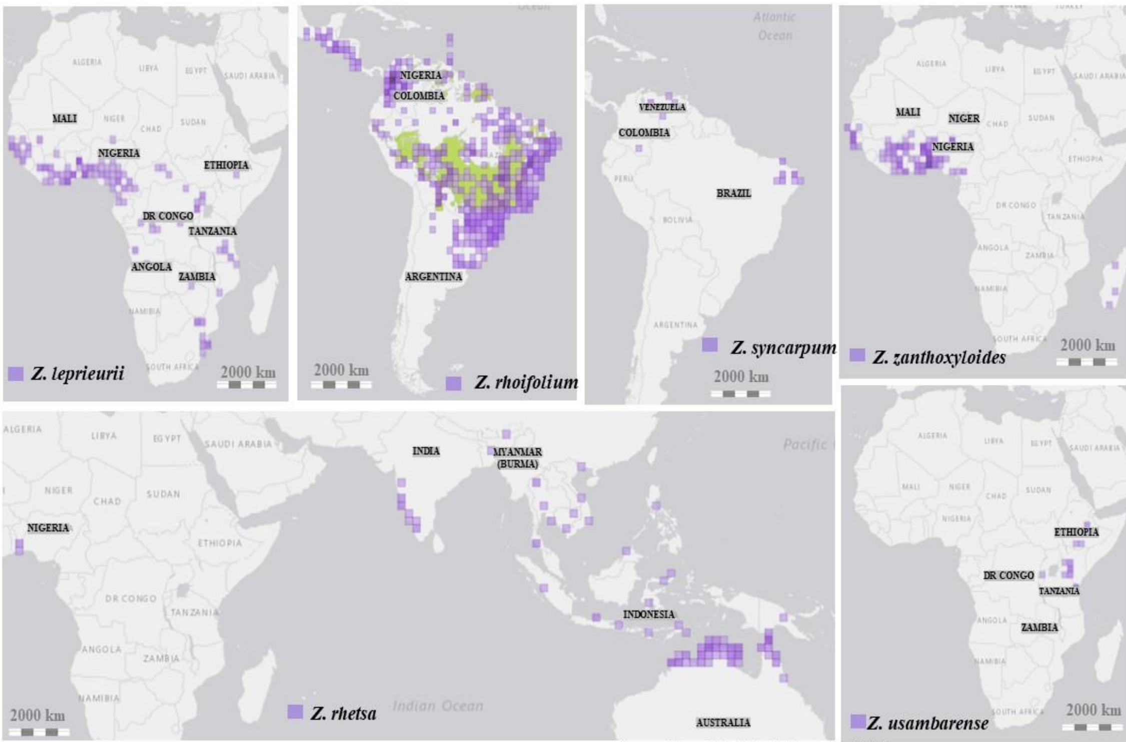
Table 1. Distribution of species from the *Zanthoxylum* genus identified in malaria management

Species	**Distribution**	**Author (Year)**
Zanthoxylum chalybeum Engl	Tanzania, Uganda, Mozambique, Namibia, South Africa, and several others in Eastern	Mguni et al. (2009)
Z. chiloperone Mart. ex Engl.	Central South America	Cebrián-torrejón et al., 2011
Z. gilletii (De Wild.) P. G. Waterman	Guinea, Sierra Leone, Kenya, Uganda, Côte d'Ivoire, Tanzania, Angola, Zimbabwe and the Democratic Republic of the Congo.	Orwa et al. (2009),-Sinan et al. (2019)
Z. heitzii heitzii (Aubrév. & Pellegr.) P.G.Waterman	West Africa	Moussavi et al. (2015), Wangensteen *et al.* (2016)
Z. holstzianum (Engl.) P.G.Waterman	Kenya,Somalia, Mozambique	Kaigongi et al., (2023)
Z. leprieurii Guill. & Perr.	Tropical Africa	Tine et al. (2020)
Z. rhetsa Roxb.) DC.	Asia	Duangyod et al., (2020)
Z. rhoifolium Lam	South America	Jan et al. (2022)
Z. syncarpum Tul.	North and South Amerca	Ross et al. (2005)
Z. simullans Hance	Tropical and subtropical	Wang et al. (2014)
Z. usambarense (Engl.) Kokwaro	Kenya, Tanzania, Mozambique, Ethiopia, Rwanda	Kirira et al.(2006), Were et al. (2010)
Z. zanthoxyloides (Lam.) Zepernich & Timler	West Africa	(Ouédraogo et al., 2019), Yaoitcha et al. (2022)



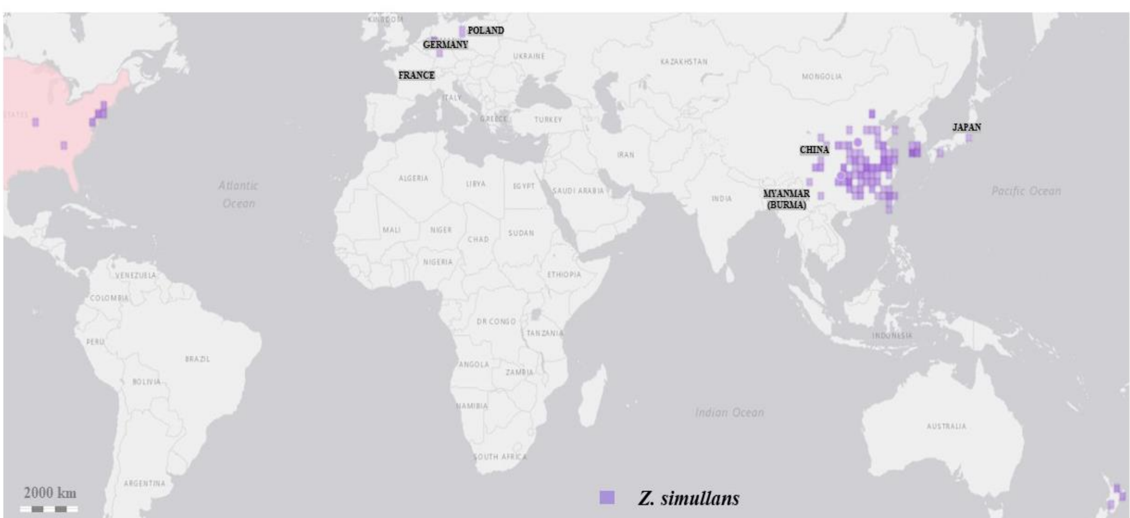
Source: Map of life (adapted: September 2024)

Figure 1a. Distribution area of the *Zanthxoylum* species used as antiplasmodial: *Z. chalybeum, Z. chiloperone, Z. gilletii, Z.heitzii* and *Z. holstzianum*



Source: Map of life (adapted: September 2024)

Figure 1b. Distribution area of the *Zanthxoylum* species used as antiplasmodial: Z. *Leprieurii*, *Z. Rhetsa*, *Z. Rhoifolium*, *Z. syncarpum*, *Z. usambarense* and *Z. zanthoxyloides*



Source: Map of life (adapted: September 2024)

Figure. 1c. Distribution area of the *Zanthxoylum* species used as antiplasmodial: *Z. simullans*

3.2. Network of researchers

For the citation author network the minimum number of documents of an author was 2 and the minimum number of citations was 1 in the VOSviewer software. The study analyzed a total of 239 authors, of which 15 were identified with 2 clusters (Figure 2). The largest cluster is displayed in red. This cluster most likely represents the core group of authors who have made substantial contributions to the area and are inextricably linked by collaborations, mutual interests, or affiliation. The second largest cluster, shown by the green color, is the next most notable group of authors. This cluster could represent a different sub-field, research group, or partnership within the larger scope of the study.

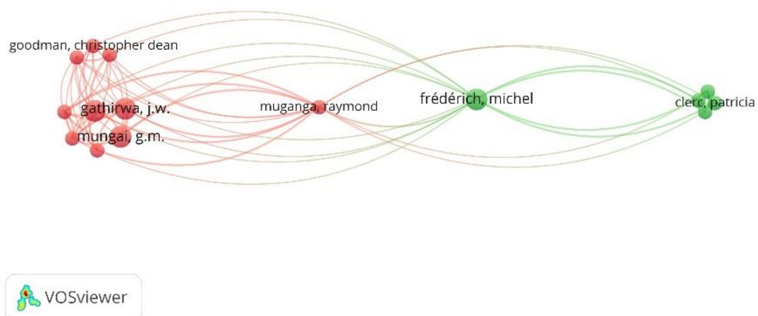


Figure 2. Citation author's network

The co-authorship network analysis employed a minimum threshold of 2 documents per author and a minimum threshold of 105 citations. This resulted in the identifying of 6 co-authors out of 223 who met the threshold (Figure 3). One cluster in red indicating a significant concentration of collaborative research efforts within this group.

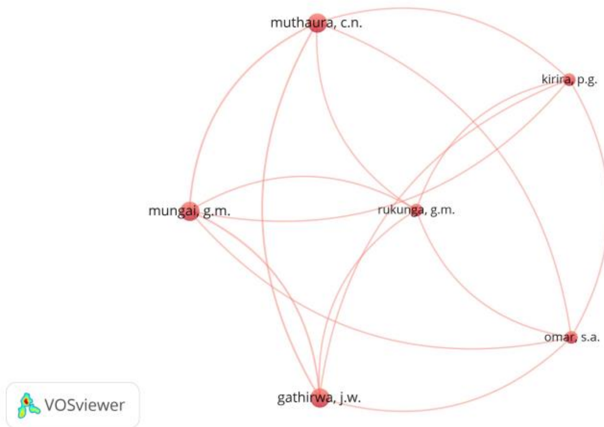


Figure 3. Coauthorship author network

For the network of cited documents, a minimum number of citations considered for a document was set to n=10 and 29 of 35 documents were found (Figure 4). The most cited document was (Bertani et al., 2005) followed by (Kirira et al., 2006). The study of (Bertani et al., 2005) investigated *Z. Rhoifolium* and other species but did not specify which compound from *Z. rhoifolium* (Rutaceae) was found to be antiplasmodial. It only mentioned that a remedy made from this plant, which is widely used among the population of French Guiana as a preventive, could inhibit more than 50% of parasite growth in vivo at around 100 mg/kg. The study have 89 citations with a FCR of 9.21 (this publication has received approximately 9.21 times more citations than average) and a RCR of 2.32 (the publication has an above average citation rate for its group 2.32 times). The study of (Kirira et al., 2006) found that the methanol extract of the stem bark of *Z. Usambarense* had an IC50 (half maximal inhibitory concentration) value < 6 µg/ml against both chloroquine-sensitive and resistant *falciparum* strains NF54 and ENT30. This study was cited 88 times with a FCR of 10 and RCR of 2.37. The two studies cited above used different approaches, the first focusing on in vivo tests and the second focusing on in vitro tests, which provide complementary evidence of the antimalarial potential of *Zanthoxylum species*.

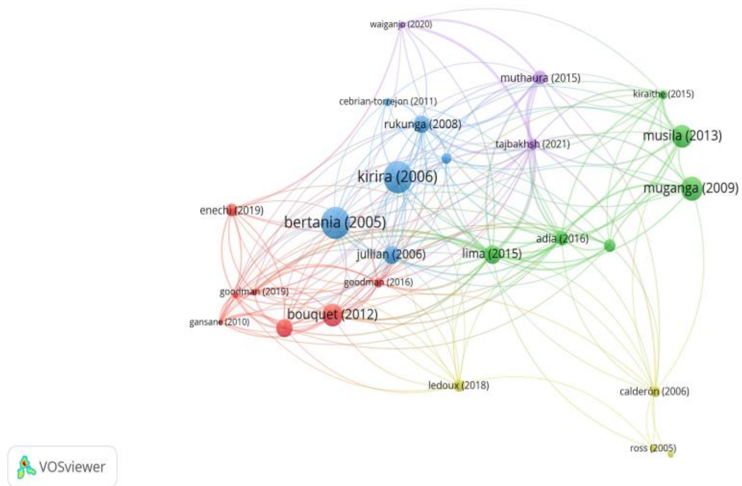


Figure 4. Citation document network

The minimum threshold for the author citation network by country was set at 2 documents per country and at least one citation per country. A total of 12 of 28 countries met the threshold set. Thus, Kenya (9 documents) was the first country with the greatest number of citations (with 35 total link strength) followed by France (6 documents, 18 total link strength) and United State (5 documents, 10 total link strength), suggesting that these countries' authors are more interested in *Zanthoxylum species* studies related to *plasmodium* (Figure 5).

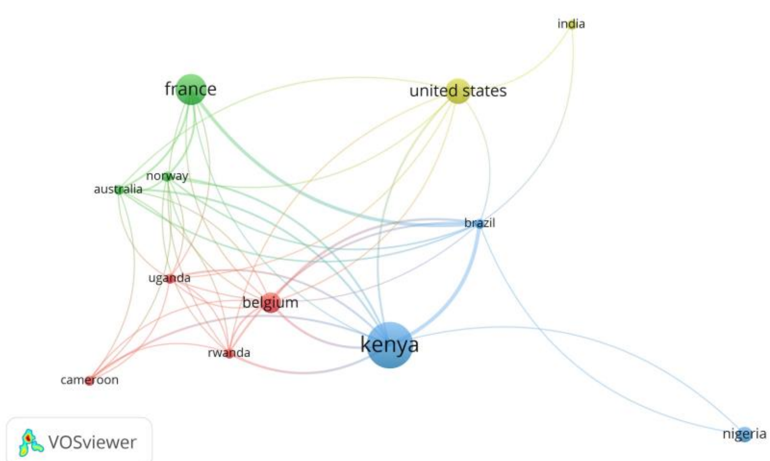


Figure 5. Author citation country network

This result reveals that Kenya is the top contributor to the *Plasmodium* field related to *Zanthoxylum* species. Kenya was top-ranked, followed by France and the United States, indicating a joint global effort in this area, combining expertise from malaria-endemic regions with resources from wealthy countries. This network demonstrates the importance of local knowledge and research capacity in the search for malaria control strategies. It also highlights the global importance of *Zanthoxylum* species and their antimalarial characteristics. However, since only 12 out of 28 countries passed the threshold criterion indicates a possible gap in global research participation, highlighting the importance of international collaboration and knowledge exchange in the fight against this disease. The small research core in some countries highlights the importance of strengthening international collaboration.

For the author citation organization network, the threshold was 2 and 40 for document and citation respectively. As a result, 12 out of 74 organizations met the criteria, and the top 10 were chosen (Figure 6). The Kenya Medical Research Institute (KEMRI) was the first with 4 documents and 17 links in total, confirming their leadership.

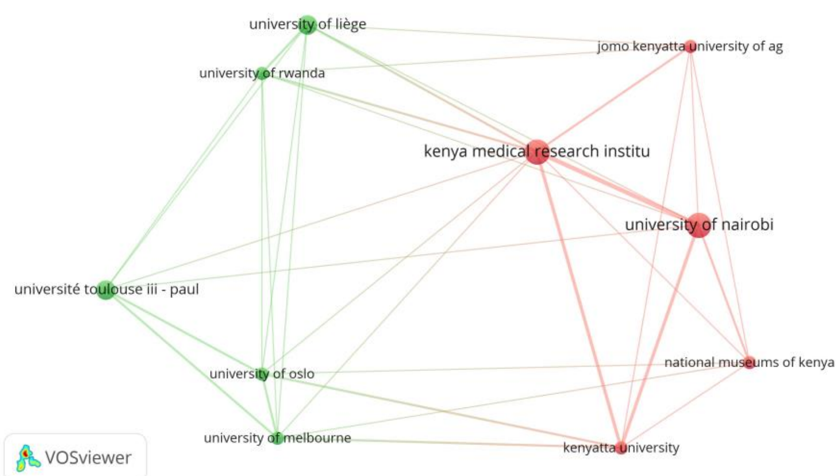


Figure 6. Citation organizations network

For the citation source network, the minimum number of documents selected in a country was n= 3 and the minimum number of citations was st at n=50. The results indicated that 3 out of 19 sources met the threshold (Figure 7).

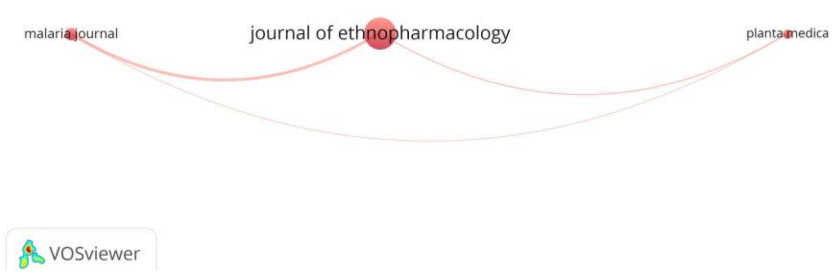


Figure 7. Citation source network

For the citation source network, the minimum number of documents selected in a country was n= 3 and the minimum number of citations was set at n=50. The results indicated that 3 out of 19 sources met the threshold (Figure 7).

The first citation source was the Journal of Ethnopharmacology with a total of 18 link strengths and 10 documents followed by Malaria Journal and Planta Medica. The first position of Ethnopharmacology suggests a strong emphasis on studies that integrate cultural and scientific approaches to medicine. At the same time, the Malaria Journal and Planta Medica are among the main sources that highlight the field's specific focus on malaria research and medicinal plant studies.

The few renowned journals can impede the distribution of key findings to larger scientific groups. This emphasizes the importance of researchers combining multiple disciplines in this sector to achieve efficient results. To increase malaria control, more journals must be published, multidisciplinary research initiatives should be encouraged, and knowledge-sharing platforms should be established between traditional medicine practitioners, pharmacologists, and malaria researchers.

3.3. Antimalarial powers of *Zanthoxylum* species

The research revealed that 12 species within the *Zanthoxylum* genus demonstrate the presence of compounds that enhance the activity against various *P. falciparum* (Table 2).

The stem barks represent 57% of the organs used as a test against *Plasmodium* strains followed by the roots (29%) (Figure.8).

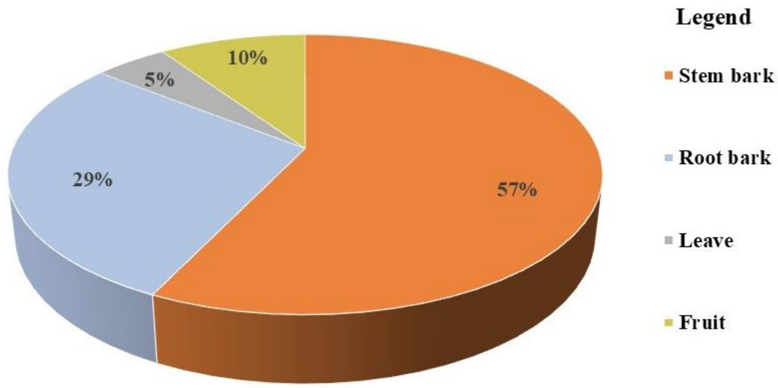


Figure 8. Percentage of species part used in test against Plasmodium strain

Laboratory tests on *Plasmodium* have focused on *Zanthoxylum* species' stem and root barks. This is thought to be due to the high concentration of antimalarial chemicals in some parts of the plant. However, it should be noted that the heavy reliance on stem and root barks not only jeopardizes the survival of wild *Zanthoxylum* populations, but also indicates a possible failure to fully explore the medicinal potential of other components of the plant. This trend highlights the critical need for more comprehensive studies that combine traditional knowledge with current scientific methodologies, emphasis sustainable harvesting practices and other parts of the plant such as leaves, fruits, and other parts of the plant. This is how the work of Guedje et al. (2016) had shown for the harvesting of bark for example it is necessary to respect a certain number of criteria to make the species sustainable.

The most frequently used extract was the methanol extract (45%), followed by the dichloromethane one (28%) (Figure 9).

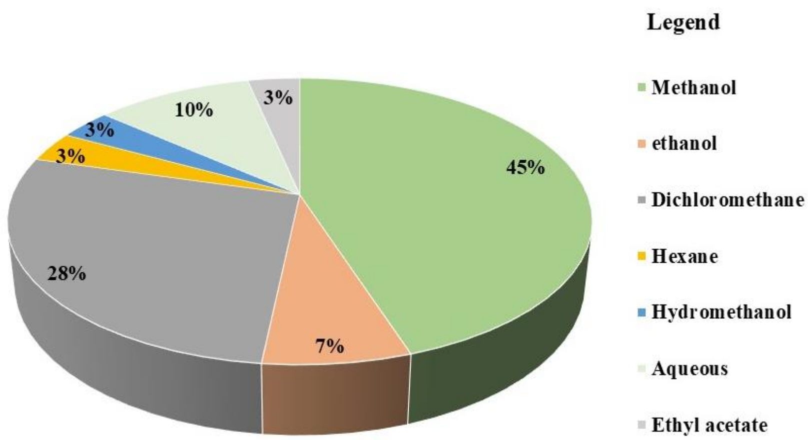


Figure 9. Extracts used in test against Plasmodium strain

It is well known (Uzor, 2020) that several compounds, including alkaloids, are involved in the antimalarial potential of plant extracts. The results suggest methanol and dichloromethane are ideal for extracting potent antiplasmodial compounds, such as alkaloids. In reality, methanol has a high solubility for many alkaloids. It is miscible with water, allowing it to extract both polar and non-polar chemicals. Still dichloromethane has a lower polarity than methanol and is therefore suitable for extracting less polar alkaloids.

Conversely, the preference for methanol and dichloromethane extracts may limit the understanding of other solvent extracts'efficacy.

There were three species of *Plasmodium* (*P. facilparum*, *P. knowlesi* (sinton and mulligan) and *P. berghei* (vincke & lips) tested by *Zanthoxyum* genus extracts and the most predominant used was *P. falciparum* (84%) (Figure 10).

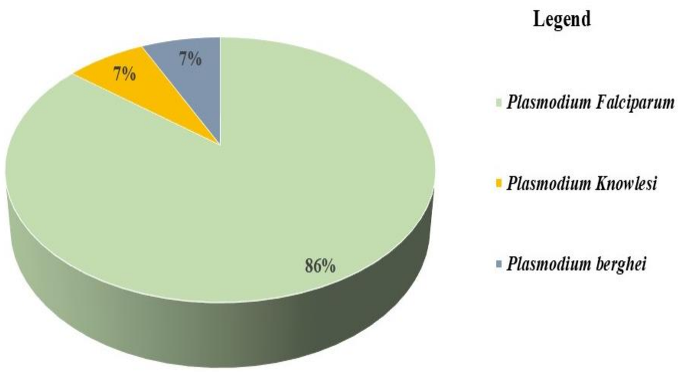


Figure. 10. *Plasmodium* species tested

The species from the *Zanthoxylum* genus was tested against a diverse range of *Plasmodium* strains, including three chloroquine-sensitive strains (D6, 3D7, and NF54) and six chloroquine-resistant strains (W2, ENT30, Dd2, FcB1, FCR3 and K1) (Figure 11).

Table 2. *Zanthoxylum* species : Type of extracts used, compounds and antimalarial activity (measured by the IC50 values) against *Plasmodium* strain

Species	Plant part	Type of extract	Type of compound	Identified Compound	Strain	IC50	Author (Year)
Z. chalybeum	Rb	Methanol	-	-	-	8.10 μg/mL	Bbosa et al. (2014)
	Rb	Methanol	-	-	W2	1.9±0.5 1.9±0.5 μg/mL	Muganga et al. (2010)
	Sb	Methanol	Alkaloid	Fagaramide	FCR3 c	2.85 μg/mL	Adia et al. (2016)
		Ethanol	-	-	NF54	3.21 μg/mL	
					FCR3 c	0.57 μg/mL	
		Aqueous			NF54	4.25 μg/mL	
Z. chiloperone .	Sb	Ethanol, dichloromethane	Alkaloid	Canthin-6-one:	D6, W2	2.0-5.3 μg/mL	Cebrián-torrejón et al. (2011)
				Trans-avicennol:	D6, W2	0.5 to 2.7 μg/mL	
Z. gilletii	Sb	Methanol, Dichloromethane	Alkaloid	Alkamide, Fagaramide	D6	0.78 μg/mL; 6.0 μg/mL	(Waterman et al. (2021)
	Sb	Methanol, Dichloromethane	Alkaloid	Nitidine	FcB1	< 5 μg/mL	Okagu et al. (2021)
	Sb	Methanol, Dichloromethane	Alkaloid	8-Acetonyldihydrochelerythrine	D6	4.06 μg/mL	(Waterman et al. (2021)
					W2	4.02 μg/mL	
					3D7	3.37 μg/mL	
	Sb		Alkaloid	Fagaramide:	D6	7.73 μg/mL	

Species	Plant part	Type of extract	Type of compound	Identified Compound	Strain	IC50	Author (Year)
		Methanol, Dichloromethane			W2	15.15 µg/mL	
					3D7	7.72 µg/mL	
Z. heitzii	Sb	Hexane	Alkaloid	dihydronitidine		0.0089 µg/ml	Goodman et al. (2016)
Z. holstzianum	Sb, Rb	Dichloromethane/methannol	Alkaloid	Nitidine	D6, W2	0.11 ± 0.01 µg/mL	Akampurira et al. (2023)
				Norchelerythrine	D6	0.15 ± 0.01 µg/mL	
		Dichloromethane/methannol	-	-	D6	2.6 ± 0.3 µg/mL	
					W2	2.5 ± 0.3 µg/mL	
Z. leprieurii	Fr	Ethyl acetate	Alkaloid	Arborinine	3D7	4.5 ± 1.0 µg/ml	Tchinda et al., (2009)
				xanthoxoline	3D7	4.6 ± 0.6 µg/ml	
Z. rhoifolium	Sb	Aqueous	Alkaloid	nitidine		IC(50)< 1 µg/mL	Correa-barbosa et al. (2023)
Z. syncarpum	Le	Methanol	Alkaloid	Syncarpamide	D6	2.04 µM	Aratikatla et al. (2017);
					W2	3.06 µM	
					3D7	3.90 µM	
					K1	2.56 µM	
Z. rhetsa	Fr	Methanol	-	-	3D7	16.21 µg/mL	Mallya and Bhitre, (2022), Mallya and Bhitre, (2022)
Z. simullans	Rb	Methanol	Alkaloid	Normelicopidine	Dd2	18.9 µg/mL	Wang et al. (2014)
Z. usambarense	Sb	Methanol extract	-	-	NF54 and ENT30	0.6< 1 µg/mL	Kirira et al. (2006)
Zanthoxylum zanthoxyloides	Sb	Dichloromethane, methan, and hydromethanol		-		1.2 µg/mL	Gansané et al. (2010)
	Rb, Sb	Methanol	Alkaloid	Bis-dihydrochelerythrinyl ether Buesgenine Chelerythrine γ-Fagarine Skimmianine Pellitorine	D6,W2	5 µg/mL	Goodman et al. (2019)
	Rb	Aqueous	Alkaloid	fagaronine	3D7	0.018 µg/ml	Kassim et al. (2005)

Note. Plant part used: Fr: Fruit, Le: Leave, Rb: Root bark, Sb: Stem bark.

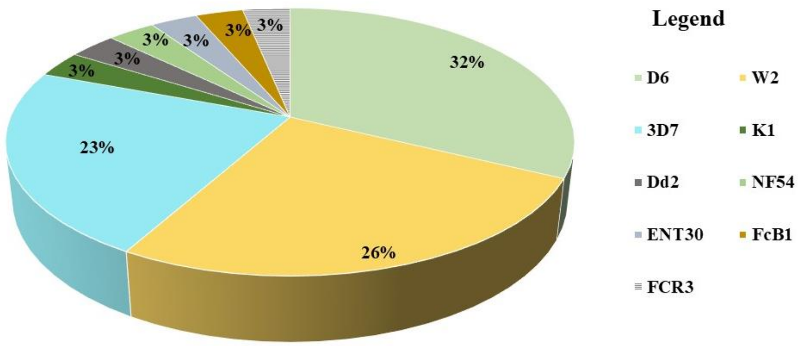


Figure 11. Strains tested against *Plasmodium*

Among tested strains, the D6 strain (32%) and the W2 strain (26%) were the most frequently tested, The study indicates that among the 12 identified species of *Zanthoxylum*, fagaronine a compound isolated from the aqueous extract of *Zanthoxylum zanthoxyloides* (Lam.) Zepernich & Timler root was the most active compound (IC50 value of 0.018 μg/ml) against *P. falciparum* strain 3D7. This was followed by the dichloromethane/methanol extract of the stem and root bark of *Z. holstzianum*, which showed activity with nitidine at an IC50 concentration of 0.11 μg/ml against both the D6 and W2 strains.

As alkaloids are primarily responsible for inhibiting *Plasmodium* in *Zanthoxylum* species, they are thought to act through multiple mechanisms of action. These compounds interact with the heme of hemoglobin, preventing its detoxification and causing toxic accumulation in the parasite (Bai et al., 2006). The study evaluates *Zanthoxylum* extracts against a wide variety of *Plasmodium* strains, encompassing both chloroquine-sensitive and resistant types. This approach offers valuable insights into the efficacy of these extracts against different malaria parasites. This shows the current challenges posed by drug resistance in malaria treatment (Gujjari et al., 2016).

Conclusion

In this study 12 species of the *Zanthoxylum* genus have been identified having significant effectiveness against diverse *Plasmodium* strains. Methanol and dichloromethane root and stem bark extracts from

Zanthoxylum species were tested on 9 strains. The most effective antiplasmodial properties are found in the stem barks of these plants. It appears that advanced research on quality, toxicity testing and in-depth clinical trials on these species is necessary but with emphasis on *Z. Zanthoxyloides* and *Z. Holstzianum* are more promising. Research should explore all parts of these previous two species and use various solvents, including methanol and dichloromethane. Providing new insight and potential treatments could be achieved by focusing on a wider range of plant components. In addition, fostering collaboration across disciplines and establishing an international network of researchers could improve the effectiveness of these efforts.

References

Adia, M. M., Emami, S. N., Byamukama, R., Faye, I. and Borg-Karlson, A.-K. (2016). Antiplasmodial activity and phytochemical analysis of extracts from selected Ugandan medicinal plants. *Journal of Ethnopharmacology*, *186*(2), 14–19. https://doi.org/10.1016/j.jep.2016.03.047

Akampurira, D., Akala, H. M., Derese, S. and Heydenreich, M. (2023). A New C─C Linked Benzophenathridine─2-Quinoline Dimer , and the Antiplasmodial Activities of Alkaloids from *Zanthoxylum holstzianum*. *Natural Products Ressource*, *37*(13), 2161–2171. https://doi.org/10.1080/14786419.2022.2034810

Aratikatla, E. K., Valkute, T. R., Puri, S. K., Srivastava, K. and Bhattacharya, A. K. (2017). Norepinephrine alkaloids as antiplasmodial agents: Synthesis of syncarpamide and insight into the structure-activity relationships of its analogues as antiplasmodial agents. *European Journal of Medicinal Chemistry*, *139*, 546–556. https://doi.org/10.1016/j.ejmech.2017.07.052

Bai, L., Zhao, Z., Cai, Z. and Jiang, Z. (2006). DNA-binding affinities and sequence selectivity of quaternary benzophenanthridine alkaloids sanguinarine , chelerythrine , and nitidine. *Bioorganic & Medicinal Chemistry*, *14*(16), 5439–5445. https://doi.org/10.1016/j.bmc.2006.05.012

Bationo, C., Cissoko, M., Katile, A., Sylla, B., Ouédraogo, A., Ouedraogo, J. B., Tougri, G., Sidzabda, C., Kompaoré, B., Moiroux, N. and Gaudart, J. (2023). Malaria in Burkina Faso : A comprehensive analysis of spatiotemporal distribution of incidence and environmental drivers , and implications for control strategies. *PLOS ONE*, *18*(9), e0290233. https://doi.org/10.1371/journal.pone.0290233

Bbosa, G. S., Mwebaza, N., Lubega, A., Musisi, N., Kyegombe, D. B. and Ntale, M. (2014). Antiplasmodial Activity of Leaf Extracts of *Zanthoxylum chalybeum* Engl . *British Journal of Pharmaceutical Research*, *4*(6), 705–713. https://doi.org/10.9734/BJPR/2014/6528

Bertani, S., Bourdy, G., Landau, I., Robinson, J. C., Esterre, P. and Deharo, E. (2005). Evaluation of

French Guiana traditional antimalarial remedies. *Journal of Ethnopharmacology*, *98*, 45–54. https://doi.org/10.1016/j.jep.2004.12.020

Cebrián-torrejón, G., Spelman, K., Leblanc, K., Muñoz-durango, K., Gutiérrez, S. T., Ferreira, E., Arias, A. R. De and Figadère, B. (2011). The antiplasmodium effects of a traditional South American remedy : *Zanthoxylum chiloperone* var . angustifolium against chloroquine resistant and chloroquine sensitive strains of Plasmodium falciparum. *Revista Brasileira de Farmacognosia Brazilian Journal of Pharmacognosy*, *21*(4), 652–661. https://doi.org/10.1590/S0102-695X2011005000104

Correa-barbosa, J., Sodré, D. F., Henrique, P., Nascimento, C. and Dolabela, M. F. (2023). Activity of the genus *Zanthoxylum* against diseases caused by protozoa : A systematic review. *Frontiers in Pharmacology*, *13*, 873208. https://doi.org/10.3389/fphar.2022.873208

Daradkeh, M., Abualigah, L., Atalla, S. and Mansoor, W. (2022). Scientometric Analysis and Classification of Research Using Convolutional Neural Networks: A Case Study in Data Science and Analytics. *Electronics (Switzerland)*, *11*(13), 2066. https://doi.org/10.3390/electronics11132066

Duangyod, T., Phuneerub, P., Maneerat, W. and Charoensub, R. (2020). Quality evaluation of *Zanthoxylum rhetsa* fruits and seeds - a Thai traditional medicine. *Indian Journal of Traditional Knowledge*, *19*(2), 335–340.

Gansané, A., Sanon, S., Ouattara, L. P., Traoré, A., Hutter, S., Ollivier, E., Azas, N., Traore, A. S., Guissou, I. P., Sirima, S. B. and Nebié, I. (2010). Antiplasmodial activity and toxicity of crude extracts from alternatives parts of plants widely used for the treatment of malaria in Burkina Faso: Contribution for their preservation. *Parasitology Research*, *106*(2), 335–340. https://doi.org/10.1007/s00436-009-1663-y

Goodman, C. D., Austarheim, I., Mollard, V., Mikolo, B., Malterud, K. E., Mcfadden, G. I. and Wangensteen, H. (2016). Natural products from *Zanthoxylum heitzii* with potent activity against the malaria parasite. *Malaria Journal*, *15*, 481. https://doi.org/10.1186/s12936-016-1533-x

Goodman, C. D., Hoang, A. T., Diallo, D., Malterud, K. E., Mcfadden, G. I. and Wangensteen, H. (2019). Anti-plasmodial Effects of *Zanthoxylum zanthoxyloides* Authors. *Planta Med*, *85*, 1073–1079.

Goodman, C. D., Hoang, A. T., Diallo, D., Malterud, K. E., McFadden, G. I. and Wangensteen, H. (2019). Anti-plasmodial Effects of *Zanthoxylum zanthoxyloides*. *Planta Medica*, *85*(13), 1073–1079. https://doi.org/10.1055/a-0973-0067

Guedje, N. M., Tchamou, N. and Lejoly, J. (2016). Tree response to bark harvest: the case of a medicinal species, *Garcinia lucida*, as source of raw materials for plant-based drug development. *Journal of Applied Biosciences*, 99, 9476–9491. https://10.4314/jab.v99i1.13

Gujjari, L., Kalani, H., Pindiprolu, S. K., Arakareddy, B. P. and Yadagiri, G. (2016). Current challenges and nanotechnology-based pharmaceutical strategies for the treatment and control of malaria. *Journal of Nanomedicine & Nanotechnology*, 7(1), 1-9. doi:10.4172/2157-7439.1000370.

Hutchins, B. I., Yuan, X., Anderson, J. M. and Santangelo, G. M. (2016). Relative Citation Ratio (RCR): A New Metric That Uses Citation Rates to Measure Influence at the Article Level. *PLoS Biology*, *14*(9). https://doi.org/10.1371/journal.pbio.1002541

Jan, B., Corrêa, S., Oliveira, L. M. De, Cristina, A. and Sá, S. (2022). What is the cause of low seed germination of *Zanthoxylum rhoifolium* Lam .? *Revista Ceres, Viçosa*, *63*(3), 358–367.

Kaigongi, M. M., Lukhoba, C. W., Musila, F. M., Taylor, M., Mbugua, R. W., Githiomi, J., Yenesew, A. and Makunga, N. P. (2023). A versatile untargeted metabolomics - driven technology for rapid phytochemical profiling of stem barks of *Zanthoxylum* species with antioxidant and antimicrobial activities. *Advances in Traditional Medicine*, *23*(3), 929–945. https://doi.org/10.1007/s13596-022-00676-w

Kassim, O. O., Loyevsky, M., Elliott, B., Geall, A., Amonoo, H. and Gordeuk, V. R. (2005). Effects of Root Extracts of *Fagara zanthoxyloides* on the In Vitro Growth and Stage Distribution of Plasmodium falciparum. *Atimicrobial Agents and Chemotheray*, *49*(1), 264–268. https://doi.org/10.1128/AAC.49.1.264

Kirby, A. (2023). Exploratory Bibliometrics : Using VOSviewer as a Preliminary Research Tool. *Publications*, *11*, 10.

Kirira, P. G., Rukunga, G. M., Wanyonyi, A. W., Muregi, F. M., Gathirwa, J. W., Muthaura, C. N., Omar, S. A., Tolo, F., Mungai, G. M. and Ndiege, I. O. (2006). Anti-plasmodial activity and toxicity of extracts of plants used in traditional malaria therapy in Meru and Kilifi Districts of Kenya. *Journal of Ethnopharmacology*, *106*, 403–407. https://doi.org/10.1016/j.jep.2006.01.017

Li, J., Jean, H., David, D., Khrystyna, F. and Lei, P. (2024). Current Status of Malaria Control and Elimination in Africa : Epidemiology , Diagnosis , Treatment , Progress and Challenges. *Journal of Epidemiology and Global Health*, *14*, 1–18.

Mallya, R. and Bhitre, M. (2022). Evaluation of Antileukemic and Antimalarial Potential of *Zanthoxylum rhetsa* DC (Rutaceae), A Well- known Spice. *Current Drug Therapy*, *17*(3), 208–216. https://doi.org/10.2174/0929866529666220426121117

Mguni, S., Mashinya, F., Khabo-Mmekoa, C. and Shai, L. J. (2009). A review of *Zanthoxylum chalybeum* Engl : Ethnomedicinal uses , pharmacology , phytochemistry and toxicology. *Journal of Medicinal Plants for Economic Development*, *7*(1), a202.

Moussavi, N., Malterud, K. E., Mikolo, B., Dawes, D., Chandre, F., Corbel, V., Massamba, D., Overgaard, H. J. and Wangensteen, H. (2015). Identification of chemical constituents of *Zanthoxylum heitzii* stem bark and their insecticidal activity against the malaria mosquito Anopheles gambiae. *Parasites & Vectors*, *8*, 503. https://doi.org/10.1186/s13071-015-1113-x

Muganga, R., Angenot, L., Tits, M. and Frédérich, M. (2010). Antiplasmodial and cytotoxic activities of Rwandan medicinal plants used in the treatment of malaria. *Journal of Ethnopharmacology*, *128*, 52–57. https://doi.org/10.1016/j.jep.2009.12.023

Okagu, I. U., Ndefo, J. C., Aham, E. C. and Teodor, E. (2021). *Zanthoxylum* Species : A Review of Traditional Uses , Phytochemistry and Pharmacology in Relation to Cancer , Infectious Diseases and Sickle Cell Anemia. *Frontiers in Pharmacology*, *12*, 1–18. https://doi.org/10.3389/fphar.2021.713090

Orwa, C., Mutua, A., Kindt, R., Jamnadass, R. and Simons, A. (2009). *Agroforestree database: a tree reference and selection guide version 4.0. World Agroforestry Centre, Kenya*. https://www.worldagroforestery.org/output/agrofoerestree-database

Ouédraogo, L., Fuchs, D., Schaefer, H. and Kiendrebeogo, M. (2019). Morphological and Molecular Characterization of *Zanthoxylum zanthoxyloides* (Rutaceae) from Burkina Faso. *Plants*, *8*(9), 353–368.

Ross, S. A., Al-azeib, M. A., Krishnaveni, K. S., Fronczek, F. R. and Burandt, C. L. (2005). Alkamides from the Leaves of *Zanthoxylum syncarpum*. *Journal of Natural Products, 68*(8), 1297–1299.

Sinan, K. I., Zengin, G., Bene, K. and Mahomoodally, M. F. (2019). South African Journal of Botany Chemistry and pharmacology of three antiplasmodial traditional medicinal plants from tropical Africa – A review. *South African Journal of Botany*, *126*, 265–276. https://doi.org/10.1016/j.sajb.2019.04.024

Tchinda, A. T., Fuendjiep, V., Sajjad, A., Matchawe, C., Wafo, P., Khan;S., Tane, P. and Choudhary, M. I. (2009). Bioactive compounds from the fruits of *Zanthoxylum leprieurii*. *Pharmacologyonline*, *1*, 406–415.

Tine, Y., Diallo, A., Gueye, R. S. and Balde, M. (2020). Variation of essential oil composition of fruits of *Zanthoxylum leprieurii* Guill . et Perr (Rutaceae) from different sample locations and during their maturation period Variation of essential oil composition of fruits of Zanthoxylum leprieurii Guill . e. *International Journal of Biological and Chemical Sciences*, *14*(2), 626–637.

Uzor, P. F. (2020). Alkaloids from Plants with Antimalarial Activity: A Review of Recent Studies. *Evidence-Based Complementary and Alternative Medicine,* 2020, Article ID 8749083. https://doi.org/10.1155/2020/8749083

Venkatesan, P. (2024). The 2023 WHO World malaria report. *The Lancet Microbe*, *5*(3), e214. https://doi.org/10.1016/S2666-5247(24)00016-8

Wang, C., Wan, J., Mei, Z. and Yang, X. (2014). Acridone alkaloids with cytotoxic and antimalarial activities from *Zanthoxylum simullans* Hance. *Pharmacognosy Magazin*, *10*(37), 73–76. https://doi.org/10.4103/0973-1296.126669

Wangensteen, H., Thanh, G., Ho, T., Tadesse, M., Miles, C. O., Moussavi, N., Mikolo, B. and Malterud, K. E. (2016). A new benzophenanthridine alkaloid and other bioactive constituents from the stem bark of *Zanthoxylum heitzii*. *Fitoterapia*. https://doi.org/10.1016/j.fitote.2016.01.012

Waterman, D. P. G., Omosa, L. K. and Okemwa, E. K. (2021). Antiplasmodial Activities of the Stem bark Extract and Compounds of Antiplasmodial Activities of the Stem bark Extract and Compounds of *Zanthoxylum gilletii* (De wild) P . G . Waterman. *Pharmacognosy Commnications*, *7*(1), 41–46. https://doi.org/10.5530/pc.2017.1.6

Were, P. S., Kinyanjui, P., Gicheru, M. M., Mwangi, E. and Ozwara, H. S. (2010). Prophylactic and curative activities of extracts from Warburgia ugandensis Sprague (Canellaceae) and *Zanthoxylum usambarense* (Engl .) Kokwaro (Rutaceae) against Plasmodium knowlesi and Plasmodium berghei. *Journal of Ethnopharmacology*, *130*(1), 158–162. https://doi.org/10.1016/j.jep.2010.04.034

Yaoitcha, A. S., Gouwakinnou, N. G., Houehanou, T. D., Ahoyo, C. C., Fandohan, A. B. and Houinato, M. R. B. (2022). Climate change impact projection on spatial distribution of *Zanthoxylum zanthoxyloides* (Lam.) Z & T. – a threatened medicinal plant in Benin (West Africa). *Agronomie Africaine*, *34*(2), 293–305. http://www.gbif.org