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PHYTOCHEMICAL AND PHARMACOLOGICAL RELEVANCE OF USING *XIMENIA CAFFRA* FOR CANCER TREATMENT IN SOUTHERN AFRICA: A REVIEW

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ABSTRACT

Ximenia caffra (X. caffra), a traditional medicinal plant is commonly used across Southern Africa for the treatment of cancer. The plant's wide use as a traditional medicine for a variety of ailments, including cancer, skin disorders and respiratory disorders, has attracted the attention of several researchers. Researchers have conducted numerous phytochemical studies on various parts of the X. caffra plant, including leaves, roots and fruits. This review intends to highlight the phytochemical profile and the pharmacological activities of X. caffra plant extracts reported by different researchers, with a special emphasis on those properties relevant to cancer treatment. We accessed peer-reviewed data from six electronic databases, namely ResearchGate, Elsevier, PubMed, Scopus, Google Scholar and ScienceDirect, to gather relevant research papers and reports. The review outcome indicated that various researchers have confirmed X. caffra extracts contain a variety of bioactive phytochemicals and a broad range of pharmacological activities, including anticancer, antibacterial, antifungal, antioxidant and anti-inflammatory properties. Toxicity studies conducted on X. caffra extracts showed moderate to no toxicity results on isolated animal cells. Most of the bioactivity studies performed on X. caffra extracts focused on in-vitro assessments. There is a need to expand the phytochemical research conducted on X. caffra extracts by performing in-vivo assessments of the bioactivities of its extracts. X. caffra seems to be a very promising source of medicinal compounds, including anticancer compounds. Further research on the isolation and identification of bioactive compounds from X. caffra using modern equipment is recommended.

***Keywords*:** *Ximenia caffra*, Anticancer, Traditional medicine, Cancer, Phytochemicals

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INTRODUCTION

The use of plants and herbs, among others, for the purpose of maintaining good health and curing diseases is known as traditional medicine, and it started many years ago before the invention of modern medicine (Matowa *et al.* 2020). Traditional medicinal practices are still present today in all countries across the world. The World Health Organisation (WHO) also recognises the existence and the importance of traditional medicine in human health, especially in the developing world where modern medicines and drugs are scarce (WHO 2019). According to studies by James *et al.* (2018) and Thomford *et al.* (2015), 80% of people in African regions with long histories of using traditional medicine rely on these medicines for their medical needs. Several countries, including Botswana, Lesotho, South Africa, Malawi and Zimbabwe, widely use traditional, complementary, and alternative medicine (TCAM), with usage ranging from 24% to 80% (Hill *et al.* 2022; Mokhesi & Modjadji 2022; Mudonhi *et al.* 2021; Peltzer 2009; Thomford *et al.* 2015). They prefer medicinal plants over synthetic medicine because of their variety, ease of accessibility, global usage, affordability, the potential for self-medication and negligible side effects (Dahlberg & Trygger 2009; Moteetee & Seleteng Kose 2016). Traditional medicine has been a component of Southern Africa's healthcare system for ages. In rural areas, where most people cannot access the few available medical facilities, traditional medicine, such as medicinal plants remain the primary means of delivering healthcare (Munodawafa 2012).

The chemical constituents of plant extracts, such as phenolics and flavonoids, play a crucial role in their biological activities, including antimicrobial, anticancer and anti-inflammatory effects. For example, *Ximenia caffra* (*X. caffra*) exhibits significant antibacterial properties, which are likely attributed to its phytoconstituents such as phenolic acids, tannins, saponins, flavonoids, steroids and alkaloids, as shown by its effectiveness against pathogens like *Salmonella typhi* and *Escherichia coli* (Chingwaru *et al.* 2020). Additionally, the presence of these bioactive compounds enhances antioxidant activities, further contributing to the plant's therapeutic potential in managing oxidative stress-related conditions (Masuku *et al.* 2020). Furthermore, the anticancer activity of these compounds may arise from their ability to inhibit tumour growth and modulate inflammatory pathways (Ahmed *et al.* 2022).

Cancer is one of the deadliest diseases in the world, accounting for an estimated 20 million new cancer cases and 9.7 million deaths globally in 2022 alone (International Agency for Research on Cancer 2024). Finding efficient management and treatment strategies for cancer, still presents a significant challenge (Chhikara and Parang 2023). Africa is rich in medicinal plants and hence researchers are becoming more interested in numerous medicinal plants found in Africa as they may provide potential novel options for treating cancer. For centuries, people have used traditional medicinal plants such as *X. caffra*, *Sclerocarya birrea*, *Parinari curatellifolia*, *Mimusops caffra*, *Syzygium cumini*, *Kigelia africana* and *Annona muricata* to treat a variety of cancers (Fakudze *et al.* 2023). These medicinal plants contain an abundant number of phytochemicals, including polyphenols with antioxidant qualities that can counteract harmful free radicals and protect tissues from oxidative stress (Ochwang'i *et al.* 2014; Unuofin *et al.* 2018).

With the development of new technologies, traditional medicinal approaches have improved and are now equally complementing modern medicinal practices. Researchers have developed and are currently using several anticancer agents of wholly herbal origin, including taxol (Sze *et al.* 2008), topotecan (Moraes *et al.* 2017), vincristine (Zishan *et al.* 2017), etoposide (Bhanot *et al.* 2011) and paclitaxel (Cragg and Newman 2005).

Different national and international cancer agencies, such as the Cancer Association of Zimbabwe (CAZ) and the National Cancer Institute (NCI), are putting in efforts on medicinal plant research to facilitate the development of improved cancer treatment and management methods. Researchers are attempting to document the traditional knowledge of medicinal plants used for cancer treatment in Southern Africa (Maroyi 2013; 2023; Matowa *et al.* 2020; Mlilo and Sibanda 2022; Shopo *et al.* 2022). *X. caffra* has been identified as a commonly used plant for cancer treatment in Southern Africa (Chivandi *et al.* 2011; Maroyi 2016; Matowa *et al.* 2020; Shopo *et al.* 2022). Previous reviews on traditional medicinal plants used in cancer treatment in Southern Africa, such as *X. caffra*, primarily concentrated on their ethnobotanical uses. This review aims to examine the phytochemical profiles and pharmacological properties of *X. caffra* in cancer treatment. Even though the phytochemical composition and the pharmacological properties of plants might be affected by the climate and geographical location of the plant, this review has been extended to the whole of Southern Africa.

REVIEW METHODOLOGY

X. caffra, which is a medicinal plant found in Southern Africa countries (Zimbabwe, Zambia, South Africa, Botswana, Malawi, Mozambique, Tanzania, Lesotho, Swaziland and Namibia), was the primary focus of this review, with a special emphasis on its phytochemical profile, pharmacological activities, and their relevance in cancer treatment in Southern Africa. This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page *et al.* 2021). The study selection process is summarised and illustrated in Figure 1.

Search Strategy

We conducted a systematic search across six academic databases, namely ResearchGate, Elsevier, PubMed, Scopus, Google Scholar and ScienceDirect, to identify studies reporting on the phytochemical composition and pharmacological activities of *X. caffra* relevant to cancer treatment. The search was conducted using the English language and utilised specific search terms, including *X. caffra*, phytochemicals, anticancer activity, antioxidant activity, ethnopharmacological uses and bioactive compounds. Additional studies were identified by screening the bibliographies of selected articles and relevant reviews.

Study Selection

The titles and abstracts of the retrieved studies were initially screened by the first author for inclusion. Full texts were then reviewed to ensure that studies met the specified inclusion criteria. The second author cross-checked the findings to confirm eligibility. Studies were included if they met the following criteria: (1) focused on the phytochemical or pharmacological aspects of *X. caffra*; (2) included in-vitro and/or in-vivo assessments; (3) published between 2004 and 2024; (4) were peer-reviewed journal articles, conference papers, or relevant reports. Studies were excluded if they were not related to *X. caffra*, did not report relevant bioactivities, or lacked sufficient data on the phytochemical composition. Duplicate publications or those reporting on the same data were resolved by selecting the most recent and comprehensive study.

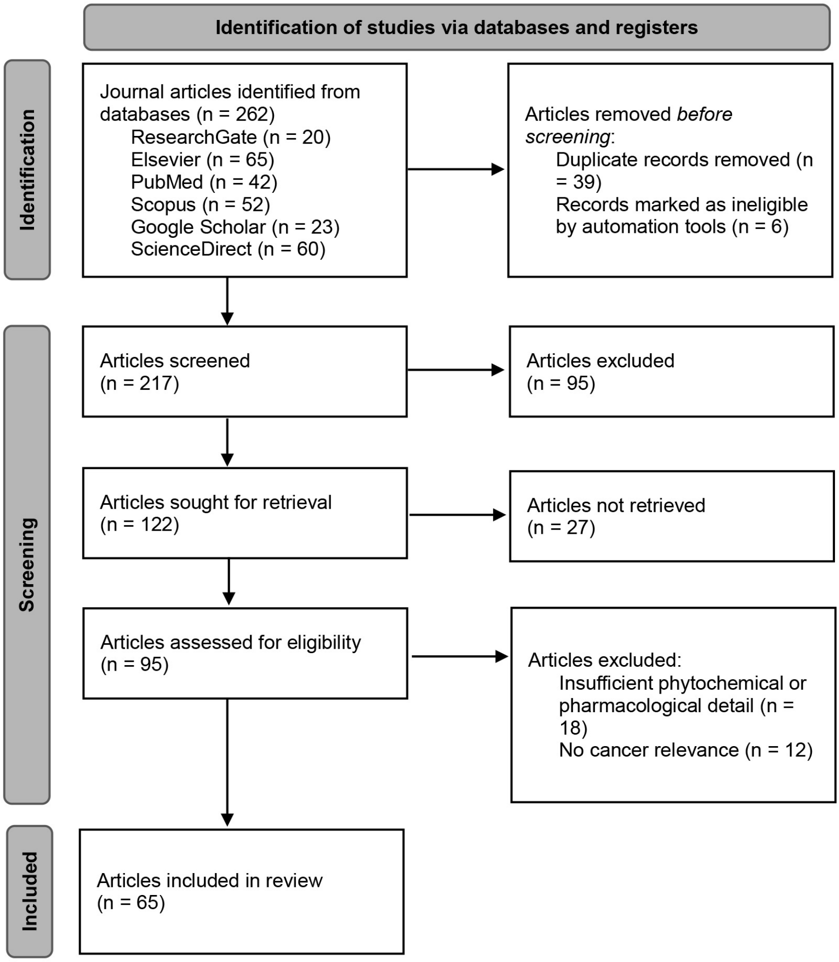

Figure 1: PRISMA flowchart of the study selection process.

Quality Assessment

The methodological quality of the included publications was assessed using a standardised checklist relevant to phytochemical and pharmacological studies. Each study was evaluated based on key criteria, including the rigour of experimental design, relevance of findings and credibility of the source. The first author conducted the assessment, which was subsequently cross-checked by the second author. Any discrepancies were resolved through discussion.

Data Extraction

Data relevant to the phytochemical profiles and pharmacological activities of *X. caffra* were extracted by the first author, focusing on study demographics, methodologies, findings and conclusions. The second author verified the accuracy of the extracted data to ensure reliability. All extracted data were compiled into a predefined data extraction form for analysis, with any disagreements resolved through consensus.

BACKGROUND ON *X. CAFFRA* PLANT

X. caffra, a member of the Olaceceae family, is a well known medicinal and traditional fruit-bearing tree. In Zimbabwe and South Africa, it is known by several common names, including Munhengeni (Shona), Mutsvanzva (Shona), Umthunduluka (Ndebele), Munampeli (Tonga) (Munodawafa 2012), and Mutshili (Venda) (Samie *et al.* 2005). *X. caffra* is a deciduous tree characterised by a dishevelled open crown, capable of reaching heights of up to 6 m in optimal conditions. The outermost layer of this plant is tough and dark grey, while its leaves are leathery and dark green (see Figure 2). The leaves are around 25 mm broad and 60 mm long, with an elliptic to lanceolate shape.

The fruit has an oval shape and green skin that becomes reddish orange when it reaches maturity, according to Orwa *et al.* (2009). The tree's sapwood is white, while its heartwood is dense and reddish brown. The little flowers are creamy green in colour (Cheikhyoussef *et al.* 2011; Van Wyk, Palgrav and Wyk 2013).

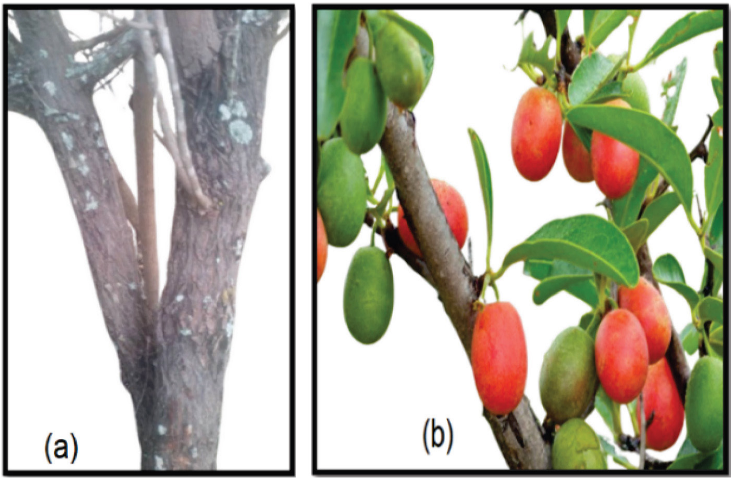

Figure 2: Photograph of *X. caffra* (a) tree trunk and (b) stem, leaves and fruits

X. caffra originated in Kenya, Tanzania, Malawi, Mozambique, Uganda, Zambia and South Africa, as Masuku *et al.* (2020) reaffirmed. According to Cheikhyoussef *et al.* (2011) as well as Van Wyk, Palgrav and Wyk 2013), *X. caffra* is extensively distributed throughout tropical sub-Saharan Africa. The tree is primarily found at medium to high altitudes, in mixed forests, and frequently found on termite mounds. Maluleke *et al.* (2024) noted that *X. caffra* is sometimes found in grasslands and rocky outcrops. *X. caffra* is among the main species in medium- to better-rainfall areas in sub-Saharan Africa.

RESULTS

Ethnopharmacological Uses

The ethnopharmacological uses of a medicinal plant serve as the foundation for modern research about the plant. Various researchers have utilised both documented and orally transmitted pharmacological information about plants to determine where to begin their investigations into medicinal plants. Different researchers have documented several ethnopharmacological uses for *X. caffra* (Chivandi *et al.* 2012; Maroyi 2016; Matowa *et al.* 2020; Shopo *et al.* 2022). According to research by Matowa *et al.* (2020), *X. caffra* fruits, roots, leaves and seeds are processed through infusions and decoctions for the treatment of a wide array of diseases, including cancers, malaria, bilharzia, diarrhoea, intestinal worms and sexually transmitted infections (STIs). According to Matowa *et al.* (2020), various *X. caffra* preparations are commonly used to treat skin, prostate, colon, blood, breast, eye and lung cancers in Zimbabwe's Manicaland Province.

X. caffra has been playing an important role in local food and traditional medicine (Maroyi 2016; Shopo *et al.* 2022). One can consume the fruit fresh or make it into a jam, as it is rich in vitamin C, proteins and minerals. The seed oil is used by the local people to soften leather, skin and for some cosmetic applications (Chivandi *et al.* 2012). As a medicinal plant, the root and leaves of *X. caffra* have been utilised for the treatment of infertility, dyspepsia and gonorrhoea (Cheikhyoussef *et al.* 2011; Mulaudzi *et al.* 2011).

The leaves of *X. caffra* have been documented for use to treat diarrhoea, dysentery, fever, cough and venereal diseases (Green *et al.* 2010). Decoctions from *X. caffra* leaves are used as a wash to soothe inflamed eyes, and infusions of the roots serve as a treatment for dysentery and diarrhoea, while powdered roots are utilised on wounds to expedite recovery (Maluleke *et al.* 2024). Tanzanians use the leaf infusion for fever, syphilis and diarrhoea, while South Africans use it as an eyesight treatment (Maroyi 2016). Researchers have shown that the powdered roots of the plant effectively control bleeding from the mouth and nose, and bovine fertility rituals use its decoction (Munodawafa 2012).

X. caffra leaves and roots are used to treat leprosy, stomach aches, constipation and pulmonary diseases (Ndhlovu and Masika 2012). In addition to being used for fertility and as a febrifuge, dried powdered leaves of *X. caffra* are applied topically to treat dermatophilosis, a skin condition caused by the bacteria *Dermatophilus congolensis* (Mulaudzi *et al.* 2011; Nair *et al.* 2013). According to (Mabogo 2012), the Venda tribe uses the leaves and/or roots as a remedy for headaches, diarrhoea, coughing and STIs. To increase desire for sex, dried powdered *X. caffra* roots are combined with soup or added to brews (Masuku *et al.* 2020). To relieve sore eyes and cure tonsillitis, a leaf decoction is utilised (Masuku *et al.* 2020). Additionally, diarrhoea and gonorrhoea infections are treated using a boiling mixture made from *X. caffra* roots (De Wet *et al.* 2012).

The medicinal uses of *X. caffra*, a plant of significant ethnopharmacological value, have been thoroughly investigated. Research studies have emphasised the medicinal properties of its fruits, roots, leaves and seeds for treating a range of illnesses, including cancers, malaria, gastrointestinal problems and STIs. In addition to its medicinal uses, *X. caffra* is also a useful ingredient in cooking and cosmetic operations.

Phytochemical Profile

This section discusses the phytochemical profile of *X. caffra*, revealing its varied chemical components. This section sheds light on the compounds that contribute to the medicinal properties of the plant. Plants that possess medicinal properties are known to contain numerous phytochemicals. Plants produce these phytochemicals as secondary metabolites which include organic compounds such as phenolic acids, tannins, saponins, flavonoids, steroids and alkaloids in response to various environmental conditions (Masuku *et al.* 2020; Mkhonto *et al.* 2023; Munodawafa 2012; Oosthuizen *et al.* 2018; Tlaamela *et al.* 2023; Zhen *et al.* 2015).

Numerous researchers have conducted phytochemical studies on *X. caffra* plants found in Southern Africa, including Zimbabwe (Masuku *et al.* 2020; Munodawafa *et al.* 2013; Ndhlala *et al.* 2006). Researchers have identified, isolated and quantified a wide range of bioactive phytochemicals from *X. caffra* using various analytical techniques, the classes are listed in Table 1.

Table 1: Classes of compounds identified in *X. caffra* by different researchers.

Class of compound	Methods used for identification	Plant part	References
Flavonoids	Thin-layer chromatography (TLC) with UV-detection and UV-Visible spectrometry	Roots and leaves	Munodawafa *et al.* (2013); Zhen *et al.* (2015); Oosthuizen *et al.* (2018); Masuku *et al.* (2020); Ndhlala *et al.* (2008)
Phenolics	Folin-Ciocalteu method	Fruits	Oosthuizen *et al.* (2018); Zhen *et al.* (2015); Masuku *et al.* (2020); Ndhlala *et al.* (2008)
Saponins	TLC with UV-detection	Leaves	Munodawafa *et al.* (2013)
Coumarins	TLC with UV-detection	Leaves	Munodawafa *et al.* (2013)
Glycosides	TLC with UV-detection Mass spectrometry	Leaves	Munodawafa *et al.* (2013); Zhen *et al.* (2015)
Tannins	TLC with UV-detection Phytochemical screening assay	Leaves, Fruits	Munodawafa *et al.* (2013); Ndhlala *et al.* (2008)
Anthraquinones	TLC with UV-detection	Leaves	Munodawafa *et al.* (2013)
Alkaloids	TLC with UV-detection	Leaves	Munodawafa *et al.* (2013)

Munodawafa *et al.* (2013) used TLC with reagent sprays and ultraviolet (UV) light detection to study the phytochemical profile of *X. caffra* found in Zimbabwe. They discovered flavonoids, saponins, coumarins, cardiac glycosides, anthraquinones, alkaloids and tannins in the plant's root and leaf extracts.

A phytochemical study in South Africa revealed the presence of significant content of phenolics in the range of 6.86 ± 0.26 to 85.5 ± 9.27 mg/g gallic acid equivalents (GAE) in *X. caffra* leaf extracts. The same *X. caffra* extracts gave a total flavonoid content in the range of 0.1–1.05 mg/g quercetin equivalent, which is much higher compared to the other plant extracts investigated in the same study (Masuku *et al.* 2020).

Oosthuizen *et al.* (2018) have also investigated the phytochemical composition of the *X. caffra* fruits, in addition to the root and leaf extracts. In their research, Oosthuizen *et al.* (2018) extracted, identified and quantified a handful of phytochemical compounds from the skin of *X. caffra* extract. In the fruit extracts of *X. caffra*, there was a total phenolic content of up to 6,487 ± 1,203 mg/l of gallic acid equivalent and up to 4,000 ± 1,480 mg/l of catechin equivalent (Oosthuizen *et al.* 2018). So, the total phenolic content was high.

Several additional researchers have identified and isolated various compounds from *X. caffra* plant extracts (Ndhlala *et al.* 2006; Oosthuizen *et al.* 2018; Tlaamela *et al.* 2023; Zhen *et al.* 2015). Researchers successfully isolated various phytochemical compounds from *X. caffra* plants found in Southern Africa, as shown in Table 2.

Table 2: Compounds isolated from *Ximenia caffra* by different researchers.

Compounds identified	**Methods used for identification**	**References**
Catechin, citric acid, epicatechin, gallic acid, hesperetin, hyperoside, isoquercitrin, kaemferol glucoside, luteolin-7-O-glucoside, procyanidin B1, procyanidin B2, quercetin-3-O-glucoside, quercetin-3-O-robinobioside, quercetin and rutin	Liquid chromatography High resolution mass spectrometry (LC-HRMS)	Oosthuizen *et al.* (2018)
Gallic acid, Catechin, Quercetin	Liquid chromatography-mass spectrometry (LC-MS)	Zhen *et al.* (2015)
Epigallocatechin gallate, Kaempferol-3-rhamnoside	Nuclear magnetic resonance (NMR) and Mass spectrometry	Tlaamela *et al.* (2023)
Vanillic acid, caffeic acid, p-coumaric acid, ferulic acid	High performance liquid chromatography (HPLC)	Ndhlala *et al.* (2008)

Oosthuizen *et al.* (2018) positively identified several compounds in *X. caffra* fruit extracts using Liquid Chromatography High-Resolution Mass Spectrometry (LC-HRMS). The same research identified aconitic acid, procyanidin and quercetin derivatives in *X. caffra* fruit extract (Oosthuizen *et al.* 2018).

On their study to evaluate the antifungal activity and potential toxicity of phytochemicals extracted from *X. caffra* leaves, Tlaamela and co-workers (Tlaamela *et al.* 2023) managed to isolate epigallocatechin gallate and kaempferol-3-rhamnoside. Epigallocatechin gallate is well known potent antioxidant and polyphenolic anti-inflammatory compound which is an abundant component of catechins in green teas (Tlaamela *et al.* 2023).

Ndhlala *et al.* (2008) successfully identified phenolic compounds, including tannins, flavonols, phenolic acids and proanthocyanins, in *X. caffra* fruit skin extracts. In 2008, Ndhlala *et al.* (2008) found that *X. caffra* fruit extracts had up to 1,125.07 ± 22.687 μg/g of total phenolics, up to 27,118 ± 1.347 μg/g of flavonoids, and up to 1.169 ± 0.054% of proanthocyanins. Ndhlala *et al.* (2008) also isolated and identified some bioactive compounds from *X. caffra*. It was proven by high performance liquid chromatography that *X. caffra* fruit extracts contained vanillic acid, caffeic acid, p-coumaric acid and ferulic acid (Ndhlala *et al.* 2008).

Overall, a lot of research conducted in Southern Africa has shown that *X. caffra* has a lot of bioactive compounds in its phytochemical profile. These include flavonoids, phenolics, saponins, coumarins, glycosides, tannins, anthraquinones and alkaloids. Researchers have isolated compounds such as epigallocatechin gallate and kaempferol-3-rhamnoside from *X. caffra* leaves, offering insights into their potential medicinal applications. Moreover, researchers have identified compounds like vanillic acid and ferulic acid in *X. caffra* fruits, indicating their significant phenolic contents and pharmacological significance. These findings highlight the potential of *X. caffra* as a source of bioactive natural chemicals and lead compounds for pharmaceutical applications.

Pharmacological Activities

X. caffra exhibits a spectrum of pharmacological activities, ranging from antimicrobial and antioxidant effects to anti-inflammatory and analgesic properties. Understanding these activities enhances our appreciation of the plant's holistic health benefits. This review focuses on anticancer, antioxidant, antimicrobial and anti-inflammatory activities and the toxicity of *X. caffra* plant extracts since they are all directly relevant to cancer treatment.

Anticancer activity

The anticancer potential of plant extracts is one of the most important properties of medicinal plants. Anticancer properties directly address the plant's potential effectiveness in targeting cancer cells, inhibiting tumour growth or inducing cancer cell death. Researchers use scientific evidence to validate the effectiveness of plant extracts against cancer cells, paving the way for their potential integration into cancer treatment protocols. Several researchers have investigated the potential anticancer activity of the *X. caffra* plant extracts on different cancer cells using in-vitro assays.

To determine the potential anticancer activity of *X. caffra* extracts, Zhen *et al.* (2015) conducted MTT assays on cultured RAW 264.7 cells (macrophage-like cancerous cells) using *X. caffra* extracts, and the results showed that the viability of RAW 264.7 cells decreased with an increase in *X. caffra* extract dose. An IC50 value of 239.0 ± 44.5 µg/ml was obtained in this study, indicating that *X. caffra* leaf extracts can inhibit the growth of RAW 264.7 cells, thus showing a cytotoxic effect.

In one research study by Gomes *et al.* (2019), the seed oils of *X. caffra* and other fruit oils have previously shown anti-proliferative responses in Caco-2 and HEK-293 cells in in-vitro studies. *X. caffra* seed oils had the most significant lethal effects on hormone-independent MDA-MB-231 breast cancer cells and showed a growth-inhibitory impact on hormone-dependent MCF-7 breast cancer cells (Gomes *et al.* 2019). *X. caffra* seed oils were found to inhibit the growth of human embryonic kidney (HEK-293) and colon cancer (Caco-2) cells in earlier research (Chivandi *et al.* 2012; Gomes *et al.* 2019).

Researchers have conducted MTT assays, revealing a dose-dependent decrease in the viability of RAW 264.7 cells with *X. caffra* leaf extracts, indicating cytotoxic effects. Additionally, studies on *X. caffra* seed oils showcased anti-proliferative effects on various cancer cell lines, including breast, kidney and colon cancer cells, showing its broad spectrum of activity. These findings provide compelling evidence supporting *X. caffra*'s potential as a valuable component in cancer treatment strategies.

We found no in-vivo anticancer studies on *X. caffra* to date in this review. However, one in-vivo study revealed the hepatoprotective property of *X. caffra* in rats (Sobeh *et al.* 2017). According to the study by Sobeh *et al.* (2017), administration of *X. caffra* root extract at a dose of 100 mg/kg significantly reduced the activities of liver enzymes; alanine aminotransferase, aspartate aminotransferase and gamma-glutamyltransferase in rats pre-treated with d-galactosamine, suggesting its protective effect on hepatocytes. This reduction in enzyme levels indicates that *X. caffra* may help mitigate liver damage, an essential factor considering the liver's role in drug metabolism and overall health during cancer treatment.

Antioxidant activity

Antioxidants are known to neutralise free radicals, which can cause oxidative stress, a key factor in cancer development. We highlight the antioxidant capacity of *X. caffra*, highlighting its role in neutralising harmful free radicals. Such antioxidative prowess is integral to preventing cellular damage from cancers and supporting overall health. *X. caffra* extract's antioxidant activity was determined by Zhen *et al.* (2015), using the ABTs assay and employing Trolox as a standard. This research showed that *X. caffra* extracts gave a total antioxidant capacity of 1.46 ± 0.01 mmol Trolox/g, which was concluded to be a significantly high antioxidant activity (Zhen *et al.* 2015).

Masuku *et al.* (2020) conducted separate research on medicinal plants found in South Africa, using the DPPH radical scavenging assay to determine the antioxidant activity of *X. caffra* against a standard antioxidant, ascorbic acid. The IC50 value for *X. caffra* extract was lower than that of ascorbic acid (1,473.3 ± 1.335 μg/ml), which means it was better at getting rid of DPPH radicals than the standard antioxidant. According to the results of the phytochemical study by Masuku *et al.* (2020), *X. caffra* showed a significant potent antioxidant activity.

In another research study to investigate phytochemicals in *X. caffra* fruit extracts, Oosthuizen *et al.* (2018) indicated that *X. caffra* fruit extracts exhibit a remarkable antioxidant capacity of up to 18.2 mg/l ascorbic acid equivalent using the N, N-Dimethyl-p-phenylenediamine dihydrochloride (DMPD) assay method. *X. caffra* had the highest antioxidant activity (95.7 ± 0.0707%) values in Munodawafa's investigation (Munodawafa 2012). Ndhlala *et al.* (2006) also discovered high antioxidant levels in *X. caffra* fruit.

Numerous investigations using diverse tests have proven the strong antioxidant properties of *X. caffra*. Research highlighting its ability to scavenge free radicals highlights its importance in reducing oxidative stress and cellular damage. Researchers using ABTs and DPPH tests have found that *X. caffra* is a very good antioxidant that works better than common antioxidants like ascorbic acid. Interestingly, its fruit extracts contain significant quantities of antioxidants, suggesting that it may help prevent illnesses linked to oxidative stress and improve general health. Together, these results highlight the importance of *X. caffra* as a natural source of antioxidants with major health benefits for people, including anticancer properties.

Antimicrobial activity

Cancer patients often have weakened immune systems, making them more susceptible to infections. The antimicrobial properties of medicinal plants could suggest their potential role in managing secondary infections in cancer patients and enhancing overall immune function during treatment (Usmani *et al.* 2021). Researchers have explored *X. caffra's* antimicrobial properties, showcasing its ability to combat various pathogens. This knowledge contributes to its potential as a multifaceted therapeutic agent. *X. caffra* leaf and root extracts were shown to be the most active plant extracts against gram-positive *Staphylococcus aureus* and *Streptococcus* Group A under antimicrobial tests using the agar-diffusion method (Munodawafa *et al.* 2013). In the same investigation, Munodawafa *et al.* (2013) showed that *X. caffra* extracts were also very strongly active against gram-negative *Escherichia coli* and *Pseudomonas aeruginosa*.

According to Munodawafa (2012), the root extract of *X. caffra*, which had an area of 10.75 ± 0.5 mm, had the highest level of microbiological inhibition against *Escherichia coli* of all the samples that were studied. *X. caffra's* minimal inhibitory concentration in the Fabry *et al.* (1998) investigations varied from 0.13 to 8 mg/ml, but values in the Munodawafa (2012) study ranged from 0.625 to 10 mg/ml. Prior research on antibacterial efficacy revealed that *X. caffra* was effective against 105 strains of bacteria from seven distinct taxonomic groups (Fabry *et al.* 1998). Fabry *et al.* (1998) have also demonstrated the plant's fungicidal and fungistatic features.

In research conducted by Tlaamela *et al.* (2023) on *X. caffra* leaf extracts, it has been established that one of the isolated compounds, epigallocatechin gallate, exhibited remarkable antifungal activity against *Candida albicans* with minimum inhibitory concentrations (MIC) of 0.5 mg/ml. Zhang *et al.* (2016) reported that epigallocatechin gallate possesses antioxidant, antimicrobial and anticancer activities, supporting the antimicrobial activity results obtained by Tlaamela *et al.* (2023). Weber *et al.* (2015) also reported the antiviral activity of epigallocatechin gallate against Chikungunya virus. Many other pharmacological studies have investigated and confirmed the biological properties of *X. caffra's* leaf and root, such as their ability to fight gonococcal, bacterial and fungal infections (Mulaudzi *et al.* 2011; Nair *et al.* 2013).

X. caffra's leaf and root extracts exhibit strong antimicrobial activity against both gram-positive and gram-negative bacteria. Research has also demonstrated its broad spectrum antimicrobial potential against pathogens like *Streptococcus* Group A, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Furthermore, studies have demonstrated the remarkable antifungal activity of isolated compounds like epigallocatechin gallate against *Candida albicans*, underscoring *X. caffra's* versatility as a therapeutic agent. Finally, pharmacological studies have demonstrated the plant's diverse biological properties, including antigonococcal, antibacterial and antifungal activities, emphasising its importance in the fight against infectious diseases.

Anti-inflammatory activity

Chronic inflammation is a well-established contributor to cancer development and progression. As described by Greten and Grivennikov (2019), inflammatory processes can promote tumorigenesis through complex interactions between cancer cells and surrounding stromal and inflammatory cells, facilitating tumour initiation, growth and metastasis. Zhao *et al.* (2021) further elucidate that chronic inflammation not only fosters tumour progression but also contributes to treatment resistance. Evaluating the anti-inflammatory properties of medicinal plants can help determine whether the plant has the potential to reduce inflammation, thereby limiting cancer risks and improving treatment outcomes. We examine the anti-inflammatory properties of different medicinal products to understand their potential to mitigate inflammatory responses. This aspect is crucial in understanding the applicability of the medicinal product in conditions marked by chronic inflammation, including cancer. Zhen *et al.* (2015) used quantitative Polymerase Chain Reaction (qPCR) to investigate the inflammatory activity of *X. caffra* leaf extracts on inflammatory enzymes and proinflammatory cytokines. *X. caffra* leaf extracts had a dose-dependent effect on the expression of inflammatory enzymes and pro-inflammatory cytokines, with a maximum reduction of 60% in (nuclear factor kappa B) NF-kB expression observed at a concentration of 312.5 µg/ml (Zhen *et al.* 2015).

In addition to the health benefits of the leaf and root extracts, seeds from *X. caffra* fruits are rich in vitamins, fatty acids and essential amino acids (Chivandi *et al.* 2011). Studies (Al-Sheddi *et al.* 2015; Costantini *et al.* 2014; Guo *et al.* 2016; Seal *et al.* 2012; Vieira *et al.* 2008) have linked these seeds to anti-inflammatory and anti-proliferative properties that may slow the growth of tumours.

Examining the potential of medicinal plants such as *X. caffra* to reduce inflammation opens up new treatment options for chronic inflammatory diseases. Research highlighted the potential of *X. caffra* leaf extracts in reducing inflammatory responses by modulating inflammatory enzymes and cytokines. Furthermore, studies have linked the nutrient-dense seeds of *X. caffra* fruits to anti-inflammatory and anti-proliferative effects, offering further therapeutic advantages. These results demonstrate the versatility of *X. caffra* as a potential treatment for inflammatory conditions, underscoring the plant's significance in both conventional and alternative medicine.

Toxicity

Assessing the toxicity profile of medicinal plants is imperative for ensuring their safe use. Researchers have conducted several studies to determine the toxicity of *X. caffra* extracts (Masuku *et al.* 2020; Moshi *et al.* 2004; Tlaamela *et al.* 2023). They did cytotoxicity tests on *X. caffra* leaf extracts and found that different solvent extracts of *X. caffra* are less harmful to TM3 Leydig cells (IC50 of 244 ± 0.004 to 749 ± 0.138 µg/ml) using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay (Masuku *et al.* 2020). The results showed that all the *X. caffra* solvent extracts kept cells alive and did not kill them, as the IC50 values were much higher than 20 µg/ml (Masuku *et al.* 2020).

Tlaamela *et al.* (2023) conducted a research study where they found that compounds isolated from *X. caffra* leaf extracts exhibited moderate toxicity against African green monkey kidney cells, concluding that these isolates are safe for medicinal applications, including oral use for combating oral candidiasis.

The Brine Shrimp Lethality Test (BSLT) was used to see how toxic the *X. caffra* extracts were. The root extract had an LC50 value of 1,590 ± 752 µg/ml and the leaf extract had an LC50 value of 1,020 ± 52.7 µg/ml. These values were compared to the known toxic plant *Nerium oleander*, which was used as a positive control and had an LC50 value of 142 ± 68.2 µg/ml (Munodawafa 2012). The results indicate that the plant is safe for use, which may explain its widespread use by traditional healers without any reported issues to date.

However, a study by Moshi *et al.* (2004) reported a markedly different LC50 value of 11.3 µg/ml for *X. caffra* extracts in the context of the BSLT, suggesting potential toxicity. We can attribute the observed differences in results to variations in collection environments, extraction methods and the duration of exposure to brine shrimp. Such variations indicate the importance of standardised protocols in toxicity assessments and suggest that *X. caffra* may indeed possess toxic properties or contain cytotoxic compounds that are not very harmful and cannot be recognised by traditional healers.

Animal toxicity studies on *X. caffra* extracts and its plant materials are limited. (Chivandi *et al.* 2016) demonstrated the potential non-toxicity of *X. caffra* kernel meal as a dietary protein source in Sprague Dawley rats. Their results indicated that substituting soybean meal with *X. caffra* kernel meal did not significantly alter serum markers related to liver and kidney function, nor did it affect blood glucose and cholesterol levels. These findings suggest that *X. caffra* is potentially non-toxic and safe for consumption, highlighting its promise as a candidate for further research in cancer treatment.

It is necessary to assess the toxicity of medicinal plants such as *X. caffra* to guarantee their safe use. There are conflicting results in the literature about the toxicity profile of extracts from *X. caffra*. Some studies indicate mild toxicity against specific cell lines, despite cytotoxicity tests showing that various solvent extracts of *X. caffra* leaves are non-toxic to cells. A long history of use without documented side effects demonstrates its relative safety. To determine acceptable usage parameters, thorough toxicity studies are necessary.

CONCLUSION

The diverse pharmacological activities of *X. caffra*, directly relevant to cancer treatment, along with its extensive ethnopharmacological history, position it as a promising candidate for cancer treatment. The review shows that *X. caffra* has significant potential as a useful resource for treating cancer due to its wide range of phytochemicals and pharmacological activities. The in-vitro antioxidant, antimicrobial and anti-inflammatory activities of the plant extracts are clear indications of their anticancer potential. The historical traditional use and documented efficacy against various cancer types underscore the need for further exploration and validation of its therapeutic benefits. While in-vitro studies have provided promising insights, there is a crucial need for more comprehensive in-vivo assessments to confirm its safety and efficacy. The discovery and isolation of bioactive compounds from *X. caffra* also opens exciting new research areas such as modification of the isolated compounds to improve activity. To fully utilise its medicinal potential, modern analytical methods must be employed to investigate *X. caffra's* anticancer potential. We highly recommend conducting in-vivo studies to fully understand *X. caffra's* therapeutic potential and facilitate its integration into mainstream healthcare practices.

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REFERENCES

AHMED, M. B., ISLAM, S. U., ALGHAMDI, A. A. A., KAMRAN, M. *et al*. (2022) Phytochemicals as chemo-preventive agents and signaling molecule modulators: Current role in cancer therapeutics and inflammation, *International Journal of Molecular Sciences*, 23(24): 15765. https://doi.org/10.3390/ijms232415765

AL-SHEDDI, E. S., FARSHORI, N. N., AL-OQAIL, M. M., MUSARRAT, J. *et al.* (2015) Portulaca oleracea seed oil exerts cytotoxic effects on human liver cancer (HepG2) and human lung cancer (A-549) cell lines, *Asian Pacific Journal of Cancer Prevention*, 16(8): 3383–3387. https://doi.org/10.7314/APJCP.2015.16.8.3383

BHANOT, A., SHARMA, R., & NOOLVI, M. N. (2011) Natural sources as potential anti-cancer agents: A review, *International Journal of Phytomedicine*, 3: 9–26.

CHEIKHYOUSSEF, A., SHAPI, M., MATENGU, K., & MU ASHEKELE, H. (2011) Ethnobotanical study of indigenous knowledge on medicinal plant use by traditional healers in Oshikoto region, Namibia, *Journal of Ethnobiology and Ethnomedicine*, 7(1): 1–11. https://doi.org/10.1186/1746-4269-7-10/TABLES/3

CHHIKARA, B. & PARANG, K. (2023) Global Cancer Statistics 2022: The trends projection analysis, *Chemical Biology Letters*, 10(1): 1–16.

CHINGWARU, C., BAGAR, T. & CHINGWARU, W. (2020) *Aqueous extracts of Flacourtia indica, Swartzia madagascariensis* and *Ximenia caffra* are strong antibacterial agents against *Shigella spp.*, *Salmonella typhi* and *Escherichia coli* O157, *South African Journal of Botany*, 128: 119–127. https://doi.org/10.1016/j.sajb.2019.10.022

CHIVANDI, E., CAVE, E., DAVIDSON, B. C., ERLWANGER, K. H. *et al.* (2012) Suppression of Caco-2 and HEK-293 cell proliferation by *Kigelia africana*, *Mimusops zeyheri* and *Ximenia caffra* seed oils, *In Vivo (Athens, Greece)*, 26(1): 99–105.

CHIVANDI, E., DAVIDSON, B., PRETORIUS, B. & ERLWANGER, K. (2011) Proximate, mineral, amino acid, fatty acid, vitamin E, phytate phosphate and fibre composition of *Mimusops zeyheri* (Red Milkwood) seed, *International Journal of Food Science and Technology*, 46(3): 555–560. https://doi.org/10.1111/j.1365-2621.2010.02518.x

CHIVANDI, E., MOYO, D., DANGAREMBIZI, R., & ERLWANGER, K. (2016) Effect of dietary *Ximenia caffra* kernel meal on blood and liver metabolic substrate content and the general clinical biochemistry of Sprague Dawley rats, *Journal of Animal Physiology and Animal Nutrition*, 100(3): 471–477. https://doi.org/10.1111/jpn.12393

COSTANTINI, S., RUSOLO, F., DE VITO, V., MOCCIA, S. *et al.* (2014) Potential anti-inflammatory effects of the hydrophilic fraction of pomegranate (*Punica granatum* L.) seed oil on breast cancer cell lines, *Molecules 2014*, 19(6): 8644–8660. https://doi.org/10.3390/MOLECULES19068644

CRAGG, G. M. & NEWMAN, D. J. (2005). Plants as a source of anti-cancer agents, *Journal of Ethnopharmacology*, 100(1–2): 72–79. https://doi.org/10.1016/J.JEP.2005.05.011

DAHLBERG, A. C. & TRYGGER, S. B. (2009) Indigenous medicine and primary health care: The importance of lay knowledge and use of medicinal plants in Rural South Africa, *Human Ecology*, 37(1): 79–94. https://doi.org/10.1007/s10745-009-9217-6

DE WET, H., NZAMA, V. N. & VAN VUUREN, S. F. (2012) Medicinal plants used for the treatment of sexually transmitted infections by lay people in northern Maputaland, KwaZulu–Natal Province, South Africa, *South African Journal of Botany*, 78: 12–20. https://doi.org/10.1016/J.SAJB.2011.04.002

FABRY, W., OKEMO, P. O. & ANSORG, R. (1998) Antibacterial activity of East African medicinal plants, *Journal of Ethnopharmacology*, 60(1): 79–84. https://doi.org/10.1016/S0378-8741(97)00128-1

FAKUDZE, N. T., SARBADHIKARY, P., GEORGE, B. P. & ABRAHAMSE, H. (2023) Ethnomedicinal uses, phytochemistry, and anticancer potentials of African medicinal fruits: A comprehensive review, *Pharmaceuticals*, 16(8): 1117. https://doi.org/10.3390/PH16081117

GOMES, M. N., AUGUSTINE, T. N., MOYO, D., & CHIVANDI, E. (2019) Differential response of breast cancer cell lines to *Kigelia africana*, *Ximenia caffra* and *Mimusops zeyheri* seed oils, *South African Journal of Botany*, 121: 463–469. https://doi.org/10.1016/J.SAJB.2018.12.017

GREEN, E., SAMIE, A., OBI, C. L., BESSONG, P. O. *et al.* (2010) Inhibitory properties of selected South African medicinal plants against Mycobacterium tuberculosis, *Journal of Ethnopharmacology*, 130(1): 151–157. https://doi.org/10.1016/J.JEP.2010.04.033

GRETEN, F. R. & GRIVENNIKOV, S. I. (2019) Inflammation and cancer: Triggers, mechanisms, and consequences, *Immunity*, 51(1): 27–41. https://doi.org/10.1016/j.immuni.2019.06.025

GUO, G., YUE, L., FAN, S., JING, S. *et al*. (2016) Antioxidant and antiproliferative activities of purslane seed oil, *Journal of Hypertension : Open Access*, 5(2): 1000218. https://doi.org/10.4172/2167-1095.1000218

HILL, J., SEGUIN, R., MANDA, A., CHIKASEMA, M. *et al*. (2022) Prevalence of traditional, complementary, and alternative medicine (TCAM) among adult cancer patients in Malawi, *Cancer Causes & Control: CCC*, 33(8): 1047–1057. https://doi.org/10.1007/S10552-022-01563-0

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER. (2024) Global cancer burden growing, amidst mounting need for services, https://www.iarc.who.int/news-events/global-cancer-burden-growing-amidst-mounting-need-for-services/ (1 February 2024).

JAMES, P. B., WARDLE, J., STEEL, A. & ADAMS, J. (2018) Traditional, complementary and alternative medicine use in Sub-Saharan Africa: A systematic review, *BMJ Global Health*, 3(5): e000895. https://doi.org/10.1136/BMJGH-2018-000895

MABOGO, D. (2012) The ethnobotany of the Vhavenda, Master diss., University of Pretoria.

MALULEKE, M. K., BOITUMELO, L. & MAROKANE-RADEBE, C. K. (2024) Exploring the biochemical constituents, medicinal properties and potential commercialization of *Ximenia caffra* Sond. for enhancing human health: A comprehensive review, *Discover Applied Sciences*, 6(1): 1–13. https://doi.org/10.1007/S42452-024-05639-1/TABLES/4

MAROYI, A. (2013) Traditional use of medicinal plants in south-central Zimbabwe: Review and perspectives, *Journal of Ethnobiology and Ethnomedicine*, 9(1), 1–18. https://doi.org/10.1186/1746-4269-9-31/FIGURES/3

MAROYI, A. (2016) *Ximenia caffra* Sond. (Ximeniaceae) in sub-Saharan Africa: A synthesis and review of its medicinal potential, *Journal of Ethnopharmacology*, 184: 81–100. https://doi.org/10.1016/J.JEP.2016.02.052

MASUKU, N. P., UNUOFIN, J. O. & LEBELO, S. L. (2020) Phytochemical content, antioxidant activities and androgenic properties of four South African medicinal plants, *Journal of Herbmed Pharmacology*, 9(3): 245–256. https://doi.org/10.34172/JHP.2020.32

MATOWA, P. R., GUNDIDZA, M., GWANZURA, L. & NHACHI, C. F. B. (2020) A survey of ethnomedicinal plants used to treat cancer by traditional medicine practitioners in Zimbabwe, *BMC Complementary Medicine and Therapies*, 20(1): 1–13. https://doi.org/10.1186/S12906-020-03046-8/TABLES/7

MKHONTO, C., MAKANANISE, V., SAGBO, I. J., MASHABELA, M. N. *et al.* (2023) UPLC–QTOF/MS tentative identification of phytochemicals from *Vernonia amygdalina* Delile acetone and ethanol leaf extracts, *Journal of Medicinal Plants for Economic Development*, 7(1): a181. https://doi.org/10.4102/JOMPED.V7I1.181

MLILO, S. & SIBANDA, S. (2022) An ethnobotanical survey of the medicinal plants used in the treatment of cancer in some parts of Matebeleland, Zimbabwe, *South African Journal of Botany*, 146: 401–408. https://doi.org/10.1016/J.SAJB.2021.11.022

MOKHESI, T. & MODJADJI, P. (2022) Usage of traditional, complementary and alternative medicine and related factors among patients receiving healthcare in Lesotho, *The Open Public Health Journal*, 15(1). https://doi.org/10.2174/18749445-V15-E2202090

MORAES, D. F. C., DE MESQUITA, L. S. S., DO AMARAL, F. M. M., DE SOUSA RIBEIRO, M. N. *et al.* (2017) Anticancer drugs from plants, *Biotechnology and Production of Anti-Cancer Compounds*, 121–142. https://doi.org/10.1007/978-3-319-53880-8_5

MOSHI, M. J., COSAM, J. C., MBWAMBO, Z. H., KAPINGU, M. *et al.* (2004) Testing beyond ethnomedical claims: Brine shrimp lethality of some Tanzanian plants, *Pharmaceutical Biology*, 42(7): 547–551. https://doi.org/10.3109/13880200490897920

MOTEETEE, A. & SELETENG KOSE, L. (2016) Medicinal plants used in Lesotho for treatment of reproductive and post reproductive problems, *Journal of Ethnopharmacology*, 194: 827–849. https://doi.org/10.1016/J.JEP.2016.10.062

MUDONHI, N., NUNU, W. N., SIBANDA, N. & KHUMALO, N. (2021) Exploring traditional medicine utilisation during antenatal care among women in Bulilima District of Plumtree in Zimbabwe, *Scientific Reports*, 11(1). https://doi.org/10.1038/S41598-021-86282-3

MULAUDZI, R. B., NDHLALA, A. R., KULKARNI, M. G., FINNIE, J. F. *et al.* (2011) Antimicrobial properties and phenolic contents of medicinal plants used by the Venda people for conditions related to venereal diseases, *Journal of Ethnopharmacology*, 135(2): 330–337. https://doi.org/10.1016/J.JEP.2011.03.022

MUNODAWAFA, T. (2012) Screening of some traditional medicinal plants from Zimbabwe for biological and anti-microbial activity, Masters diss., University of Zimbabwe.

MUNODAWAFA, T., CHAGONDA, L. S. & MOYO, S. R. (2013) Antimicrobial and phytochemical screening of some Zimbabwean medicinal plants, *Journal of Biologically Active Products from Nature*, 3(5–6): 323–330. https://doi.org/10.1080/22311866.2013.782759

NAIR, J. J., MULAUDZI, R. B., CHUKWUJEKWU, J. C., VAN HEERDEN, F. R. *et al.* (2013) Antigonococcal activity of *Ximenia caffra* Sond. (Olacaceae) and identification of the active principle, *South African Journal of Botany*, 86: 111–115. https://doi.org/10.1016/J.SAJB.2013.02.170

NDHLALA, A. R., MUCHUWETI, M., MUPURE, C., CHITINDINGU, K. *et al.* (2008) Phenolic content and profiles of selected wild fruits of Zimbabwe: *Ximenia caffra*, *Artobotrys brachypetalus* and *Syzygium cordatum*, *International Journal of Food Science & Technology*, 43(8): 1333–1337. https://doi.org/10.1111/J.1365-2621.2007.01611.X

NDHLALA, A. R., MUPURE C. H., CHITINDINGU, K., BENHURA, M. A. N. *et al.* (2006) Antioxidant potentials and degrees of polymerization of six wild fruits, *Scientific Research and Essay*, 1(3): 087–092.

NDHLOVU, D. N. & MASIKA, P. J. (2012) Ethno-veterinary control of bovine dermatophilosis and ticks in Zhombe, Njelele and Shamrock resettlement in Zimbabwe, *Tropical Animal Health and Production*, 45(1): 525–532. https://doi.org/10.1007/S11250-012-0253-7/TABLES/6

OCHWANG'I, D. O., KIMWELE, C. N., ODUMA, J. A., GATHUMBI, P. K. *et al*. (2014) Medicinal plants used in treatment and management of cancer in Kakamega County, Kenya. *Journal of Ethnopharmacology*, 151(3): 1040–1055. https://doi.org/10.1016/J.JEP.2013.11.051

OOSTHUIZEN, D., GOOSEN, N. J., STANDER, M. A., IBRAHIM, A. D. *et al*. (2018) Solvent extraction of polyphenolics from the indigenous african fruit *ximenia caffra* and characterization by LC-HRMS. *Antioxidants 2018*, 7(8): 103. https://doi.org/10.3390/ANTIOX7080103

ORWA, C., MUTUA, A., KINDT, R., JAMNADASS, R. *et al*. (2009) Agroforestree Database: A tree reference and selection guide, Version 4.

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I. *et al*. (2021) The PRISMA 2020 statement: An updated guideline for reporting systematic reviews, *BMJ 2021*, 372: n71. https://doi.org/10.1136/bmj.n71

PELTZER, K. (2009) Utilization and practice of traditional/complementary/alternative medicine (TM/CAM) in South Africa, *African Journal of Traditional, Complementary, and Alternative Medicines*, 6(2): 175–185.

SAMIE, A., OBI, C., BESSONG, P. & NAMRITA, L. (2005) Activity profiles of fourteen selected medicinal plants from Rural Venda communities in South Africa against fifteen clinical bacterial species, *African Journal of Biotechnology*, 4(12): 1443–1451.

SEAL, S., CHATTERJEE, P., BHATTACHARYA, S., PAL, D. *et al.* (2012) Vapor of volatile oils from litsea cubeba seed induces apoptosis and causes cell cycle arrest in lung cancer cells. *PLOS ONE*, 7(10): e47014. https://doi.org/10.1371/JOURNAL.PONE.0047014

SHOPO, B., MAPAYA, R. J. & MAROYI, A. (2022) Ethnobotanical study of medicinal plants traditionally used in Gokwe South District, Zimbabwe, *South African Journal of Botany*, 149: 29–48. https://doi.org/10.1016/J.SAJB.2022.05.052

SOBEH, M., MAHMOUD, M. F., ABDELFATTAH, M. A. O., EL-BESHBISHY, H. A. *et al.* (2017) Hepatoprotective and hypoglycemic effects of a tannin rich extract from *Ximenia americana* var. caffra root. *Phytomedicine*, 33: 36–42. https://doi.org/10.1016/j.phymed.2017.07.003

SZE, D. M. Y., MILLER, K. & NEILAN, B. (2008) Development of taxol and other endophyte produced anti-cancer agents. *Recent Patents on Anti-Cancer Drug Discovery*, 3(1): 14–19. https://doi.org/10.2174/157489208783478685

THOMFORD, N., DZOBO, K., CHOPERA, D., WONKAM, A. *et al*. (2015) Pharmacogenomics implications of using herbal medicinal plants on African populations in health transition, *Pharmaceuticals*, 8(3): 637–663. https://doi.org/10.3390/ph8030637

TLAAMELA, D. M., MAHLO, S., ABDALLA, M. & MCGAW, L. (2023) Antifungal activity and toxicity of bioactive compounds isolated from the leaf of *Ximenia caffra* Sond. var. natalensis, *Journal of Medicinal Plants for Economic Development*, 7(1): a219. https://doi.org/10.4102/jomped.v7i1.219

UNUOFIN, J. O., OTUNOLA, G. A. & AFOLAYAN, A. J. (2018) Polyphenolic content, antioxidant and antimicrobial activities of *vernonia mespilifolia* less. used in folk medicine in the Eastern Cape Province, South Africa, *Journal of Evidence-Based Integrative Medicine*, 23. https://doi.org/10.1177/2515690X18773990

USMANI, J., KHAN, T., AHMAD, R. & SHARMA, M. (2021) Potential role of herbal medicines as a novel approach in sepsis treatment, *Biomedicine & Pharmacotherapy*, 144: 112337. https://doi.org/10.1016/J.BIOPHA.2021.112337

VAN WYK, B., PALGRAV, K. C. & WYK, P. V. (2013). *Field Guide to Trees of Southern Africa*, (Vol. 1, 2nd ed.). Penguin Random House. https://doi.org/10.4081/pb.2012.br1

VIEIRA, C. R., MARQUES, M. F., SOARES, P. R., MATUDA, L. *et al*. (2008) Antiproliferative activity of Pterodon pubescens Benth. seed oil and its active principle on human melanoma cells, *Phytomedicine*, 15(6–7): 528–532. https://doi.org/10.1016/J.PHYMED.2007.08.003

WEBER, C., SLIVA, K., VON RHEIN, C., KÜMMERER, B. M. *et al.* (2015) The green tea catechin, epigallocatechin gallate inhibits chikungunya virus infection, *Antiviral Research*, 113: 1–3. https://doi.org/10.1016/J.ANTIVIRAL.2014.11.001

WORLD HEALTH ORGANISATION. (2019). WHO global report on traditional and complementary medicine 2019.

ZHANG, X., WANG, J., HU, J. M., HUANG, Y. W. *et al*. (2016) Synthesis and biological testing of novel glucosylated epigallocatechin gallate (EGCG) derivatives, *Molecules 2016*, 21(5): 620. https://doi.org/10.3390/MOLECULES21050620

ZHAO, H., WU, L., YAN, G., CHEN, Y. *et al*. (2021) Inflammation and tumor progression: Signaling pathways and targeted intervention, *Signal Transduction and Targeted Therapy*, 6(263). https://doi.org/10.1038/s41392-021-00658-5

ZHEN, J., GUO, Y., VILLANI, T., CARR, S. *et al.* (2015) Phytochemical analysis and anti-inflammatory activity of the extracts of the African medicinal plant *Ximenia caffra*, *Journal of Analytical Methods in Chemistry*, 2015(1): 948262. https://doi.org/10.1155/2015/948262

ZISHAN, M., SAIDURRAHMAN, S., ANAYATULLAH, A., AZEEMUDDIN, A. *et al*. (2017) Natural products used as anti-cancer agents, *Journal of Drug Delivery and Therapeutics*, 7(3): 11–18. https://doi.org/10.22270/jddt.v7i3.1443