# A Review on Medicinal Plants Used in The Management of Male Infertility Associated with Diabetes Mellitus in Thengwe, Limpopo Province, South Africa

Murendeni Nethengwe, Kunle Okaiyeto, Chinyerum S. Opuwari & Oluwafemi O. Oguntibeju

***Abstract*—** Diabetes mellitus is a metabolic chronic disease characterized by persistent hyperglycemia resulting in oxidative stress. Excessive production of reactive oxidative species (ROS) through the mitochondrial electron transport chain and other pathways destroys the macromolecules such as proteins, lipids, and DNA thereby leading to an inflammatory response involving the excessive production of cytokines, which leads to the augmentation of the production of ROS and subsequently leads to tissue damage. One of the complications of diabetes mellitus is male infertility which results from reproductive tissue damage. Oxidative stress and chronic inflammation in the male reproductive tissue pose a great risk in the development of male infertility. Although, synthetic drugs are conventionally used in the treatment of diabetes and its complications, the cost implications and adverse effects associated with the use of the drugs cannot be overemphasized. Hence, the quest for cost-effective alternative with fewer side effects such as natural products are highly imperative. Therefore, the present review aimed at providing available ethnobotanical information about medicinal plants used in Thengwe, Limpopo Province in the management of diabetes and its complications such as male infertility.

***Keywords*—** Diabetes mellitus-related male infertility, inflammation, oxidative stress, medicinal plants.

## I. INTRODUCTION

Diabetes mellitus (DM) is a non-communicable metabolic disease defined by different complications that is caused by hyperglycaemia (Wang *et al*., 2021). Hyperglycaemia is the hallmark of DM and a consequence of the alterations in the secretion and/or action of insulin (insulin resistance) (Mudau *et al*., 2022). Major predisposing factors, including genetic predisposition, obesity, poor food, and other lifestyle selections, are linked to insulin resistance and pancreatic beta cell degeneration (Kumar et al., 2021). Hyperglycaemia is implicated in complications such as cardiovascular disease, nephropathy, neurodegenerative diseases, and male infertility (Abou Zeid *et al*., 2021; Johnson *et al*., 2019; Nanti *et al*., 2019). The increased blood glucose molecules react with macromolecules in the body, altering and damaging them (Roxo *et al*., 2019). The rise in DM prevalence contributes to the rise in male infertility, and is a great financial and public health concern (Temidayo & Stefan, 2017). The link between DM and male infertility is mitigated by the excessive production of reactive oxidative species and inflammatory cytokines, led by hyperglycaemia (Oguntibeju, 2019).

The exposure of cells to high glucose levels causes the mitochondria to produce excess ROS and leads to oxidative stress (Nolfi-Donegan *et al*., 2020), an instigator of the progression of DM-related complications (Olofinsan *et al*., 2022). Furthermore, the interaction of glucose molecules with other macromolecules also increase ROS (Fishman *et al*., 2018). ROS are highly reactive and unstable and can easily oxidise other molecules such as proteins, lipids, and DNA thereby damaging them (Hosseini *et al*., 2019). Oxidative stress occurs when the production of ROS exceeds their elimination by antioxidants (Kurutas, 2016). Immune cells release inflammatory cytokines in response to tissue damage (Nna *et al*., 2019). The damage caused by both high levels of glucose and oxidative stress leads to the excessive release of inflammatory cytokines, causing more damage (Nna *et al*., 2019). The high levels of inflammatory cytokines, and oxidative stress in the male reproductive organs is detrimental to the production and maturation of spermatozoa, and can lead to male infertility (Agarwal *et al*., 2018).

The prevalence of DM has risen more in developing countries compared to developed countries, with DM being the second leading cause of death in South Africa. A large number of people (415 million) worldwide are affected by DM, and it is estimated that double the amount will be affected by 2040 (Ibrahim *et al*., 2019). It is also estimated that approximately 5% of the world's population may be

Murendeni Nethengwe is with the Cape Peninsula University of Technology, Bellville, South Africa

Kunle Okaiyeto is with the Cape Peninsula University of Technology, Bellville, South Africa

Chinyerum Opuwari is with the University of Western Cape, Bellville, South Africa

Oluwafemi, O, Oguntibeju is with the Cape Peninsula University of Technology, Bellville, South Africa

diabetic by the year 2030 (Abou Zeid *et al*., 2021). A rapid rise in the prevalence of DM from 4.5% to 12.7% in South Africa was recorded between the years 2010 to 2019 (Grundlingh et al., 2022). Besides the rise in mortality, DM reduces the quality of life and increases the number of males affected by infertility issues (Johnson et al., 2019). It has been recorded that 50% of infertility cases involve male-related causative factors (Abdillahi & Van Staden, 2012). There is currently no known cure for DM, however, drugs such as metformin, glibenclamide, insulin, acarbose, and miglitol are prescribed to diabetic patients for the management of DM complications (Liu *et al*., 2018; Lv & Guo, 2020). These drugs are reported to decrease blood glucose levels, ameliorate oxidative stress and inflammation, and inhibit enzymes responsible for the breakdown of carbohydrates into glucose molecules (Ibrahim *et al*., 2019). Currently prescribed drugs are accompanied by side effects, and high production costs (Innalegwu *et al*., 2022). The disadvantages behind the use of synthetic drugs in the treatment of DM complications show a need in a more cost-effective and efficacious method of treatment (Ibrahim *et al*., 2019). The pathway link between DM and male infertility has led to further investigation and findings of an alternative therapeutic way of treating male infertility in diabetic individuals.

The use of medicinal plants dates back to the existence of humankind (Petrovska, 2012). Over 80% of the African population use medicinal plants as a form of treatment (Nanti *et al*., 2019). Although the mechanisms behind the effectiveness of these plants was not yet investigated, ancient people continued to utilise them as food and to treat ailments (Aremu, 2022). Presently, more information about medicinal plants obtained from ethnobotanical surveys and biomedical studies has been published. Through available publications, it is evident that medicinal plants contain nutrients and phytochemicals such as polyphenols, alkaloids, and flavonoids which are key to the effectiveness of these plants *(Alabi et al*., 2019; Joseph *et al*., 2017; Moichela *et al*., 2021).

In Thengwe community of Limpopo Province, South Africa, traditional healers traditionally treat DM and male infertility using medicinal herbs. Phytochemicals in these medicinal plants can ameliorate oxidative stress and inflammation, thereby treating DM and male infertility (Nna *et al*., 2019). The different plants used by these Vhavenda people for the treatment of DM have been published, however, the potential of the same plants in the treatment of male infertility in diabetic patients is not well established. Additionally, there are more medicinal plants known and used by traditional healers regardless of their appearance in the literature. The documentation of more plants in the treatment of DM, and their potential benefits in specifically treating male infertility could lead to further investigation of the mechanisms of action of these plants, and an increase in their use to lower the prevalence of male infertility. More studies on the different plants used in traditional medicine could pave a way to more discovery of suitable dosage, preparation, and method of administration, for a more efficacious way of treatment. Improvement and more documentation of the use of medicinal plants could create a safer (less adverse effects), more accessible and more effective way of treating DM and related male infertility.

## II. Methodology

### A. Study area

The ethnobotanical survey was carried out in Thengwe village in Limpopo, South Africa. Thengwe village lies in the far North of Limpopo province between coordinates 22° 24' 0.0"-23° 36' 0.0" S and 29° 12' 0.0" and 31° 12' 0.0" E. Figure 1 represents the location of Thengwe village.

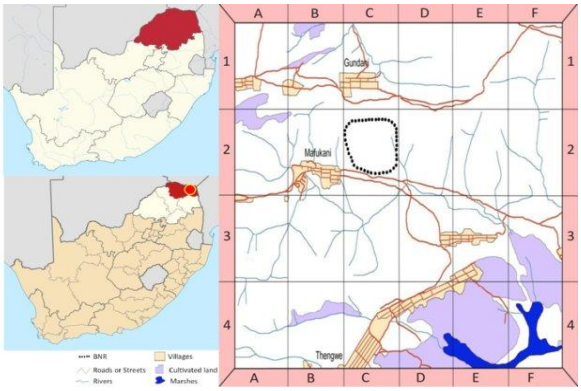


Fig 1. The location of Thengwe village in Limpopo province, South Africa, with the indication of the Brackenridgea Nature reserve in Mafukani (Tiawoun *et al*., 2019).

### B. Data collection

An ethnobotanical survey was carried out at Thengwe village in Limpopo, South Africa, through a structured one-on-one interview with 5 traditional healers about the medicinal plants used in the treatment of DM-related male infertility, together with their local names. Approval to get this information was obtained from the Chief of Tshidongololwe village. Information about medicinal plants used in Limpopo for the treatment of DM-related male infertility was obtained from publications found in different databases such as, PubMed, Scopus, Science Direct, Wiley, and Springer, by searching for keywords such as, diabetes mellitus, male infertility, medicinal plants, and Limpopo.

## III. Results and Discussion

Amongst others, the following plants were found in Thengwe village, Limpopo, South Africa. This study recorded 10 taxa used in the treatment of both DM and the resulting treatment of male infertility. The method of preparation for these medicinal plants was found to be majorly concoction and administration was done orally. These plants were also identified in the literature and their benefits in DM and in male infertility were linked. The information on the selected plants is also represented in Table 1.

TABLE I:

Ethnobotanical information for plants used for the treatment of DM-related male infertility in Thengwe village, Limpopo Province, South Africa. Local names of the plants are indicated in brackets.

| Name of plant | Part used for DM-related male infertility | Dosage | Method of preparation and administration | Other known benefits |
|---|---|---|---|---|
| *Androstachys johnsonii* (Musimbiri) | Leaves | 250 ml per day for 2 weeks | Orally (water decoction) | Sexually transmitted diseases |
| *Annona senegalensis (*Muembe) | Leaves Roots | 1 Tablespoon 3 times a day | Orally (water infusion) | Erectile dysfunction, malaria, and intestinal worms. |
| *Brackenridgea zanguebarica* (Mutavhatsindi) | Roots | 250 ml per day for 2 weeks | Orally (water decoction) | Healing of wounds |
| *Garcinia livingstonei (*Mupimbi) | Leaves, roots, and stem | 2 shots 3 times a day for 7 days | Orally (ethanol infusion) | Stomach cramps, bacterial infections |
| *Peltophorum africanum* (Musese) | Leaves Roots and bark | 250 ml per day for 2 weeks | Orally (water decoction) | Viral infections |
| *Rhoicissus tridentate* (Murumbul ambudzana) | Stem | Half a cup per day for 2 weeks | Orally (water infusion) | unknown |
| *Securidaca longepedunculata* (Mpesu) | Stem bark | Half a cup per week for 4 weeks | Orally (water decoction) | Sexually transmitted diseases |
| *Senna petersiana* (Munemben embe) | Leaves Seeds | Half a cup per week for 2 weeks | Orally (ethanol infusion) | Stomach cramps |
| *Terminalia sericea* (Mususu) | Roots Bark Leaves | 250 ml per day for 2 weeks | Orally (water decoction) | Bacterial infections |
| *Ximenia caffra (*Mutshili) | Roots Leaves Fruits | One cup per day for 2 weeks | Orally (water decoction) | unknown |

Traditional healers (informants of the present study) were mainly male, although randomly selected. They reported that their way of knowing and locating these plants for any treatment was through divine communication with the ancestors. The most used parts of medicinal plants for the treatment of DM and male infertility were the roots and leaves, followed by the stem bark, fruits and seeds. The vast availability of medicinal plants in Thengwe village supports the medical route popularly taken by the citizens of the area. Traditional healers in Limpopo have reported the use of *Androstachys johnsonii* (Musimbiri in Tshivenda), also known as Lebombo ironwood, as a treatment for DM and male infertility. *Androstachys johnsonii* is a tall (15 m) evergreen plant found in areas of Africa with very dry soil and low rainfall (Gandiwa *et al*., 2011). In addition to its effect on male infertility treatment, the leaves of *Androstachys johnsonii* have been recorded to have an aphrodisiac effect on men (Maroyi, 2013). Besides the report from traditional healers, the treatment of DM-related complications by *Androstachys johnsonii* extract is not well investigated. *Androstachys johnsonii* has also been used to treat bacterial infections (Georginah *et al*., 2012).

**Fig 2.** *Androstachys johnsonii* (Musimbiri).

Some medicinal plants have been recorded as food or food additives. *Annona senegalensis* (Muembe in Tshivenda), also known as "Wild custard apple" is a shrub (2-11m tall) with smooth green leaves that have brownish hair on the dorsal side, a greyish-brownish stem, and green fruits that turn yellow and orange when ripe (Okhale *et al*., 2016). These plants are found in hot climates next to river banks in forests (Okhale *et al*., 2016). The fruits of A. *senegalensis* are edible, with the flowers used as a seasoning in foods (Donhouedé *et al*., 2022). Supporting the evidence that this plant has been used in the treatment of DM and its complications, it was reported that the leaf extracts of A. *senegalensis* are beneficial

in the reduction of blood glucose (Ibrahim *et al*., 2019; Nanti *et al*., 2019). Furthermore, the effect of A. *senegalensis* in the treatment of DM is linked to its antioxidant and anti-inflammatory capacity (Ibrahim *et al*., 2019).

The compounds in A. *senegalensis* such as hexadecanoic acid, methyl ester, 1,3-octadecenal, and bis (2-methylpropyl) ester are associated with the inhibitory effect of the leaf extract of the plant on α-amylase and α-glucosidase, leading to the amelioration of hyperglycaemia (Ibrahim *et al*., 2019). Previous studies have showed that phytochemicals such as flavonoids, saponosides, triterpenes and tannins are constituents of A. *senegalensis*, corroborating the findings that this plant has antioxidant effects (Nanti *et al*., 2019; Okhale *et al*., 2016). The roots of the plant are prepared by the traditional healers in Limpopo to treat male infertility (Mahwasane *et al*., 2013). Similar to this report, infusions of the roots of the plant are prepared in Nigeria for the treatment of erectile dysfunction, another male reproduction complication accompanying DM (Okhale *et al*., 2016). It was also reported that the concoction prepared with A. *senegalensis* treats malaria and intestinal worms (Donhouedé *et al*., 2022).

Fig 3. *Annona senegalensis* (Muembe).

Brackenridgea *zanguebarica* is known as Mutavhatsindi by the Vhavenda people. It has green leaves, and a yellow-pigmented stem and grows up to 10 m tall in tropical areas (Möller *et al*., 2010**;** Rasethe, 2022). The B. *zanguebarica* plants are fenced at the Brackenridgea Nature Reserve in Thengwe, Limpopo where their harvest is controlled, due to the species being endangered (Rasethe, 2022). Several superstitions and witchcraft reports follow the use of B. *zanguebarica* which has been known to be a way to protect the plants from being overused (Rasethe, 2022). Traditional healers also used the roots of B. *zanguebarica* for the healing of wounds, and later switching to the leaves of the plant for the same purpose, due to raised conservation strategies. Isolation of phenolic compounds from B. *zanguebarica* has revealed the presence of different flavonoids in the crude root extract (Möller *et al*., 2010).

Fig 4. Brackenridgea *zanguebarica* (Mutavhatsindi).

*Garcinia livingstonei* (Mupimbi in Tshivenda), also known as “African mangosteen” is a small evergreen plant with very small leaves found in high temperature areas. *Garcinia livingstonei* is known for its antioxidant and anti-inflammatory effects in the treatment of DM complications (Joseph *et al*., 2017). Compounds such as morelloflavone, morelloflavone-7-sulphate, guttiferone A, sargaol (Mulholland *et al*., 2013), amentoflavone, 4’momomethoxy amrentoflavone (Kaikabo & Eloff, 2011), and phenols (flavonoids and alkaloids) (Joseph *et al*., 2017) have been isolated from the leaves, roots and stem of *Garcinia livingstonei*. The identification of the different compounds in the plant supports the benefits of the plant in treating DM-related male infertility. The leaves of this plant are also used to relieve stomach cramps.

Fig 5. *Garcinia livingstonei* (Mupimbi).

*Peltophorum africanum* is well known as Musese by the Vhavenda people. Phytochemical screening of the leaves of P. *africanum* revealed the availability of phytochemical compounds such as tannins, flavonoids and saponins, contributing to the antioxidant effect of the plant (Abou Zeid *et al*., 2021). In addition to these compounds, P. *africanum* also contains catechin, and bergenin, a C-galloylglycoside, adding to the antioxidant capacity of the plant (Theo *et al*., 2009). The antioxidant capacity of this plant could possibly explain its therapeutic effect in the amelioration of hyperglycaemia and the treatment of male infertility. Although the method of extraction differs in some studies compared to the method used (water extraction) by the selected traditional healers in Limpopo, findings show the antidiabetic effect of this plant through the inhibition of α-amylase (Abou Zeid *et al*., 2021). A previous ethnobotanical study has recorded the use of the roots and bark of P. *africanum* in the treatment of male infertility (Abdillahi & Van Staden, 2012; Theo *et al*., 2009). P. *africanum* is also beneficial in the treatment of viral

infections due to its ant-inflammatory effect (Adebayo et al., 2017). The reduction of proinflammatory cytokines caused by P. *africanum* could contribute to its benefit in the treatment of DM-related male infertility.

Fig 6. Peltophorum africanum (Musese).

*Rhoicissus tridentate* (Murumbulambudzana in Tshivenda), also known as “Wild grape” is a shrub with wedged green to black leaves and greenish-yellow flowers, known for its benefit in the treatment of DM (Aremu, 2022; Mukundi *et al*., 2015). Traditional healers have reported that the plant is mostly used for the treatment of sexually transmitted diseases (Nazer *et al*., 2019).The identification of phenols, flavonoids, saponins and tannins in the stems of R. *tridentate* suggests the antioxidant and anti-inflammatory effect of the plant, which explains the amelioration of the DM complications, including male infertility (Mukundi *et al*., 2015). Very few publications report the benefits of this plant in DM complications.

Fig 7. *Rhoicissus tridentate* (Murumbulambudzana).

*Securidaca longepedunculata* (Mpesu in Tshivenda) is popularly known as “Violet tree”, grows up to 6 m tall and produces purplish-green fruits (Abubakar *et al*., 2022). The plant is mostly used for the treatment of erectile dysfunction, and for aphrodisiac effects. Its roots and stem bark are known by traditional healers for the treatment of both DM and male infertility (Innalegwu *et al*., 2022; Musa *et al*., 2022). This plant is known to contain useful phytochemicals such as flavonoids, xanthones, terpenes, and steroids with a high capacity to ameliorate oxidative stress (Innalegwu *et al*., 2022). A previous study also identified antioxidants such as saponins, flavonoids and terpernoidsin the stem bark of the plant (Adefolaju *et al*., 2019). Root-bark extracts of S. *longepedunculata* affect the testicular parameters of rabbits and improve fertility (Chika *et al*., 2017), which may be attributed to the bioactive compound content of this plant. The treatment with S.*longepedunculata* on rats has shown the effect of this plant in the improvement of both sperm concentration and sperm motility, and could possibly reverse DM effects in the spermatozoa (Chika *et al*., 2017).

Fig 8. Securidaca longepedunculata (Mpesu)

*Senna petersiana* (known as Munembenembe in Tshivenda) has been recorded for its benefit in the treatment of DM complications through the inhibition of α-amylase and α-glucosidase (Mudau *et al.*, 2022; Olofinsan *et al*., 2022). The hypoglycaemic effect of this plant is also linked to the pancreatic lipase inhibitory capacity of its leaf extracts (Olofinsan *et al*., 2022). Leaves contain phenolic compounds such as flavonoids that boost the plant’s antioxidant capacity (Olofinsan *et al*., 2022). The leaves of S. *petersiana* possess an antioxidant effect through the activation of antioxidant enzymes thereby ameliorating oxidative stress (Olofinsan *et al*., 2022). Activation of these enzymes in the testes could be a possible mechanism behind the treatment of male infertility. The use of the seeds S. *petersiana* for the treatment of male infertility in traditional medicine is recorded (Rajkovic *et al*., 2022).

Fig 9. *Senna petersiana* (Munembenembe).

*Terminalia sericea* **(**Mususu in Tshivenda) is one of the popular medicinal plants in Africa (Anokwuru *et al*., 2020). It is a small plant that grows up to 8 m tall well known as “Silver cluster leaf” (Anokwuru *et al*., 2020). It is used as an antibiotic due to its microbial effect (Nel *et al*., 2020). The stem of T. *sericea* is used in the treatment of DM complications due to its effect on inhibiting carbohydrate hydrolysis enzymes such as α-amylase and α-glucosidase

(Nkobole *et al*., 2011). The reduction of blood glucose could possibly contribute to the reduction of macromolecule damage in the male reproductive organs, thereby reducing male infertility. The bark of this plant also possesses high antioxidant capacity suggested to be caused by the availability of phytochemicals such as catechin, epicatechin, gallocatechin, β-sitosterol, β-sitosterol-3-acetate, and lupeol in the stem bark (Nkobole *et al*., 2011). Flavonoids (rutinoside and quercetin galloyl-glucoside) were isolated from the leaves of T. *sericea* in support of the antioxidant content of the plant (Sobeh *et al*., 2019).

Fig 10. *Terminalia sericea* (Mususu).

*Ximenia caffra* (Mutshili in Tshivenda), also known as sour plum, is a shrub that grows in tropical areas in African countries such as Tanzania, Namibia, Limpopo and Botswana (Sobeh *et al*., 2017). The poor and dry soil in the Thengwe farms in Limpopo favour the existence of these plants (Jacob *et al*., 2021). X. *caffra* has a stem with grey to black barks, and green to creamy white flowers that can sometimes be reddish-pink (Jacob *et al*., 2021). X. *caffra* is known for its multiple benefits and its commercial use, due to the use of its oils for cosmetics, and the consumption of its fruits and nuts (Maroyi, 2016). The leaves and roots of X. *caffra* are used for the treatment of male infertility (Sobeh *et al*., 2017). Phytochemical analysis of the roots of this plant revealed the identification of compounds such as tannins and other flavonoids such as catechins, epicatechins and quecetin explaining the antioxidant capacity of the plant (Nkosi *et al*., 2022; Sobeh *et al*., 2017). In corroboration of this finding, the antioxidant capacity of the leaves of X. *caffra* was measured and found to be high and of potential in the treatment of DM complications (Jacob *et al*., 2021). The association of the treatment of DM and male infertility by this plant is linked to the amelioration of hyperglycaemia and the increase levels of insulin (Sobeh *et al*., 2017). A study conducted by Nkosi and colleagues also supported the evident hypoglycaemic effect of the plant deduced from the α-amylase and α-glucosidase inhibitory effect of the fruits it produces (Nkosi *et al*., 2022).

Fig 11. *Ximenia caffra* (Mutshili).

## IV. Conclusion

Male infertility is a home-breaker in many countries of the world. It is eminent to seek solution to male infertility all ways possible including herbal approach. The present study reviewed 10 plants used in Thengwe village, Limpopo in the treatment of DM-related male infertility. This shows the vast possibility of the discovery and improvement of more ways to treat male infertility associated with DM. Findings from the present study revealed there is limited studies documented on the reviewed plants. The indigenous knowledge of medicinal plants is valuable resources for health management. Knowledge of traditional medicine use need to be protected through proper documentation of recipes enumerations. It is obvious that traditional knowledge on the use of medicinal plants must be recorded before it is lost to future generations. The paucity of scientific literature information on the pharmacological activities of some plant species demonstrates the need for more ethnobotanical survey studies to capture and document the folk medicinal use of plants in South Africa and around the world. This study will provide a foundation for future phytochemical and pharmacological investigations into the beneficial medicinal properties of such plants. Rather than relying exclusively on trial and error resulting from random screening procedures, adequately documented traditional knowledge may address challenges in identifying plants with medicinal uses that could find new applications for the beneficial of all humans.

## References

[1] Abdillahi, H. S., & Van Staden, J. (2012). South African plants and male reproductive healthcare: Conception and contraception. *Journal of Ethnopharmacology*, *143*(2), 475–480. https://doi.org/10.1016/j.jep.2012.06.047

[2] Abou Zeid, A. H., El Hawary, S. S., Mohammed, R. S., Ashour, W. E. S., Ahmed, K. A., Sabry, O. M., & Attia, H. N. (2021). Metabolite Profiling of Peltophorum africanum Sond. & Saraca indica L. Leaves via HR-UPLC/PDA/ESI/MS Analysis and Assessment of their Anti-Diabetic Potential. *Journal of Biologically Active Products from Nature*, *11*(5–6), 442–466. https://doi.org/10.1080/22311866.2021.1943523

[3] Abubakar, U. S., Danmalam, U. H., Ibrahim, H., Maiha, B. B., Hadiza, R. J., & Abdullahi, M. S. (2022). *LCMS / MS Analysis of the Ethylacetate Extract of Securidaca longipedunculata Fresen ( Polygalaceae ) Stem Bark*. *March*.

[4] Adebayo, S. A., Steel, H. C., Shai, L. J., & Eloff, J. N. (2017). Investigation of the Mechanism of Anti-Inflammatory Action and Cytotoxicity of a Semipurified Fraction and Isolated Compounds From the Leaf of Peltophorum africanum (Fabaceae). *Journal of Evidence-*

*Based Complementary and Alternative Medicine*, *22*(4), 840–845. https://doi.org/10.1177/2156587217717417

[5] Adefolaju, O., Arannilewa, J., Olowo, A., & State, K. (n.d.). *Effect of* Administration *of Aqueous Extract of Securidaca Longepedunculata Stem Bark on Enzymes of the Small Intestine Allozan Induced Diabetic Rat*. 1–8.

[6] Agarwal, A., Rana, M., Qiu, E., AlBunni, H., Bui, A. D., & Henkel, R. (2018). Role of oxidative stress, infection and inflammation in male infertility. *Andrologia*, *50*(11), 1–13. https://doi.org/10.1111/and.13126

[7] Alabi, T. D., Brooks, N. L., & Oguntibeju, O. O. (2019). Antioxidant Capacity, Phytochemical Analysis and Identification of Active Compounds in Anchomanes difformis. *The Natural Products Journal*, *10*(4), 446–458. https://doi.org/10.2174/2210315509666190422155347

[8] Anokwuru, C. P., Tankeu, S., van Vuuren, S., Viljoen, A., Ramaite, I. D. I., Taglialatela-Scafati, O., & Combrinck, S. (2020). Unravelling the antibacterial activity of terminalia sericea root bark through a metabolomic approach. *Molecules*, *25*(16). https://doi.org/10.3390/MOLECULES25163683

[9] Aremu, A. O. (2022). *Commercialization Potential of Six Selected Medicinal Plants* Commonly *Used for Childhood Diseases in South Africa : A Review*.

[10] Chika, C. I., Luka, M., & Azubuike, U. S. (2017). *Effect of Securidaca* longepedunculata *root-bark methanol extract on testicular morphometry of New Zealand rabbits*. *9*(December), 361–367. https://doi.org/10.5897/JVMAH2017.0586

[11] Donhouedé, J. C. F., Salako, K. V., Gandji, K., Idohou, R., Tohoun, R., Hounkpèvi, A., Ribeiro, N., Ribeiro-Barros, A. I., Glèlè Kakaï, R., & Assogbadjo, A. E. (2022). Food and medicinal uses of Annona senegalensis Pers.: a country-wide assessment of traditional theoretical knowledge and actual uses in Benin, West Africa. *Journal of Ethnobiology and Ethnomedicine*, *18*(1), 1–15. https://doi.org/10.1186/s13002-022-00510-2

[12] Fishman, S. L., Sonmez, H., Basman, C., Singh, V., & Poretsky, L. (2018). The role of advanced glycation end-products in the development of coronary artery disease in patients with and without diabetes mellitus: A review. In *Molecular Medicine* (Vol. 24, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s10020-018-0060-3

[13] Gandiwa, E., Chikorowondo, G., Zisadza-Gandiwa, P., & Muvengwi, J. (2011). Structure and composition of Androstachys johnsonii woodland across various strata in Gonarezhou National Park, southeast Zimbabwe. *Tropical Conservation Science*, *4*(2), 218–229. https://doi.org/10.1177/194008291100400209

[14] Georginah, M. M., Ligavha-mbelengwa, M. H., & Bhat, R. B. (2012). Antimicrobial *activity of Androstachys johnsonii Prain*. *11*(103), 16767–16771. https://doi.org/10.5897/AJB11.2352

[15] Grundlingh, N., Zewotir, T. T., Roberts, D. J., & Manda, S. (2022). Assessment of prevalence and risk factors of diabetes and pre-diabetes in South Africa. *Journal of Health, Population and Nutrition*, *41*(1), 1–12. https://doi.org/10.1186/s41043-022-00281-2

[16] Hosseini, S. S., Gol, A., & Khaleghi, M. (2019). The effects of the lactobacillus acidophilus ATCC 4356 on the oxidative stress of reproductive system in diabetic male rats. *International Journal of Reproductive BioMedicine*, *17*(7), 495–504. https://doi.org/10.18502/ijrm.v17i7.4861

[17] Ibrahim, A., Umar, I. A., Aimola, I. A., & Mohammed, A. (2019). Inhibition of key enzymes linked to diabetes by Annona senegalensis Pers (Annonaceae) leaf in vitro. *Journal of Herbal Medicine*, *16*(November 2017), 100248. https://doi.org/10.1016/j.hermed.2018.11.004

[18] Innalegwu, A., Maimuna, D., Umar, B., Jimoh, O., & Rukayya, T. (2022). Antidiabetic potentials of green‐synthesized alpha iron oxide nanoparticles using stem extract of Securidaca longipedunculata. *International Nano Letters*, *12*(3), 281–293. https://doi.org/10.1007/s40089-022-00377-x

[19] Jacob, A. D., Dauda, J. A., Daniel, O. A., Nayo, R. O., Maji, D. C., & Umar, I. (2021). *Assessment of Free Radical Scavenging Potency and In-vitro Antioxidant Analysis of Ximenia caffra ( Sour Plum ) Leaf*. *9*(2), 1–7.

[20] Johnson, A., Cheng, S. C., Tsou, D., & Kong, Z. L. (2019). Attenuation of reproductive dysfunction in diabetic male rats with timber cultured Antrodia cinnamomea ethanol extract. *Biomedicine and Pharmacotherapy*, *112*(1), 1–13. https://doi.org/10.1016/j.biopha.2019.108684

[21] Joseph, K. S., Bolla, S., Joshi, K., Bhat, M., Naik, K., Patil, S., Bendre, S., Gangappa, B., Haibatti, V., Payamalle, S., Shinde, S., Dewir, Y. H., & Murthy, H. N. (2017). Ermittlung der chemischen Zusammensetzung und des Nährstoffgehaltes anhand der Fettsäurezusammensetzungen bei der afrikanischen Mangostane (Garcinia livingstonei). *Erwerbs-Obstbau*, *59*(3), 195–202. https://doi.org/10.1007/s10341-016-0311-9

[22] Kaikabo, A. A., & Eloff, J. N. (2011). Antibacterial activity of two biflavonoids from Garcinia livingstonei leaves against Mycobacterium smegmatis. *Journal of Ethnopharmacology*, *138*(1), 253–255. https://doi.org/10.1016/j.jep.2011.08.023

[23] Kumar, S., Behl, T., Sachdeva, M., Sehgal, A., Kumari, S., Kumar, A., Kaur, G., Narayan, H., & Bungau, S. (2021). Implicating the effect of ketogenic diet as a preventive measure to obesity and diabetes mellitus. *Life Sciences*, *264*(October 2020), 118661. https://doi.org/10.1016/j.lfs.2020.118661

[24] Kurutas, E. B. (2016). The importance of antioxidants which play the role in cellular response against oxidative/nitrosative stress: Current state. *Nutrition Journal*, *15*(1), 1–22. https://doi.org/10.1186/s12937-016-0186-5

[25] Liu, M. L. I. N., Wang, M. L., Lv, J. J. U. N., Wei, J. I. E., & Wan, J. U. N. (2018). *Glibenclamide exacerbates adriamycin‐induced cardiotoxicity by activating oxidative stress‐induced endoplasmic reticulum stress in rats*. 3425–3431. https://doi.org/10.3892/etm.2018.5862

[26] Lv, Z., & Guo, Y. (2020). Metformin and Its Benefits for Various Diseases. Frontiers *in Endocrinology*, *11*(April), 1–10. https://doi.org/10.3389/fendo.2020.00191

[27] Mahwasane, S. T., Middleton, L., & Boaduo, N. (2013). An ethnobotanical survey of indigenous knowledge on medicinal plants used by the traditional healers of the Lwamondo area, Limpopo province, South Africa. *South African Journal of Botany*, *88*, 69–75. https://doi.org/10.1016/j.sajb.2013.05.004

[28] Maroyi, A. (2013). Traditional use of medicinal plants in south-central Zimbabwe: Review and perspectives. *Journal of Ethnobiology and* Ethnomedicine, *9*(1). https://doi.org/10.1186/1746-4269-9-31

[29] 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

[30] Moichela, F. T., Adefolaju, G. A., Henkel, R. R., & Opuwari, C. S. (2021). Aqueous leaf extract of Moringa oleifera reduced intracellular ROS production, DNA fragmentation and acrosome reaction in Human spermatozoa in vitro. *Andrologia*, *53*(1), 1–11. https://doi.org/10.1111/and.13903

[31] Möller, M., Suschke, U., Nolkemper, S., Schneele, J., Distl, M., Sporer, F., Reichling, J., & Wink, M. (2010). Antibacterial, antiviral, antiproliferative and apoptosis-inducing properties of Brackenridgea zanguebarica (Ochnaceae) . *Journal of Pharmacy and Pharmacology*, *58*(8), 1131–1138. https://doi.org/10.1211/jpp.58.8.0015

[32] Mudau, T. E., Olowoyo, J. O., & Amoo, S. O. (2022). Ethnobotanical assessment of medicinal plants used traditionally for treating diabetes in Vhembe district, Limpopo Province, South Africa. *South African Journal of Botany*, *146*, 304–324. https://doi.org/10.1016/j.sajb.2021.10.016

[33] Mukundi, M. J., Mwaniki, N. E. N., Piero, N. M., Murugi, N. J., Daniel, A. S., Peter, G. K., & Alice, M. N. (2015). *Journal of Developing Drugs In Vivo Anti-diabetic Effects of Aqueous Leaf Extracts of Rhoicissus tridentata in Alloxan Induced Diabetic Mice*. *4*(3). https://doi.org/10.4172/2329-6631.1000131

[34] Mulholland, D. A., Mwangi, E. M., Dlova, N. C., Plant, N., Crouch, N. R., & Coombes, P. H. (2013). Non-toxic melanin production inhibitors from Garcinia livingstonei (Clusiaceae). *Journal of Ethnopharmacology*, *149*(2), 570–575. https://doi.org/10.1016/j.jep.2013.07.023

[35] Musa, D. D., Rabiu, M., & Buah, J. (2022). *ETHNOBOTANICAL SURVEY OF PLANTS USED IN TREATMENT OF DIABETES BY THE HAUSA-FULANI TRIBALS IN KATSINA STATE NIGERIA*. *March*.

[36] Nanti Goore, G. C. G., Nene Bi, S. A., Toure, A., & Traore, F. (2019). Assessment of the antioxidant and anti-diabetic activity of Annona Senegalensis and Hallea Ledermannii in alloxan-induced diabetic rats. *Pharmacologyonline*, *1*, 319–336.

[37] Nazer, M., Abbaszadeh, S., Darvishi, M., Kheirollahi, A., Shahsavari, S., & Moghadasi, M. (2019). The Most Important Herbs Used in the

Treatment of Sexually Transmitted Infections in Traditional Medicine. *Sudan Journal of Medical Sciences*, *14*(2), 41–64. https://doi.org/10.18502/sjms.v14i2.4691

[38] Nel, A. L., Murhekar, S., Matthews, B., White, A., & Cock, I. E. (2020). The interactive antimicrobial activity of Terminalia sericea Burch ex DC. leaf extracts and conventional antibiotics against bacterial triggers of selected autoimmune inflammatory diseases. *South African Journal of Botany*, *133*, 17–29. https://doi.org/10.1016/j.sajb.2020.06.013

[39] Nkobole, N., Houghton, P. J., Hussein, A., & Lall, N. (2011). Antidiabetic activity of Terminalia sericea constituents. *Natural Product Communications*, *6*(11), 1585–1588. https://doi.org/10.1177/1934578x1100601106

[40] Nkosi, N. J., Shoko, T., Manhivi, V. E., Slabbert, R. M., Sultanbawa, Y., & Sivakumar, D. (2022). Metabolomic and chemometric profiles of ten southern African indigenous fruits. *Food Chemistry*, *381*(August 2021), 132244. https://doi.org/10.1016/j.foodchem.2022.132244

[41] Nna, V. U., Bakar, A. B. A., Ahmad, A., Eleazu, C. O., & Mohamed, M. (2019). Oxidative stress, NF-κB-mediated inflammation and apoptosis in the testes of streptozotocin–induced diabetic rats: Combined protective effects of malaysian propolis and metformin. *Antioxidants*, *8*(10), 1–23. https://doi.org/10.3390/antiox8100465

[42] Nolfi-Donegan, D., Braganza, A., & Shiva, S. (2020). Mitochondrial electron transport chain: Oxidative phosphorylation, oxidant production, and methods of measurement. *Redox Biology*, *37*, 1–9. https://doi.org/10.1016/j.redox.2020.101674

[43] Oguntibeju, O. O. (2019). Type 2 diabetes mellitus, oxidative stress and inflammation: examining the links. *International Journal of Physiology*, Pathophysiology *and Pharmacology*, *11*(3), 45–63. http://www.ncbi.nlm.nih.gov/pubmed/31333808%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC6628012

[44] Okhale, S., Akpan, E., Fatokun, O., Esievo, K., & Kunle, O. (2016). Annona senegalensis Persoon (Annonaceae): A review of its ethnomedicinal uses, biological activities and phytocompounds. *Journal of Pharmacognosy and Phytochemistry*, *5*(2), 211–219.

[45] Olofinsan, K. A., Erukainure, O. L., Msomi, N. Z., & Islam, S. (2022). *Senna petersiana inhibits key digestive enzymes and modulates dysfunctional enzyme activities in oxidative pancreatic injury*. *12*(May), 300–311. https://doi.org/10.4103/2221-1691.350178

[46] Petrovska, B. B. (2012). Historical review of medicinal plants’ usage. Pharmacognosy *Reviews*, *6*(11), 1–5. https://doi.org/10.4103/0973-7847.95849

[47] Rajkovic, J., Chen, Y., Sharifi-rad, J., Tutuncu, S., Aydar, E. F., & Topkaya, C. (n.d.). *A Review of Recent Studies on the Antioxidant and Anti-Infectious Properties of Senna Plants Infectious Properties of Senna Plants*. *Dc*.

[48] Rasethe, M. T. (2022). In situ conservation challenges of Brackenridgea zanguebarica Oliv.: A South African case study. *Biodiversitas*, *23*(8), 3876–3883. https://doi.org/10.13057/biodiv/d230803

[49] Roxo, D. F., Arcaro, C. A., Gutierres, V. O., Costa, M. C., Oliveira, J. O., Lima, T. F. O., Assis, R. P., Brunetti, I. L., & Baviera, A. M. (2019). Curcumin combined with metformin decreases glycemia and dyslipidemia, and increases paraoxonase activity in diabetic rats. *Diabetology and Metabolic Syndrome*, *11*(1), 1–8. https://doi.org/10.1186/s13098-019-0431-0

[50] Sobeh, M., Mahmoud, M. F., Abdelfattah, M. A. O., El-Beshbishy, H. A., El-Shazly, A. M., & Wink, M. (2017). Hepatoprotective and hypoglycemic effects of a tannin rich extract from Ximenia americana var. caffra root. *Phytomedicine*, *33*(May), 36–42. https://doi.org/10.1016/j.phymed.2017.07.003

[51] Sobeh, M., Mahmoud, M. F., & Hasan, R. A. (2019). *Chemical composition ,* antioxidant *and hepatoprotective activities of methanol extracts from leaves of Terminalia bellirica and Terminalia sericea ( Combretaceae )*. 1–22. https://doi.org/10.7717/peerj.6322

[52] Temidayo, So., & Stefan, S. P. (2017). Diabetes mellitus and male infertility. *Asian Pacific Journal of Reproduction*, *7*(1), 6. https://doi.org/10.4103/2305-0500.220978

[53] Theo, A., Masebe, T., Suzuki, Y., Kikuchi, H., Wada, S., Obi, C. L., Bessong, P. O., Usuzawa, M., Oshima, Y., & Hattori, T. (2009). Peltophorum Africanum, a traditional South African medicinal plant, contains n anti HIV-1 constituent, betulinic acid. *Tohoku Journal of Experimental Medicine*, *217*(2), 93–99. https://doi.org/10.1620/tjem.217.93

[54] Tiawoun, M. A. P., Tshisikhawe, M. P., & Gwata, E. T. (2019). Investigation of current threats to the existence of Brackenridgea zanguebarica in a small geographic area in Vhembe, Limpopo Province, South Africa. *Biodiversitas*, *20*(6), 1487–1495. https://doi.org/10.13057/BIODIV/D200601

[55] Wang, X., Li, Q., Han, X., Gong, M., Yu, Z., & Xu, B. (2021). Electroacupuncture Alleviates Diabetic Peripheral Neuropathy by Regulating Glycolipid-Related GLO/AGEs/RAGE Axis. *Frontiers in Endocrinology*, *12*(July), 1–13. https://doi.org/10.3389/fendo.2021.655591