

Review on Literature of the Plant *Elephantorrhiza Elephantine* on its Healing Properties and Recent Acquired Knowledge of its Medicinal Activities (2000-2020)

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ABSTRACT

Background: The current review article outlines current findings in literature from undertaken studies and review articles on the plant *Elephantorrhiza elephantine* from the past 20 years to date. The information presented in this article will include the following aspects of the plant. The plant description and taxonomy, ethnomedical uses, phytochemistry and pharmacology of *Elephantorrhiza elephantine*. The article looks to discuss existing hurdles in research found on this plant and how to integrate any previous research with what is currently done in research on the plant. It aims on guiding the path of future research direction on the plant *Elephantorrhiza elephantine*. **Methods:** A total of 40 articles were selected and read through. The articles selected had included literature publications with the keywords such as; *Elephantorrhiza elephantine*, plant description, taxonomic of the plant, ethno medicinal usages, phytochemicals, pharmacological properties and plant toxicity, which were published between the years 2000 – 2021. There were 32 articles relevant for this review article and 2 dissertation that were written between the criteria of years. **Results:** The ethnomedical uses of *Elephantorrhiza elephantine* have been investigated by various authors on the anti-microbial activities, anti-inflammatory, anticancer and in ethnoveterinary medicine on how the plant provides relief to individuals with illnesses/disease through its traditional uses. These studies have been conducted on both animals and humans. The experiments performed used the crude extract derived from parts of the plant such as the roots and leaves. These plant parts have phytochemical compounds that are extracted using varying polar solvents. In the animal studies, acetone extracts of *E. elephantine* roots demonstrated significant activity against a tick-borne disease in cattle livestock and parasite worms in goats. In humans, the dried leaf extracts of *E. elephantine* was also subjected to various polar solvents and water, investigated for phytochemical content, antioxidant, anti-inflammatory, anti-diabetic and cytotoxic activities, using standard methods. It was reported that the ethanol extract yielded the highest phytochemical content. **Conclusion:** The gap in knowledge has narrowed on medicinal plants effects of healing properties. This lead by extensive research carried out trying to understand the benefits of traditional medication and why majority of the population uses it as they primary healthcare choice. Investigating the mechanism of action of *E. elephantine* on its antimicrobial, anti-diabetic, antimalarial, anti-inflammatory and wound healing could lead to an enhanced understanding on the medicinal properties of the plant extracts and a commercialisation of a product in future. **Key words:** Medicinal plants, Phytochemical content, Antimicrobial, Plant extracts.

INTRODUCTION

The plant *Elephantorrhiza elephantine*

Elephantorrhiza elephantine (Burch) Skeels is a plant used extensively in the southern African countries as a source of food and to treat diseases and conditions caused by pathogenic microorganisms.¹⁻⁴ *Elephantorrhiza elephantine* is a member of the *Fabaceae* family and of the genus *Elephantorrhiza*. This species, *elephantine*, is spread widely among the southern African countries of Botswana; Namibia, Lesotho and provinces like Limpopo, North West, Mpumalanga, Free State, Eastern Cape, Northern Cape and KwaZulu-Natal in South Africa.^{5,6} *Elephantorrhiza elephantine* has many known names amongst different indigenous countries and documented literature. It is known as *elandsbean* (in English); *mupangara* (in Shona), *intolwane* (in Xhosa and Zulu); *mositsane* (in Sotho and Tswana) and *elandsboontjies* (in Afrikaans).⁷⁻¹¹ The plant image is represented in (Figure1a). The plant grows naturally in open grassy slopes and hillsides, and produces red roots that look like

sweet potatoes.⁹ The reddish root seen in (Figure 1b) is the most commonly used part of the plant in traditional medicine² and is used as remedy for the following conditions/diseases: diarrhoea and dysentery; diabetes,³ chest complaints, heart conditions, hypertension, syphilis, infertility in women, bladder problems, urinary tract infections, waist pain in infants, fever and haemorrhoids.^{4,12}

The plant description of *Elephantorrhiza elephantine* and taxonomy

Elephantorrhiza elephantine is a perennial low shrub with stems up to 90 cm tall at ground level and from the woody end of an elongated, often thickened rhizome up to 8 m long. The leaves consist of 2-4 pairs of pinnae in lower leaves and 7-17 pairs in upper ones, where the axis is up to 10 cm long.^{3,12} The scientific classification of *Elephantorrhiza elephantine* derives from the Kingdom *Plantae*; the Phylum *Tracheophyta*, the Class *Magnoliopsida*, the Order *Fabales*, the Family *Fabaceae*, the Genus *Elephantorrhiza* and Species *elephantine*.^{13,14}

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Figure 1a: The plant's image. (Modimolle, Nov 2014).



Figure 1b: The reddish roots (prota4u.org).

Ethnomedical uses

Elephantorrhiza elephantina's healing properties has been explored respectively in both humans and animals. In animals, according to McGaw et al.,¹⁵ studies done in the past decade between 2009 – 2019 has reported that traditional plants are commonly used in ethnoveterinary medicine amongst South African rural livestock which is a common feature still seen. Ethnoveterinary medicine may play an important role in relieving conditions such as wounds, skin diseases, mild diarrhoea and intestinal worms and tick-borne disease in livestock and not limited to these mentioned. *Elephantorrhiza elephantina* was one of the many plants reported in the survey, used to conduct the study amongst the many other plants used for a variety of commonly encountered animal diseases and afflictions. This study supports that greater interest has been shown recently in documenting ethnoveterinary medicine (EVM), as with ethnobotanical medicine used in treating

humans and animals.¹⁵ In the past decade, efforts have been made to publish the varying uses of medicinal plants in South African EVM in greater detail, as were their biological activity investigations relating directly to their ethnoveterinary use by McGaw and Eloff.⁵ In the same article a downfall in the survey was identified, where the author of the article Martin et al.,¹⁶ mentioned that the shortcomings of employing such a system included inefficacy or toxicity of remedies, there was uncertainty over dosing regimens and lack of standardisation, as well as unavailability of plant material during certain seasons of the year.¹⁶ The study conducted surveys in some of the provinces in South Africa, in places like Limpopo and the North-west province. This identified that not all provinces were analysed, provinces that were not mentioned were the Eastern Cape, the Free State and KwaZulu-Natal province. Further investigation in the mentioned provinces could be included in future studies as they have a high rate of breeding rural livestock and it could yield significant results towards the medicinal research in EVM and the plant is known to grow within these provinces (pza.sanbi.org/elephantorrhiza-elephantina, 2019). In the animal studies, acetone extracts of *E. elephantina* roots demonstrated significant activity against a tick-borne disease in cattle livestock¹⁷ and parasite worms in goats.¹⁸

In humans, *E. elephantina* has been reported to be used against conditions such as diarrhoea, blood purifying, ulcers, skin wounds, cleansing of the womb, infertility of the women, urinary tract infections in both men and women and the relief of fevers caused by illnesses associated with pathogenic bacteria in humans.^{1,2,12} The plant's extract using different polar solvents such as ethanol, methanol and aqueous solution have demonstrated relief to diarrhoea, wound disease, fever and fertility problems in women.^{6,9,15,16,19,20} The plant's roots are widely reported to be used in mixtures or solely in treatment of the conditions. The other parts such as the leaves are seldom used when treating conditions.^{6,16} The traditional uses of *E. elephantina* extract in the treatment of diarrhoea is much researched and widely reported.^{1,2,9,12,21} Researchers have subjected microorganisms associated with gut flora such as *Escherichia coli* and *Streptococcus* species to mainly the plant's roots and recently the leaves extract for further investigation aimed to understand and isolate phytochemical compounds like phenol; flavonoids and tannins reported to be responsible for antidiarrheal and antibacterial activities.^{2,12,22} Further investigation of how the mechanism of action of the plant extract works could be assessed and also establish their safety and efficacy. The gut flora has the potential to become pathogenic and causes diarrhoea^{2,12,21} and that is the reason why the above mentioned pathogens are commonly used in antidiarrheal and antibacterial studies of other authors as they are known to be opportunistic pathogen and part of the gut flora.

However, since roots are reported to be used more, the overexploitation for the root of the plant *E. elephantina* has put the plant on the Red Data List of medicinal plants in the Southern African regions since the beginning of the 2000s.^{6,12,23} When a population of *elephantina* is destroyed, the chance of regeneration is limited as they are known to grow in relatively natural areas. These are in rural areas or areas with an open row(s) of grass on land that is surrounded with fewer homes or buildings. The plant shows evidence of an unusual type of germination where the seedling buries its *plumule* (the bud within the embryo from which the stem and leaves develop) and shoots, thus arising from well below the ground surface (pza.sanbi.org/elephantorrhiza-elephantina, 2019).²⁴ They are not weedy in character even though a large colony of these plants may seem that way. In trying to preserve the livelihood of the plant, this has led to scientist exploring other parts of the plant putting the focus on the leaves. Recent research by Olaokun et al.,⁶ explored the phytochemical content, anti-diabetes, anti-inflammatory, antioxidant and cytotoxic activity of leaf extracts of *Elephantorrhiza elephantina*. It's reported there is a lack of information on the leaves' biological activity and not much reports on the plants' anti-diabetic

activity in humans and animals.^{5,6,15,16,22} The dried leaves extracts of *E. elephantine* were subjected to the following solvents; acetone, ethanol, cold water and hot water and investigated for polyphenolic, tannin and flavonoid content, antioxidant, anti-inflammatory, anti-diabetic and cytotoxic activities, using standard methods. Olaokun et al.,⁶ reported that the phenolic and flavonoid contents of the ethanol extract were the highest to acetone. In addition, the inhibition of α -amylase activity by the ethanol extracts was the strongest to acetone and water. Furthermore, the ethanol extract was the least cytotoxic which was subjected on mouse cells against H4IIE liver and differentiated C2C12 muscle cells (myotubules). However, for the other assays, the hot water extract was the most active than the ethanol and acetone. The hot water extract in a concentration dependent manner stimulated the highest C2C12 glucose utilisation activity in addition to exhibiting the strongest antioxidant and anti-inflammatory activities.⁶ Water and alcohol are used in preparing herbal remedies in traditional practice, indicating the significance of the results. According to a study by,⁶ was the most recent study conducted reporting the biological activities of *E. elephantine* leaf extracts. This indicates that they are still opportunity to do further investigate on the leaves of this plant where it is subjected to other solvents of various polarity such as hexane, ethanol and acetone. The analysis of the study shows that the leaves can be used as an alternative, ensuring the long-term usage and preservation of the livelihood of the plant. However, more investigation should be conducted to gain more scientific evidence on the plant's leaf extract. This will prevent the plant from being dug up which would cause it to die; instead, only the leaves would be harvested extending the plant's lifetime and allowing the leaves to bloom once more. As a result, if the plant is dug up, this method of self-preservation would not be possible. Plant self-preservation may help to ensure the plant's existence and may even prevent extinction.

METHODS AND MATERIAL

A review of literature search on the plant species was undertaken by the use of different electronic databases such as Google Scholar, ScienceDirect, Sabinet ePublication, African Journals, PubMed using keywords such as; *Elephantorrhiza elephantine*, plant description, taxonomic of the plant, ethno medicinal usages, phytochemicals, pharmacological properties and plant toxicity. A total of 60 articles were selected and analysed. The articles selected had included literature publications with the keywords mentioned above and these articles were published between the years 2000 – 2021. Although articles that dated back from the 1900s were used as early reference literature. There were 32 articles relevant for this review article and 2 dissertations that were written between the criteria of years. There were eighteen (18) articles that were excluded based on the relevance of information needed for the article. An observation was made on where current research on the plant *Elephantorrhiza elephantine* is established, what was previously researched on the plant and what more could be investigated to expand our knowledge in literature and identify what challenges could be overcome in the years to come research.

Phytochemicals of the different parts of the plant

Plants' secondary metabolites known as phytochemicals play an important role in reducing the occurrences of many diseases such as diabetes, syphilis, dysentery, fever, hypertension and haemorrhoids.^{6,25} The phytochemical compounds like glycosides, phenols, saponins and tannins which are detected in the plants extract help in the relief of illnesses/healing of wounds with the rich medicinal activity as mentioned in previous literature of^{1,3,22,26} and therefore supports the ethno pharmacological uses of the plant. Phytochemicals are plant-derived molecules (PDMs) known to be a rich source of diverse compounds found in different parts of a plant when extracted using a solvent that could serve as the basis for rational drug design.²⁷ Research

has lead into investigating the phytochemical properties found in the roots/rhizomes and leaves of the plant *E. elephantine*. In these parts of the plant, investigations on which phytochemicals are commonly found as the plant's extracts. The phytochemicals of *Elephantorrhiza elephantine* ranges and includes namely gallic acid, glucoside, flavonoid, phenols, tannins and phytosterols.^{4,21,22,28}

Rhizomes/Roots

According to Mthembu,²⁸ findings from the aqueous and methanol extract of the rhizomes includes flavonoids and have indicated the presence of 5.8-22.3% tannins found in the rhizome of the plant. Tannins is the main compound found in the roots of the plant.^{3,11,26} An additional finding from the study of,²⁸ indicted that 16.8% of sugars were detected in the rhizomes of the plant. The following sugars found in the rhizome of *E. elephantine* were b-sitosterol, gallic acid, methyl gallate, catechin and pentahydroxyflavan, among other compounds. The compounds detected were mainly phenolic compounds with a flavonoid skeleton.²⁸ The paper reported on the plant's good antioxidant activity when tested against and compared to the antioxidant activity of green tea. These results were significant indication of scientific evidence of *E. Elephantine* supporting the plant's ability of antioxidant properties.²⁸

Elephantorrhiza elephantine leaves

Kudumela and Masoko,²² findings reported using the following solvents; n-hexane, dichloromethane, acetone, and methanol for extraction. The phytochemical compounds that were detected in the leaves were flavonoids, cardiac glycosides, alkaloids, steroids and tannins. The Thin Layer Chromatography (TLC) fingerprint profiling of the plant extracts and spectrophotometric methods for quantitative determination were used to support the phytochemistry detections, it was resulted in the study that terpenoids and saponins were not detected as extracts of *Elephantorrhiza elephantine* using TLC. However, the phenolic, tannins and flavonoid content of *E. elephantine* was reported to be the third highest in the study when compared to the other plants. The phytochemicals which could be responsible for medicinal activity in medicinal plants are commonly steroids, tannins, flavonoids and glycosides which were present in all the plants selected for the study.²² Terpenoids and saponins are seen as compounds responsible for antibacterial activity^{22,28} and this could be an indication that *Elephantorrhiza elephantine's* medicinal activity when using the leaves may result from other phytochemical compounds. Kudumela and Masoko,²² used the plant's dried leaf as they were avoiding problems associated with fresh plant material such as bacterial and fungal contamination since most plants live in a mutualistic relationship with microorganisms. The phytochemical compounds such as phenols, tannins and saponins have therapeutic value and may possess one or more biological activity hence the importance of preliminary screening of phytochemicals when studying medicinal plants.

Pharmacological studies

Investigations on the plant's antimicrobial activity and toxicity has been performed in the past decade^{1,5,6} using different solvents with ranging polarisations to extract the phytochemical compounds of *Elephantorrhiza elephantine*. Minimum Inhibitory Concentration (MIC) and disc diffusion methods were used to investigate the antimicrobial activity, assays like TLC and spectrophotometry amongst others were used as qualitative and quantitative assays to investigate which phytochemical compounds are obtainable within the plant.²²

The toxicity of the plant was investigated by subjecting the extract against mouse cells against H4IIE liver and differentiated C2C12 muscle cells (myotubules). The results in previous studies^{6,20,22,28} have indicated that the phenolic and flavonoid compounds extracted from

Elephantorrhiza elephantine's roots and leaves do pose antimicrobial activity which may inhibit bacterial infections which ultimately leads to the healing of infections caused by the microorganism. The plants phytochemical compounds of *E. elephantine* may use different phytochemicals for antimicrobial activity/healing properties. This could explain the different mechanisms/mode of actions which the plant uses or have a stronger affinity to inhibit microorganisms because of the solvents used to extract the compounds than the mechanism used by conventional antibiotics that were also derived from medicinal plants years ago. The active phytochemical compounds found in newly investigated medicinal plants could be different or ineffective since bacteria may have developed resistance against the mechanism of inhibition. Therefore, new plant species investigation could be of clinical value in new development for the treatment of infectious diseases caused by pathogenic microorganisms.²

However,²⁹ expresses that as much as research has been done on the medicinal plant *E. elephantine* for evidence of anti-microbial; anti-inflammatory, anti-malaria, anti-diabetic and wound healing,^{9,19,20,30} no confirmation was acknowledged from researchers for any further development of product and commercialised. Maharaj et al.²⁹ further highlights that the past literature evidence compiled should have already led to the commercialisation of pharmaceutical products in respect to antimicrobial product. However, due to the lack of product to show, this indicates that more research is needed with more corresponding data of past research to strengthen the knowledge before pharmaceutical companies would invest in commercialisation of products.²⁹ This poses questions towards research as to whether scientist are collecting information as part of the natural drug discovery paradigm or whether they interpreting the traditional uses correctly and undertaking biological assays using correct screening and appropriate models and also understanding mechanism of action and safety fully. This highlights that there are gaps within the science studies which should lead to more investigation performed on *E. elephantine* sampled and found in other provinces of the country where the plant is prominent, geographic factors do influence secondary metabolites produced by plants. This will be used for comparison of old research to new research and provide a broader sight of knowledge on *E. elephantine* medicinal properties and strengthen the scientific findings. This review corroborates with²⁹ in that *Elephantorrhiza elephantine* has several scientific reports to prove efficacy through pharmacological studies by the research studies conducted in antibacterial, anti-inflammatory and anti-diabetic but not limited to these mentioned^{6,12,22,28} but not much has been done on the safety. These studies illustrated scientific evidence which validates the traditional uses of the plant. A documented commercialization of a product from the plant *Elephantorrhiza elephantine* was made by Council for Scientific and Industrial Research (CSIR) on the plant's extract from the roots for the management and treatment of Benign Prostate Hyperplasia (BPH)²⁸ and placed on the commercial market. In literature, medicinal uses of the plant *Elephantorrhiza elephantine* have been reported to treat disease such as Urinary tract infections (UTIs) and bladder infection however, not limited to the ones mentioned but fewer research documentation was found regarding its benefits against cancer. Mthembu²⁸ had conducted studies which included the investigation of anticancer using plant extracts from *E. elephantine*. The CSIR led a research using the study of,²⁸ which has made known that the extract of *E. elephantine* has potent activity in inhibiting the 5-alpha reductase enzyme which is responsible for converting testosterone to dihydrotestosterone (DHT). Dihydrotestosterone is a causative factor in the progression of BPH.^{29,31} In addition the mode of action of inhibitors of the 5-alpha reductase enzyme could also be used for the treatment of male pattern baldness.³² This led the CSIR to developing a synthetic product of the extract of the plant for the management and treatment of male pattern baldness. A product is licenced by the CSIR who filed a patent ³³[Patent No US 9,061,023 B2] on the extracts of

E. elephantine for the management and treatment of benign prostatic hyperplasia (BPH).The discovery was licensed to Afriplex a South African botanical manufacturing company (<https://www.csir.co.za/csir-and-afriplexpartners-bringing-health-solutions>) and the product is currently traded as Folicin A/T for BPH and male pattern baldness (<https://afriplex.co.za/what-we-do/product-manufacturing/active-ingredients/>).²⁹ This is a singular case in which the product developed from *E. elephantine* extract, especially for BPH and male pattern baldness since the plant was not documented to be traditionally used towards such an illness/diseases. This could rather be linked to some of the traditional use of the plant by individuals with "bladder or urinary" problems and based on its anti-bacterial properties. This indicates that research that produces satisfying results with enough scientific evidence in the case of study found in the article,²⁹ product commercialisation is possible. This leads to question on what more can be done to close the gap of knowledge and produce more supporting evidence for this plant to achieve more health benefiting products manufacturing.

CONCLUSION

The gap of knowledge on medicinal plants has narrowed down in the past decade because of extensive research carried out by different scientist trying to better understand the benefits of traditional medication and why majority of the population still uses it as they primary healthcare choice. However, some of the research has been questioned on whether or not appropriate studies or guidelines that will lead to authentication of traditional medicines from the plant extracts for their formal incorporation into the healthcare system will follow through. There are still gaps in understanding the mode of action on how the plant extract inhibit the various microorganisms subjected to it, its anti-diabetic properties and antimalarial properties has not been thoroughly investigated but more literature has come forth on the phytochemistry, toxicity and anticancer properties of the plant species whereby a BPH product has been commercialized from the root crude extracts *Elephantorrhiza elephantine*.²⁹ Furthermore, different parts of the plant such as the leaves have been researched as an alternative instead of the root to preserve the plant as it has been listed on the red list database. Further investigating and understanding the mode of action of *E. elephantine* on its mechanism of action on the plants antimicrobial, anti-diabetic, antimalarial, anti-inflammatory and wound healing could lead to a better understanding on the medicinal properties of the plant extracts and a commercialization of a product in future.

LIST OF ABBREVIATIONS

EVM	Ethno veterinary medicine
PDM	Plant-derived molecules
TLC	Thin Layer Chromatography
MIC	Minimum Inhibitory Concentration
CSIR	Council for Scientific and Industrial Research
BPH	Benign Prostate Hyperplasia
UTI	Urinary tract infections
DHT	Dihydrotestosterone

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Radebe T, wrote and made the corrections to the article.

Mfengwana PH and Olivier D read and approved the final manuscript.

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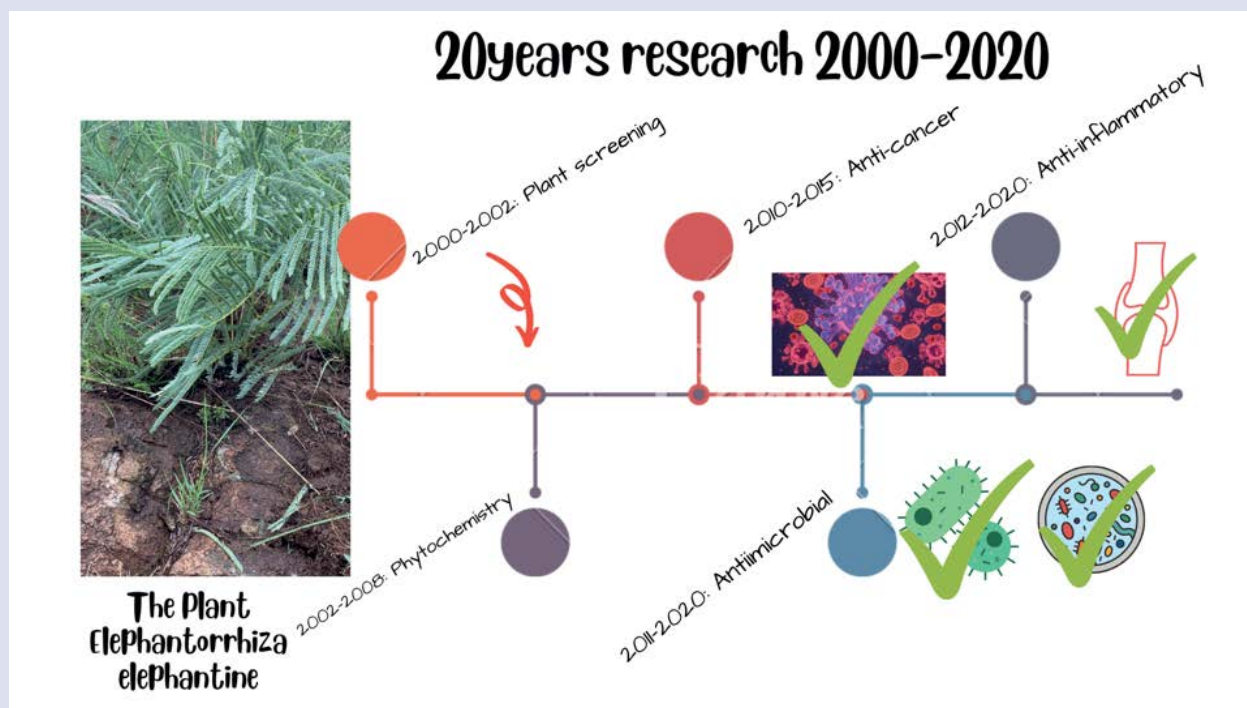
Not applicable.

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GRAPHICAL ABSTRACT



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