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A synthesis and review of ethnomedicinal uses, phytochemistry and biological activities of *Antidesma venosum* E. Mey. ex Tul. (Phyllanthaceae)

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Abstract

Antidesma venosum is an evergreen to semi-deciduous tree used traditionally to treat various human and animal diseases. This review aims to provide an overview and critically analyze the ethnomedical uses, phytochemistry and biological activities of *A. venosum*. The results of the current study are based on literature survey conducted using various search engines such as Elsevier, Pubmed, Google Scholar, PubMed, Springer, Science Direct, Taylor and Francis, and pre-electronic sources such as books, book chapters, scientific journals and other grey literature. The bark, fruit, leaf, root and stem bark decoction or infusion of *A. venosum* are mainly used for magical rituals, as anthelmintic and ethnoveterinary medicine, and traditional cure for epilepsy, hernia, malaria, skin infections, oral candidiasis, snakebites, sexually transmitted infections, abdominal pains, menstrual problems, respiratory infections, infertility, and gastrointestinal infections. The chemical constituents identified from *A. venosum* include essential oils, isoquinoline alkaloids, triterpenoids, lactones, phytosterols, saponins, cardiac glycosides, tannins and flavonoids. The species possesses a wide range of biological activities which include antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, antischistosomal, mutagenic and cytotoxicity activities. *Antidesma venosum* is a valuable medicinal plant species, and future research should focus on animal experiments aimed at assessing toxicity and clinical efficacy of species extracts.

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INTRODUCTION

Antidesma venosum E. Mey. Ex Tul. is a small tree of the Phyllanthaceae family. The genus name *Antidesma* L. is derived from the Greek words "*anti*" meaning "*for*" and "*demos*" meaning "band" about the bark of the species used for cordage (Palmer and Pitman, 1972). The species name "*venosum*" is a Latin word which means "conspicuously veined" about the bold veining of the leaves (Palmer and Pitman, 1972). The synonyms of *A. venosum* include *A. bifrons* Tul., *A. boivinianum* Baill., *A. fuscocinereum* Beille, *A. neriifolium* Pax & K. Hoffm. And *A. tomentosa* Fenzl. *Antidesma venosum* has been recorded in coastal bushveld, woodland, forest margins and grassland in tropical Africa (Palgrave, 2002). The fruits of *A. venosum* are edible in Benin, Ethiopia, Kenya, Mozambique, South Africa and Zimbabwe. The stems of *A. venosum* are used as chewing sticks in Ghana while the leaves of the species are browsed by game and livestock. The bark of *A. venosum* is traded as a traditional medicine in informal herbal medicine markets in South Africa and Tanzania.

Therefore, this review aims to provide a comprehensive appraisal of the ethnomedicinal uses, phytochemistry and biological activities of *A. venosum*.

MATERIALS AND METHODS

An extensive literature survey related to *A. venosum* was conducted using various search engines such as Elsevier, Pubmed, Google Scholar, Springer, Science Direct, Taylor and Francis, and pre-electronic sources such as books, book chapters, scientific journals and other grey literature. The literature search was conducted using keywords such as "*Antidesma venosum"*, "medicinal uses of *Antidesma venosum"*, "phytochemicals of *Antidesma venosum"*, "biological activities of *Antidesma venosum"*, "ethnobotany of *Antidesma venosum",* and various other synonyms of the plant species.

RESULTS AND DISCUSSION

Medicinal uses of *Antidesma venosum*

The bark, fruit, leaf, root, stem, stem bark and twig decoction or infusion of *A. venosum* are mainly used for magical rituals, as anthelmintic and ethnoveterinary medicine, and traditional medicine for epilepsy, hernia, malaria, menstrual problems, skin infections, oral candidiasis, snakebites, sexually transmitted infections, abdominal pains, respiratory infections, infertility and gastrointestinal infections (Table 1, Figure 1). In South Africa, the leaves of *A. venosum* are mixed with those of *Zanthoxylum capense* (Thunb.) Harv., *Trimeria grandifolia* (Hochst.) Warb., *Graderia scabra* Benth. and *Canthium inerme* (L. f.) Kuntze as traditional medicine for stomach complaints. Arnold and Gulumian (1984) argued that the roots of *A. venosum* are mixed with those of *Combretum paniculatum* Vent. and *Grewia microthyrsa* K. Schum. ex Burret or are mixed with those of *Artabotrys brachypetalus* Benth., *Dichrostachys cinerea* (L.) Wight & Arn. and *Zantedeschia aethiopica* (L.) Spreng. As remedies for infertility. In Nigeria, the stem bark of *A. venosum* is mixed with the grass, *Hyparrhenia subplumosa* Stapf as traditional medicine for mental illness (Ibrahim *et al.*, 2008).

Phytochemistry of *Antidesma venosum*

A variety of chemical compounds have been isolated and identified from *A. venosum*, including essential oils, an isoquinoline alkaloid, triterpenoids, lactones and phytosterols (Table 2).

Other phytochemical compounds identified from the leaves, roots and stem bark of *A. venosum* include carbohydrate, saponins, cardiac glycosides, reducing sugars, steroid, tannins and flavonoids.

Biological activities of *Antidesma venosum*

Pharmacological research revealed that different extracts of *A. venosum* and compounds isolated from the species have various biological activities such as antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, antischistosomal, mutagenic and cytotoxicity activities.

Antibacterial activities

(Mayekiso *et al.*, 2009) evaluated the antibacterial activities of acetone leaf extracts of *A. venosum* against *Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis* and *Enterococcus coli* using the following microdilution method. The extract exhibited activities against the tested pathogens with minimum inhibitory concentration (MIC) values as low as 0.02 mg/ml (Mayekiso *et al.*, 2009). Fawole *et al.* (2009a) evaluated the antibacterial activities of dichloromethane, petroleum ether and ethanol extracts of *A. venosum* leaves against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus* using the microdilution technique with neomycin (100.0 μg/ml) as a positive control. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.7 mg/ml to 9.4 mg/ml (Fawole *et al.*, 2009a). Mwangomo *et al.* (2012) evaluated the antibacterial activities of crude, petroleum ether, dichloromethane and methanol extracts of *A. venosum* roots and stem bark against *Streptococcus faecalis, Bacillus cereus, Bacillus subtilis, Bacillus anthracis, Klebsiella pneumoniae, Salmonella typhi, Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Shigella flexneri* using the broth microdilution method with gentamicin as a positive control. The extracts exhibited activities against the tested pathogens with MIC values ranging from 0.02 mg/ml to 5.0 mg/ml (Mwangomo *et al.*, 2012). Magadula *et al.* (2013) evaluated the antibacterial activities of the compounds (3R,4R,5S)-4-hydroxy-5-methyl-3-tetradecanyl γ-lactone, friedelin, lupeol and β-sitosterol isolated from the root bark and stem bark of *A. venosum* against *Enterococcus faecalis*, *Staphylococcus aureus*, *Bacillus cereus*, *Streptococcus pyogenes*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Shigella flexneri* using broth microdilution method with gentamicin as a positive control. All compounds exhibited activities against tested pathogens with MIC values ranging from 0.2 mg/ml to >2.5 mg/ml (Magadula *et al.*, 2013). Shengo *et al.* (2013); Shengo and Mundongo (2020) evaluated the antibacterial activities of crude extracts of *A. venosum* stem against *Klebsiella pneumoniae*, *Salmonella typhii* and *Proteus mirabilis* using agar dilution method. The extract exhibited activities against

Table 1: Medicinal uses of Antidesma venosum

Medicinal use	Part used	Country	Reference
Abdominal pains	Fruits, leaves, roots and twigs	DRC, South Africa, Tanzania	(Chhabra *et al.*, 1993)
Anthelmintic	Roots	DRC and South Africa	(Palgrave, 2002)
Aphrodisiac	Roots	DRC	(Mbayo *et al.*, 2016)
Backache	Stem	Tanzania	(Choi *et al.*, 2015)
Blennorrhoea	Roots	DRC	(Mbayo *et al.*, 2016)
Body pains	Roots	South Africa	(Palgrave, 2002)
Diabetes	Roots	DRC	(Mbayo *et al.*, 2016)
Epilepsy	Roots	Malawi and Tanzania	(Moshi *et al.*, 2005)
Expulsion of retained placenta	Roots	Tanzania	(Chhabra *et al.*, 1993)
Fish poison	Leaves	Tanzania	(Neuwinger, 2004)
Gastro-intestinal problems (diarrhoea, dysentery, gastritis and stomachache)	Leaves, roots and stem bark	DRC, Mozambique, Namibia, Nigeria, South Africa and Tanzania	(Mbayo *et al.*, 2016)
Stomach complaints	Leaves mixed with those of Zanthoxylum capense (Thunb.) Harv., Trimeria grandifolia (Hochst.) Warb., Graderia scabra Benth. and Canthium inerme (L. f.) Kuntze	South Africa	(Arnold and Gulumian, 1984)
Hernia	Roots and stem bark	Mozambique and Tanzania	(Chhabra *et al.*, 1993)
Hypertension	Leaves	Guinea	(Kabine *et al.*, 2015)
Infertility	Roots	DRC, South Africa and Tanzania	(Chhabra *et al.*, 1993)
Infertility	Roots mixed with those of Combretum paniculatum Vent. and Grewia microthyrsa K. Schum. ex Burret	South Africa	(Arnold and Gulumian, 1984)
Infertility	Roots mixed with those of Artabotrys brachypetalus Benth., Dichrostachys cinerea (L.) Wight & Arn. and Zantedeschia aethiopica (L.) Spreng.	South Africa	(Arnold and Gulumian, 1984)
Liver complaints	Roots	Kenya	(Chhabra *et al.*, 1993)
Magical rituals and charm	Leaves and roots	Malawi and Tanzania	(Augustino, 2011)

Continued on next page

Table 1 continued

Medicinal use	Part used	Country	Reference
Menstrual problems	Roots	DRC, South Africa and Tanzania	(Chhabra *et al.*, 1993)
Malaria	Leaves and roots	DRC and Tanzania	(Chhabra *et al.*, 1993; Mbayo *et al.*, 2016)
Mental illness	Stem bark mixed with Hyparrhenia subplumosa Stapf	Nigeria	(Ibrahim *et al.*, 2008)
Oral candidiasis	Roots	Namibia and Tanzania	(Kisangau *et al.*, 2007)
Respiratory infections (chest pain, cough and tuberculosis)	Roots	Namibia, South Africa and Tanzania	(Chhabra *et al.*, 1993)
Schistosomiasis	Roots	Tanzania	(Chhabra *et al.*, 1993)
Sexually transmitted infections (gonorrhoea syphilis and venereal diseases)	Roots	DRC, Mozambique and Tanzania	Chhabra *et al.* (1993)
Skin infections (abscess and acne)	Fruits and roots	Angola, DRC and South Africa	(Mbayo *et al.*, 2016)
Snakebites	Bark, leaves and roots	DRC and Tanzania	(Mbayo *et al.*, 2016)
Tonic	Roots	South Africa	(Arnold and Gulumian, 1984)
Toothache	Roots	DRC	(Mbayo *et al.*, 2016)
Ulcers	Bark	Tanzania	(Chhabra *et al.*, 1993)
Uterine prolapse	Roots	Tanzania	(Chhabra *et al.*, 1993)
Vomiting	Roots	Mozambique	(Arnold and Gulumian, 1984)
Ethnoveterinary medicine (anthelmintic and wounds)	Stem and stem bark	Kenya and Côte d'Ivoire	(Njoroge *et al.*, 2010)

Table 2: Phytochemical compounds isolated from Antidesma venosum

Phytochemical compound	Value	Plant part	Reference
1-methyl-2,4-bis(1-methylethenyl)-cyclohexane (%)	1.7	Leaves	(Egharevba *et al.*, 2015)
3,7,11,15-tetramethyl-(E,E)-1,6,10,14-Hexadecatetraen-3-ol (%)	1.6	Leaves	(Egharevba *et al.*, 2015)
(3R,4R,5S)-4-hydroxy-5-methyl-3-tetradecanyl γ-lactone	-	Root bark	(Magadula *et al.*, 2013)
14-Heptadecenal (%)	0.1	Leaves	(Egharevba *et al.*, 2015)
Antidesmone	-	Leaves	(Bringmann *et al.*, 2000, 2001)
Betulinic acid	-	Root bark	(Magadula *et al.*, 2012)
Caryophyllene (%)	7.1	Leaves	(Egharevba *et al.*, 2015)
Caryophyllene oxide (%)	4.7	Leaves	(Egharevba *et al.*, 2015)
cis-1,2- Cyclohexanedimethanol (%)	0.4	Leaves	(Egharevba *et al.*, 2015)
(R)-(+)-Citronellal (%)	29.0	Leaves	(Egharevba *et al.*, 2015)
Citronellol (%)	0.03	Leaves	(Egharevba *et al.*, 2015)
Citronellyl acetate (%)	12.0	Leaves	(Egharevba *et al.*, 2015)
Condensed tannin (%)	0.7	Leaves	(Fawole *et al.*, 2009b)
Docosane (%)	1.1	Leaves	(Egharevba *et al.*, 2015)
epifriedelanol	-	Root bark	(Magadula *et al.*, 2012)
Eucalyptol (%)	3.2	Leaves	(Egharevba *et al.*, 2015)
β-Eudesmene (%)	0.6	Leaves	(Egharevba *et al.*, 2015)
α-Farnesene (%)	0.6	Leaves	(Egharevba *et al.*, 2015)
(E)-β-Farnesene (%)	0.2	Leaves	(Egharevba *et al.*, 2015)
Farnesol (%)	0.6	Leaves	(Egharevba *et al.*, 2015)
Farnesyl acetone (%)	0.9	Leaves	(Egharevba *et al.*, 2015)
Flavonoid (mg CE/g)	2.8	Leaves	(Fawole *et al.*, 2009b)
Friedelin	-	Root bark and stem bark	(Magadula *et al.*, 2012, 2013)

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Table 2 continued

Phytochemical compound	Value	Plant part	Reference
Gallotannin (μg GAE/g)	0.8	Leaves	(Fawole *et al.*, 2009b)
cis-Geranylacetone (%)	1.1	Leaves	(Egharevba *et al.*, 2015)
Heneicosane (%)	0.6	Leaves	(Egharevba *et al.*, 2015)
Hexahydrofarnesyl acetone (%)	0.1	Leaves	(Egharevba *et al.*, 2015)
Humulene (%)	0.9	Leaves	(Egharevba *et al.*, 2015)
trans-β-Ionone (%)	0.5	Leaves	(Egharevba *et al.*, 2015)
Isopulegol (%)	2.2	Leaves	(Egharevba *et al.*, 2015)
Lupeol	-	Stem bark	(Egharevba *et al.*, 2015)
Methyl citronellate (%)	1.3	Leaves	(Egharevba *et al.*, 2015)
Neo-Menthol (%)	0.4	Leaves	(Egharevba *et al.*, 2015)
Neryl acetate (%)	0.9	Leaves	(Egharevba *et al.*, 2015)
Pheophytin A	-	Root bark	(Magadula *et al.*, 2012)
Phytol (%)	4.1	Leaves	(Egharevba *et al.*, 2015)
Presqualene acetate	-	Root bark	(Magadula *et al.*, 2012)
Presqualene alcohol	-	Root bark	(Magadula *et al.*, 2012)
β-sitosterol	-	Root bark and stem bark	(Magadula *et al.*, 2013)
Stigmasterol	-	Stem bark	(Magadula *et al.*, 2013)
Tetracosane (%)	6.0	Leaves	(Egharevba *et al.*, 2015)
Tetradecanal (%)	7.0	Leaves	(Egharevba *et al.*, 2015)
n-Tridecan-1-ol (%)	0.7	Leaves	(Egharevba *et al.*, 2015)
(Z)-7-Hexadecenal (%)	2.6	Leaves	(Egharevba *et al.*, 2015)
(Z)-7-Tetradecenal (%)	0.2	Leaves	(Egharevba *et al.*, 2015)
α-tocopherol	-	Root bark	(Magadula *et al.*, 2012)
Toddaculin	-	Root bark	(Magadula *et al.*, 2012)
Total phenolics (mg GAE/g)	13.0	Leaves	(Fawole *et al.*, 2009b)
(Z)-2,6,10-trimethyl-1,5,9-Undecatriene (%)	0.6	Leaves	(Egharevba *et al.*, 2015)

Salmonella typhii and *Proteus mirabilis* with MIC values ranging from 6.3 mg/ml to 12.5 mg/ml (Shengo *et al.*, 2013; Shengo and Mundongo, 2020). Tor-Anyiin and Yakumbur (2012) evaluated the antibacterial activities of methanol, ethyl acetate, n-pentanol and water extracts of stem bark of *A. venosum* against *Staphylococcus aureus, Escherichia coli* and *Salmonella typhi* using the agar well diffusion method. The extracts exhibited activities against tested pathogens with the zone of inhibition ranging from 0.3 mm to 6.3 mm (Tor-Anyiin and Yakumbur, 2012). Adegoke *et al.* (2013) evaluated the antibacterial activities of methanol and ethanol leaf extracts of *A. venosum* against *Staphylococcus aureus*, *Escherichia coli*, *Proteus Vulgaris*, *Salmonella typhi*, *Streptococcus lactis* and *Shigella* spp. Using the agar well diffusion method with gentamycin (1.0 μg/ml) as a positive control. The extracts exhibited activities against tested pathogens with a zone of inhibition ranging from 6.0 mm to 21.0 mm, MIC and minimum bactericidal concentration (MBC) values ranged from 6.3 mg/ml to 12.5 mg/ml and 6.3 mg/ml to 50.0 mg/ml, respectively (Adegoke *et al.*, 2013). (Shirinda *et al.*, 2019) evaluated the antibacterial activities of aqueous and organic extracts of *A. venosum* leaves against *Bacteroides fragilis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides vulgatus, Clostridium difficile, Clostridium perfringens, Fusobacterium nucleatum, Fusobacterium varium, Helicobacter pylori, Escherichia coli* and *Enterococcus faecalis* using the microdilution method. The extracts exhibited the best activities against *Clostridium perfringens* with MIC value of 60.0 μg/mL (Shirinda *et al.*, 2019).

Antimycobacterial activities

Mayekiso *et al.* (2009) also evaluated the antimycobacterial activities of acetone leaf extracts of *A. venosum* against *Mycobacterium fortuitum* and *Mycobacterium smegmatis* using the serial microdilution method. The extract exhibited activities against the tested pathogens with MIC values as low as 0.02 mg/ml (Mayekiso *et al.*, 2009). Mmushi *et al.* (2010) evaluated the antimycobacterial activities of acetone, dichloromethane, hexane and methanolic extracts of *A. venosum* leaves against *Mycobacterium smegmatis* using the broth microdilution with rifampicin as a positive control. The extracts exhibited activities with MIC values ranging from 0.3 mg/ml to 1.3 mg/ml and total activity ranging from 16.0 ml/g to 126.6 ml/g (Mmushi *et al.*, 2010).

Antifungal activities

Fawole *et al.* (2009a) evaluated the antifungal activities of dichloromethane, petroleum ether, and ethanol extracts of *A. venosum* leaves against *Candida albicans* using the microdilution technique with amphotericin B as a positive control. The extracts exhibited activities against tested pathogen with MIC values ranging from 3.1 mg/ml to 6.3 mg/ml (Fawole *et al.*, 2009a). Mwangomo *et al.* (2012) evaluated the antifungal activities of crude, petroleum ether, dichloromethane and methanol extracts of *A. venosum* roots and stem bark against *Candida albicans* and *Cryptococcus neoformans* using the broth microdilution method with fluconazole as a positive control. The extracts exhibited activities against tested pathogens with MIC values ranging from 2.5 mg/ml to 5.0 mg/ml (Mwangomo *et al.*, 2012). Magadula *et al.* (2013) evaluated the antifungal activities of the compounds (3R,4R,5S)-4-hydroxy-5-methyl-3-tetradecanyl γ-lactone, friedelin, lupeol and β-sitosterol isolated from the root bark and stem bark of *A. venosum* against *Candida albicans* and *Cryptococcus neoformans* using broth microdilution method with fluconazole as a positive control. All compounds, except for friedelin, exhibited weak activities against the tested pathogens with MIC values of >2.5 mg/ml (Magadula *et al.*, 2013).

Anti-inflammatory activities

Fawole *et al.* (2009b) evaluated the anti-inflammatory activities of *A. venosum* by assessing the ability of dichloromethane, ethanol, petroleum ether and water leaf extracts of the species to inhibit cyclooxygenase 1 and 2 (COX 1 and COX 2) enzymes. The dichloromethane, ethanol and petroleum ether extracts showed suitable activities against COX 1 enzymes with inhibition of prostaglandin synthesis of 72.8% to 103.0% at the highest test concentration of 250 μg/mL (Fawole *et al.*, 2009b).

Antioxidant activities

Kabine *et al.* (2015) evaluated the antioxidant activities of methanol, water and ethyl acetate extracts of *A. venosum* leaves using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay with quercetin as a positive control. The extract exhibited activities with percentage inhibition of about 80.0% (Kabine *et al.*, 2015).

Antischistosomal activities

(Sparg *et al.*, 2000) evaluated the antischistosomal activities of crude extracts of *A. venosum* roots against the schistosomula of *Schistosoma haematobium* with praziquantel as a positive control. The schistosomula were placed into a culture medium to which the plant extract was added. The extract exhibited activities at 12.5 mg/ml, killing 33.3% of the schistosomula worms and killing 100.0% of the

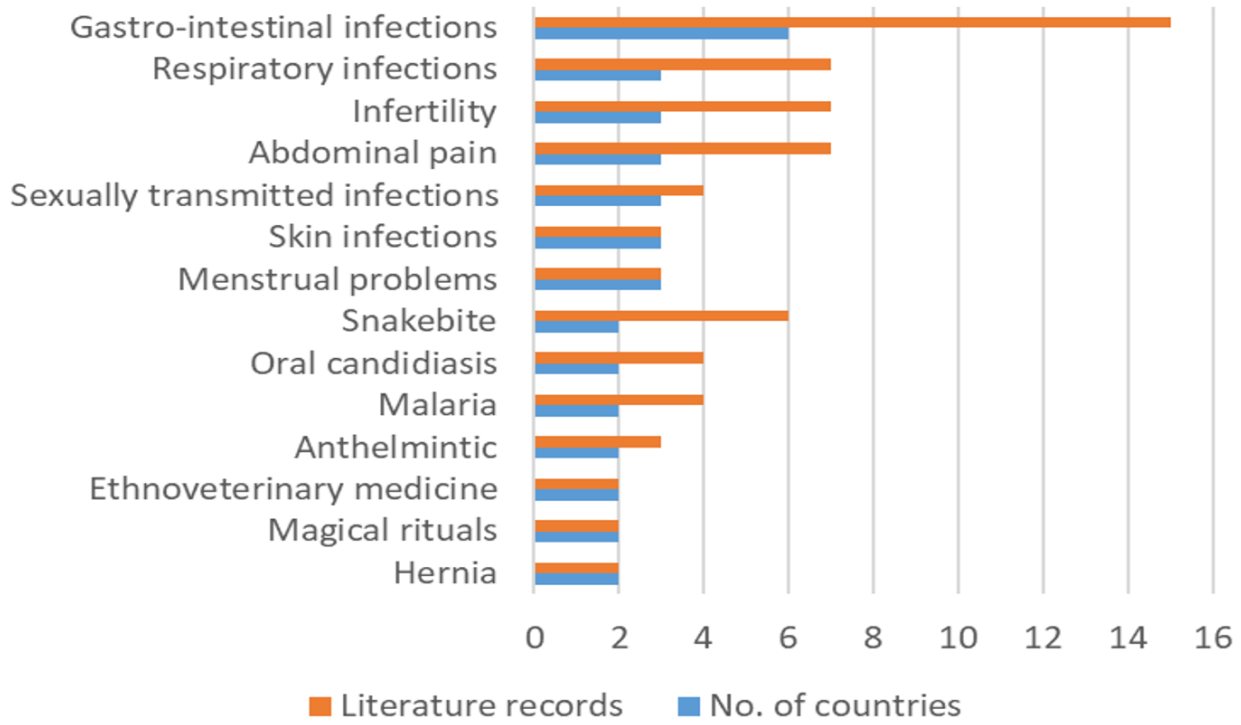

Figure 1: Medicinal uses of Antidesma venosum based on literature records

worms at a concentration of 1.6 mg/ml in comparison to MIC value was 1.0 μg/ml exhibited by the positive control (Sparg *et al.*, 2000).

Mutagenic activities

Elgorashi *et al.* (2002) evaluated the mutagenic activities of dichloromethane and 90.0% methanol extracts of leaf twigs of *A. venosum* using the Ames test, micronucleus test, comet assay and VITOTOX® test. The dichloromethane extract exhibited mutagenicity or DNA damage and chromosomal aberrations in the micronucleus test and comet assay (Elgorashi *et al.*, 2002). Taylor *et al.* (2003) evaluated the mutagenic activities of dichloromethane extract of leaves and twigs of *A. venosum* using the Ames test, micronucleus test, comet assay and VITOTOX® test. The extracts exhibited activities in the micronucleus test and comet assay (Taylor *et al.*, 2003).

Cytotoxicity activities

Steenkamp *et al.* (2009) evaluated the cytotoxicity activities of crude root extracts of *A. venosum* against human adenocarcinoma cells of the cervix (HeLa), human breast cells (MCF-12A), lymphocytes (both resting and stimulated) as well as primary porcine hepatocytes using the using 3-(4,5-dimethyl-2- thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay. The acute systemic toxicity of the crude extract was determined using the BioTox™ and vertebrate test against *Vibrio fischerii* and *Poecilia reticulata*, respectively. The extract exhibited concentration-dependent activities with half-maximal inhibitory concentration (IC_{50}) values of 25.4 μg/ml and 44.0 μg/ml against HeLa and MCF-12A cells, respectively. The extract caused 100% mortality of the bacterial pathogens indicating that the species is cytotoxic and possesses acute systemic toxicity (Steenkamp *et al.*, 2009). Mwangomo *et al.* (2012) evaluated the cytotoxicity activities of crude, petroleum ether, dichloromethane and methanol extracts of *A. venosum* roots and stem bark using the brine shrimp lethality test with cyclophosphamide as a positive control. The extracts exhibited activities with half-maximal lethal concentration (LC_{50}) values ranging from 25.5 μg/ml to 80.3 μg/ml (Mwangomo *et al.*, 2012).

CONCLUSIONS

This review showed that several phytochemicals characterize A. venosum and the species exhibited antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, antischistosomal, mutagenic and cytotoxicity activities. However, the majority of these biological activities lack bio guided isolation strategies and mechanisms of action. Therefore, future research should focus on pharmacokinetics, mechanisms of action and structural activity relationships of the compounds of the species. Future research should also focus on animal experiments aimed at assessing toxicity and clinical

efficacy of species extracts.

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Conflict of Interest

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