Evaluation of Medicinal uses, Phytochemistry and Biological Activities of *Adenia gummifera* (Harv.) Harms

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Abstract: *Adenia gummifera* (Harv.) Harms is a climber or liane widely used as traditional medicine throughout its distributional range in tropical Africa. *Adenia gummifera* occurs naturally in the Democratic Republic of Congo (DRC), Eswatini, Ethiopia, Kenya, Malawi, Mozambique, Seychelles, Somalia, South Africa, Tanzania, Uganda, Zambia and Zimbabwe. This study is aimed at providing a critical review of the medicinal uses, phytochemistry and biological activities of *A. gummifera*. Documented information on the medicinal uses, phytochemistry and biological activities of *A. gummifera* was collected from several online sources, which included Scopus, Google Scholar, PubMed and Science Direct. Additional information was gathered from pre-electronic sources such as book chapters, books, journal articles and scientific publications sourced from the university library. This study showed that the species is widely used as an emetic and a protective charm, and, as traditional medicine for infertility, sexually transmitted infections, gastro-intestinal infections, leprosy, respiratory infections, malaria and menstrual problems. Phytochemical compounds identified from the species include polyacetylenic diepoxide, alkaloids, flavonoids, flavonol, modeccin, proanthocyanidins, tetraphyllin, phenolics, polyphenol and tannins. Pharmacological research revealed that *A. gummifera* extracts and compounds isolated from the species have antibacterial, antifungal, acetylcholinesterase inhibitory (AChEI), anaesthetic, antioxidant, antiplasmodial and cytotoxicity activities. Future research on *A. gummifera* should focus on detailed phytochemical evaluations including toxicological, *in vivo* and clinical studies to corroborate the traditional medical applications of the species.

Keywords: *Adenia gummifera*, ethnopharmacology, herbal medicine, indigenous pharmacopeia, Passifloraceae.

INTRODUCTION

Adenia gummifera (Harv.) Harms is a robust, semi-woody climber or liane belonging to the Passifloraceae family. The genus *Adenia* Forssk. consists of approximately 100 species, the majority of these being perennial succulent herbs, vines, lianas, shrubs and trees [1]. The genus name *Adenia* Forssk. is derived from a Greek name "*aden*" meaning "glandular enlargement" in reference to a pair of glands at the top of the petiole or leaves of some *Adenia* species [2]. The species name "*gummifera*" means producing gum or resin [2]. The synonyms of *A. gummifera* include *A. rhodesica* Suess., *Modecca gummifera* Harv. and *Ophiocaulon gummifera* (Harv.) Harv. The stems of *A. gummifera* are thick, hairless, bluish-green in colour and produce whitish powder in older stems. The height of *A. gummifera* ranges from 5 cm to 15 m [2] and the stems exude reddish pungent fluid when cut. The leaves are simple, alternate, three-lobed, dark grey-green above, glaucous on the underside and distinctly three-veined from the base. The flowers are small, greenish-yellow in colour, axillary, and hanging on loose drooping heads. The fruit is an oval capsule, light green to reddish in colour with a smooth, pitted or rough leathery to smooth shell. *Adenia gummifera* occurs naturally in the Democratic Republic of Congo (DRC), Eswatini, Ethiopia, Kenya, Malawi, Mozambique, Seychelles, Somalia, South Africa, Tanzania, Uganda, Zambia and Zimbabwe [3,4]. *Adenia gummifera* has been recorded on rocky slopes, termite mounds, ravines in dry and moist forests, forest margins, savanna woodlands and bushland at an altitude ranging from 50 m to 2020 m above sea level [3,4].

The leaves of *A. gummifera* are cooked as leafy vegetables in some countries in tropical Africa [4,5]. The roots and stems of *A. gummifera* are sold as traditional medicines in informal herbal medicine markets in Botswana, Mozambique, Gauteng and KwaZulu-Natal provinces in South Africa [6-9]. *Adenia gummifera* is widely used as a disinfectant around the house [10,11] while roots and stems of the species are widely used as fish poison [12-15]. Wink and Van Wyk [11] categorized *A. gummifera* as an extremely hazardous cell toxin which disturbs the gastro-intestinal tract resulting in vomiting, diarrhoea, convulsions, kidney, and liver damage. However, a patent was registered in Kenya, highlighting the use of herbal concoction of *A. gummifera* mixed with *Anthocleista grandiflora* Gilg, *Asparagus africanus* Lam., *Bersama abyssinica* Fresen., *Clematis hirsuta* Guill. & Perr., *Clutia kilimandscharica* Engl., *Croton macrostachyus* Hochst. ex Delile, *Dovyalis abyssinica* (A. Rich.) Warb., *Ekebergia capensis* Sparrm., *Periploca linearifolia*

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Table 1: Medicinal uses of *Adenia gummifera*

Medicinal use	Part used	Country	Reference
Anaemia	Root decoction taken orally	Kenya and Tanzania	[4,12,14,15,23,29]
Antihelmintic	Root decoction taken orally	Mozambique	[9]
Biliousness	Leaf and stem infusions taken orally	South Africa and Tanzania	[2,12,17,18,23-25]
Colic	Aerial part decoction taken orally	Tanzania	[12,23]
Cosmetic	Leaf, root and stem infusions	South Africa and Tanzania	[12,17,18]
Depression	Leaf, root and stem infusions taken orally	South Africa	[2,24,25,30-33]
Diabetes	Stem bark decoction taken orally	DRC	[20]
Emetic	Fruit and root decoction taken orally	Eswatini, South Africa, Tanzania and Zimbabwe	[10-12,17,18,23,25,26,30,31,33,34]
Epilepsy	Root infusion taken orally	South Africa and Zimbabwe	[2,26,27]
Fibroids	Root and stem bark decoction taken orally	Kenya	[35,36]
Gastro-intestinal problems (cholera, diarrhoea, dysentery and stomach ache)	Root decoction taken orally	Kenya, Malawi, South Africa, Tanzania and Zimbabwe	[2,4,12,14,15,23,26-28]
Headache	Root and stem decoction taken orally	Kenya	[37]
Hydrocele	Root decoction taken orally	Tanzania	[12,23]
Induce labour	Leaves, roots, stems and stem bark applied topically	DRC and Mozambique	[19,20]
Infertility	Aerial part, leaf, root and stem decoction taken orally	Kenya, Mozambique, South Africa and Tanzania	[2,5,12,19,23,25,28,35,38,39]
Infertility	Roots mixed with those of *Xylopia parviflora* Spruce	South Africa	[40]
Leprosy	Root decoction taken orally	Eswatini, Kenya, Mozambique, South Africa and Tanzania	[2,4,10-12,15,17,18,23,25,31,34,41]
Madness	Root infusion taken orally	Zimbabwe	[26]
Malaria	Leaf and root decoction taken orally	Eswatini, Mozambique and South Africa	[2,4,10-12,17,18,24,25,31,34]
Menstrual problems	Root and stem infusion taken orally	Kenya, South Africa and Zimbabwe	[5,18,25-27,35]
Menstrual problems	Roots mixed with those of *Maesa lanceolata* Forssk., *Nymphaea capensis* Thunb., *Osyris lanceolata* Hochst. & Steud. and *Piper capensis* L. f.	South Africa	[40]
Oral candidiasis	Root and stem decoction taken orally	Tanzania	[42,43]
Painful uterus	Root infusion taken orally	Zimbabwe	[26]
Pains	Root decoction taken orally	Tanzania	[23]
Prevent abortion	Leaf and root infusion taken orally	Zimbabwe	[26]
Protective charm (ward-off evil spirits)	Leaves, roots and stems	Kenya, Malawi, South Africa and Tanzania	[15,17,18,23,32,44,45]
Respiratory infections (chest pains, colds, cough and tuberculosis	Root and stem decoction taken orally	Kenya, Mozambique and South Africa	[9,18,37,41,45]
Rheumatism	Root decoction applied topically	Malawi and Zimbabwe	[15,26]
Scabies	Root decoction applied topically	Tanzania	[12,23]

(Table 1). Continued.

Medicinal use	Part used	Country	Reference
Sexually transmitted infections (gonorrhoea and venereal diseases)	Root decoction taken orally	Kenya, Malawi, South Africa, Tanzania and Zimbabwe	[2,4,12,14,15,23,27,28,46]
Gonorrhoea	Roots mixed with leaves of *Erianthemum dregei* (Eckl. & Zeyh.) Tiegh. and stems of *Sarcophyte sanguinea* Sparrm.	South Africa	[47]
Venereal diseases	Roots mixed with those of *Dicoma anomala* Sond.	Zimbabwe	[26,48]
Snake bite	Root decoction applied topically	Kenya and Tanzania	[12,14]
Wounds	Leaf, root and stem decoction applied topically	Kenya and Mozambique	[9,19,28]
Ethnoveterinary medicine (foot and mouth, pustular stomatitis and retained placenta)	Leaves	Tanzania and Uganda	[21,22]
Foot and mouth	Leaves mixed with those of *Dodonaea viscosa* (L.) Jacq., *Indigofera arrecta* A. Rich. and *Solanum nigrum* L.	Tanzania	[21]

Quart.-Dill. & A. Rich., *Plantago palmata* Hook. f., *Prunus africana* (Hook. f.) Kalkman, *Rhamnus prinioides* L'Hér. and *Vachellia nilotica* (L.) P.J.H. Hurter & Mabb. that is used as traditional medicine used against human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) opportunistic infections [16]. It is, therefore, within this context that the current study was undertaken aimed at documenting the pharmacological properties, phytochemistry and medicinal uses of *A. gummifera.*

Medicinal uses of *Adenia gummifera*

The medicinal uses of *A. gummifera* have been recorded in DRC, Eswatini, Kenya, Malawi, Mozambique, South Africa, Tanzania, Uganda, Zambia and Zimbabwe, representing 76.9% of the countries where the species is indigenous. Major medicinal applications of *A. gummifera* that have been recorded in three countries and supported by at least three literature records include the use of the species as an emetic and a protective charm and, as a traditional medicine for infertility, sexually transmitted infections, gastro-intestinal infections, leprosy, respiratory infections, malaria and menstrual problems (Table **1**; Figure **1**). Other medicinal applications of *A. gummifera* recorded in at least two countries include the use of the species as cosmetic [12,17,18], to induce labour [19,20], and ethnoveterinary medicine [21,22], and a traditional medicine for anaemia [14,23], biliousness

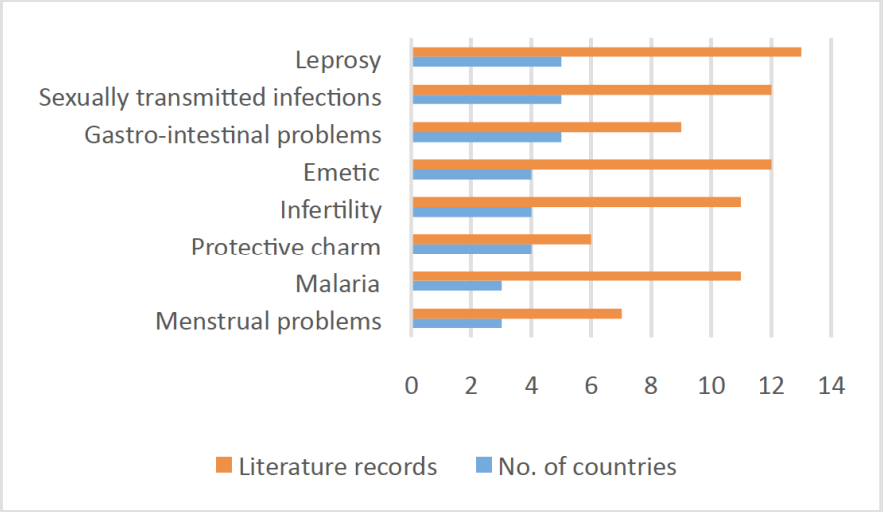

Figure 1: Medicinal applications of *Adenia gummifera* derived from literature records.

[2,12,17,18,23-25], epilepsy [2,26,27], rheumatism [15,26], snake bite [12,14] and wounds [9,19,28].

Phytochemistry of *Adenia gummifera*

Okem *et al.* [49] quantified heavy metals in stems of *A. gummifera* (Table **2**). A wide variety of compounds including a polyacetylenic diepoxide, gummiferol, alkaloids, flavonoids, modeccin, proanthocyanidins, tetraphyllin, flavonol, phenolics, polyphenol and tannins have been identified from the aerial parts, leaves, roots, root bark and stems of *A. gummifera* (Table **2**). Some of these phytochemical compounds may be responsible for the pharmacological properties exhibited by the species.

Biological Activities of *Adenia gummifera*

Pharmacological research revealed that different extracts of *A. gummifera* and compounds isolated from the species have various biological activities such as antibacterial, antifungal, acetylcholinesterase inhibitory (AChEI), anaesthetic, antioxidant, antiplasmodial and cytotoxicity activities.

Antibacterial Activities

Mujovo [25] evaluated the antibacterial activities of acetone extracts of *A. gummifera* leaves against *Bacillus cereus* ATCC 11778, *Bacillus subtilis* ATCC 6051, *Bacillus pumilus* ATCC 7061, *Staphylococcus aureus* ATCC 12600, *Enterecoccus faecalis* ATCC 292192, *Enterobacter cloacae* ATCC 13047, *Escherichia coli* ATCC 11775, *Klebsiella pneumoniae* ATCC 13883, *Pseudomonas aeruginosa* ATCC 33584 and *Serratia marcescens* ATCC 1380 using the agar dilution method with streptomycin sulfate (10.0 µg/ml - 100.0 µg/ml) as a positive control. The extract exhibited activities against the tested pathogens with minimum inhibitory concentration (MIC) values ranging from 1.0 mg/ml to 5.0 mg/ml [25]. Okem *et al*. [49] evaluated the antibacterial activities of acetone extracts of *A. gummifera* stems against *Escherichia coli* ATCC 11775 and *Staphylococcus aureus* ATCC 12600 using microdilution method with neomycin as the a positive control. The extracts exhibited activities with MIC values ranging from 0.4 mg/mL to 12.0 mg/mL [49].

Table 2: Phytochemical Composition of *Adenia gummifera*

Compound	Value	Plant part	Reference
Aluminium (mg/kg)	21.7 – 41.6	Stems	[49]
Cadmium (mg/kg)	0.04	Stems	[49]
Chromium (mg/kg)	5.8 – 6.3	Stems	[49]
Copper (mg/kg)	4.1	Stems	[49]
Flavonoids (mg CTE/g)	0.02	Stems	[49]
Flavonoids (mg quercetin/g)	1.1	Stems	[31]
Gummiferol	-	Leaves	[38]
Iron (mg/kg)	70.3 – 165.5	Stems	[29,49]
Lead (mg/kg)	0.7	Stems	[49]
Manganese (mg/kg)	23.8 – 32.8	Stems	[49]
Mercury (mg/kg)	0.8 – 3.1	Stems	[49]
Modeccin	-	Aerial parts and roots	[11]
Nickel (mg/kg)	2.8 – 6.5	Stems	[49]
Proanthocyanidins (mg quercetin/g)	1.1	Stems	[31]
Tetraphyllin B	-	Aerial parts and roots	[11]
Tin (mg/kg)	76.4 – 77.0	Stems	[49]
Total flavonol (mg quercetin/g)	1.1	Stems	[31]
Total phenolic content (mg GAE/g)	0.1 – 0.2	Stems	[49]
Total polyphenol (mg tannic acid/g)	8.2	Stems	[31]
Zinc (mg/kg)	28.4 – 34.3	Stems	[49]

Antifungal Activities

Tawonezvi [50] evaluated the antifungal activities of ethanol, aqueous and methanol extracts of *A. gummifera* root bark against *Candida albicans* and *Rhodotorula* spp. using the agar well diffusion and broth dilution methods. The aqueous and ethanol extracts exhibited activities with zone of inhibition ranging from 10.0 mm to 37.0 mm and the MIC values ranging from 61.0 mg/ml to 72.0 mg/ml [50].

Acetylcholinesterase Inhibitory (AChEI) Activities

Adewusi and Steenkamp [51] evaluated the acetylcholinesterase inhibitory (AChEI) activities of ethyl acetate extract of *A. gummifera* roots using the Ellman's colorimetric method with galanthamine as a positive control. The extract exhibited dose-dependent AChEI activities with half maximal inhibitory concentration (IC_{50}) value of 0.02 mg/mL [51].

Anaesthetic Activities

Ngarivhume *et al.* [52] evaluated the anaesthetic activities of aqueous extracts of *A. gummifera* stem against *Apis mellifera* (African honeybee) using *in vitro* diffusion method. The extract exhibited anaesthetic activities with a concentration up to 6.0% and excessive exposure was lethal [52].

Antioxidant Activities

Adedapo *et al.* [31] evaluated the antioxidant activities of methanol extracts of the stems of *A. gummifera* using the 2,2'-azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), 1,1-Diphenyl-2-picrylhydrazyl (DPPH) and ferrous reducing antioxidant property (FRAP) assays with ascorbic acid, butylated hydroxytoluene (BHT), catechin and quercetin as positive controls. The extract exhibited activities with reducing ability of 159.1 mm Fe (II)/g while the DPPH radical scavenging activity at a concentration of 0.1 mg/ml which reached 60.0% [31].

Antiplasmodial Activities

Kraft *et al.* [53] evaluated the *in vitro* antiplasmodial activities of petrol ether: ethylacetate (1:1) extracts of the aerial parts of *A. gummifera* using the [^{3}H] hypoxanthine incorporation assay against the chloroquine sensitive and chloroquine-resistant strains of *Plasmodium falciparum*. The extract exhibited weak activities [53].

Cytotoxicity Activities

Fullas *et al.* [38] evaluated the cytotoxicity activities of the polyacetylenic diepoxide compound gummiferol isolated from the leaves of *A. gummifera* using KB cytotoxicity-guided fractionation against the KB human cell lines. The compound exhibited activities with median effective dose (ED_{50}) value of 1.1 µg/ml in the human epidermoid carcinoma (KB) cell line assay [38].

CONCLUSION

Van Wyk *et al.* [10], Wink and Van Wyk [11] argued that *A. gummifera* is poisonous and, therefore, there is a need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. Therefore, the widespread use of *A. gummifera* as food plant and source of traditional medicines throughout its distributional range suggest that the species is not taken at toxic dosages. But the use of *A. gummifera* as food and for the treatment of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies of the bark, fruits, leaves, roots and seeds, and compounds isolated from the species are necessary.

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CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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