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EVALUATION OF MEDICINAL USES, PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES OF *GREWIA OCCIDENTALIS* L. (MALVACEAE)

Alfred Maroyi
Department of Botany, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa; Phone/Fax: 0027406022322; E-mail: amaroyi@ufh.ac.za

Abstract
*Grewiaoccidentalis*L. is a shrub or small tree widely used as traditional medicine in southern Africa.The current study critically reviewed the medicinal uses, phytochemistry and pharmacological properties of *G. occidentalis*. Results of the current study are based on literature survey conducted using various search engines such as Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis, and pre-electronic sources such as books, book chapters, scientific journals and other grey literature obtained from the University library. This study revealed that *G. occidentalis*is used mainly to ease childbirth and hasten labour, as ethnoveterinary medicine, and traditional medicine for bladder ailments, impotence, infertility, respiratory infections, sores and wounds. Pharmacological research identified flavonoids, lipids, phenolics, tannins and triterpenoids from the bark, fruits, leaves, roots and wood of the species. The crude extracts of *G. occidentalis*and phytochemical compounds isolated from the species exhibited antibacterial, antigonococcal, antifungal, anti-HIV, anti-inflammatory, antioxidant and uterotonic activities.*Grewiaoccidentalis*should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological properties.

Keywords: Ethnopharmacology, *Grewiaoccidentalis,* herbal medicine, indigenous knowledge, Malvaceae, southern Africa, Tiliaceae

1. Introduction

Grewiaoccidentalis L. (Figure 1) is a shrub or small tree belonging to the Malvaceae family or the mallows. Evidence from recent molecular analysis has established that *G. occidentalis* belongs to the expanded Malvaceae family as opposed to its previous association with the Tiliaceae family [1-3]. Recent research has resulted in expansion of the family Malvaceae to include families such as Bombacaceae, Sterculiaceae and Tiliaceae[1-3]. The family Malvaceae consists of approximately 250 genera and 4200 species which are mostly herbs or shrubs [4,5]. The genus *Grewia* L. is a pantropical genus with about 300 recognised species of trees, shrubs and lianas distributed throughout the Old World [1]. The genus name *Grewia* is in honour of Nehemiah Grew (1641-1712) an English botanist, physician, author and microscopist, who is considered to be among the founders of plant anatomy as a branch of scientific research [6-8]. The species name *occidentalis* means "from the west" [6-8]. The synonyms of *G. occidentalis* include *G. chirindae*Baker.f.,*G. microphylla*Weim. and*G. rudatisii*Burret[9,10]. The English common names of *G. occidentalis* include "assegai wood", "cross berry", "four corner", "bow wood", "button wood", "dew berry", "pink donkey berry" and "star flower".

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Figure 1: *Grewiaoccidentalis*: A branch showing leaves, flowers and fruits (photo: BT Wursten)

Grewiaoccidentalis is an evergreen to semi-deciduous multi-stemmed shrub or small tree with tangled crown that can grow to a height of 10 metres [7]. *Grewiaoccidentalis* sometimes occurs as a climber in closed evergreen forest and has a tendency to scramble. The bark of *G. occidentalis* is smooth and grey to grey-brown in colour. Leaves of *G. oocidentalis* are simple and alternate, lanceolate to ovate in shape, light green and thinly textured but smooth with three prominent veins from the leaf base [7]. The flowers are pink to dark mauve in colour, showing yellow stamens in central mass, occurring in clusters and situated opposite the leaves. The fruit of *G. occidentalis* is reddish brown in colour, slightly fleshy and shiny drupe when mature, four-lobed and characteristically square in shape. *Grewiaoccidentalis*has been recorded in a variety of habitats such as mountain slopes, thornveld, forest margins, open woodland, bushveld, thicket, wooded grassland, arid highlands, arid Karoo, riverine bush, coastal dune bush and evergreen montane forests [11]. *Grewiaoccidentalis*has been recorded in Eswatini, Lesotho, Mozambique, South Africa and Zimbabwe at an altitude ranging from sea level to 2075 m above sea level [10]. The branches and bark which contain gum and tannin are tough, strong and fibrous and used to make string or rope [12,13]. *Grewiaoccidentalis* is variable and divided into two varieties, namely *G. occidentalis* var. *occidentalis* occurring in Zimbabwe and South Africa, and *G. occidentalis* var. *littoralis* Wild confined to coastal and sand dunes in Mozambique [9]. The leaves of *G. occidentalis* are browsed by game and livestock [14]. The ripe fruits are eaten by humans, often collected and dried for later use [7,13,15-17]. The leaves of *G. occidentalis* are used as leafy vegetables in South Africa [15,16,18-21].

Roots of *G. occidentalis* are an ingredient of a herbal mixture known as "isihlambezo" used to induce or augment labour and as postnatal medication to expel the afterbirth, and often administered to animals to expel the placenta and treatment of endometritis[12,22-24]. The "isihlambezo" ingredients include roots of *G. occidentalis, Agapanthus africanus* (L.) Hoffmans (roots), *Callilepislaureola* DC. (roots), *Cliviaminiata* (Lindl.) Bosse (leaves), *Combretumerythrophyllum* (Burch.) Sond. (roots), *Crinum* spp. (bulb), *Gomphocarpusfruticosus* (L.) W.T. Aiton (roots), *Gunneraperpensa*L. (rhizomes), *Gymnanthemumcorymbosum* (Thunb.) H. Rob. (roots), *Pentanisiaprunelloides* (Klotzsch) Walp. (roots), *Rhoicissustridentata*(L.f.) Wild & R.B. Drumm. subsp. *cuneifolia*(Eckl. &Zeyh.) Urton(roots), *Scadoxuspuniceus*(L.) Friis&Nordal(bulb) and *Typhacapensis* (Rohrb.) N.E.Br. (rhizome) 12,22-24]. It is therefore, within this context that this study was undertaken aimed at reviewing the medicinal uses, phytochemistry and pharmacological properties of *G. occidentalis*.

2. Materials and methods

Several electronic databases were searched which included Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis. Additional information was obtained from pre-electronic sources such as books, book chapters, scientific journals and other grey literature obtained from the University library. The relevant terms *Grewiaoccidentalis*was paired with keywords such as "medicinal uses of *Grewiaoccidentalis"*, "phytochemicals of *Grewiaoccidentalis"*, "biological activities of *Grewiaoccidentalis"*, "pharmacological properties of *Grewiaoccidentalis",* "ethnobotany of *Grewiaoccidentalis",* and various other synonyms and common names of the plant species. The ultimate goal of this search was to explore articles that investigated the medicinal uses, phytochemical and biological activities of *G. occidentalis.*

3. Results and discussion

3.1 Medicinal uses of *Grewiaoccidentalis*

The bark, leaf, root and twig decoctions or infusions of *G. occidentalis*are mainly usedto ease childbirth and hasten labour, as ethnoveterinary medicine, and traditional medicine for bladder ailments, impotence, infertility, respiratory infections, sores and wounds (Table 1; Figure 2). Research by De Wet and Ngubane[25] showed that the roots of *G. occidentalis* are mixed with those of *Rhoicissusdigitata* (L.f.) Gilg& M. Brandt, *Crotalaria monteiroi*Taub. ex Baker f., *Brideliacatharticа*Bertol., *Garcinia livingstonei* T. Anderson and *Commiphoraneglecta* I. Verd. to cleanse blood, as postpartum, and traditional medicine for infertility and menstrual problems. Research by Robert and Robert[13] showed that the bark and twigs of *G. occidentalis*are mixed with leaves of *Centellaasiatica* (L.) Urb. as traditional medicine for ear problems, insect and tick bites, scratches and wounds. Similarly, research by Muthaphuli[26] and Semenya and Maroyi [2] showed that the bark of *G. occidentalis*is mixed with bark of *Cassia abbreviata*Oliv. and*Ficussycomorus* L. as traditional medicine for diabetes mellitus. According to Dold and Cocks [28], the leaves of *G. occidentalis*are mixed with those of *Oleaeuropaea* L. subsp. *africana* (Mill.) P.S. Green and *Zanthoxylumcapense* (Thunb.) Harv. and the sap of *Aloe ferox* Mill. asethnoveterinary medicine for gallsickness in stock.

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Table 1: Medicinal uses of Grewiaoccidentalis

Medicinal use	Parts used and preparation	Country	Reference
Bladder ailments	Rootbark	South Africa	[8,29-36]
Blood cleansing	Roots mixed with those of *Rhoicissusdigitata* (L.f.) Gilg& M. Brandt, *Crotalaria monteiroi*Taub. ex Baker f., *Brideliacathartica*Bertol., *Garcinia livingstonei*T. Anderson and *Commiphoraneglecta* I. Verd.	South Africa	[25]
Boils	Roots	Lesotho	[30,37,38]
Charm and rituals	Stem and wood	Lesotho and South Africa	[39-42]
Diabetes mellitus	Bark mixed with bark of *Cassia abbreviata*Oliv. and *Ficussycomorus* L.	South Africa	[26,27]
Ear problems	Bark and twigs which are mixed with leaves of *Centellaasiatica* (L.) Urb.	South Africa	[13]
Ease childbirth and hasten labour	Leaves, roots and twigs	South Africa	[6,8,9,13,15,30,31,33,35,36,43-47]
Impotence	Leaves, roots and twigs	Eswatini and South Africa	[6,9,13,15,36,44,46,48,49]
Infertility	Leaves, roots and twigs	Eswatini and South Africa	[6,9,13,15,36,43-46,48,50,51]
Infertility	Roots mixed with those of *R.digitata, C.monteiroi, B.cathartica, G.livingstonei* and *C.neglecta*	South Africa	[25]
Insect and tick bites	Bark and twigs which are mixed with leaves of *C.asiatica*	South Africa	[13]
Menstrual problems	Roots mixed with those of *R.digitata, C.monteiroi, B.cathartica, G.livingstonei* and *C.neglecta*	South Africa	[25]
Postpartum	Leaves, roots and twigs	South Africa	[13]
Postpartum	Roots mixed with those of *R.digitata, C.monteiroi, B.cathartica, G.livingstonei* and *C.neglecta*	South Africa	[25]
Respiratory infections (sore throat and tuberculosis)	Roots	South Africa	[52-56]
Scratches	Bark and twigs which are mixed with leaves of *C.asiatica*	South Africa	[13]
Sexually transmitted infections (syphilis and venereal diseases)	Roots	South Africa	[15,34,57]
Sores and wounds	Bark, leaves and twigs	Eswatini, Lesotho and South Africa	[6-9,12,13,21,30,32,33,35-38,44,47-49,58-61]
Wounds	Bark and twigs which are mixed with leaves of *C. asiatica*	South Africa	[13]
Tonic	Roots	South	[49]

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		Africa	
Ethnoveterinary medicine (anthelmintics, gallsickness, heartwater and wounds)	Bark, leaves and twigs	South Africa	[62-66]
Gallsickness in stock	Leaves mixed with those of *Oleaeuropaea*L. subsp. *africana*(Mill.) P.S. Green and *Zanthoxylumcapense*(Thunb.) Harv. and the sap of *Aloe ferox* Mill.	South Africa	[28]

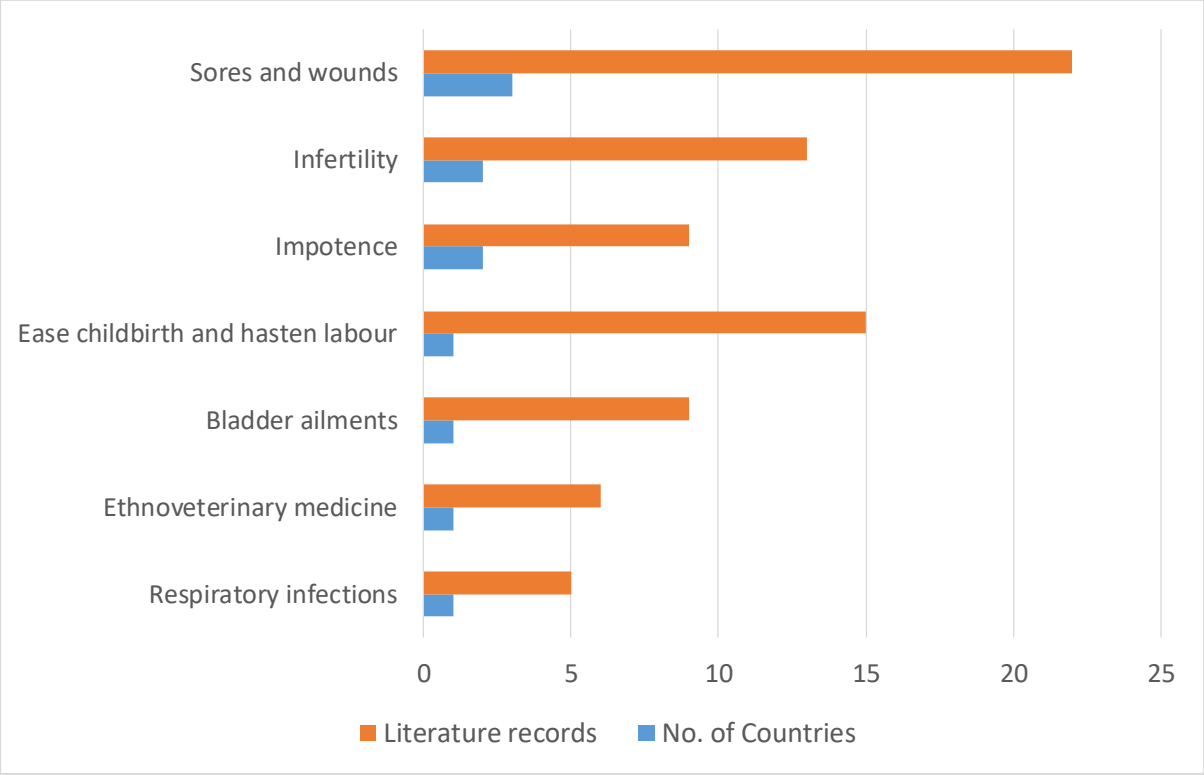

Figure 2: Medicinal uses of *Grewiaoccidentalis*in southern Africa

3.2Nutritional and phytochemistry of *Grewiaoccidentalis*

Some researchers identified nutritional elements and phytochemical compounds from the bark, fruits, leaves, roots and wood of *G. occidentalis* (Table 2). The phytochemical compounds identified from the bark, fruits, leaves, roots and wood of *G. occidentalis* include flavonoids, lipids, phenolics, tannins and triterpenoids (Table 2). Someofthesephytochemicalcompoundsmayberesponsibleforthe pharmacological activities associated with *G. occidentalis*.

Table 2: Nutritional and phytochemistry of *Grewiaoccidentalis*

Nutritional and chemical compound	Value	Plant part	Reference
Acid detergent fibre (%)	27.0	Leaves	[67]
Ash (%)	12.7	Leaves	[67]
Calcium (mg/100g)	183.0	Leaves	[19]
Condensed tannins (% LCE)[a]	0.2	Roots	[57]
Coniferaldehyde ((E)-4-hydroxy-3-methoxy-cinnamaldehyde)	-	Bark and wood	[31]
Copper (%)	10.0	Leaves	[67]
Crude fibre (%)	14.4	Leaves	[67]

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Crude protein (%)	6.0	Leaves	[67]
Flavonoids (µg CAE/g)[b]	1.2	Roots	[57]
Gallotannin (µg GAE/g)[c]	13.2	Roots	[57]
Iron (%)	187.5	Leaves	[67]
Lipid (%)	2.6	Fruits	[68]
Magnesium (mg/100g)	130.0	Leaves	[19]
Manganese (%)	96.0	Leaves	[67]
Neutral detergent fibre (%)	32.8	Leaves	[67]
Oleanonic acid	-	Bark and wood	[31]
Phosphorous (mg/100g)	76.0	Leaves	[19]
Potassium (mg/100g)	579.0	Leaves	[19]
Protein (%)	2.6	Fruits	[68]
Sinapaldehyde ((E)-4-hydroxy-3,5-dimethoxycinnam aldehyde)	-	Bark and wood	[31]
Sodium (mg/100g)	78.0	Leaves	[19]
Syringaldehyde (4-hydroxy-3,5-dimethoxybenzaldehyde)	-	Bark and wood	[31]
Total phenolics (mg GAE/g)[c]	11.7	Roots	[57]
Vitamin C (mg/100g)	18.4	Leaves	[19]
Zinc (mg/100g)	1.1	Leaves	[19]

[a]Values expressed as percentage leucocyanidin equivalents (LCE) per gram plant extracts

[b]Values expressed as catechin equivalents (CTE) per gram of plant extracts

[c]Values expressed as gallic acid equivalent (GAE) per gram of plant extracts

3.3 Pharmacological properties of *Grewiaoccidentalis*

The following biological activities have been reported from the leaves, roots and shoots of *G. occidentalis*as well as phytochemical compounds isolated from the species: antibacterial [34,57,59,69,70], antigonococcal[34,57], antifungal [34,57], anti-HIV [34,57], anti-inflammatory [34,71], antioxidant [33,72] and uterotonic[31] activities.

3.3.1 Antibacterial activities

Grierson and Afolayan [59] evaluated the antibacterial activities of acetone, methanol and water extracts of *G. occidentalis* shoots against *Bacillus cereus, Bacillus pumilus, Bacillus subtilis, Micrococcus kristinae, Staphylococcus aureus, Enterobacter cloacae, Escherichia coli, Klebsiellapneumoniae, Pseudomonas aeruginosa* and *Serratiamarcescens* using the agar diffusion method. The methanol extract exhibited activities against all tested pathogens with minimum inhibitory concentration (MIC) values ranging from 1.0 mg/ml to 4.0 mg/ml [59]. Pretorius et al. [69] evaluated the antibacterial activities of crude extract of *G. occidentalis* leaves at a concentration of 50 mg/ml against *Clavibactermichiganense*pv. *michiganense, Agrobacterium tumefaciens, Erwiniacarotovora*pv. *carotovora, Xanthomonascampestris*pv. *phaseoli* and *Pseudomonas solanacearum* using the agar diffusion method with dimethyl dodecyl ammonium chloride as a positive control. The extract exhibited activities against *Pseudomonas solanacearum* with inhibition zone of 7.0 mm whichcompared favourably with inhibition zone of 12.0 mm exhibited by the positive control [69].Mulaudzi[34] and Mulaudzi et al. [57] evaluated the antibacterial activities of ethanol, dichloromethane, water and petroleum ether extracts of G. occidentalis roots against *Escherichia coli, Staphylococcus aureus, Klebsiellapneumoniae* and *Bacillus subtilis* using the microdilution method with neomycin (0.1 mg/ml) as a positive control. The extracts exhibited activities against the tested pathogens with the MIC values ranging from 0.8 mg/ml to >12.5 mg/ml [34,57].Lall et al. [70] evaluated antibacterial activities of ethanol extract of *G. occidentalis* leaves against *Mycobacterium smegmatis, Mycobacterium tuberculosis* and *Propionibacterium acnes* using micro-dilution technique with ciproflaxin and tetracycline as positive controls. The extract exhibited weak activities against tested pathogens with MIC values ranging from 500.0 µg/mL to >1000.0 µg/mLin comparison to MIC values of 0.3 µg/mL and 0.8 µg/mL exhibited by the positive controls ciproflaxin and tetracycline, respectively [70].

3.3.2 Antigonococcal activities

Mulaudzi[34] and Mulaudzi et al. [57] evaluated the antigonococcal activities of ethanol, dichloromethane and petroleum ether extracts of *G. occidentalis* roots against *Neisseria gonorrhoeae* through determination of clear

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zones of inhibition with ciprofloxacin as a positive controls. The extracts exhibited moderate activities with percentage inhibition ranging from 44.0% to 53.0% [34,57].

3.3.3 Antifungal activities

Mulaudzi[34] and Mulaudzi et al. [57] evaluated the antifungal activities of ethanol, dichloromethane, water and petroleum ether extracts of *G. occidentalis* roots against *Candida albicans* using the microdilution method with amphotericin B as a positive control. The extracts exhibited activities against the tested pathogen with MIC and minimum fungicidal concentration (MFC) values ranging from 1.6 mg/ml to 6.3 mg/ml and 3.1 mg/ml to 6.3 mg/ml, respectively [34,57].

3.3.4 Anti-HIV activities

Mulaudzi[34] and Mulaudzi et al. [57] evaluated the anti-HIV activities of methanol and water extracts of *G. occidentalis* roots against a non-radioactive HIV-1 reverse transcriptase colorimetric ELISA kit with combivir and kaletra as positive controls. The extracts exhibited activities with inhibition percentage of 55.0% at 1.0 mg/ml and half maximal inhibitory concentration (IC_{50}) values ranging from 0.9 mg/ml to 0.1 mg/ml, which were comparable to IC_{50} values of 0.06 mg/ml to 0.3 mg/ml exhibited by the positive control [34,57].

3.3.5 Anti-inflammatory activities

Mulaudzi[34] and Mulaudzi et al. [71] evaluated the anti-inflammatory activities of aqueous, dichloromethane, 80% ethanol and petroleum ether extracts of *G. occidentalis* roots against the cyclooxygenase (COX-1 and COX-2) enzymes. The dichloromethane and petroleum ether extracts exhibited activities towards both COX-1 and COX-2 with percentage inhibition of at least 70.0% [34,71].

3.3.6 Antioxidant activities

Steenkamp et al. [33] evaluated the antioxidant activities of aqueous and methanol extracts of *G. occidentalis* bark by assessing their ability to scavenge the hydroxyl radical (HO•) as measured by means of electron spin resonance spectrometery with the spin trap α-phenyl-N-tert-butylnitrone. For water and methanol extracts, the hydroxyl radical scavenging activities were 58.0% and 78.%, respectively [33].Moustafa et al. [72] evaluated the antioxidant activities of methanol extracts of *G. occidentalis* leaf using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay with ascorbic acid as a positive control. The extract exhibited free radical scavenging activities of 94.7% and half maximal effective concentration (EC_{50}) value of 11.9 µg/ml which was comparable to EC_{50} value of 4.1 µg/ml exhibited by the positive control [72].

3.3.7 Uterotonic activities

Mulholland et al. [31] evaluated the uterotonic activities of aqueous extract and an off-line supercritical extract of *G. occidentalis* using the uterine muscle tissue of a pregnant guinea pig. Research by Mulholland et al. [31] revealed that the uterotonic activities exhibited by the species were due to the compounds oleanonic acid and coniferaldehyde ((E)-4-hydroxy-3-methoxycinnamaldehyde).

4. Conclusion

The present review summarizes the medicinal uses, phytochemistry and pharmacological properties of *G. occidentalis*. Based on presented information, there is not yet enough data correlating the medicinal uses of the species with its phytochemical and pharmacological properties. Detailed studies on phytochemical, pharmacological properties, toxicological properties, *in vivo* and clinical research involving both extracts and compounds isolated from the species are required.

Conflict of interest

No conflict of interest is associated with this work.

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