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# Phytochemicals, bioactivities of *Euclea natalensis*: A review

**Khaled Rashed***

*Department of Pharmacognosy, National Research Centre, 33 El-Bohouth st.-Dokki, Giza, P.O.12622, Egypt*

## Abstract

*Euclea natalensis* is from family Ebenaceae. It is widely used for curing bronchitis, pleurisy, chronic asthma and urinary tract infections by the Zulus, in South Africa. It is traditionally used as herbal medicine for several human diseases and ailments in tropical Africa. It has a high degree of consensus on abdominal pains, antidote for snake bites, diabetes, diarrhoea, malaria, roundworms, stomach problems, toothache, venereal diseases and wounds. Several ethnopharmacological studies have shown that crude extracts and chemical compounds from *E. natalensis* demonstrated many biological activities both in vitro and *in vivo*, which included antibacterial, antidiabetic, antifungal, antimycobacterial, antiviral, antioxidant, antiplasmodial, larvicidal, antischistosomal, molluscicidal, dentin permeability and hepatoprotective activities.

**Keywords:** *Euclea natalensis*, chemical compounds, bioactivities.

***Correspondence Info:**
Dr. Khaled Rashed
Department of Pharmacognosy,
National Research Centre,
33 El-Bohouth st.-Dokki, Giza, P.O.12622, Egypt

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## 1. Introduction

*Euclea natalensis* A. DC. Is from family Ebenaceae It is widely distributed in tropical, subtropical Africa and is common on the East Coast of South Africa. The roots of this plant are being used for curing bronchitis, pleurisy, chronic asthma and urinary tract infections by the Zulus. The roots are also used as a dye, for skin infections caused by Mycobacterium leprae and to relieve headache and toothache by the local inhabitants of South Africa [1].

According to previous investigations, roots of *E. natalensis* have been found to be antibacterial against Mycobacterium tuberculosis and a number of Gram-positive and Gram-negative bacterial species [2, 3]. *Euclea natalensis* is a widely used as herbal medicine in South Africa and the species is an ingredient of a commercial herbal concoction or formula called imbiza [4].

The imbiza formula or prescription is in clinical use, sold in informal markets, medicinal herbal markets and pharmacies in South Africa. Imbiza is a general term for a class of purgative medicines which affect internal cleansing system, often administered as a vaginal douche, a drink or an emetic [5]. Imbiza has also gained popularity in South Africa as an immune booster and as a tonic used to treat and manage various minor and chronic illnesses [6]. Imbiza is used as herbal concoction for ailments such as colds, chest infections, skin infections, diabetes, tuberculosis, cancer and symptoms of human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) [7].

Traditional healers in South Africa prescribe imbiza for women's fertility problems, as a blood purifier, scrofula and for chest complaints [7]. Imbiza is also traditionally used to facilitate pregnancy by preparing the uterus to accept a fetus. Apart from *E. natalensis*, imbiza also contain roots of *Polygala fruticosa* P. J. Bergius, *Raphionacme* spp., bulbous roots of *Crinum* spp. and *Cyrtanthus obliquus* (L. f.) Aiton and the root barks of *Zanthoxylum capense* (Thunb.) Harv, *Capparis tomentosa* Lam. and *Rauvolfia caffra* Sond[4]. The aim of the current review is to comprehensively document information on phytochemistry and biological activities of *E. natalensis* to understand its ethnopharmacological value as traditional herbal medicine.

## 2. Chemical compounds

Several chemical constituents have been isolated from *E. natalensis*, mainly compounds belonging to naphthoquinone and pentacyclic terpenoids classes.

Lopes and Paul [8] isolated two pentacyclic terpenoids, betulin and lupeol from the root bark of *E. natalensis*, while Tannock [9] isolated naphthoquinones, namely isodiospyrin and mamegakinone 4 from the same species. King *et al*. [10] isolated natalenone from the root bark of E. natalensis, while Ferreira *et al*. [11] isolated natalenone hydroxydiospyrin, euclanone, galpinone ,methylnaphthazarin and neodiospyrin from the same species. Khan *et al*. [12] isolated lupeol, mamegakinone, diospyrin and 7-methyljuglone from the root bark of *E. natalensis* while Khan [13] isolated 4,8-dihydroxy-6-methyl-1-tetralone (shinanolone) from the same species . Weigenand *et al*. [14] isolated betulin, lupeol, shinanolone , lupene-3-isoferulate and octahydroeuclein from the root bark of E. natalensis. Similarly, Lall *et al*. [15] isolated betulin, lupeol, shinanolone, 20(29)-lupene-3-isoferulate, octahydroeuclein and -sitosterol from the root bark of *E. natalensis*. Van der Kooy [16] isolated isodiospyrin, mamegakinone, neodiospyrin, diospyrin, 7-methyljuglone , shinanolone and 5-hydroxy-4-methoxy-2-nathaldehyde from the root bark of *E. natalensis*. Van der Kooy *et al*. [17] isolated isodiospyrin, mamegakinone, neodiospyrin, diospyrin, 7-Methyljuglone and shinanolone from root bark of E. natalensis. Bapela *et al*. [18] assessed the correlation between plant growth and accumulation of diospyrin, 7-methyljuglone and shinanolone in seeds and seedlings of *E. natalensis*, but the compounds accumulated at variable rates and no trend could be established between their synthesis and seedling growth. Bapela *et al*. [19] assessed seasonal variation of isodiospyrin and neodiospyrin, diospyrin, 7-methyljuglone and shinanolone from wild plants of *E. natalensis* but no defining pattern was established in the synthesis and accumulation of levels of these compounds within the species. Bapela *et al*. [20] assessed effect of nitrogen, phosphorus and potassium fertilizers on accumulation of isodiospyrin, neodiospyrin , diospyrin, 7-methyljuglone and shinanolone. A significantly positive correlation was established between the concentration of isodiospyrin, neodiospyrin, diospyrin, 7-methyljuglone and shinanolone with fertilization from field-grown seedlings. Joubert *et al*. used high performance liquid chromatography (HPLC) to quantify the concentration of diospyrin and 7-methyljuglone in roots of *E. natalensis*. The concentration of diospyrin was higher (about 2750 mg/kg) than the concentration of 7-methyljuglone which was about 450 mg/kg. Joubert *et al*. [21] argued that the observed variation in naphthoquinones concentration could be due to the age of the roots harvested, wound and environmental or other stress factors. Cooper and Owen-Smith [22] showed that *E. natalensis* leaves contain >5% condensed tannins.

## 3. Bioactivities

### 3.1 Antidiabetic Activities

Nkobole *et al*. [23] evaluated antidiabetic activities of acetone root extracts of *E. natalensis* by assessing in vitro β-glucosidase and α-amylase enzyme assays. The plant extracts demonstrated inhibition of 92.6, 0.04% and 74.5, 0.04%at 0.2mg/mL on β-glucosidase and α -amylase, respectively.

### 3.2 Antioxidant effect

Nkobole *et al*. [23] evaluated antioxidant activities of acetone root extracts of E. natalensis using 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) free radical assay. The DPPH scavenging activity of the plant extract was 94.4, 0.01% which was comparable to 95.8, 0.01% demonstrated by the control, Vitamin C. Nkobole *et al*. [23] also evaluated antioxidant activities of the compounds lupeol and β-sitosterol isolated from the stem bark of *Terminalia sericea* using DPPH free radical assay. The compound lupeol proved high radical activity, exhibiting half maximal effective concentration ($EC_{50}$) values of 3.66 µM, which was comparable to the $EC_{50}$ values of 2.52 µM demonstrated by the control, Vitamin C [23]. Lall *et al*. [24] evaluated antioxidant activities of *E. natalensis* ethanolic shoot extracts using the DPPH free radical assay. The IC50 value of the extracts against DPPH free radical was found to be 22.55, 2.93 g/mL against 4.34, 0.48 µg/mL exhibited by the control, ascorbic acid [67]. These results obtained by Lall *et al*. [24] and Nkobole *et al*. [23] are important as intake of antioxidant rich herbal medicines scavenge free radicals and modulate oxidative stress-related degenerative effects.

### 3.3 Antibacterial Activity

Khan and Nkunya [25] evaluated antibacterial activities of *E. natalensis* root bark extract against *Escherichia coli* and *Staphylococcus aureus*. The extract was active against Staphylococcus aureus exhibiting 15–20 mm inhibition zone. Khan and Nkunya [25] evaluated antibacterial activities of the compounds mamegakinone, diospyrin and 7-methyljuglone isolated from *E. natalensis* roots against *Bacillus anthracis*, *Bacillus cereus*, *Clostridium perfringens*, *Corynebacterium diphtheriae, Escherichia coli, Haemophilus influenzae, Klebsiella aerogenes, Neisseria gonorrhoeae, Pseudomonas aureginosa, Salmonella Heidelberg, Shigella dysenteriae, Shigella flexnerii* and *Staphylococcus aureus*. The compounds were active against most of the bacteria except *Escherichia coli* and *Pseudomonas aureginosa*, with inhibition zone demonstrated by the pathogens ranging from 8 mm to 24 mm [25].

**3.4 Antimycobacterial Activity**

Lall and Meyer [26] evaluated antimycobacterial activities of acetone and water root extracts of *E. natalensis* against drug-resistant and drug-sensitive strains of Mycobacterium tuberculosis H37Rv using the agar plate method. Acetone and water extracts inhibited the growth of Mycobacterium tuberculosis at a concentration of 0.5 mg/mL. Lall and Meyer [26] evaluated the acetone and water extracts using a rapid radiometric method against Mycobacterium tuberculosis and obtained a MIC value of 0.1 mg/mL against the strains.

**3.5 Antiplasmodial and Larvicidal Activities**

Clarkson *et al*. [27] evaluated antiplasmodial activities of aqueous, dichloromethane, dichloromethane and methanol (1:1) root and stem extracts of *E. natalensis* against *Plasmodium falciparum* using the parasite lactate dehydrogenase assay. *Euclea natalensis* dichloromethane and methanol (1:1) root and leaf extract showed promising activities with $IC_{50}$ values of 5.1 µg/mL and 5.3 µg/mL, respectively [27]. The antiplasmodial properties demonstrated by *E. natalensis* imply that the species could be a promising candidate for further investigation as plant-based antimalarial agent. Historically, some of the antimalarial drugs have been derived from herbal medicines or from structures modeled on medicinal plant lead compounds and these include the quinoline-based antimalarials as well as artemisinin and its derivatives. Maharaj *et al*. [28] evaluated larvicidal activities of roots and stem dichloromethane extracts of *E. natalensis* by exposing the third instar *Anopheles arabiensis* larvae to the extracts with acetone and distilled water as controls. The root and stem extracts exhibited 100% mortality after 48 and 96 h of exposure, respectively [28].

**3.3 Antiviral potential**

The acetone extract of *E. natalensis* showed moderate antiviral activity against HSV-1, at concentrations of 0.1 to 0.02 mg/mL as shown by the reduction of virus-induced cytopathogenic effects and the protection of cells in a cell viability assay. The compound diospyrin exhibited no inhibitory effects while water extracts exhibited weak activity at a concentration of 0.2 mg/mL which corresponded to a 42% cytopathic effect. Mahapatra *et al*. [29] evaluated the HIV-1 reverse transcriptase inhibition activities of the compound 7-methyljuglone isolated from the roots of *E. natalensis* and its synthetic derivatives against recombinant HIV-1 enzyme using non-radioactive HIV-RT colorimetric assay. The compound 7-methyljuglone and synthesized compounds exhibited potent inhibitory activities ranging from 70% to 100% at 100 µg/mL [29].

**3.7 Hepatoprotective Effect**

Lall *et al*. [30] evaluated in vitro hepatoprotective activities of E. natalensis ethanolic shoot extracts on human HepG2 cells. The hepatoprotective activities of *E. natalensis* extracts were tested *in vivo* using a rat model of isoniazid and rifampicin-induced hepatotoxicity. *Euclea natalensis* showed a hepatoprotective effect (50% at 12.5 µg/mL) and the ability to increase T-helper 1 cell cytokines Interleukin, Interleukin 2 and Interferon by up to 12-fold and the ability to decrease the T-helper 2 cell cytokine Interleukin 10 fourfold when compared to baseline cytokine production [30].

**3.8 Cytotoxicity and Toxicity**

Lall *et al*. [31] evaluated cytotoxicity of crude chloroform extract of the roots of *E. natalensis*, diospyrin 11 and 7-methyljuglone 12 by exposing different concentrations of samples to green monkey kidney cells (Vero) and a mouse macrophage cell line, J774A.1. Cytotoxicity results for the Vero cell line showed that the crude extract and diospyrin 11 had 50% maximal inhibitory concentration ($IC_{50}$) values of 64.87 and 17.78 µg/mL, respectively. The concentration of 7-methyljuglone that effected a 90% reduction of growth of Mycobacterium tuberculosis Erdman within J774.1 macrophages was 0.57 µg/mL [31]. Similarly, Lall *et al*. [32] evaluated cell toxicity of root extracts of *E. natalensis* by determining the effect of the crude extracts and diospyrin on the monolayers of primary vervet monkey kidney (VK) cells. The dose of the plant samples that inhibited 50% cell growth ($ID_{50}$) after the incubation period was 0.1 mg/mL and 0.2 mg/mL for acetone and water extracts, respectively. The compound diospyrin 11 exhibited an $ID_{50}$ value of 0.02 mg/mL on VK cells. The water extract from the roots of the plant was the least toxic to cell cultures and inhibited the replication of HSV-1 moderately at a concentration of 0.2 mg/mL [32]. More *et al* evaluated cytotoxicity of ethanol leaf extracts of E. natalensis using the XTT (sodium 30-[1-(phenyl amino-carbonyl)-3,4-tetrazolium]-bis-[4-methoxy-6-nitro) benzene sulphonic acid hydrate) assay method. The extracts showed cytotoxicity activity on the Vero cell line with $IC_{50}$ value of 285.1, 4.9 µg/mL.

## 4. Conclusion

*Euclea natalensis* is an important and frequently used herbal medicines in tropical Africa. The species is widely used for human diseases and ailments such as abdominal pains, antidote for snake bites, diabetes, diarrhoea, malaria, roundworms, stomach problems, toothache and venereal diseases.

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