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Systematic Review

Evaluation of Medicinal Uses, Phytochemistry and Biological Activities of *Combretum vendae* A.E. Van Wyk (Combretaceae)

Alfred Maroyi

Department of Biotechnology and Biological Sciences, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa

Abstract

Combretum vendae A.E. Van Wyk, commonly known as “Venda bushwillow”, is a deciduous shrub or small tree endemic to the Blouberg and Soutpansberg mountain ranges in the Limpopo province in South Africa. A critical review is presented here that focuses on the medicinal uses, phytochemicals and *in vitro* biological activities of *C. vendae*. To this end, multidisciplinary scientific publications, which included books, book chapters and scientific journals obtained from the university library and scientific databases such as PubMed®, Web of Science, Scopus®, Google Scholar, SciELO, ScienceDirect® and SpringerLink® were surveyed for the medicinal uses, phytochemical and *in vitro* biological activities of *C. vendae*. The leaf or root decoctions of *C. vendae* are taken orally or applied topically as traditional medicine for bacterial and fungal infections, blood purification, leprosy and as an ophthalmic. Phytochemical compounds identified from *C. vendae* include flavonoids, polyphenolics, tannins, proanthocyanidin, anthocyanin, saponins, terpenoids, steroids, cardiac glycosides and flavanols. The phytochemical compounds isolated from *C. vendae* and its extracts demonstrated antibacterial, antifungal, anti-inflammatory, antioxidant, antiplatelet and cytotoxicity activities. Future research on *C. vendae* should focus on detailed phytochemical, pharmacological and toxicological evaluations, as well as *in vivo* and clinical studies.

Key words: Combretaceae, *Combretum vendae*, materia medica, traditional ecological knowledge, Venda bushwillow

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Corresponding Author: Alfred Maroyi, Department of Biotechnology and Biological Sciences, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Combretum vendae A.E. Van Wyk, commonly known as "Venda bushwillow," is a deciduous shrub or small tree that belongs to the Combretaceae family, commonly known as the white mangrove, Indian almond, or bush willow family. *Combretum vendae* is endemic to the Limpopo province in South Africa in the Blouberg and Soutpansberg mountain ranges in deep red and rocky sandy soils derived from weathered quartzitic sandstone and quartzite^{1,2}, which is a core component of the Soutpansberg Centre of Plant Endemism³. Soutpansberg Centre of Plant Endemism is a regional biological hotspot characterized by high concentrations of endemic species^{2,3}. *Combretum vendae* is exclusively found in the distinct, narrow and restricted ecological and floristic zones of the Blouberg and Soutpansberg mountain ranges¹. Therefore, *C. vendae* is "strict-endemic" or a "local and narrow endemic" or "narrowly restricted endemic" taxon, as the species is confined to a relatively small area but well-defined geographical area based on current species records and distributions⁴. Evaluation of the conservation status of *C. vendae* using the World Conservation Union (IUCN) Red Data categories⁵. Some 15 years after its discovery resulted in categorizing the species as "insufficiently known" due to a lack of information about the condition of the species' habitat, its population and other environmental factors⁶. Currently, the conservation status of *C. vendae* is categorized as of Least Concern on the IUCN Categories and Criteria Version 3.1, as the population of the species is stable⁷. Literature records show that "local and narrow endemics", "narrowly restricted endemics" or "strict-endemics" are often amongst the taxa that are most sensitive to habitat fragmentation or modification, disturbance and environmental changes and are therefore, at highest risk of extinction⁸. The majority of endemic species that are collected from the wild as herbal medicines need human intervention or protection via *in situ* and *ex situ* conservation as both anthropogenic threats and natural environmental changes such as the restricted distribution and specialized habitats of the species, small or declining population size, over-collection or harvesting of the species by local communities often make endemic species more vulnerable to extinction⁴. For example, the leaves and roots of *C. vendae* are used as sources of traditional medicines in the Limpopo province in South Africa⁹.

Previous research showed that endemic plant species have a lot of potential as a possible source of pharmaceutical drugs and health-promoting products for managing and treating a wide range of human and animal diseases or

ailments¹⁰⁻¹⁴. In this context, therefore, "local and narrow endemics", "narrowly restricted endemics" or "strict-endemics" such as *C. vendae* deserve special attention in terms of ethnopharmacological research, as any unfavorable change in the habitat might negatively affect species population. Moreover, research by Rummun *et al.*¹⁵ showed that endemic plants are usually inaccessible to traditional healers and local communities as these species are rare and usually protected by national conservation laws. Therefore, traditional ecological knowledge associated with "local and narrow endemics", "narrowly restricted endemics" or "strict-endemics" such as *C. vendae* is at risk of being lost as this information is not properly documented. This traditional ecological knowledge about *C. vendae* accumulated from the past to the present is extremely important and of great value in ethnopharmacological research. Thus, this review provides an analysis of medicinal uses of *C. vendae* in South Africa, its phytochemistry and *in vitro* biological activities.

MATERIALS AND METHODS

A systematic review of the medicinal uses, phytochemicals and *in vitro* biological activities of *Combretum vendae* was conducted following the Preferred Reporting Items for systematic reviews and meta-analyses (PRISMA) guidelines. The search string used in this study consisted of the following terms: ("medicinal plant" OR "botanical medicine" OR "phytomedicine" OR "phytochemical" OR "in vitro biological activities" OR "ethnobotany") AND ("knowledge" OR "indigenous" OR "culture" OR "traditional" OR "*Combretum vendae*"). The peer-reviewed literature search was performed using PubMed®, Web of Science, Scopus®, Google Scholar, SciELO, ScienceDirect® and SpringerLink® databases. Additional scientific publications, which included books, book chapters and scientific journals, were obtained from the university library. The study inclusion criteria focused on studies that explored the medicinal uses, phytochemical and *in vitro* biological activities of *C. vendae*. Exclusions were made for articles that did not address these issues. In addition to this, scientific papers published as abstracts only, conference papers, technical reports, dissertations and these were excluded. The number of articles appraised for full inclusion in the study amounted to 35 (Fig. 1), published from 1962 to 2025, a long period to capture literature on the medicinal uses, phytochemical and *in vitro* biological activities of *C. vendae*.

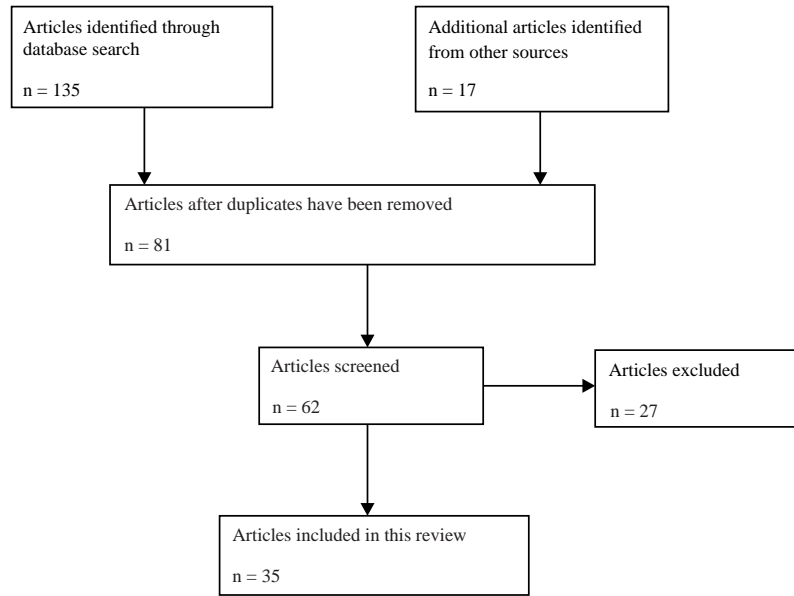


Fig. 1: PRISMA flow diagram presenting the systematic review undertaken in this study

RESULTS AND DISCUSSION

Taxonomy and morphological description of *Combretum vendae*: The genus *Combretum* Loefl. consists of approximately 276 species with a pantropical distribution, mainly in tropical Asia and Africa, but absent in the Pacific Islands and most of Australia¹⁶. About 140 *Combretum* species have been recorded in tropical Africa and approximately 20 species are endemic to Madagascar¹⁷. Therefore, the highest number of *Combretum* species occurs in tropical Africa, with the centre of diversity of the genus on the African continent¹⁸. The genus *Combretum* comprises trees, shrubs and lianas characterized by leaves that are opposite, whorled, or rarely alternate, with entire margins, lacking stipules or having very small stipules and with persistent petioles that often form hooked spines¹⁹. The flowers are bisexual, actinomorphic, with an inferior ovary and winged fruits, or rarely an unwinged nut¹⁶. The genus name '*Combretum*' is of classical origin, as the name was first used by the Roman naturalist, natural philosopher, naval and military commander Gaius Plinius Secundus, known in English as Pliny (23-79 AD), used in reference to an unknown plant²⁰. The name was later reused by the Swedish botanist Pehr Löfving (31 January 1729-22 February 1756) for the *Combretum* genus²⁰. The species name "*vendae*" is in reference to the Venda area in the Limpopo province in South Africa, where the type specimen was collected from¹.

Combretum vendae is a deciduous shrub or small tree growing up to 5 m in height¹. The main stems, fairly widely spaced at ground level, arise from a substantial root

system. The bark is smooth, with inconspicuous, longitudinal reticulation, similar to the bark of species such as *C. caffrum* (Eckl. & Zeyh.) Kuntze, *C. erythrophyllum* (Burch.) Sond., *C. kraussii* Hochst. and *C. woodii* Dümmer¹. The bark is smooth and grey in colour with lighter grey areas arranged in more or less and circumferential bands. The young branchlets are covered with white or greyish hairs. The leaves are simple, opposite, rarely alternate, broadly elliptic to obovate in shape, green in colour above and waxy, while the underside is grey-green in colour, velvety or glabrous with conspicuously raised intersecondary veining. The leaf apex is obtuse to rounded, forming a slender tip, sometimes twisted, while the base is acute to rounded and shallowly lobed, the margin entire. The flowers which appear in September to October are cream to light yellow in colour and their sepals are tinged red or purple, occurring in the axils of the leaves. The winged and broadly elliptic fruits appear in March to August, which are green in colour at first and become dark, wine-red. *Combretum vendae* has been recorded in acidic, clay, rocky and sandy soils on the higher slopes of the Blouberg, Soutpansberg and Thengwe areas of the Limpopo province in South Africa on rocky and deep red sandy soils²¹. Hahn² regards *C. vendae* as a complex species, dividing it into two distinct varieties. Variety *vendae*, which is characterized by leaves with have pubescent lower surface, unlike variety *glabrata* N. Hahn, which has its leaf undersurface being densely glabrous to tomentose². *Combretum vendae* is often confused with a closely related to, *C. nelsonii* Dümmer^{1,2}, which is a multi-stemmed shrub or small tree and *C. collinum* Fresen. subsp. *gazense* (Swynn. & Bak f.)

Table 1: Medicinal uses of *Combretum vendae*

Medicinal use	Part used	References
Bacterial and fungal infections	Leaf decoction applied topically	Watt and Breyer-Brandwijk ²²
Blood purification	Leaf decoction taken orally	Watt and Breyer-Brandwijk ²² , Suleiman <i>et al.</i> ²³ , Dzoyem and Kuete ²⁴ and Ahmed <i>et al.</i> ²⁵
Leprosy	Leaf decoction applied topically	Watt and Breyer-Brandwijk ²² , Suleiman <i>et al.</i> ²³ , Dzoyem and Kuete ²⁴ and Ahmed <i>et al.</i> ²⁵
Ophthalmic	Leaf decoction applied topically	Watt and Breyer-Brandwijk ²² , Suleiman <i>et al.</i> ²³ , Dzoyem and Kuete ²⁴ and Ahmed <i>et al.</i> ²⁵

Table 2: Phytochemical composition of *Combretum vendae* leaves

Phytochemical compound	Formula	References
Acacetin	C ₁₆ H ₁₂ O ₅	Komape <i>et al.</i> ³⁰
Apigenin	C ₁₅ H ₁₀ O ₅	Komape <i>et al.</i> ³⁰ and Eloff <i>et al.</i> ³¹
Arjunolic acid	C ₃₀ H ₄₈ O ₅	Ejidike <i>et al.</i> ³²
Borneol	C ₁₀ H ₁₈ O	Grimsey <i>et al.</i> ²⁷
Camphor	C ₁₀ H ₁₆ O	Grimsey <i>et al.</i> ²⁷
Cineole	C ₁₀ H ₁₈ O	Grimsey <i>et al.</i> ²⁷
Corosolic acid	C ₃₀ H ₄₈ O ₄	Ejidike <i>et al.</i> ³²
Isomenthol	C ₁₀ H ₂₀ O	Grimsey <i>et al.</i> ²⁷
Isomycorene	C ₁₀ H ₁₆	Grimsey <i>et al.</i> ²⁷
Limonene	C ₁₀ H ₁₆	Grimsey <i>et al.</i> ²⁷
Maslinic acid	C ₃₀ H ₄₈ O ₄	Ejidike <i>et al.</i> ³²
Terpineol	C ₁₀ H ₁₈ O	Grimsey <i>et al.</i> ²⁷
Ursolic acid	C ₃₀ H ₄₈ O ₃	Ejidike <i>et al.</i> ³²

Table 3: Proximate, mineral and trace metals composition of ashes, leaves and stems of *Combretum vendae*²⁶

Mineral	Value	Plant part
Ash (%)	9.0-13.0	Leaves and stems
Moisture (%)	8.0	Leaves
Protein (%)	7.0-14.0	Leaves and stems
Energy (kj)	14.0-17.0	Leaves and stems
Calcium (mg/mL)	3.9-26.3	Leaves and stems
Cobalt (mg/mL)	0.2-0.7	Leaves and stems
Copper (ppm)	0.1-0.4	Leaves and stems
Iron (ppm)	0.1-2.5	Leaves and stems
Manganese (mg/mL)	0.1-1.8	Leaves and stems
Magnesium (g/kg dry matter)	2.1-22.3	Leaves and stems
Nickel (mg/mL)	0.3-1.9	Leaves and stems
Potassium (g/kg dry matter)	8.7-51.7	Leaves and stems
Sodium (mg/mL)	2.1-6.7	Leaves and stems
Zinc (ppm)	0.4-0.6	Leaves and stems

Okafor¹, which is characterized by greyish leaves that are covered by woolly hairs¹. Other *Combretum* species associated with *C. vendae* include *C. apiculatum* Sond., *C. collinum* subsp. *gazense*, *C. hereroense* Schinz, *C. moggii*, *C. molle*, *C. mossambicense* (Klotzsch) Engl. and *C. zeyheri* Sond¹.

Medicinal uses of *Combretum vendae*: The leaf or root decoctions of *C. vendae* are taken orally or applied topically as traditional medicine for bacterial and fungal infections, blood purification, leprosy and ophthalmic (Table 1). *Combretum vendae* is closely related to species such as *C. caffrum*, *C. collinum*, *C. erythrophyllum*, *C. kraussii* and *C. woodii*¹, therefore, its medicinal applications are much the same as these species. In South Africa, *Combretum* species such as *C. apiculatum*, *C. caffrum*, *C. collinum*, *C. erythrophyllum*, *C. hereroense*, *C. imberbe*, *C. kraussii*, *C. molle*, *C. paniculatum* and *C. zeyheri* are used for coughs, infertility, venereal diseases, stomach problems, sores and wounds²².

Phytochemistry and pharmacological properties of *Combretum vendae*:

Qualitative and quantitative phytochemical analyses of *C. vendae* leaves, stems and ashes revealed the presence of flavonoids, polyphenolics, tannins, proanthocyanidin, anthocyanin, saponins, terpenoids, steroids, cardiac glycosides and flavonols²⁵⁻²⁷ (Table 2). *Combretum vendae* is a good source of proteins, energy, minerals such as calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium and zinc (Table 3). The protein content of 7.0 to 14.0% exhibited by *C. vendae* implies that the browse value of the species is higher than other *Combretum* species, such as *C. imberbe*, which have leaves and twigs containing only 4.0% protein²⁸. Although no digestibility value of the leaves, branches, twigs, or fruits of *C. vendae* to livestock or game could be found in the literature, the species is a potential forage for ruminants as the species is an important source of micro and macro elements, as well as classical nutrients such as proteins and energy²⁹. Some of the phytochemical compounds isolated

from *C. vendae* leaves and its crude extracts exhibited antibacterial, antifungal, anti-inflammatory, antioxidant, antiplatelet and cytotoxicity activities, supporting some of its traditional medicinal uses.

Antibacterial activities: Ahmen *et al.*³³ evaluated the antibacterial activities of the acetone extract of *C. vendae* leaves against *Enterococcus faecalis*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* using the microplate dilution method with gentamicin as a positive control. The acetone extract of the species showed activities against the tested pathogens exhibiting minimum inhibition concentration (MIC) values which ranged from 0.16 mg/mL to 0.31 mg/mL³³. Suleiman *et al.*²³ assessed the antibacterial properties of hexane, acetone, dichloromethane and methanol extracts of *C. vendae* leaves against *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* using a two-fold serial microdilution assay with gentamicin as a positive control. The extracts showed antibacterial activities against the tested pathogens, exhibiting MIC values which ranged from 0.08 mg/ml to 2.5 mg/mL²³. Ahmed *et al.*²⁵ assessed the antibacterial properties of dichloromethane, water, ethyl acetate and butanol extracts of *C. vendae* leaves against *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* using the microdilution method with gentamicin as a positive control. The extracts demonstrated activities against the tested pathogens, exhibiting MIC values ranging from 39.0 to 625.0 µg/mL²⁵. Komape *et al.*³⁰ evaluated the antibacterial activities of acetone, hexane, chloroform, dichloromethane and methanol extracts of *C. vendae* leaves and the phytochemical compound acacetin isolated from the species against *Enterococcus faecalis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* using the serial microplate dilution method with ampicillin as a positive control. The extracts and the phytochemical compound demonstrated activities against the tested pathogens, exhibiting MIC values ranging from 0.08 to 2.5 mg/mL³⁰. Anokwuru *et al.*³⁴ assessed the antibacterial properties of the methanol extract of *C. vendae* leaves against *Shigella sonnei*, *Staphylococcus aureus*, *Escherichia coli*, *Staphylococcus epidermidis*, *Bacillus cereus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Salmonella typhimurium* and using the microdilution method with ciprofloxacin as a positive control. The extracts showed antibacterial activities against the tested pathogens, exhibiting MIC values which ranged from

0.25 mg/mL to >3.0 mg/mL³⁴. Grimsey *et al.*²⁷ evaluated the antibacterial activities of the methanol extract of *C. vendae* leaves against *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Escherichia coli* using the broth microdilution assay with ciprofloxacin, ampicillin, gentamycin, oxacillin and methicillin as positive controls. The extracts demonstrated activities against the tested pathogens exhibiting MIC values ranging from 115.0 to 460.0 µg/mL²⁷.

Antifungal activities: Suleiman *et al.*²³ assessed the antifungal properties of dichloromethane, acetone, methanol and hexane extracts of *C. vendae* leaves against *Microsporum canis*, *Aspergillus fumigatus*, *Sporothrix schenckii*, *Candida neoformans* and *Candida albicans* using a two-fold serial microdilution assay with amphotericin B as a positive control. The extracts showed antifungal activities against the tested pathogens, exhibiting MIC values which ranged from 0.08 to 2.5 mg/mL²³. Ahmed *et al.*²⁵ assessed the antifungal properties of ethyl acetate, dichloromethane, water and butanol extracts of *C. vendae* leaves against *Aspergillus fumigatus*, *Candida albicans* and *Cryptococcus neoformans* using the microdilution assay with amphotericin B as a positive control. The extracts showed antifungal activities against the tested pathogens, exhibiting MIC values which ranged from 19.0 to 1250.0 µg/mL²⁵.

Anti-inflammatory activities: Ahmed *et al.*²⁵ evaluated the anti-inflammatory activities of the crude extracts of *C. vendae* leaves by determining the inhibition of 15-lipoxygenase (15-LOX) using soybean lipoxygenase type 1-B. The extract demonstrated lipoxygenase inhibitory capacity by exhibiting a Median Lethal Concentration (LC₅₀) value of 22.3 µg/mL²⁵.

Antioxidant activities: Suleiman *et al.*³⁵ assessed the antioxidant properties of the methanol extract of *C. vendae* leaves using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay with L-ascorbic acid as a positive control. The extract showed antioxidant activities exhibiting a maximal effective concentration (EC₅₀) value of 4.4 µg/mL³⁵. Ahmed *et al.*²⁵ assessed the antioxidant properties of ethyl acetate, water, butanol and dichloromethane extracts of *C. vendae* leaves using the ferric reducing antioxidant power (FRAP), 2,2'-azino-bis (3-ethylbenzothiazoline)-6-sulphonic acid (ABTS) and DPPH free radical scavenging methods with trolox and ascorbic acid as positive controls. The extracts showed ferric reducing antioxidant power activities and EC₅₀ values which ranged from 0.25 to 23.9 µg/mL for

ABTS and DPPH, respectively²⁵. Mathipa *et al.*²⁶ evaluated the antioxidant activities of 70% acetone extract of *C. vendae* leaves using the DPPH free radical scavenging assay with ascorbic acid as a positive control. The extract exhibited dose-dependent activities with scavenging activities ranging from 60.0 to 80.0%²⁶.

Antiplatelet activities: Suleiman *et al.*³⁵ evaluated the antiplatelet activities of the methanol extract of *C. vendae* leaves using the *in vitro* platelet aggregation method with aspirin as the positive control. The extract demonstrated antiplatelet properties exhibiting an EC₅₀ value of 0.06 µg/mL³⁵.

Cytotoxicity activities: Suleiman *et al.*³⁵ assessed the cytotoxicity properties of methanol extract of *C. vendae* leaves against the Vero monkey kidney cell line using the 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT) method with berberine chloride as a positive control and the hemagglutination method. The extract exhibited cytotoxicity properties with agglutination occurring at 1.3 mg/mL and demonstrated a hemagglutination assay titer value of 0.8³⁵.

CONCLUSION

The current study showed that leaf or root decoctions of *C. vendae* are taken orally or applied topically as traditional medicine for bacterial and fungal infections, blood purification, leprosy and also used as an ophthalmic. The species is also characterized by phytochemical compounds such as flavonoids, polyphenolics, tannins, proanthocyanidin, anthocyanin, saponins, terpenoids, steroids, cardiac glycosides and flavonols. While *C. vendae* has a long history of human association and use, it has not received wide acknowledgment for its various medicinal uses. *Combretum vendae* has great potential as a medicinal plant characterized by several ethnomedicinal applications and ethnopharmacological properties. To realize the full potential of *C. vendae*, future studies should explore additional active phytochemical compounds using various *in vitro* and *in vivo* models.

SIGNIFICANCE STATEMENT

This study discovered the medicinal importance of *Combretum vendae* A.E. Van Wyk, a South African endemic species traditionally used for treating bacterial and fungal infections, blood purification, leprosy and

ophthalmic conditions. The plant was shown to contain diverse phytochemical compounds, including flavonoids, tannins, saponins, terpenoids, steroids and cardiac glycosides, which are responsible for its antibacterial, antifungal, antioxidant, anti-inflammatory and cytotoxic properties. These findings highlight its potential as a promising natural source of novel bioactive agents for therapeutic development. This study will help researchers to uncover the critical areas of phytochemical and pharmacological evaluation that many were not able to explore. Thus, a new theory on the ethnopharmacological significance of *C. vendae* may be arrived at.

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