

# *Nidorella ivifolia*: a review of its botany, medicinal uses, phytochemistry and biological activities

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## Abstract

*Nidorella ivifolia* is a perennial shrub widely used as herbal medicine in southern Africa. This study is aimed at providing a critical review of the botany, medicinal uses, phytochemistry and biological activities of *N. ivifolia*. Documented information on the botany, medicinal uses, phytochemistry and biological activities of *N. ivifolia* was collected from several online sources which included BMC, Scopus, SciFinder, Google Scholar, Science Direct, Elsevier, Pubmed and Web of Science. Additional information on the botany, medicinal uses, phytochemistry and biological activities of *N. ivifolia* 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 leaves and roots of *N. ivifolia* are used as herbal medicines for backache, hyperventilation, sprains, swollen feet and hands, blood pressure, depression, pain, rheumatism, headache, pleuritic pain, postnatal cleansing, diabetes, stomach problems, convulsions, inflammation, influenza, heart problems, fever and respiratory problems. Several phytochemical compounds including diterpene acids,  $5\alpha$ -hydroxy,10β-hydroxyprintzianic acid, conyscabraic acid, hautriwaic acid, nidoresedaic acid, printziaic acid, cardiac glycosides, saponins and tannins have been identified from the leaves of *N. ivifolia*. Pharmacological research revealed that *N. ivifolia* crude extracts and essential oils isolated from the species have antibacterial, antimycobacterial, antifungal, antiplasmodial, antiprotozoal and cytotoxicity activities. *Nidorella ivifolia* should be subjected to further phytochemical, pharmacological activities.

Keywords: Asteraceae, Compositae, ethnopharmacology, herbal medicine, indigenous pharmacopeia, Nidorella ivifolia

# INTRODUCTION

Nidorella ivifolia (L.) J.C. Manning & Goldblatt is a perennial shrub belonging to the Asteraceae or Compositae family. The family Asteraceae is an important source of pharmaceutical drugs such as artemisinin, developed from the leaves of Artemisia annua L.1-8 Asteraceae is one of the largest families of flowering plants in the world, with about 1600 genera and 23,000 species found almost everywhere in the world except in Antarctica.<sup>9</sup> Several members of the family Asteraceae are characterized by phytochemical compounds such as acetophenones, caffeoylquinic acids, phloroglucinol, polyphenols, pyrrolizidine alkaloids, polyacetylenes, chalcone, flavonoids and diterpenoids.<sup>10,11</sup> Several species of the family Asteraceae are characterized by analgesic, anti-allergic, antibacterial, antidiabetic, antifungal, antiviral, anti-inflammatory, antimigraine, antioxidant, antiproliferative, antipyretic, antitumor, antiulcer. cardiotonic, and neuroprotective and neurotoxicity activities.9-13 Nidorella ivifolia and other related species such as N. anomala Steetz, N. auriculata DC., N. microcephalla Steetz, N. pinnata (L.f) J.C. Manning & Goldblatt and N. resedifolia DC. are used as herbal medicines in tropical Africa.<sup>14-16</sup> The leaves of N. *ivifolia* are cooked as leafy vegetables in Namibia.<sup>17,18</sup> Leaves and stems of N. ivifolia are sold as herbal medicines in the informal herbal medicines markets in the Eastern Cape province in South Africa.<sup>19</sup> Nidorella ivifolia is one of the important medicinal plants in South Africa and the species is included in the book "medicinal plants of South Africa", a photographic guide to the most commonly used plant medicines in the country, including their botany, main traditional uses and active ingredients.<sup>20</sup> Research by Van  $Wyk^{21}$  showed that the leaves of *N. ivifolia* have

commercial potential as herbal medicines for inflammation, colds and fever in South Africa. It is within this context that this review was undertaken aimed at reviewing the botany, medicinal uses, phytochemical and biological activities of *N. ivifolia* so as to provide the baseline data required in evaluating the therapeutic potential of the species.

# Botanical profile of Nidorella ivifolia

The genus Nidorella Cass. comprises about 15 species that are restricted in distribution to eastern and southern Africa.<sup>22-30</sup> Both morphological and molecular data showed that species of *Nidorella* Cass. and those of *Conyza* Less. are closely related.<sup>23,27,31,32</sup> Synonyms associated with N. ivifolia include Baccharis halimifolia Moench, B. ivaefolia L., Conyza ivifolia (L.) Less., C. scabrida DC., Erigeron dentatus Burm.f., E. ivifolius Sch. Bip., Fimbrillaria baccharoides Cass., Marsea ivifolia Kuntze and Pluchea scabrida DC.<sup>23-26,29,30</sup> Nidorella ivifolia is an erect, multi-stemmed, slender shrub with willowy branches up to 2 metres in height, <sup>30</sup> with minutely hairy stems bearing aromatic leaves.<sup>18,33</sup> Leaves are petiolate, elliptic to lanceolate in shape, three-nerved from the base and leaf margins that are sharply serrate. The flower heads are inconspicuous, disciform, borne in flattopped clusters, in dense terminal corymbs which are cream-coloured to pale yellow in colour. The fruits of N. ivifolia are small nutlets that are dispersed by means of bristly seed hairs. The species has been recorded in Botswana, Lesotho, Mozambique, Namibia, South Africa, Swaziland and Zimbabwe.<sup>23,25,26,28-30</sup> Nidorella ivifolia has been recorded near streams and in sandstone slopes, streambeds or forest margins at an altitude ranging from 5 m to 1920 m above sea level.<sup>25,29,30</sup>

# Medicinal uses of Nidorella ivifolia

The leaves and roots of *N. ivifolia* are used as herbal medicines for backache, hyperventilation, sprains, swollen feet and hands, blood pressure, depression, pain, rheumatism, headache, pleuritic pain, postnatal cleansing,

diabetes, stomach problems, convulsions, inflammation, influenza, heart problems, fever and respiratory problems (Table 1, Figure 1). The roots of *N. ivifolia* are used as a substitute for *Anemone caffra* Harv. for magical purposes in South Africa.<sup>34,35</sup>

Medicinal use	Parts used	References
Arthritis	Leaves	Philander <sup>36</sup>
Backache	Leaves	Nortje and Van Wyk <sup>37</sup> ; Hulley and Van Wyk <sup>38</sup>
Bladder infections	Leaves	De Beer and Van Wyk <sup>39</sup>
Blood pressure	Leaves	Hulley and Van Wyk <sup>38</sup> ; Thring and Weitz <sup>40</sup> ; Balogun and Ashafa <sup>41</sup>
Convulsions	Leaves	Hutchings et al. <sup>35</sup> ; Thring and Weitz <sup>40</sup> ; Watt and Breyer-Brandwijk <sup>42</sup> ; Hutchings and Van Staden <sup>43</sup> ; Ojewole <sup>44</sup> ; Sobiecki <sup>45</sup> ; Stafford et al. <sup>46</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Masondo et al. <sup>48</sup>
Depression	Roots	Semenya et al. <sup>49</sup> ; Semenya and Potgieter <sup>50</sup> ; Mogale et al. <sup>51</sup>
Diabetes	Leaves	Van Wyk et al. <sup>20</sup> ; Philander <sup>36</sup> ; Nortje and Van Wyk <sup>37</sup> ; Thring and Weitz <sup>40</sup> ; Thring et al. <sup>52</sup> ; Afolayan and Sunmonu <sup>53</sup> ; Odeyemi and Bradley <sup>54</sup>
Eye problems	Leaves	Thring and Weitz <sup>40</sup>
Fever	Leaves	Van Wyk et al. <sup>20</sup> ; Van Wyk <sup>21</sup> ; Hutchings et al. <sup>35</sup> ; Philander <sup>36</sup> ; Nortje and Van Wyk <sup>37</sup> ; Hulley and Van Wyk <sup>38</sup> ; Thring and Weitz <sup>40</sup> ; Watt and Breyer-Brandwijk <sup>42</sup> ; Thring et al. <sup>52</sup> ; Scott et al. <sup>55</sup> ; McGaw et al. <sup>56</sup>
Fractures	Leaves	Thring and Weitz <sup>40</sup> ; Hutchings <sup>57</sup>
Gall	Leaves	Philander <sup>36</sup>
Gout	Leaves	Philander <sup>36</sup>
Headache	Leaves	Hutchings et al. <sup>35</sup> ; Hulley and Van Wyk <sup>38</sup> ; Thring and Weitz <sup>40</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Van Wyk et al. <sup>58</sup>
Heart problems	Leaves	Van Wyk et al. <sup>20</sup> ; Hutchings et al. <sup>35</sup> ; Philander <sup>36</sup> ; Hulley and Van Wyk <sup>38</sup> ; De Beer and Van Wyk <sup>39</sup> ; Thring and Weitz <sup>40</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Thring et al. <sup>52</sup> ; Van Wyk et al. <sup>58</sup> ; Van Wyk <sup>59</sup> ; Van Wyk and Gorelik <sup>60</sup> ;
Hyperventilation	Leaves	Hutchings et al. <sup>35</sup> ; Sobiecki <sup>45</sup>
Infertility	Leaves	Hulley and Van Wyk <sup>38</sup>
Inflammation	Leaves	Van Wyk et al. <sup>20</sup> ; Van Wyk <sup>21</sup> ; Hutchings et al. <sup>35</sup> ; Philander <sup>36</sup> ; Hulley and Van Wyk <sup>38</sup> ; Thring and Weitz <sup>40</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Thring et al. <sup>52</sup> ; Scott et al. <sup>55</sup>
Influenza	Leaves	Van Wyk et al. <sup>20</sup> ; Philander <sup>36</sup> ; Hulley and Van Wyk <sup>38</sup> ; De Beer and Van Wyk <sup>39</sup> ; Thring and Weitz <sup>40</sup> ; Thring et al. <sup>52</sup> ; Van Wyk <sup>59</sup> ; Van Wyk and Gorelik <sup>60</sup> ; Seaman <sup>61</sup>
Kidney problems	Leaves	Hulley and Van Wyk <sup>38</sup>
Magical purposes	Roots used as a substitute for <i>Anemone caffra</i> Harv.	Gerstner <sup>34</sup> ; Hutchings et al. <sup>35</sup>
Pains	Leaves	Van Wyk et al. <sup>20</sup> ; Hulley and Van Wyk <sup>38</sup> ; De Beer and Van Wyk <sup>39</sup>
Pleuritic pain	Roots	Hutchings et al. <sup>35</sup> ; Thring and Weitz <sup>40</sup> ; Hutchings and Van Staden <sup>43</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Seaman <sup>61</sup>
Postnatal cleansing	Leaves	Hutchings et al. <sup>35</sup> ; Hulley and Van Wyk <sup>38</sup> ; De Beer and Van Wyk <sup>39</sup> ; Thring and Weitz <sup>40</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Van Wyk et al. <sup>58</sup>
Respiratory problems (chest complaints, colds, and coughs)	Leaves	Van Wyk et al. <sup>20</sup> ; Van Wyk <sup>21</sup> ; Hutchings et al. <sup>35</sup> ; Philander <sup>36</sup> ; Hulley and Van Wyk <sup>38</sup> ; De Beer and Van Wyk <sup>39</sup> ; Thring and Weitz <sup>40</sup> ; Watt and Breyer-Brandwijk <sup>42</sup> ; Hutchings and Van Staden <sup>43</sup> ; Wentzel and Van Ginkel <sup>47</sup> ; Thring et al. <sup>52</sup> ; McGaw et al. <sup>56</sup> ; Van Wyk et al. <sup>58</sup> ; Van Wyk <sup>59</sup> ; Van Wyk and Gorelik <sup>60</sup> ; Seaman <sup>61</sup>
Rheumatism	Leaves	Van Wyk et al. <sup>20</sup> ; Philander <sup>36</sup> ; Thring and Weitz <sup>40</sup> ; Thring et al. <sup>52</sup>
Sores	Leaves	Scott et al. <sup>35</sup>
Spastic colon	Leaves	Hulley and Van Wyk <sup>38</sup>
Sprains	Leaves	Thring and Weitz <sup>40</sup> ; Hutchings <sup>57</sup>
Stomach problems (diarrhoea and dysentery)	Leaves	Van Wyk et al. <sup>20</sup> ; Hulley and Van Wyk <sup>38</sup> ; De Beer and Van Wyk <sup>39</sup> ; Thring and Weitz <sup>40</sup> ; Scott et al. <sup>55</sup> ; Van Wyk et al. <sup>58</sup> ; Van Wyk <sup>59</sup> ; Van Wyk and Gorelik <sup>60</sup>
Swollen feet and hands	Leaves	Nortje and Van Wyk <sup>37</sup> ; De Beer and Van Wyk <sup>39</sup>
Tonic	Leaves	Hulley and Van Wyk <sup>38</sup>
Toothache	Leaves	Hulley and Van Wyk <sup>38</sup>
Wounds	Leaves	Long <sup>62</sup>
Ethnoveterinary medicine (gallsickness)	Leaves	Hutchings et al. <sup>35</sup>



Figure 1. Medicinal applications of Nidorella ivifolia derived from literature records

# Phytochemistry and biological activities of Nidorella ivifolia

A number of diterpene acids which include  $5\alpha$ -hydroxy,10 $\beta$ -hydroxyprintzianic acid, conyscabraic acid, hautriwaic acid, nidoresedaic acid, printziaic acid and derivatives of these have been identified in the aerial parts of *N. ivifolia*.<sup>63,64</sup> Scott et al.<sup>55</sup> identified cardiac glycosides, saponins and tannins from the leaves of *N. ivifolia*.

The following biological activities have been reported from the flower, leaf and twig extracts of *N. ivifolia* and essential oils isolated from the species: antibacterial,  $^{52,61,65}$  antimycobacterial,  $^{61}$  antifungal,  $^{52,61,65,66}$  antiplasmodial,  $^{67}$  antiprotozoal  $^{68}$  and cytotoxicity  $^{68}$  activities.

# Antibacterial activities

Seaman<sup>61</sup> evaluated the antibacterial activities of acetone and methanol leaf extracts of *N. ivifolia* against *Staphylococcus aureus, Enterococcus faecalis, Bacilus cereus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Serratia odorifera* and *Moraxella catarrhalis* using broth microdilution method with neomycin and ciprofloxacin as positive controls. The extracts showed activities against tested pathogens with minimum inhibitory concentration (MIC) values ranging from 0.5 mg/ml to 16.0 mg/ml.<sup>61</sup> Thring et al.<sup>52</sup> evaluated antibacterial activities of aqueous, methanol, ethanol and ethyl-acetate leaf extracts of *N. ivifolia* against *Staphylococcus aureus, Pseudomonas aeruginosa* and *Mycobacterium smegmatis* using the discdiffusion assay and two-fold serial dilution with ciprofloxacin as a positive control. The extracts were active against Staphylococcus aureus and Mycobacterium smegmatis with zone of inhibition ranging from 0.5 mm to 4.0 mm which are comparable to 2.0 mm to 4.0 mm exhibited by the positive control. The MIC values ranged from 0.3 mg/ml to 5.0 mg/ml.<sup>52</sup> Samie et al.<sup>65</sup> evaluated antibacterial activities of essential oils isolated from N. ivifolia against Acinetobacter calcoaceticus, Bacilus cereus, Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Micrococcus kristinae, Salmonella typhi, Proteus vulgaris, Serratia marsecens and Streptococcus faecalis using the microdilution method. The essential oil exhibited activities against all tested pathogens with both MIC and minimum bactericidal concentration (MBC) values ranging from 1.0 mg/ml to >7.5 mg/ml.<sup>65</sup>

# Antimycobacterial activities

Seaman<sup>61</sup> evaluated the antimycobacterial activities of acetone and aqueous leaf extracts of *N. ivifolia* against *Mycobacterium smegmatis* and *Mycobacterium aurum* using broth microdilution technique and *Mycobacterium tuberculosis* using BACTEC susceptibility testing with rifampicin and ciprofloxacin as positive controls. The extracts exhibited activities with MIC values ranging from 0.3 mg/ml to 4.0 mg/ml.<sup>61</sup>

## Antifungal activities

Seaman<sup>61</sup> evaluated the antifungal activities of methanol and acetone leaf extracts of N. ivifolia against Candida albicans using the broth microdilution method with nystatin as a positive control. The methanol and acetone extracts exhibited activities with MIC values of 4.0 mg/ml and 8.0 mg/ml, respectively.<sup>61</sup> Thring et al.<sup>52</sup> evaluated antifungal activities of aqueous, methanol, ethanol and ethyl-acetate leaf extracts of N. ivifolia against Candida albicans using the disc-diffusion assay and two-fold serial dilution with amphotericin B as a positive control. The extracts exhibited activities with MIC values ranging from 0.6 mg/ml to 5.0 mg/ml.<sup>52</sup> Samie and Nefefe<sup>66</sup> evaluated antifungal activities of essential oils isolated from N. ivifolia against Fusarium verticillioides. Fusarium nygamai, Fusarium oxysporum, Fusarium proliferatum and Fusarium graminearum using the agar diffusion and microdilution methods with nystatin as a positive control. The essential oils exhibited activities against Fusarium nygamai, Fusarium oxysporum and Fusarium proliferatum with the zone of inhibition ranging from 8.0 mm to 13.0 mm. The MIC and minimum fungicidal concentration (MFC) values against all tested pathogens ranged from 0.5 mg/ml to 3.8 mg/ml and 0.5 mg/ml to >7.5 mg/ml, respectively.<sup>66</sup> Samie et al.<sup>65</sup> evaluated antifungal activities of essential oils isolated from N. ivifolia against Candida albicans, Candida glabrata, Candida krusei, Candida parapsilosis, Candida tropicalis and Cryptococcus neoformans using the microdilution method. The essential oil exhibited activities against all tested pathogens with MIC and MFC values ranging from 0.1 mg/ml to 7.5 mg/ml and 0.5 mg/ml to >7.5 mg/ml, respectively.<sup>65</sup>

# **Antiplasmodial activities**

Clarkson et al.<sup>67</sup> evaluated antiplasmodial activities of flower, leaf and twig aqueous, dichloromethane and methanol (1:1) extracts of *N. ivifolia* against *Plasmodium falciparum* using the parasite lactate dehydrogenase (pLDH) assay. The dichloromethane and methanol (1:1) flower, leaf and twig extracts exhibited activities with half maximal inhibitory concentration (IC<sub>50</sub>) values ranging from 7.8 µg/ml to 11.5 µg/ml.<sup>67</sup>

#### Antiprotozoal activities

Mokoka et al.<sup>68</sup> evaluated antiprotozoal activities of dichloromethane: methanol (1:1) leaf extracts of *N. ivifolia* against *Plasmodium falciparum, Trypanosoma cruzi, Trypanosoma brucei rhodesiense* and *Leishmania donovani* with benznidazole (IC<sub>50</sub> = 0.5 µg/mL), chloroquine (IC<sub>50</sub> = 0.05 µM), melarsoprol (IC<sub>50</sub> = 0.03 µM) and miltfosine (IC<sub>50</sub> = 0.2 µg/mL) as reference drugs. Determination of the activities of the extracts against these pathogens was done using Almar Blue, resazurin and the <sup>3</sup>H-hypoxanthine incorporation assays. The extracts exhibited activities with IC<sub>50</sub> values ranging from 6.7 µg/mL to 49.4 µg/mL.<sup>68</sup>

# Cytotoxicity activities

Mokoka et al.<sup>68</sup> evaluated the cytotoxicity activities of dichloromethane: methanol (1:1) leaf extracts of *N. ivifolia* 

against the rat myoblast L6 cells with podophyllotoxin (IC<sub>50</sub> = 0.05  $\mu$ M) as a reference drug. The extract exhibited very little toxicity towards the myoblasts L-6 cells with IC<sub>50</sub> value of 48.1  $\mu$ g/mL.<sup>68</sup>

#### CONCLUSION

The present review summarizes the botany, medicinal uses, phytochemistry and pharmacological properties of *N. ivifolia*. Based on presented information, there is not yet enough data correlating the ethnomedicinal uses of the species with its phytochemical and pharmacological properties. Detailed studies on the pharmacokinetics, *in vivo* and clinical research involving both extracts and compounds isolated from the species are required. Therefore, future research should focus on the molecular modes or mechanisms of action, pharmacokinetics and physiological pathways for specific extracts of the species including identification of the bioactive compounds of the species and their associated pharmacological activities.

#### **Conflict of interest**

The author declares that there is no conflict of interest regarding the publication of this paper.

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