Helichrysum nudifolium (L.) Less.: Review of its Medicinal Uses, Phytochemistry and Biological Activities

Alfred Maroyi

Medicinal Plants and Economic Development (MPED) Research Centre, Department of Botany, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa

Abstract: Helichrysum nudifolium is a valuable and well-known medicinal plant species in southern Africa. The current study critically reviewed the medicinal uses, phytochemistry and biological activities of H. nudifolium. Information on medicinal uses, phytochemistry and biological activities of H. nudifolium was collected from multiple internet sources which included Scopus, Google Scholar, Elsevier, Science Direct, Web of Science, Pubmed, SciFinder and BMC. Additional information was gathered from pre-electronic sources such as journal articles, scientific reports, theses, books and book chapters obtained from the University library. This study showed that H. nudifolium is mainly used as ethnoveterinary medicine, as colic and herbal medicine for fever, headache, swellings, infertility, pregnancy and postpartum problems. Pharmacological research revealed that H. nudifolium extracts have antibacterial, antymycobacterial, antifungal, anti-HIV, GABAA-benzodiazepine receptor-binding, anticancer, anti-inflammatory, antiprostasmodial, antiprotocoal and cytotoxicity activities. There is need for experimental animal studies, randomized clinical trials and target-organ toxicity studies involving H. nudifolium crude extracts and compounds isolated from the species. Future should also focus on evaluation of pharmacological properties of compounds isolated from H. nudifolium.

Keywords: Asteraceae, Helichrysum nudifolium, ethnopharmacology, herbal medicine, southern Africa.

INTRODUCTION

Helichrysum nudifolium (L.) Less. is a perennial herb or small shrub which belongs to the Asteraceae or Compositae family. The species has been recorded in Angola, Botswana, Burundi, Cameroon, Democratic Republic of Congo (DRC), Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Rwanda, Sierra Leone, South Africa, South Sudan, Sudan, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe and Yemen [1-3]. Helichrysum nudifolium shows enormous variation in terms of its growth form, with plants from different geographical areas often having different appearances. In the formal taxonomic revision of the species, Beentje [2] described three different varieties namely H. nudifolium var. nudifolium, H. nudifolium var. oxyphyllum (DC.) Beentje and H. nudifolium var. pilosellum (L.f.) Beentje. However, most ethnobotanical and ethnopharmacological literature do not separate H. nudifolium into specific varieties, but rather to H. nudifolium sensu lato, and this is the approach that has been adopted in this study. The height of H. nudifolium ranges from 10 to 150 cm, with annual stems emanating from stout, perennial underground, woody rootstock [1-3]. The leaves are long, thin, narrowly elliptic to ovate, glabrous or hairy, cauline, broad-based and clasping. The inflorescence is branched, consisting of loose flower heads which are pale yellow to pale brown in colour. Helichrysum nudifolium has been recorded in grassland, wooded grassland, thicket, disturbed areas and on roadsides at an altitude ranging from 5 m to 2810 m above sea level [1-3].

The leaves, roots, stems and twigs of H. nudifolium are primary sources of herbal medicines in tropical Africa. Due to the popularity of the species as herbal medicine, the leaves and stems of H. nudifolium are sold as herbal medicines in the herbal medicine informal markets in Gauteng and Mpumalanga provinces in South Africa [4,5]. Helichrysum nudifolium is also one of the important medicinal plants in South Africa, 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 [6]. Helichrysum nudifolium is commonly known as hottentot's tea in southern Africa as the aromatic young leaves are used as a tea-substitute or herbal tea in Lesotho [7], South Africa [8] and Swaziland [9]. Research by Van Wyk and Gorelik [10] showed that the leaves of H. nudifolium are used as a substitute for common tea (that is, Camellia sinensis (L.) Kuntze) or as a hot beverage, that is herbal tea or tisane, primarily consumed as food but also as herbal medicine for colds and chest complaints. According to Van Wyk [11], the leaves of H. nudifolium have commercial potential as remedies for colds and chest complaints in South Africa. Therefore, H. nudifolium is an integral
part of traditional pharmacopoeia in southern Africa with potential contribution to primary health care of local communities in the region. Therefore, this is the rationale behind the current study, aimed at providing a critical appraisal of the existing ethnomedicinal value, phytochemistry and biological activities of *H. nudifolium* as well as exploring the potential of the species as herbal medicine.

### Medicinal Uses

The leaves, roots, stems, twigs and the whole plant parts of *H. nudifolium* are used as herbal medicines against 29 human and animal diseases in tropical Africa (Table 1). *Helichrysum nudifolium* is mainly used to treat fever (six citations in three countries), colic and headache (five citations in two countries each), swellings (four citations in two countries), infertility

<table>
<thead>
<tr>
<th>Disease</th>
<th>Parts used</th>
<th>Country</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergies</td>
<td>Leaves</td>
<td>South Africa</td>
<td>[14]</td>
</tr>
<tr>
<td>Antipyretic</td>
<td>Roots</td>
<td>South Africa</td>
<td>[8,12]</td>
</tr>
<tr>
<td>Aphrodisiac</td>
<td>Whole plant</td>
<td>Lesotho and South Africa</td>
<td>[7]</td>
</tr>
<tr>
<td>Burns</td>
<td>Leaves</td>
<td>Swaziland</td>
<td>[9]</td>
</tr>
<tr>
<td>Burnt as incense</td>
<td>Leaves</td>
<td>Lesotho and Swaziland</td>
<td>[7,9]</td>
</tr>
<tr>
<td>Catarrh</td>
<td>Leaves and roots</td>
<td>South Africa</td>
<td>[8,12,15]</td>
</tr>
<tr>
<td>Chest problems</td>
<td>Leaves and roots</td>
<td>South Africa</td>
<td>[6,8-10,12,16-21]</td>
</tr>
<tr>
<td>Colds</td>
<td>Leaves, roots, stems and whole plant</td>
<td>South Africa</td>
<td>[6,8,10,15-18,20-23]</td>
</tr>
<tr>
<td>Colic</td>
<td>Leaves, roots and whole plant</td>
<td>Lesotho and South Africa</td>
<td>[12,13,16,23,24]</td>
</tr>
<tr>
<td>Cough</td>
<td>Leaves, roots and whole plant</td>
<td>South Africa</td>
<td>[6,15-17,21,25,26]</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Leaves, roots and whole plant</td>
<td>South Africa</td>
<td>[26-30]</td>
</tr>
<tr>
<td>Fever</td>
<td>Leaves and roots</td>
<td>Lesotho, South Africa and Swaziland</td>
<td>[6,9,12,13,16,17]</td>
</tr>
<tr>
<td>Flu</td>
<td>Leaves</td>
<td>South Africa</td>
<td>[22]</td>
</tr>
<tr>
<td>Headache</td>
<td>Leaves and whole plant</td>
<td>South Africa and Swaziland</td>
<td>[6,9,16,31-33]</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Roots</td>
<td>Uganda</td>
<td>[34]</td>
</tr>
<tr>
<td>Infections</td>
<td>Leaves and twigs</td>
<td>South Africa</td>
<td>[6]</td>
</tr>
<tr>
<td>Infertility</td>
<td>Whole plant</td>
<td>Malawi and South Africa</td>
<td>[24,35]</td>
</tr>
<tr>
<td>Infertility in women</td>
<td>Whole plant mixed with <em>Commelina africana</em> L. and <em>Salvia triangularis</em> Thunb.</td>
<td>South Africa</td>
<td>[12]</td>
</tr>
<tr>
<td>Internal sores</td>
<td>Leaves and roots</td>
<td>South Africa</td>
<td>[16]</td>
</tr>
<tr>
<td>Pregnancy and postpartum problems</td>
<td>Whole plant</td>
<td>Malawi and South Africa</td>
<td>[24,35]</td>
</tr>
<tr>
<td>Menstrual pain</td>
<td>Whole plant</td>
<td>South Africa</td>
<td>[6,26]</td>
</tr>
<tr>
<td>Otitis</td>
<td>Leaves</td>
<td>Swaziland</td>
<td>[9]</td>
</tr>
<tr>
<td>Pain</td>
<td>Leaves and twigs</td>
<td>South Africa</td>
<td>[6]</td>
</tr>
<tr>
<td>Pulmonary infections</td>
<td>Leaves</td>
<td>South Africa</td>
<td>[8,12,15,25]</td>
</tr>
<tr>
<td>Rectal prolapse</td>
<td>Whole plant</td>
<td>South Africa</td>
<td>[23]</td>
</tr>
<tr>
<td>Skin infections</td>
<td>Leaves</td>
<td>South Africa</td>
<td>[14]</td>
</tr>
<tr>
<td>Swellings</td>
<td>Leaves</td>
<td>Lesotho and South Africa</td>
<td>[7,12,13,17]</td>
</tr>
<tr>
<td>Weaning</td>
<td>Roots</td>
<td>South Africa</td>
<td>[36]</td>
</tr>
<tr>
<td>Wounds</td>
<td>Leaves, roots and whole plant</td>
<td>South Africa</td>
<td>[6,14-16,23,25,37,38]</td>
</tr>
<tr>
<td>Ethnoveterinary medicine (black leg)</td>
<td>Leaves</td>
<td>Lesotho</td>
<td>[7,12,13]</td>
</tr>
</tbody>
</table>
Squalene from aerial parts, flowers and leaves of *Helichrysum nudifolium* (Table 2). Future research should focus on the isolation and identification of bioactive compounds in the utilized plant parts, particularly aerials parts, stems and roots and evaluate the biological activities of these compounds.

### Biological Activities

The following biological activities have been reported from *H. nudifolium* crude extracts: antibacterial [15,18,42], antimycobacterial [18], antifungal [15,18], anti-HIV [43,44], GABA benzodiazepine receptor-binding [45], anticancer [19], anti-inflammatory [32], antiplasmodial [46], antiprotozoal [47] and cytotoxicity [42,43,44,47] activities.

### Antibacterial Activities

Matsheka [15] evaluated the antibacterial activities of acetone extracts of aerial parts of *H. nudifolium* against *Bacillus cereus*, *Bacillus pumilus*, *Bacillus subtilis*, *Micrococcus kristinae*, *Staphylococcus aureus*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Serratia marcescens* using agar dilution method. The extract exhibited activities against all tested pathogens with the exception of *Klebsiella pneumoniae* and *Serratia marcescens* with minimum inhibitory concentration (MIC) value of 1.0 mg/ml [15]. Seaman [18] evaluated the antibacterial activities of acetone and methanol root and leaf extracts of *H. nudifolium* against *Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Serratia odorifera* and *Moraxella catarrhalis* using disc diffusion and broth micro-dilution methods with neomycin and ciprofloxacin as positive controls. The extracts showed activities against *Staphylococcus aureus*, *Enterococcus faecalis* and *Bacillus cereus* with MIC values ranging from 0.5 mg/ml to >8.0 mg/ml [18]. Lourens et al. [42] evaluated antibacterial activities of chloroform: methanol (1:1) leaf and stem extracts of *H. nudifolium* against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus cereus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* using the 96-well microplate method with ciprofloxacin as the positive control. The extracts exhibited activities against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus cereus* and *Klebsiella pneumoniae* with MIC values ranging from 0.02 mg/ml to 4.0 mg/ml [42].

### Antimycobacterial Activities

Seaman [18] evaluated the antimycobacterial activities of acetone and water leaf and root extracts of *H. nudifolium* (Table 2). Future research should focus on the isolation and identification of bioactive compounds in the utilized plant parts, particularly aerials parts, stems and roots and evaluate the biological activities of these compounds.
**H. nudifolium** against *Mycobacterium smegmatis* and *Mycobacterium aurum* using broth micro-dilution technique and *Mycobacterium tuberculosis* using BACTEC susceptibility testing with rifampicin and ciprofloxacin as positive controls. The extracts exhibited activities with MIC values ranging from 1.0 mg/ml to 16.0 mg/ml [19].

**Antifungal Activities**

Mathekga [15] evaluated the antifungal activities of acetone extracts of aerial parts of *H. nudifolium* against Aspergillus flavus, Aspergillus niger, Cladosporium cladosporioides, Cladosporium cucumerinum, Cladosporium sphaerospermum and Phytophthora capsici using agar dilution method. The extract exhibited activities against all tested pathogens with MIC values of 0.1 mg/ml [15]. Seaman [18] evaluated the antibacterial activities of acetone and methanol leaf and root extracts of *H. nudifolium* against Candida albicans using disc diffusion and broth micro-dilution methods with neomycin and ciprofloxacin as positive controls. The extract showed activities with MIC values ranging from >2.0 mg/ml to 8.0 mg/ml [18].

**Anti-HIV Activities**

Heyman [43] evaluated anti-HIV activities of methanol: water and chloroform extracts of aerial parts of *H. nudifolium* on vero African green monkey kidney cells using the cytopathic effect (CPE) inhibition assay with acyclovir (0.75 µg/ml) as a positive control. The methanol: water extract showed slight toxicity with cytopathic effect of 100.0 µg/ml in comparison to 0.8 µg/ml exhibited by the positive control [43]. Heyman et al. [44] evaluated anti-HIV activities of dichloromethane and methanol: water extracts of aerial parts of *H. nudifolium* using the DeCIPhR method. The dichloromethane extract exhibited activities with the median lethal concentration (LC50) value of 48.0 µg/mL [44].

**GABA(A)-Benzodiazepine Receptor-Binding Activities**

Stafford et al. [45] evaluated GABA-A-benzodiazepine receptor-binding activities of ethanol leaf extracts of *H. nudifolium* using the GABA-A-benzodiazepine receptor-binding assay. The extract showed dose-dependent activities [45].

**Anticancer Activities**

Fouche et al. [19] evaluated anticancer activities of dichloromethane root extracts of *H. nudifolium* against a panel of three human cell lines (breast MCF7, renal TK10 and melanoma UACC62). The extract showed moderate activities with total growth inhibition (TGI) values ranging from 8.4 µg/ml to 33.5 µg/ml [19].

**Anti-Inflammatory Activities**

Jäger et al. [32] evaluated aqueous and ethanolic leaf extracts of *H. nudifolium* in an *in vitro* assay for cyclooxygenase (COX) inhibitors with indomethacin (0.5µg) as the positive control. The ethanolic extract of *H. nudifolium* showed inhibition of 96% which was higher than 66.5% inhibition exhibited by the indomethacin control. Based on these results, there might be a rationale for the ethnopharmacological claim that *H. nudifolium* possess anti-inflammatory properties.

**Antiplasmodial Activities**

Clarkson et al. [46] evaluated the antiplasmodial activities of dichloromethane: methanol (1:1) and water extracts of whole plant parts of *H. nudifolium* against *Plasmodium falciparum* using the parasite lactate dehydrogenase assay. The dichloromethane: methanol (1:1) extract showed promising activities with half maximal inhibitory concentration (IC50) value of 6.8 µg/ml. The promising antiplasmodial activities exhibited by *H. nudifolium* show that the plant could serve as an antimalarial agent as the species is used as a remedy for fever in Lesotho, South Africa and Swaziland [6,9,12,13,16,17].

**Antiprotozoal Activities**

Mokoka et al. [47] evaluated antiprotozoal activities of dichloromethane: methanol (1:1) whole plant parts extracts of *H. nudifolium* against *Plasmodium falciparum*, *Trypanosoma cruzi*, *Trypanosoma brucei rhodesiense* and *Leishmania donovani* with benznidazole (IC50 = 0.5 µg/mL), chloroquine (IC50 = 0.05 µM), melarsoprol (IC50 = 0.03 µM) and milftosine (IC50 = 0.2 µg/mL) as reference drugs. The extract exhibited activities with IC50 values ranging from 9.4 µg/mL to 43.9 µg/mL [47].

**Cytotoxicity Activities**

Heyman [43] evaluated cytotoxicity activities of chloroform and methanol: water extracts of aerial parts of *H. nudifolium* on Vero African green monkey kidney cells using the XTT (sodium 3′-[1-(phenyl amino-carbonyl)-3,4-tetrazolium]-bis-[4-methoxy-6-nitro] benzene sulfonic acid hydrate) method with
zearalenone as a positive control. The chloroform extract exhibited IC$_{50}$ value of <3.1 µg/ml which was comparable to 1.3 µg/ml exhibited by the positive control, while methanol: water extract exhibited IC$_{50}$ value of 138.4 µg/ml [43]. Lourens et al. [42] evaluated in vitro cytotoxicity activities of chloroform: methanol (1:1) leaf and stem extracts of *H. nudifolium* [against transformed human kidney epithelial (Graham) cells, MCF-7 breast adenocarcinoma and SF-268 glioblastoma cells] at a concentration of 0.1 mg/ml using the sulforhodamine B (SRB) assay. The extract exhibited Graham cell growth ranging from 35.3% to 83.9% at the tested concentration [42], implying that the species maybe toxic against Graham cells. Mokoka et al. [47] evaluated the cytotoxicity activities of dichloromethane: methanol (1:1) whole plant extracts of *H. nudifolium* against rat myoblast L6 cells with podophyllotoxin (IC$_{50}$ = 0.05 µM) as a reference drug. The extract exhibited very little toxicity towards the myoblasts L-6 cells with IC$_{50}$ value of 47.7 µg/mL [47]. Heyman et al. [44] evaluated cytotoxicity activities of dichloromethane and methanol: water extracts of aerial parts of *H. nudifolium* using the DeCIPhR method. The dichloromethane extract exhibited activities with median lethal dose (LD$_{50}$) value of >50.0 µg/mL [44].

**CONCLUSION**

The diverse medicinal uses of *H. nudifolium* and the preliminary phytochemical and pharmacological evaluations carried so far indicates its potential as herbal medicine. The documented preliminary diverse pharmacological activities are directly or indirectly involved in a range of physiological processes which offers protection against growth of undesirable microbes and free radicals. Although contemporary ethnopharmacological research involving *H. nudifolium* is promising, it is too preliminary and sometimes too general to be used to explain and support some of the medicinal uses of the species. There is need for evaluation of the clinical significance of the antioxidant properties, cytotoxicity and toxicity using in vivo models.

**CONFLICT OF INTEREST**

The author declares that he has no conflict of interest.

**ACKNOWLEDGEMENTS**

I would like to express my gratitude to the National Research Foundation (NRF), South Africa and Govan Mbeki Research and Development Centre (GMRDC), University of Fort Hare for financial support to conduct this study.

**REFERENCES**


[18] Seaman T. The antimicrobial and antimycobacterial activity of plants used for the treatment of respiratory ailments in Southern Africa and the isolation of anacardic acid from...


