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# *Morinda officinalis* How. – A comprehensive review of traditional uses, phytochemistry and pharmacology

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## ARTICLE INFO

*The list of chemical compounds using PubChem CID's immediately:*
Monotropein (PubChemCID:73466)
Asperuloside tetraacetate (PubChemCID:443336)
Asperuloside (PubChemCID:84298)
Asperulosidic acid (PubChemCID: 11968867)
Deacetyl asperulosidic acid (PubChemCID: 12315349)
Morofficinaloside (PubChemCID:10453987)
Morindolide (PubChemCID:10397184)
Physcion (PubChemCID: 10639)
Rubiadin-1-Methyl ether (PubChemCID:96191)
Rubiadin (PubChemCID: 124062)
2-hydroxy-3-hydroxymethy-lanthraquinone (PubChem CID:44445519)
1-hydroxy-anthraquinone (PubChemCID:8512)
1-hydroxy-2-methyl anthraquinone (PubChemCID:160817)
2-hydroxy-3-hydroxymethylanthraquinone (PubChemCID:44445519)
Tectoquinone (PubChemCID:6773)

## ABSTRACT

*Ethnopharmacological relevance:* The medicinal plant *Morinda officinalis*How. (MO) and its root have long been used in traditional medicines in China and northeast Asia as tonics for nourishing the kidney, strengthening the bone and enhancing immunofunction in the treatment of impotence, osteoporosis, depression and inflammatory diseases such as rheumatoid arthritis and dermatitis.

*Aim of the review:* This review aims to sum up updated and comprehensive information about traditional usage, phytochemistry, pharmacology and toxicology of MO and provide insights into potential opportunities for future research and development of this plant.

*Methods:* A bibliographic investigation was performed by analyzing the information available on MO in the internationally accepted scientific databases including Pubmed, Scopus and Web of Science, SciFinder, Google Scholar, Yahoo, Ph.D. and M.Sc. dissertations in Chinese. Information was also obtained from some local and foreign books on ethnobotany and ethnomedicines.

*Results:* The literature supported the ethnomedicinal uses of MO as recorded in China for various purposes. The ethnomedical uses of MO have been recorded in many regions of China. More than 100 chemical compounds have been isolated from this plant, and the major constituents have been found to be polysaccharides, oligosaccharides, anthraquinones and iridoid glycosides. Crude extracts and pure compounds of this plant are used as effective agents in the treatment of depression, osteoporosis, fatigue, rheumatoid arthritis, and infertility due to their anti-depressant, anti-osteoporosis, pro-fertility, anti-radiation, anti-Alzheimer disease, anti-rheumatoid, anti-fatigue, anti-aging, cardiovascularprotective, anti-oxidation, immune-regulatory, and anti-inflammatory activities. Pharmacokinetic studies have demonstrated that the main components of MO including monotropein and deacetyl asperulosidic acid are distributed in various organs and tissues. The investigation on acute toxicity

*Abbreviations:* MO, *Morinda officinalis* How.; HNMR, nuclear magnetic resonance spectroscopy; IR, infrared spectroscopy; MS, mass spectrometry; $^{1}$HNMR, urine nuclear magnetic resonance $^{1}$H; TCM, traditional Chinese medicine; SFDA, State Food and Drug Administration; i.p., intraperitoneal injection; p.o., per os; COPD, chronic obstructive pulmonary disease; DRL72-s, differential reinforcement of low-rate72-s; 5-HTP, 5-hydroxytryptamine; SOD, superoxide dismutase; WBC, white blood cell; CNS, central nervous system; PTSD, Post-traumatic stress disorder; BDNF, brain-derived neurotrophic factor; GSK-3β, glycogen Synthase Kinase-3β; PSD95, Postsynaptic density-95; NGF, the nerve growth factors; HPA, hypothalamic-pituitary-adrenal; HAMD-17, the Hamilton depression scale-17; HAMA, Hamilton anxiety scale; BMD, bone mineral density; OPG, osteoprotegerin; DPD, Deoxypyridinoline; TRAP, tartrate resistant acid phosphates; ACTH, Adrenocorticotropic hormone; CORT, Corticosterone; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; IL-lβ, interleukin-lβ; ALP, alkaline phosphatase; BGP, bone gla protein; TGF-1β, transforming growth factor beta; BMSCs, bone marrow stromal cells; Cbfαl, core-banding factor α1; CAII, carboni canhydrase II; JNK, c-Jun N-terminal kinases; NF-κB, nuclear factor kappaB; CTR, calcitonin receptor; M-CSF, macrophage colonystimulation factor; RANKL, receptor activator of NF-κB ligand; BMP-2, bone morphogenetic protein-2; DKK-1, Diekkopf-1; RUNX2, Runt-related Transcription Factor 2; OPN, Osteopontin; MAPK, the mitogen-activated protein kinase; ERK, extracellular signal-regulated kinases; BMC, bone mineral content; LPL, lipoprotein lipase; HL, hepaticlipase; SDH, succino dehydrogenase; CAT, catalase; FSH, Follicle-Stimulating Hormone; LH, luteinizing hormone; MSTD, the mean seminiferous tubule diameter; FSHR, follicle-stimulating hormone receptor; ABP, androgen binding protein; AsAb, antisperman tibody; GnRH, gonadotrophin-releasing hormone; TJ, upregulate tight junction; HPGA, hypothalamus-pituitary-gonadal axis; CIP, capture incubation period; GSH-Px, glutathione pemxidase; LTP, long-term potentiation; Bcl-2, B cell leukemia-2 gene product; IRI, ischemia-reperfusion injury; CK, creatine kinase; BUN, blood urea nitrogen; SCr, serum creatinine; AMI, acute myocardial infarction; HUVECs, human umbilical vein endothelial cells; CTX, cyclophosphamide; COX-2, cyclooxygenase-2; DAI, disease activity index; MPO, myeloperoxidase

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1, 3-dihydroxy-2-methoxyanthraquinone (PubChemCID:14189688)
2-methoxyanthraquinone (PubChemCID:18646)
Alizarin-2-Methyl ether (PubChemCID:23669622)
Digiferruginol (PubChemCID:32209)
Lucidin-ω-Ethyl ether (PubChem CID:28578)
2-hydroxy-1-methoxy-anthraquinone (PubChemCID:80309)
Mannose (PubChemCID:18950)
Nystose (PubChemCID:166775)
Hexasaccharide (PubChemCID: 3082034)
Heptasaccharide (PubChem CID: 44630346)
Sucrose (PubChemCID: 5988)
Trisaecharide (PubChemCID: 10206531)
Inulotriose (PubChemCID: 101708615)
Inulotetraose (PubChem CID: 101708615)
Inulopentaose (PubChemCID:101110146)
1-kestose (PubChemCID: 440080)
Fumaric acid (PubChemCID:444972)
Succinic acid (PubChemCID:1110)
1-hexanol (PubChem CID:8103)
N-hexadecanoic acid (PubChem CID:985)
3-methyl-benzaldehyde (PubChem CID:12105)
(Z,Z)-9,12-octadecadienoic acid (PubChem CID:5280450)
Bicyclo[4,2,0]octa-1,3,5-trien-7-O (PubChem CID:354193)
Benzeneacetaldehyde (PubChem CID:998)
Pentadecanoic acid (PubChem CID:13849)
N-Nonanal (PubChem CID:31289)
L-Camphor (PubChem CID:230921)
L-borneol (PubChem CID:10049)
Ar-Curcumene (PubChem CID:92139)
β-sesquiphelandrene (PubChem CID:12315492)
α-zingiberene (PubChem CID:92776)
β-bisabolene (PubChem CID:10104370)
Stigmasterol (PubChem CID: 5280394)
Daucosterol (PubChem CID:5742590)
β-sitosterol (PubChemCID: 222284)
Scopoletin (PubChem CID:5280460)

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and genotoxicity indicated that MO is nontoxic. There have no reports on significant adverse effect at a normal dose in clinical application, but MO at dose of more than 1000 mg/kg may cause irritability, insomnia and unpleasant sensations in individual cases.

*Conclusion:* MO has emerged as a good source of traditional medicines. Some uses of this plant in traditional medicines have been validated by pharmacological investigations. However, the molecular mechanism, structure-activity relationship, and potential synergistic and antagonistic effects of its multi-components such as polysaccharides, oligosaccharides, anthraquinones and iridoid glycosides need to be further elucidated, and the structural feature of polysaccharides also need to be further clarified. Sophisticated analytical technologies should be developed to comprehensively evaluate the quality of MO based on HPLC-fingerprint and content determination of the active constituents, knowing that these investigations will help further utilize this plant.

## 1. Introduction

The genus *Morinda* (Rubiaceae), which includes 102 species, is distributed in tropical, subtropical and temperate regions (Flora of China, 2015). *Morinda citrifolia* L.(Wong et al., 2002), *Morinda lucida* (Koumaglo et al., 1992) and *Morinda officinalis*. aHowre commonly used traditional medicinal plants. *Morinda citrifolia* L., also known as noni, which contains a number of anthraquinones and anthraquinone glycosides, fatty acids and their derivatives, iridoids and iridoid glycosides, lignans, neolignans, flavonol glycosides, phenylpropanoids, saccharides, triterpenoids and fatty acids (Levand and Larson, 1979), has been used traditionally as a folk remedy for many diseases, including diabetes, hypertension and cancer in Polynesia, South and Southeast Asia, Northeastern Australia and the Caribbean owing to its diversity biological activities, including analgesic, antibacterial, anti-cancer, anti-inflammatory, antioxidant, anti-tubercular, cancer-chemopreventive and cardiovascular actions (Saludes et al., 2002; Yanine et al., 2006). *Morinda lucida*, an important plant in traditional medicine in West Africa, has been shown to possess a variety of biological activity, such as anti-inflammatory, antipyretic, analgesia, anti-malarial, anti-diabetic, anticancer, and insecticidal activity, as well as promoting gastric emptying and intestinal motility (Moses et al., 2014). *Morinda officinalis* How. has long been used as tonics for the action of nourishing kidney, strengthening bone and enhancing immune function in the treatment of impotence, menstrual disorders, osteoporosis, diabetes, rheumatoid arthritis and dermatitis in China and northeast Asia (Song et al., 2015). In this review, we focused on the ethno-botany, phytochemistry, pharmacology and clinical application of *Morinda officinalis* How.

*Morinda officinalis* How (MO), which is a lianoid shrub, has been cultivated in subtropical and tropical areas for more than 200 years (Lin et al., 2010), and is one of the best-known herbs in Asia, especially in southern China. The root of this plant, named *"Bajitian"* in traditional Chinese medicine (TCM), has long been used as a tonic or nutrient supplement for alleviating a wide spectrum of diseases, including impotence (Wang et al., 2016), osteoporosis, rheumatoid arthritis (Ye et al., 2013a, 2013b), dermatitis, depression (Zhang et al., 2000a, 2000b) and Alzheimer disease. A variety of biological activities of MO root have been reported, including anti-depressant (Zou and Zhang, 2012), anti-osteoporosis, pro-fertility, anti-radiation (Zhang et al., 2013), anti-Alzheimer disease, anti-rheumatoid (Ye et al., 2013a, 2013b), anti-fatigue (Zhang et al., 2009), anti-aging, cardio vasculo-protective, anti-oxidation (Li et al., 2008a, 2008b), immune-regulatory (Chen et al., 2003a, 2003b), and anti-inflammatory activities (Kim et al., 2005). In addition, phytochemical investigations have demonstrated the presence of polysaccharides and oligosaccharides, anthraquinones, iridoid glucosides and volatile oil in MO root (Chen and Xue, 1987).