

COMPARATIVE REVIEW OF MORINDA SPECIES: PHYTOCHEMISTRY, MEDICINAL PROPERTIES, AND THERAPEUTIC POTENTIAL

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ABSTRACT

The genus *Morinda* (family Rubiaceae) comprises several species renowned for their medicinal properties, including *Morinda citrifolia*, *Morinda coreia*, and *Morinda officinalis*. These plants have been used in traditional medicine for centuries across various cultures in Southeast Asia and the Pacific Islands. This review compares the phytochemical composition, pharmacological properties, and therapeutic potential of different *Morinda* species, highlighting the similarities and differences among them. Studies indicate that *Morinda* species are rich in bioactive compounds such as anthraquinones, flavonoids, and alkaloids, which contribute to their antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. Despite the promising therapeutic benefits of these plants, further clinical trials and toxicological studies are necessary to establish their safety and efficacy in human health applications.

KEYWORDS: *Morinda* species, Phytochemistry, Medicinal plants, *Morinda citrifolia*, *Morinda coreia*, Pharmacological properties.

1. INTRODUCTION

The genus *Morinda*, comprising over 80 species, is a rich source of bioactive compounds and has long been utilized in traditional medicine systems, particularly in Southeast Asia, the Pacific Islands, and Africa. The most well-known species, *Morinda citrifolia* (noni), has been widely studied for its numerous health benefits. Other species, such as *Morinda coreia* and *Morinda officinalis*, also exhibit significant medicinal potential. This review aims to compare the phytochemical profiles, pharmacological activities, and therapeutic applications of these *Morinda* species to identify their unique and shared benefits and to assess their potential for modern therapeutic use.

Here is a botanical introduction of each

- ***Morinda citrifolia* L. (Noni)**

Family: Rubiaceae

Morinda citrifolia, commonly known as noni, is a small evergreen tree or shrub native to Southeast Asia and widely distributed across the Pacific Islands, India, and tropical regions of Australia. It typically grows up to 3–10 meters in height and is characterized by its glossy, dark green, opposite leaves, which are large, elliptic to ovate, and conspicuously veined. The plant produces small, white, tubular flowers that are borne in clusters. Its most recognizable feature is the multiple, ovoid fruit, which turns yellowish- white upon ripening and emits a pungent odor. features the distinctive, pungent, multiple fruit along with its glossy, dark green leaves. The globose clusters of white tubular flowers and bumpy fruits are characteristic.

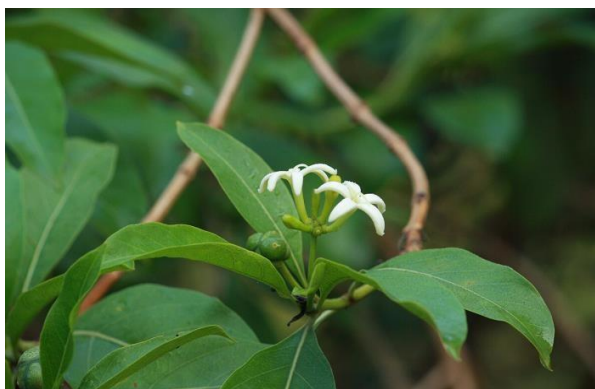


- ***Morinda coreia* Buch.-Ham. (Syn. *Morinda tinctoria* Roxb.)**

Family: Rubiaceae

Morinda coreia, also known as **Indian mulberry**, is a medium-sized deciduous tree

distributed across South and Southeast Asia, particularly India, Sri Lanka, and Myanmar. It can reach 15–20 meters in height and is distinguished by its rough, greyish bark and opposite, elliptic to lanceolate leaves. The plant produces small, white flowers arranged in dense heads, which develop into yellow to reddish drupaceous fruits. *M. coreia* is valued for its timber, natural dye (morindone from the roots), and medicinal properties, its dense, spherical flower heads situated close to the stem.



***Morinda officinalis* F.C.**

Family: Rubiaceae

Morinda officinalis is a perennial climbing shrub native to southern China and widely cultivated in subtropical Asia. It is distinguished by its slender, twining stems and opposite, leathery, lanceolate leaves with entire margins. The plant produces cluster of small, tubular, white to yellowish flowers, followed by multiple, small drupes. The roots (*Radix Morindae officinalis*) are the primary medicinal part and are thick, cylindrical, and yellowish-brown. They are widely used in traditional Chinese medicine, where the plant is classified as a yang-tonifying herb.



2. Phytochemistry of Morinda Species

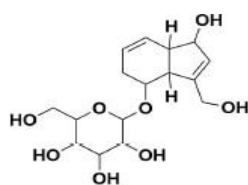
2.1 Overview of Chemical Constituents

The chemical composition of Morinda species varies, but they share several common bioactive compounds that contribute to their medicinal properties. These include anthraquinones, flavonoids, triterpenoids, alkaloids, and glycosides.

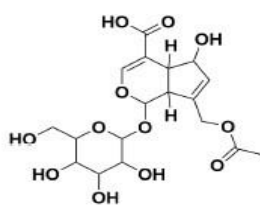
- *Morinda citrifolia* (Noni)

1. Iridoids

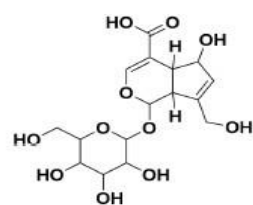
Iridoids are a fascinating group of compounds that can be found in many different types of plants and insects, such as the *Aspidistra*, *Gentianae*, *Lamiaceae*, *Lauraceae*, *Rubiaceae*, *Sedum*, and *Verbenaceae* families, as well as in insects, including butterflies. Iridoids are a subclass of monoterpenoids and are acetal derivatives of iridodial. Natural iridoids possess the basic skeleton of a cyclopentadiene-fused pyran ring. Iridoids can be divided into iridoid glycosides, secoiridoids glycosides, bis-iridoids, and nonglycosidic iridoids. Iridoids have been shown to have many different biological activities, including anti-inflammatory, antibacterial, antiviral, neuroprotective, hepatoprotective, hypoglycemic, antitumor, and antioxidant activities.



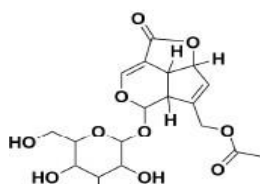
Aucubin



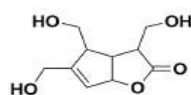
Asperulosidic acid



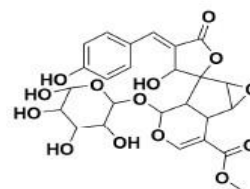
Deacetylasperulosidic acid



Asperuloside



Morindacin



Citrifolinoside A

2. Anthraquinones

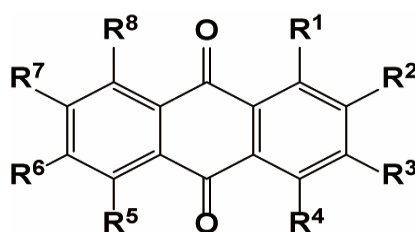
Anthraquinones are a class of organic compounds defined by a core structure of three fused benzene rings—the anthracene nucleus—with two ketone functionalities at positions 9 and 10, forming the anthraquinone (9,10-anthracenedione) scaffold. This tricyclic system is widely distributed across the natural world, being prevalent in plants (notably in rhizomes and bark), fungi, lichens, and insects, and is recognized for contributing both pigmentation

and bioactivity.

In *Morinda citrifolia*, anthraquinones represent one of the key bioactive groups, particularly concentrated in the roots. The pharmacological profile of anthraquinones is tightly linked to the nature and positioning of substituent groups on the core skeleton. Polar substituents—such as hydroxyl, carboxyl, or glycosidic moieties—generally enhance antimicrobial activity, whereas derivatization with sugar chains may attenuate antioxidant capabilities. Specifically, hydroxyl-rich anthraquinones have strong free radical-scavenging properties and are capable of modulating antioxidant pathways and inhibiting the generation of reactive oxygen species.

Among the anthraquinones isolated from *M. citrifolia*, damnacanthal is particularly noteworthy due to its ability to inhibit various tyrosine kinases, underpinning its potential as an antineoplastic agent. Additional anthraquinones identified in the species include alizarin, morindadiol, nordamnacanthal, rubiadin, ibericin, tectoquinone, lucidin, damnacanthol ω ethyl ether, lucidin ω butyl ether, rubiadin ω methyl ether, rubiadin ω ethyl ether, rubiadin ω propyl ether, and 1hydroxy2methyl9,10anthraquinone.

Moreover, a comprehensive study identified a novel anthraquinone, moricitrifone, alongside seven known congeners in the fruits of *M. citrifolia*. These compounds exhibited significant antiproliferative effects across human cancer cell lines—including HL-60, SMMC- 7721, A-549, MCF-7, and SW480—with inhibitory concentrations (IC₅₀) ranging from approximately 0.26 \pm 0.05 to 16.58 \pm 0.18 μ M, comparable to the standard chemotherapeutic doxorubicin.



3. Coumarins

Coumarins are naturally occurring heterocyclic compounds comprising a benzopyrone (2H1benzopyran2one) core structure, which consists of a benzene ring fused to a pyrone (lactone) ring. Over 1,300 coumarins have been identified across diverse biological sources including plants, bacteria, and fungi with notable prevalence in families such as *Leguminosae* (*Fabaceae*), *Rosaceae*, *Rutaceae*, *Apiaceae* (*Umbelliferae*), *Lamiaceae*, *Clusiaceae*, and others.

These compounds exhibit a wide array of biological activities, including antioxidant, antiinflammatory, antibacterial, anticoagulant, antiviral, antifungal, anticancer, neuroprotective, antihypertensive, antihyperglycemic, anticonvulsant, and antitubercular effects.

The pharmacological behavior of coumarins is strongly influenced by their substituent patterns. For example.

Orthophenolic hydroxyl groups on the benzene ring enhance both antioxidant and antitumor effects.

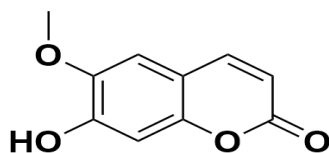
Aryl substituents at the C4 position confer potent activities including antiHIV, antitumor, antiinflammatory, and analgesic effects.

C3 phenylcoumarin moieties are associated with significant antioxidant and antiHIV activities.

Hydroxylated derivatives (e.g., esculetin, fraxetin, daphnetin) generally display strong antioxidant capabilities by scavenging reactive oxygen species and enhancing endogenous antioxidant enzyme systems.

Regarding antiinflammatory mechanisms, coumarins can inhibit enzymes such as cyclooxygenase (COX) and lipoxygenase (LOX), thereby reducing the synthesis of proinflammatory mediators like prostaglandins and leukotrienes. For instance, in experimental models, esculetin effectively reduced oxidative stress and inhibited inflammation, while comparisons among 1,2benzopyrone, umbelliferone, and esculetin demonstrated varying degrees of antiinflammatory and antioxidant potency.

In *Morinda citrifolia* (noni), the primary coumarin identified is scopoletin (7hydroxy6methoxycoumarin), particularly in leaf extracts. Scopoletin has shown notable biochemical activities, including antiinflammatory, antioxidant, antiangiogenic, and apoptotic effects in various in vitro and in vivo models. However, a specific concentration figure (e.g., 6 mg/g in leaf water extract) could not be corroborated from available sources.



Scopoletin

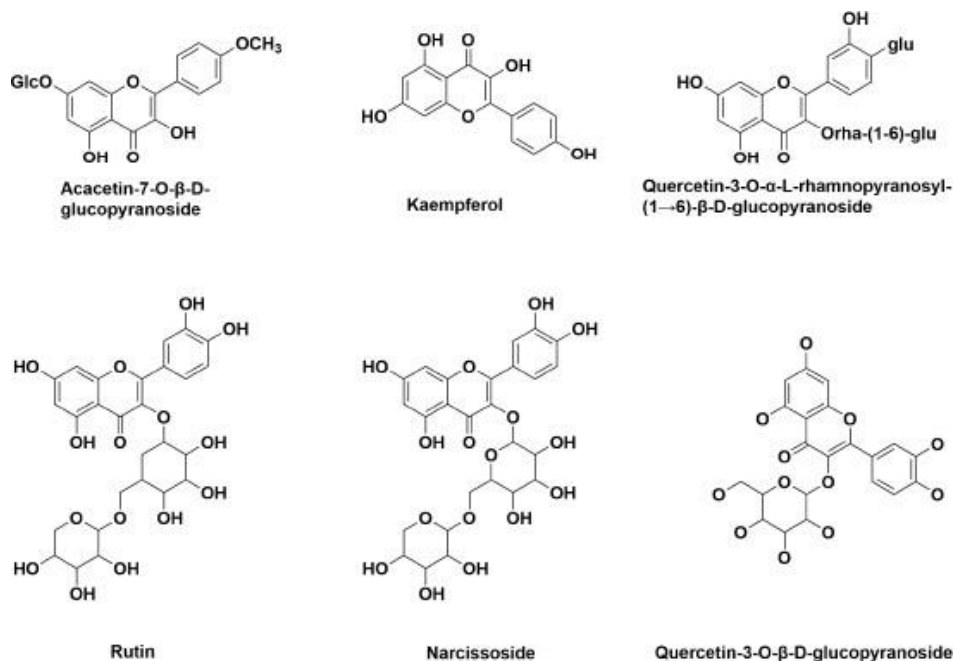
4. Flavonoids

Flavonoids are plant-specific polyphenolic secondary metabolites characterized by a 15carbon skeleton ($C_6-C_3-C_6$) comprising two aromatic rings (A and B) connected by a three-carbon bridge that forms a heterocyclic ring (ring C). Their structural subclasses include flavones, flavonols, flavanones, flavan3ols, isoflavones, anthocyanidins, neoflavonoids, and chalcones). These compounds exist in aglycone forms or as glycosides, with the latter being the predominant form in dietary sources.

Flavonoids exert numerous pharmacological effects, including anticancer, antioxidant, anti-inflammatory, and vasoprotective activities. They enhance cellular antioxidant defenses such as superoxide dismutase, glutathione peroxidase, and catalase scavenge reactive oxygen species, chelate transition metals, and inhibit prooxidant enzymes like cyclooxygenase and lipoxygenase. Structurally, features such as a 2,3double bond conjugated with a 4oxo group, plus hydroxyl groups at positions 3, 5, 7, and the B-ring's 3',4'-OH groups, are crucial for antioxidant potency.

In *Morinda citrifolia* (noni), total flavonoid content is a key quality marker for extracts and is typically quantified using rutin as the standard reference. Content can vary based on fruit maturity, with a consistent upward trend observed as ripening progresses. One study reported total flavonoid levels of 234.42 mg/L in noni juice and 12.56–14.48 g/kg in fruits.

The following flavonoids have been identified in *M. citrifolia*: acacetin7O β Dglucopyranoside
kaempferol rutin narcissoside quercetin
quercetin3O β Dglucopyranoside
quercetin3O α Lrhamnopyranosyl(1 \rightarrow 6) β Dglucopyranoside
5,7dimethylapigenin4'O β Dgalactopyranoside.



5. Polysaccharides

Polysaccharides are highmolecularweight biomacromolecules composed of more than ten monosaccharide units linked via glycosidic bonds, widely present in nature and noted for diverse bioactivities such as immunomodulatory, antiinflammatory, antioxidant, antitumor, and hypoglycemic effects.

In *Morinda citrifolia* (noni), polysaccharides represent significant functional components especially pectic heteropolysaccharides rich in galacturonic acid and galactose, with smaller proportions of rhamnose and glucose. These pectic components play a crucial role in fruit tissue integrity and softening during ripening.

Extraction of noni polysaccharides typically involves aqueous extraction (e.g., of juice or puree) followed by ethanol-mediated precipitation to isolate the crude polysaccharide fraction. Alternative methods such as ultrasound-assisted and pulsed electric field-assisted extraction have been developed to enhance yield, reduce temperature exposure, and preserve bioactivity; ultrasound-assisted extraction has achieved yields as high as ~11.1% and produced polysaccharides with notably stronger antioxidant properties.

Interestingly, the crude polysaccharide content decreases as fruit maturity increases, with reported values dropping from approximately 1.72 g per 100 g in less ripened fruit to 1.07 g per 100 g in ripe (yellow–white) fruit. This trend is likely due to enzymatic degradation of cell wall polysaccharides (e.g., pectin methylesterases and polygalacturonases), leading to

solubilization and reduced extractable content.

Functionally, noni polysaccharides exhibit antiinflammatory activity *in vivo*. For example, administration of noni-derived polysaccharides reduced carrageenan-induced paw edema, suppressed leukocyte migration, and alleviated inflammatory nociception in animal models. Additionally, a polysaccharide-rich fraction from noni juice (noni-ppt) displayed antitumor and immunomodulatory properties, enhancing survival in tumor-bearing mice through activation of peritoneal exudate cells and release of immune mediators (TNF α , IL1 β , IL12, IFN γ , NO), effects that were attenuated by immunosuppressants indicative of an immune-mediated mechanism.

Further investigations revealed that noni polysaccharide-rich fractions can synergize with doxorubicin chemotherapy, eliciting T CD8⁺ lymphocyte proliferation and maintaining antioxidant capacity suggesting promise as a potential adjuvant in cancer therapy.

Lastly, polysaccharide fractions derived from fermented noni (via *Lactobacillus*) demonstrated robust immunostimulatory effects *in vitro* and *in vivo*, including elevated NO production, cytokine (IL1 β , IL6, TNF α) release, iNOS/COX2 expression, and enhanced NK cell activity and immune cell numbers in lymphoid tissues of mice.

6. Nutrient Composition of *Morinda citrifolia* (Noni) Fruit

Minerals constitute approximately 8.4% of the dry matter in noni fruit, with potassium being the most abundant mineral in the puree measured at approximately 214.34 mg per 100 g dry matter. Other detected minerals include calcium, iron, sodium, selenium, magnesium, phosphorus, and sulfur.

Further analysis reveals that noni fruit is characterized as high in potassium and low in sodium, a profile that may support vascular health and aid in blood pressure regulation.

Regarding vitamins, vitamin C (ascorbic acid) is the most prominent, with levels ranging from 24 to 158 mg per 100 g dry matter. In noni puree specifically, vitamin C content is approximately 1.13 mg/g.

Additional data indicate that flavonoid and mineral content can vary with fruit maturity and geographical origin suggesting these values are influenced by factors such as ripeness, cultivation conditions, and processing methods

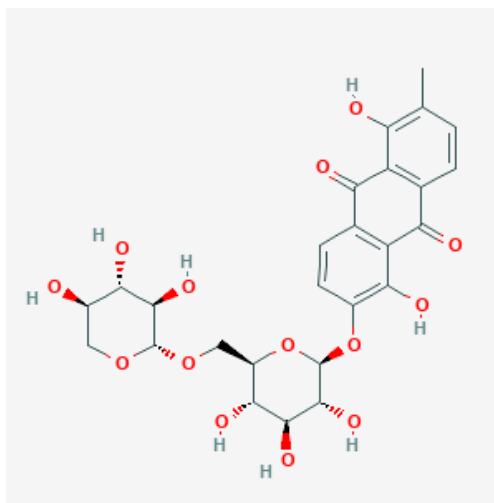
- *Morinda coreia*

1. Yopaaoside B.

Type & Class: Iridoid glycoside, molecular formula $C_{26}H_{28}O_{14}$, molecular weight 564.15 Da.

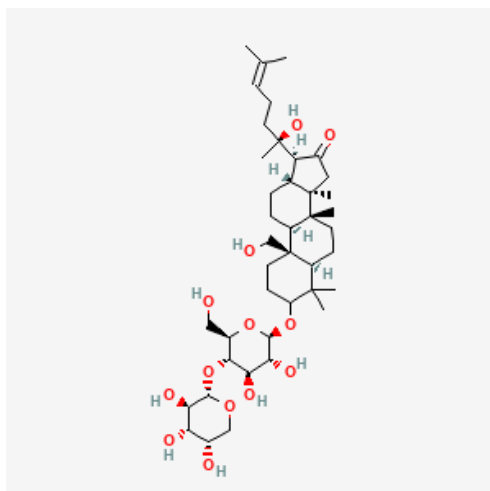
Structure: Based on JGLOBAL chemical data, Yopaaoside B is a cyclopenta[c]pyran with a β -D-glucopyranosyloxy substituent, multiple hydroxyls, and a carboxylic acid methyl ester.

Significance: Iridoid glycosides like this typically contribute to plant defense through anti-inflammatory, antimicrobial, or deterrent activities.

**2. Yopaaoside A (Peracetylated Derivative)**

Type & Class: A peracetylated variant of Yopaaoside A, with formula $C_{37}H_{38}O_{20}$, molecular weight ~802.7 Da.

Structure: It is structurally similar to Yopaaoside B but includes acetyl groups on hydroxyls, increasing lipophilicity. Utility of Derivatives: Such peracetylation is often used in structural elucidation and to improve compound stability or extraction.

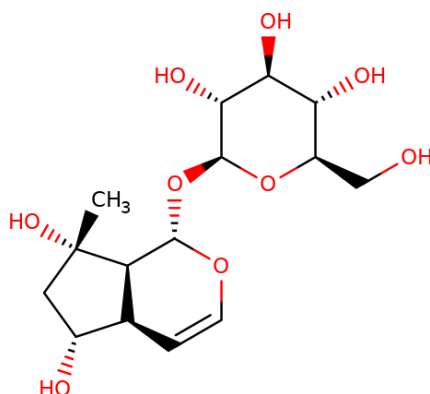


3. 6-O-Acetylscandoside

Type & Class: Iridoid glycoside, molecular formula $C_{18}H_{24}O_{12}$, molecular weight ~432.13 Da.

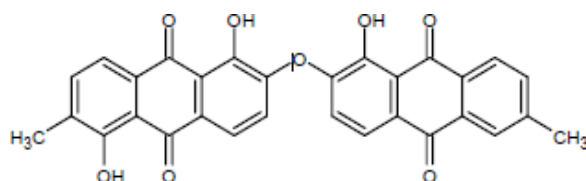
Structure: Features a cyclopenta[c]pyran backbone (iridoid skeleton) with a glucose moiety esterified by an acetyl group at the 6-hydroxyl position.

Biological Insight: Acetylated iridoids like this are known for modulating anti-inflammatory or enzyme-inhibitory pathways.



4. Bianthraquinone (Morind aquinone)

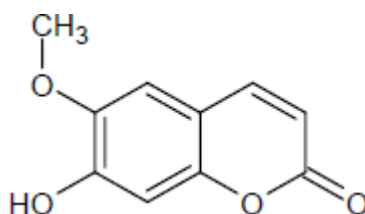
A novel compound, Morindaquinone, classified as a bianthraquinone, was isolated from the roots of *Morinda coreia* alongside twelve known anthraquinones (e.g., soranjidiol, rubiadin-1-methyl ether, tectoquinone, nordamnacanthol, damnacanthol, etc.) during a phytochemical investigation. This discovery marked the first identification of a bianthraquinone within the *Morinda* genus. The term signifies a dimer composed of two anthraquinone units linked together most likely via carbon–carbon bonds. The image provided visually represents this dimeric anthraquinone structure, characteristic of Morindaquinone. Each anthraquinone consists of a three-ringed aromatic scaffold with carbonyl groups at positions 9 and 10. The bianthraquinone reflects two such cores covalently connected—forming a larger, conjugated scaffold.



5. Scopoletin

Also known as 7-Hydroxy-6-methoxy-2H-1-benzopyran-2-one; also known as

6methoxyesculetin, esculetin-6-methyl ether, or Gelseminic acid. Molecular formula: $C_{10}H_8O_4$, with a molar mass of approximately 192.17 g/mol. Structure: It is a coumarin derivative featuring a benzene ring fused with a lactone (pyrone) ring, bearing a hydroxyl group at the 7-position and a methoxy group at the 6-position. It exhibits antimicrobial, antifungal, anticancer, anti-angiogenic, antidiabetic, antihypertensive, hepatoprotective, neuroprotective, immunomodulatory, and anti-aging effects, and functions as an inhibitor of enzymes such as acetylcholinesterase, choline acetyltransferase, monoamine oxidase, and aldose reductase.

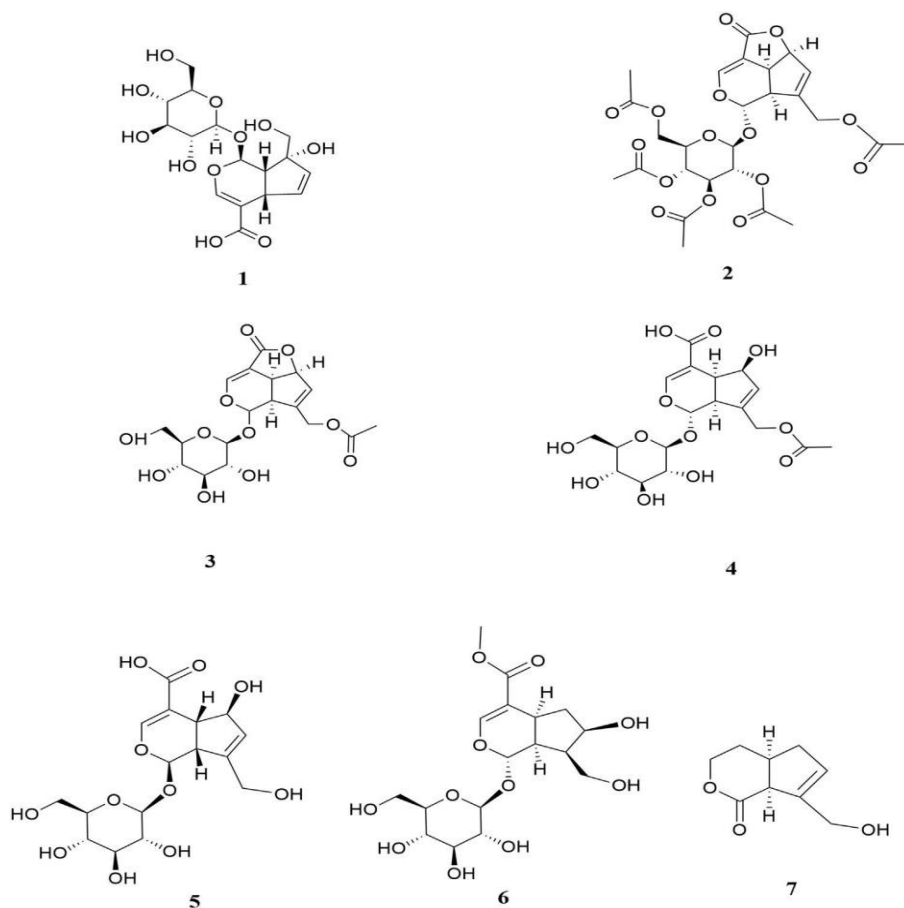


- *Morinda officinalis*

1. Iridoid glycosides

They are among the primary active constituents of the root of *Morinda officinalis*. Ethanol extracts of the root have yielded seven such compounds monotropein, asperuloside tetraacetate, asperuloside, asperulosidic acid, deacetylasperulosidic acid, morofficaloside, and morindolide. Of these, monotropein is the most abundant, comprising nearly 2.0% of the root's composition.

These iridoid glycosides, and particularly monotropein, have demonstrated significant antiinflammatory activity. In murine macrophages stimulated with lipopolysaccharide (LPS), monotropein markedly suppressed the production of proinflammatory mediators such as nitric oxide (NO), tumor necrosis factor α (TNF α), interleukin1 β (IL1 β), along with reduced expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase2 (COX2). These effects are attributed to its inhibition of NF κ B signaling pathways.



2. Anthraquinones

They are a key class of bioactive compounds isolated from the root of *Morinda officinalis* (MO). These derivatives are characterized by hydroxyl and/or methoxy substitutions on the anthraquinone core, and typically feature a single carbon-containing side chain. In total, seven anthraquinone compounds have been extracted from the ethanolic root extract of MO, along with one coumarin (scopoletin).

These include.

Physcion Rubiadin 1 methyl ether

2-Hydroxy-1-methoxyanthraquinone

1,2-Dihydroxy-3-methylanthraquinone

1,3,8-Trihydroxy-2-methoxyanthraquinone

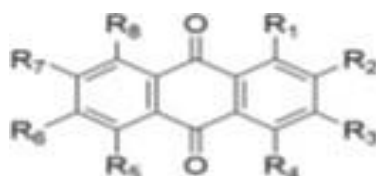
2-Hydroxymethyl-3-hydroxyanthraquinone

2-Methoxyanthraquinone

Scopoletin (a coumarin).

These anthraquinones exhibit promising antiosteoporotic properties, demonstrated through both *in vitro* and *ex vivo* studies. Notably, Moreover, further research focused on three specific anthraquinones 1,3,8 trihydroxy-2-methoxyanthraquinone 2-hydroxy-1-methoxyanthraquinone, and rubiadin revealed their ability to: Decrease bone

resorption pit formation, reduce multinucleated osteoclast numbers, and suppress TRAP and cathepsin K activity in co-cultured osteoblast and bone marrow cells. Enhance osteoclast apoptosis and improve the osteoprotegerin (OPG)/RANKL expression ratio in osteoblasts. Modulate signaling pathways, including inhibition of JNK and NFκB activity, and downregulate calcitonin receptor (CTR) and carbonic anhydrase II (CA II) expression in osteoclasts.



3. Polysaccharides, Mono- and Oligosaccharides

Saccharides form another significant class of active constituents in the root of *Morinda officinalis* (MO). Among the oligosaccharides isolated are.

Bajijiasu, mannose, nystose, 1Ffructofuranosyl nystose, inulintype hexasaccharide, inulintype heptasaccharide, sucrose, and various inulintype small oligosaccharides— namely trisaecharide (trisaccharide), inulotriose, inulotetraose, and inulopentaose.

Research has leveraged these oligosaccharides in particular, an inulin-type approach for therapeutic development, including new treatments targeting mild to moderate depression. Clinical studies, including randomized controlled trials involving 1,384 participants, found that *Morinda officinalis* oligosaccharide (MOO) capsules had comparable efficacy to conventional antidepressants and demonstrated a similar safety profile.

Further mechanistic insights reveal that MOO exerts its antidepressant effects via modulation of the gut microbiota–5-HTP–serotonin pathway. Specifically, MOO boosts tryptophan hydroxylase (TPH) activity and suppresses 5-hydroxytryptophan decarboxylase (5HTPDC) in the gut microbiota, increasing 5-hydroxytryptophan (5HTP) levels, which crosses into the bloodstream and eventually elevates serotonin in the brain.

Switching to polysaccharides, these have traditionally been extracted via hot water followed by ethanol precipitation. Four homogeneous polysaccharides MOHPI, MOHPII, MOHPIII, and MOHPIV were then separated through ion-exchange and size-exclusion chromatographic methods.

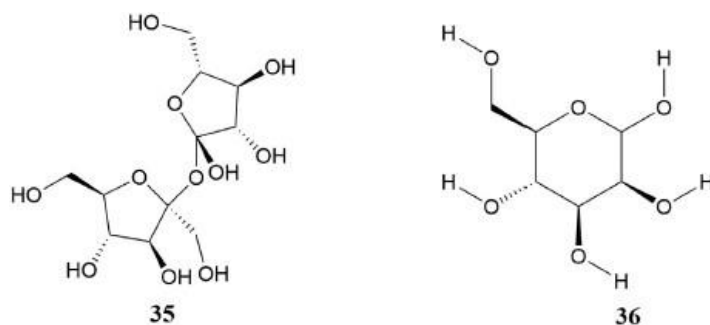
Characterization of these polysaccharides reveals.

MOHPI: A small oligosaccharide (~2,000 Da), mainly composed of glucose and fructose.

MOHPIII: A glycoprotein (~35,000 Da), containing arabinose, xylose, glucose, fructose, and galactose.

MP1: A linear inulin-type fructan (~2,165 Da) with β -(2 \rightarrow 1)-linked fructose units.

MP2 and MP3: Acidic polysaccharides (~19,494 Da and ~27,705 Da, respectively), rich in galacturonic acid, arabinose, and galactose.

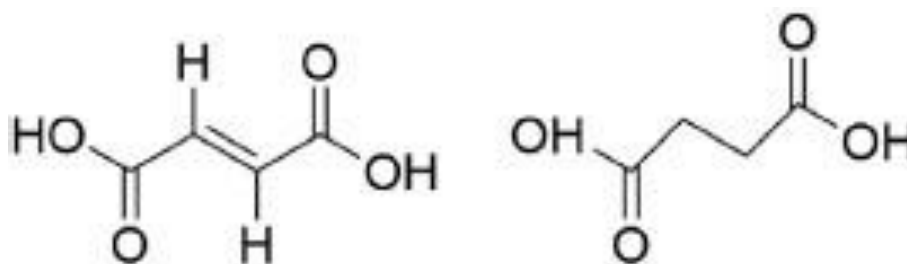


4. Volatile Oils

Volatile oils from *Morinda officinalis* root are rich and diverse, traditionally obtained through steam distillation. One study using LCMS and computational methods detected 34 compounds, accounting for 77.4% of the total oil. These include key terpenoids such as borneol, α -zingiberene, α -curcumene, L-hexanol, β -sesquiphellandrene, 2furanamine, n-nonanal, Lcamphor, and β -bisabolene.

Another analysis identified 15 major volatile components, totaling 87.95% of the oil. Highlights include borneol, 2,6-bis(1,1dimethylethyl)-2methylphenol, and hydrocarbons like n-heptadecane, iso-heptadecane, n-octadecane, and iso-eicosane. Fatty acids such as tetradecanoic acid, pentadecanoic acid, and 9-hexadecenoic acid, along with their ethyl esters and Nphenyl1naphthalenamine, were also prominent.

Additionally, a broader profiling reported up to 37 volatile constituents, with dominant components including n-hexadecanoic acid, 3methyl benzaldehyde, (Z,Z)-9,12-octadecadienoic acid, oleic acid, borneol, bicyclo[4.2.0]octa1,3,5-trien-7-one, 2methyl9,10-anthracenedione, and pentadecanoic acid.



Study & Coverage	Key Components Identified
34 compounds (77.4%)	Borneol; α -zingiberene; α -curcumene; L-hexanol; β -sesquiphellandrene; 2-furanamine; n-nonanal; L-camphor; β -bisabolene
15 compounds (87.95%)	Borneol; 2,6-bis(...)2-methylphenol; n-heptadecane; iso-heptadecane; n-octadecane; iso-eicosane; tetradecanoic acid; pentadecanoic acid; 9-hexadecenoic acid; ethyl esters; N-phenyl-1-naphthalenamine
37 constituents	n-hexadecanoic acid; 3-methyl benzaldehyde; (Z,Z)-9,12-octadecadienoic acid; oleic acid; borneol; bicyclo[4.2.0]octa-1,3,5-trien-7-one; 2-methyl-9,10-anthracenedione; pentadecanoic acid

2.2 Comparative Chemical Profiles

Table 2: below summarizes the main bioactive compounds found in different *Morinda* species.

Compound	<i>Morinda citrifolia</i>	<i>Morinda coreia</i>	<i>Morinda officinalis</i>
Anthraquinones	Morindone	Morindone	Morindine
Flavonoids	Scopoletin	Quercetin	Kaempferol
Alkaloids	Alkaloids (e.g., Noniine)	Morindine	Morindine
Triterpenoids	β -sitosterol	Triterpenes	Triterpenoids
Glycosides	Noni Glycosides	Glucosides	-

3. Pharmacological Properties

3.1 ANTIOXIDANT ACTIVITY

The antioxidant activity of *Morinda* species is primarily due to the high levels of phenolic compounds and flavonoids.

- ***Morinda citrifolia* (Noni)**

Polymers such as polyphenols, iridoids, scopoletin, and polysaccharides are identified as the principal antioxidant-active constituents in *M. citrifolia*.

Findings from Recent Studies

Phenolic Extract in NAFLD Model (Mice)

Supplementation with *M. citrifolia* fruit phenolic extract (NFE) significantly mitigated high-fat diet-induced nonalcoholic fatty liver disease (NAFLD) by modulating oxidative stress,

inflammation, insulin resistance, and liver metabolism. This effect is also linked with beneficial shifts in gut microbiota composition and metabolomic pathways such as glutathione metabolism and the pentose phosphate pathway.

Noni Fruit Water Extract (NFW) & Polysaccharides (NFP)

In mice fed a high-fat diet, both NFW (10 mL/kg) and NFP (50–200 mg/kg) reduced body and liver weight gains. NFP significantly enhanced liver SOD and GPx activities, elevated the antioxidant trolox equivalent capacity (TEAC), lowered malondialdehyde (MDA) levels, and upregulated Nrf2 expression while downregulating NFκB signaling indicating robust antioxidant and anti-inflammatory effects.

Noni Wine & Nrf2 Activation

Fermented noni wine (40 mL/kg/day) improved systemic antioxidant capacity in highfat diet mice. It modulated lipid metabolism, increased energy expenditure, and activated the Nrf2 antioxidant pathway.

Fermented Noni Juice (FNJ) in Diabetic Models

In insulin-resistant HepG2 cells and diabetic db/db mice, FNJ (3–5%) enhanced glucose uptake, attenuated oxidative stress by increasing SOD and GPx activity while reducing ROS and MDA, activated the Nrf2/ARE signaling cascade, and restored gut microbiota diversity.

Polysaccharide (NFP) & GutLiver Axis

In highfat diet rats, NFP (100 mg/kg) alleviated hepatic oxidative stress and inflammation by modulating short-chain fatty acids (SCFAs), intestinal barrier integrity, and gut microbiota composition.

- ***Morinda coreia***

Antioxidants are compounds that protect cells from damage caused by free radicals. Antioxidants such as thiols or ascorbic acid (vitamin C) may also act to inhibit free radical reactions. The ability of the isolate to scavenge free radicals was confirmed by estimating its DPPH radical scavenging activity. Five different concentrations of the pure compound (10, 50, 75, 100, and 250 µg/mL) were prepared. To each, 3 mL of DPPH (0.1 mM in ethanol) solution was added. The reaction mixture was incubated in complete darkness for 30 minutes, after which its absorbance was measured at 517 nm. Results were compared with ascorbic acid, a standard antioxidant. Percentage radical scavenging activity (%RS) was

calculated. The isolated compound demonstrated significant, dose-dependent antioxidant efficacy comparable to that of ascorbic acid. At the highest concentration 250 µg/mL the compound exhibited extremely high scavenging efficiency (94.86%), surpassing ascorbic acid at the same concentration (92.93%). The IC₅₀ value for the tested compound was determined to be 75.2 µg/mL.

- ***Morinda officinalis***

Aqueous extracts of *Morinda officinalis* demonstrate notable scavenging activity against hydroxyl radicals ($\cdot\text{OH}$) and superoxide anion radicals ($\text{O}_2^{\cdot-}$).^[1]

The acidic polysaccharide (APMO) derived from *M. officinalis* exhibits strong antioxidative potential in vitro: it effectively scavenges DPPH radicals, chelates ferrous ions, and protects rat erythrocytes from H₂O₂-induced hemolysis.^[2]

Oligosaccharides isolated from *M. officinalis* have been shown to preserve the integrity of human sperm DNA exposed to H₂O₂, as evidenced by confocal micro-Raman spectroscopy.^[3]

In mouse models subjected to exhaustive swimming, *M. officinalis* aqueous extracts enhanced physical endurance, boosted the activities of antioxidant enzymes SOD (superoxide dismutase) and GSHPx (glutathione peroxidase), and reduced malondialdehyde (MDA) levels in the myocardium, liver, and serum.^[4-5]

Similarly, administering 4.5 mg/kg of the aqueous extract for eight weeks to overtrained rats extended their time to exhaustion, increased SOD, GSHPx, Ca²⁺ATPase, and Na⁺K⁺ATPase activities in skeletal muscle, and enhanced muscle antioxidative capability during exercise. However, these animal studies lacked positive controls and employed only a single dosage, limiting reliability and precluding dose–response analysis.

3.2 ANTI-INFLAMMATORY EFFECTS

All three *Morinda* species have demonstrated anti-inflammatory properties, though the mechanisms may vary slightly.

- ***Morinda citrifolia* (Noni)**

Inflammation plays a pivotal role in the onset and progression of many chronic and serious diseases. Research suggests that *M. citrifolia* suppresses inflammatory responses via various

pathways, mediated by key constituents such as phenolic compounds, polysaccharides, and specific proteins. Its anti-inflammatory efficacy has been validated across diverse experimental setups including LPS-induced cellular models, colitis, esophagitis, rheumatoid arthritis, pneumonia, edema, and steatohepatitis.

In Vitro Cellular Models Noni Seed Extract in Macrophages *M. citrifolia* seed extract significantly inhibited nitric oxide (NO) production and reduced inducible nitric oxide synthase (iNOS) expression and tumor necrosis factor- α (TNF α) levels in LPS-activated RAW264 cells exceeding the effects of seed oil, leaf, or fruit extracts.

Traditional Herbal Formulations Thai Herbal Formulation (PTP) A traditional Thai blend incorporating *M. citrifolia* demonstrated strong anti-inflammatory activity in rat models, effectively reducing edema in response to both ethyl phenylpropionate (ear swelling) and carrageenan or arachidonic acid (paw swelling). Fermented Noni Juice in Gout Model.

In an acute gouty arthritis model, fermented noni juice lowered expression of NLRP3 and TNF- α , leading to pronounced reduction of monosodium urate-induced ankle swelling.

Noni Fruit Juice Phytochemicals

Five compounds isolated from Hawaiian noni fruit juice asperulosidic acid, rutin, nonioside A, a specific trienoate glucoside, and tricetin effectively inhibited NO production and suppressed IKK α / β , I κ B α , NF κ B p65, iNOS, and COX2 in LPS-stimulated RAW264.7 cells.

- ***Morinda Coreia***

Antiinflammatory refers to the property of a substance that reduces inflammation or swelling. Such agents relieve pain by combating inflammation, unlike opioids, which act on the central nervous system to block pain signaling to the brain. In this study, the protease inhibition and prevention of protein degradation activities of AEM were quantified and represented as percentages of inhibition. At a concentration of 100 μ g/mL, AEM exhibited approximately $44.10 \pm 0.26\%$ protease inhibition and $44.38 \pm 0.58\%$ prevention of protein degradation. The membranestabilizing property of AEM was evaluated using a red blood cell hemolysis assay, demonstrating that AEM stabilizes erythrocyte membranes with around $69.36 \pm 0.20\%$ inhibition of cell lysis.

In the current investigation, the *in vitro* antiinflammatory activity of *M. tinctoria* extract (AEM) was determined by assessing its ability to inhibit proteases and prevent protein

denaturation. The findings suggest that the experimental extract was effective in inhibiting protease activity by up to about 44% and significantly prevented protein degradation. Moreover, the membranestabilizing property of *M. tinctoria* previously unreported was revealed in our study, showing promise in protecting against cell membrane damage. The AEM extract was found to consist of quinones, steroids, terpenoids, phenols, glycosides, and tannins, and displayed strong antiinflammatory properties in *in vitro* models.

- ***Morinda officinalis***

Methanol extracts of *Morinda officinalis* (MEMO) exhibit significant anti-inflammatory and antinociceptive effects. In both *in vitro* and *in vivo* models, MEMO suppresses the expression of inducible nitric oxide synthase (iNOS), cyclooxygenase2 (COX2), and tumor necrosis factor α (TNF α) by downregulating NF κ B activation. This suppression is accompanied by inhibition of I κ B degradation and reduced NF κ B binding activity, highlighting its mechanism of action via NF κ B pathway interference.^[6]

The iridoid glycoside monotropein, derived from *M. officinalis* roots, is a key contributor to its pharmacological activity. Administered orally at 20 and 30 mg/kg/day, monotropein significantly decreases pain-related behaviors in mice (hot plate test and writhing assay) and reduces carrageenan-induced paw edema in rats, supporting its antinociceptive and anti-inflammatory efficacy.^[7]

On a molecular level, monotropein impedes LPS-induced inflammatory responses in RAW 264.7 macrophages by downregulating mRNA expression of iNOS, COX2, TNF α , and interleukin1 β (IL1 β). It also attenuates NF κ B signaling by reducing NF κ B's DNA binding activity, preventing I κ B α phosphorylation and degradation, and ultimately inhibiting NF κ B translocation to the nucleus. In a DSS-induced colitis rat (or mouse) model, monotropein alleviates disease activity index (DAI), decreases myeloperoxidase (MPO) activity, and lowers expression of inflammatory proteins in colon mucosa, effects attributed to suppression of NF κ B activation.^[8-9]

3.3 ANTIMICROBIAL ACTIVITY

Several *Morinda* species have shown antimicrobial effects.

- ***Morinda citrifolia* (Noni)**

Antimicrobial efficacy is commonly assessed using the disk diffusion. Using sequential extraction of dried *M. citrifolia* root powders (hexane, dichloromethane, ethyl acetate, ethanol), the following antibacterial activities were observed.

Hexane extract inhibited *Staphylococcus aureus*, *S. epidermidis*, and *Bacillus cereus* with inhibition zones of approximately 4.0 mm, 6.5 mm, and 5.0 mm, respectively.

Dichloromethane extract showed the strongest activity against *Escherichia coli*, with an inhibition zone of about 5.5 mm, and also demonstrated moderate activity against the Gram-positive strains.

Ethyl acetate extract was most active against *Pseudomonas aeruginosa* (≈ 5.5 mm zone) and displayed moderate activity against *S. epidermidis* (~ 4.5 mm).

In antitubercular assays via the microplate Alamar Blue method.

Dichloromethane root extract had a minimum inhibitory concentration (MIC) of 50 $\mu\text{g/mL}$ against *Mycobacterium tuberculosis*.

Other extracts including hexane, ethyl acetate, ethanol, and aqueous root extracts were inactive (MIC > 100 $\mu\text{g/mL}$).

Independent studies report that an ethanolic leaf extract of *M. citrifolia* achieved 89% inhibition of *M. tuberculosis* at 100 $\mu\text{g/mL}$.

Additionally, in a dental context:

A water extract of noni outperformed conventional disinfectants and photodynamic therapy in disinfecting dental metal–ceramic crowns in an experimental model.

Noni-derived cerium oxide nanoparticles exhibited bacteriostatic activity against both Gram-positive and Gram-negative bacteria, with efficacy exceeding that of amoxicillin.

- ***Morinda coreia***

An antimicrobial is an agent capable of killing microorganisms or inhibiting their growth, including the formation of thin spores. In that study, different concentrations of n-hexane and chloroform extracts from *M. coreia* were loaded into wells and left to air dry. A total of 100 μL of a suspension containing *H. pylori* (1×10^8 CFU/mL; McFarland 2) in PBS was uniformly spread on BHI medium. A well was punched into the agar and filled with varying concentrations of the extracts. After 72 hours of incubation, both extracts exhibited anti-*H. pylori* activity, each producing a 7 mm zone of inhibition notably at 0.4 mg/mL for the n-hexane extract and 2.4 mg/mL for the chloroform extract using the agar well method.

Antimicrobial activity of *M. coreia* was also assessed against *A. niger*, where methanol extracts of leaves, bark, and fruit all showed inhibition. However, against *A. oryza*, inhibition was observed only with the bark sample. Additionally, *Salmonella* cultures were inhibited by the leaf methanol extract.

- ***Morinda officinalis***

The essential oil extracted from *Morinda officinalis* roots (yield: ~0.03%) and its 2-methylbenzaldehyde derivatives display potent acaricidal activity against both *Dermatophagoides spp.* (dust mites) and *Haemaphysalis longicornis* (a tick species). Remarkably, these extracts are several times more effective than DEET in both fumigant and contact bioassays.

For instance, in fumigant assays, 2,4,5-trimethylbenzaldehyde achieved LD₅₀ values of approximately 0.21, 0.19, and 0.68 µg/cm³ against *D. farinae*, *D. pteronyssinus*, and *H. longicornis*, respectively illustrating dramatically greater toxicity than DEET.

Additionally, *Morinda officinalis* oil and certain analogues (notably 2,3-dihydroxybenzaldehyde) induced a visible color change in dust mites, turning them from colorless to dark brown offering a built-in mite indicator that may aid in allergen detection or monitoring.

3.4 Other Therapeutic Benefits

- ***Morinda citrifolia* (Noni)**

1. HYPOGLYCEMIC ACTIVITY OF MORINDA CITRIFOLIA

Morinda citrifolia (noni) has been traditionally utilized in Indonesia and Polynesia for managing diabetes. Scientific investigations have substantiated its potential as a natural remedy for type 2 diabetes through various mechanisms.

Enzyme Inhibition: Noni components exhibit inhibitory effects on key enzymes involved in carbohydrate metabolism. Molecular docking and dynamics simulations have demonstrated that ursolic acid, a triterpenoid found in noni, binds effectively to human pancreatic α-amylase, suggesting its potential as a therapeutic agent for diabetes management.

α-Glucosidase Inhibition: A study identified 15 compounds in noni seeds with α-glucosidase inhibitory activity. Among them, scopoletin, quercetin, and caffeic acid exhibited significant inhibitory effects, with IC₅₀ values of 160, 133, and 120 µmol·L⁻¹, respectively.

In Vivo Efficacy: In a study involving streptozotocin-induced diabetic rats, administration of fermented noni juice significantly reduced fasting blood glucose levels and improved liver tissue glycogen content, demonstrating its hypoglycemic and hepatoprotective activities.

Combination Therapy: A polyherbal formulation combining noni, mango, and pineapple extracts demonstrated enhanced α -amylase and α -glucosidase inhibitory activities *in vitro*. This combination also showed significant blood glucose reduction in an *in vivo* rat model, suggesting potential for synergistic effects in diabetes management.

2. ANTICANCER ACTIVITY OF *MORINDA CITRIFOLIA*

Over the past five years, *Morinda citrifolia* (noni) has garnered significant attention for its potential anticancer properties, particularly due to its rich content of anthraquinone compounds. These compounds have demonstrated notable antiproliferative effects across various cancer cell lines.

Key Bioactive Compounds

Morindone: This anthraquinone has shown selective cytotoxicity against colorectal cancer cell lines such as HCT116, LS174T, and HT29. In molecular docking studies, morindone exhibited strong binding affinities to key oncogenic targets, including β -catenin, MDM2-p53, and KRAS, suggesting its potential as an effective therapeutic agent against colorectal cancer.

Rubiadin: Another anthraquinone compound, rubiadin, has demonstrated significant cytotoxicity against colorectal cancer cell lines. Its mechanism involves binding to β -catenin, MDM2-p53, and KRAS, similar to morindone, indicating its potential as a multitarget anticancer agent.

Nordamnacanthal and Damnacanthal: These compounds have exhibited potent cytotoxic effects against various cancer cell lines, including T-lymphoblastic leukemia (CEM-SS) and breast carcinoma (MCF-7). Notably, nordamnacanthal displayed stronger activity than damnacanthal, highlighting the importance of specific structural features in their anticancer efficacy.

Lucidin: Lucidin has been identified as a potent inhibitor of DNA topoisomerase II, an enzyme crucial for DNA replication and cell division. Its inhibitory effect on this enzyme underscores its potential as an anticancer agent.

- *Morinda coreia*

1. ANTIDIABETIC ACTIVITY

Diabetes mellitus commonly known as diabetes is a metabolic disease characterized by elevated blood sugar levels. This occurs when the body fails to produce adequate insulin or cannot effectively utilize the insulin it does produce. In the study, rats were fasted overnight and administered a single intraperitoneal injection of freshly prepared streptozotocin (STZ) at 55 mg/kg body weight, dissolved in 0.1 M citrate buffer (pH 4.5). To mitigate drug-induced hypoglycemia, the animals received 5% glucose solution overnight. Control rats received citrate buffer only. Rats were classified as diabetic if their blood glucose exceeded 250 mg/dL on the third day post-STZ injection. Treatment commenced on the fourth day and continued for 30 days.

Diabetic rats displayed a marked increase in blood glucose and a decrease in body weight compared to controls. Treatment with *Morinda tinctoria* (MTR) or insulin markedly lowered blood glucose and restored body weight gain to near-normal levels. Additionally, diabetic rats showed a significant decrease in total hemoglobin and a significant increase in glycosylated hemoglobin (HbA1c) and plasma insulin levels. Administration of MTR or insulin reversed these effects, restoring total hemoglobin and HbA1c to near-control levels.

These outcomes align with findings from Pattabiraman and Muthukumaran (2011), who demonstrated that *M. tinctoria* aqueous fruit extract given to STZ-diabetic rats for 30 days significantly reduced blood glucose and lipid peroxidation, while enhancing plasma insulin and the activities of antioxidant enzymes such as catalase, superoxide dismutase (SOD), reduced glutathione (GSH), and glutathione peroxidase (GPx) in liver and kidney tissues.

2. ANTICANCER ACTIVITY

Cancer is characterized by abnormal cell growth that proliferates uncontrollably. Anticancer agents act by targeting cancer cells to either induce cell death or inhibit their proliferation. In that study, ultrafiltered protein fractions were examined for cytotoxic effects on selected cancer cell lines using the MTT assay. Various concentrations (2– 100 µg/mL) of the ultrafiltered proteins were applied to cells cultured in 96-well plates containing DMEM with 10% FBS for 24 hours. Following incubation, the culture medium was replaced with fresh medium and incubated with 50 µL of MTT solution for 4 hours in a CO₂ incubator. Subsequently, the medium was removed, and 200 µL of DMSO was added to dissolve the

resulting formazan crystals. Absorbance was measured at 570 nm, and cell viability percentages were calculated. In untreated (control) Vero cells, intact, distinct DNA bands were observed indicating viable cells while DNA fragmentation characteristic of apoptosis was detected in A549 cancer cells treated with ultrafiltered proteins derived from the leaves of *Morinda pubescens*, suggesting the induction of apoptotic cell death via these protein fractions.

- ***Morinda officinalis***

1. IMMUNOMODULATORY ACTIVITY

Oral administration of *Morinda officinalis* (MO) aqueous extract at 4.5 g/kg for 10 days significantly counteracted cyclophosphamide (CTX)-induced immunosuppression in mice. This treatment restored white blood cell (WBC) counts, enhanced the clearance of colloidal carbon by mononuclear phagocytes, and stimulated macrophage phagocytic activity.^[10]

In in vitro culture, MO aqueous extract at concentrations of 50 mg/mL and 5 mg/mL promoted the proliferation of CD34⁺ hematopoietic progenitor cells and enhanced colony formation in the FUGM assay, indicating a stimulatory effect on hematopoietic stem cell proliferation and differentiation.^[11]

When administered to CTX-immunosuppressed mice, crude MO polysaccharides (at 10, 30, and 50 mg/kg) as well as purified homogeneous fractions MOPI3a and MOPA2a, improved immune function. Observed benefits included increased immune organ indices, enhanced macrophage phagocytosis, and elevated lymphocyte transformation rates.^[12]

Likewise, MO oligosaccharides given at 25 and 50 mg/kg markedly enhanced splenocyte proliferation and antibody production in mice. Importantly, this immunopotentiality occurred without affecting the proliferation of Peyer's patch cells in vitro, suggesting a selective enhancement of systemic immune responses.^[13]

However, these studies share common limitations: none included a positive control, and the use of a single dose level limits the reliability of the findings and precludes analysis of dose-response relationships.

2. MEMORY ENHANCEMENT AND ANTIALZHEIMER'S EFFECTS

Aqueous extracts of *Morinda officinalis* (MO) effectively counteract learning and memory impairments induced by D-galactose in rodent models. In mice subjected to 4 weeks of

Dgalactose treatment, oral administration of *MO* extract at doses ranging from 11.25 to 45 g/kg significantly enhanced performance in the Morris water maze. This cognitive improvement was accompanied by reductions in aldose reductase (AR) activity and serum levels of glycated hemoglobin (HbA1c), fructosamine, advanced glycation end-products (AGEs), and their receptor (RAGE), thereby attenuating brain cell damage.^[14]

In a complementary rat model of Alzheimer's disease induced by combined Dgalactose and sodium nitrite for 30 days *MO* extract administered at 15, 30, and 60 mg/kg markedly improved performance in the stepdown test. These doses also elevated cerebral superoxide dismutase (SOD) activity and reduced malondialdehyde (MDA) levels, as well as both the mRNA expression and enzymatic activity of monoamine oxidaseB (MAOB).^[15]

It is notable that these two studies report drastically different *MO* dosage ranges spanning more than two orders of magnitude which complicates direct comparisons and raises questions about dose consistency and translational relevance.

3. ANTIRHEUMATOID ARTHRITIS ACTIVITY OF *MORINDA OFFICINALIS*

Morinda officinalis (*MO*) has long been utilized in traditional Chinese medicine for the treatment of rheumatoid arthritis. Recent research has shed light on its anti-arthritic properties.

Ethanol Extracts in RA Models

Ethanol extracts of *MO* significantly reduced paw swelling and decreased serum levels of key inflammatory cytokines including TNF α , IL1 β , and IL6 in rat models of adjuvant-induced arthritis. These extracts also inhibited ankle swelling, lowered levels of prostaglandin E2, and reduced acetic acid-induced writhing responses in mice, demonstrating both anti-inflammatory and analgesic efficacy.

Iridoid Glycoside (MOIG) Effects and Mechanism

Isolated iridoid glycosides from *MO* (MOIG), when administered to rats with Complete Freund's Adjuvant (CFA)-induced arthritis at doses of 50–200 mg/kg, effectively attenuated symptoms of RA. This included reductions in paw swelling, arthritic scores, body weight loss, spleen index, and inflammatory markers such as IL1 β , IL6, and IL17a. Histological analysis further confirmed mitigation of synovial hyperplasia and joint damage.

At the cellular level, MOIG suppressed inflammation in LPS-stimulated RAW 264.7

macrophages by decreasing NO production, and downregulating iNOS, COX2, and inflammatory cytokines. It also inhibited the activation of the NFκB and MAPK signaling pathways critical drivers of inflammation by reducing phosphorylation of ERK, JNK, p38, and IκBα, as well as nuclear translocation of NFκB p65.

4. Therapeutic Applications

4.1 Traditional and Modern Uses

- ***Morinda citrifolia* (Noni)**

Has been traditionally used to treat a variety of conditions, including pain, infections, and skin disorders. Its popularity in modern health products is attributed to its broad-spectrum therapeutic effects.

- ***Morinda Coreia***

Is used traditionally for pain relief, fever reduction, and as an anti-inflammatory agent. Its modern applications are focused on its potential for treating chronic conditions like diabetes and arthritis.

- ***Morinda officinalis***

Has been used in traditional Chinese medicine for its adaptogenic properties and to treat conditions such as fatigue, stress, and pain.

4.2 Clinical and Preclinical Evidence

While clinical studies on *Morinda* species are still limited, there is increasing evidence supporting their pharmacological effects. For example, several studies have highlighted the potential of *Morinda citrifolia* in managing diabetes and hypertension, while *Morinda coreia* has shown promise in anti-inflammatory and antimicrobial applications.^[16]

5. Safety and Toxicity

Despite their medicinal benefits, the safety of *Morinda* species must be thoroughly evaluated. For instance, high doses of *Morinda citrifolia* may cause liver toxicity in some individuals, and excessive consumption of *Morinda coreia* has been linked to mild gastrointestinal discomfort.^[17]

6. CONCLUSION

The genus *Morinda* encompasses several species with notable pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, and anticancer effects. While

Morinda citrifolia is the most well-studied and widely used species, *Morinda coreia* and *Morinda officinalis* also offer significant therapeutic potential. Future research should focus on comparative clinical studies, dose standardization, and safety profiles to facilitate the integration of these plants into modern medicine.

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