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Review Article

Morin: A Powerful Potential Flavonoid for Human

Sampda Jain *, Yogesh Yadav, Manoj Sharma

School of Studies in Pharmaceutical Sciences, Jiwaji University Gwalior (Madhya Pradesh), India, 474001

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*For Correspondence:

Sampda Jain, School of Studies in Pharmaceutical Sciences, Jiwaji University Gwalior (Madhya Pradesh), India, 474001

Abstract

Objective: A bioflavonoid obtained from plants in the Moraceae family, morin exhibits strong pharmacological potential because of its hepatoprotective, neuroprotective, cardioprotective, anti-inflammatory, antioxidant, and anticancer effects. It is a promising therapeutic agent for diseases like diabetes, cancer, and neurodegenerative disorders because of its low toxicity and capacity to alter important cellular signaling pathways like Nrf2/HO-1 and EGFR.

Data Sources: Its antioxidant mechanism effectively reduces oxygen species that are reactive and oxidative damage through the Nrf2/HO-1 pathway, potentially preventing neurodegenerative diseases.

Study Selection: The effectiveness of morin has been proven in both Parkinson's disease and colitis models, highlighting its neuroprotective and anti-inflammatory properties, anti-oxidant, cardioprotective, anti-diabetic, synergistic effects. Morin's anti-inflammatory properties, whereby it reduces glial activation and improves tissue recovery.

Summary of Contents of the Article: Morin acts as a non-competitive inhibitor of PTP1B in anti-diabetic studies, thereby enhancing insulin sensitivity. Its anti-cancer effects consist in increasing death by caspase activation and blocking of metastases in breast cancer. Morin also guards against liver damage, neurotoxicity, and myocardial ischemia-reperfusion injury.

Conclusion: Although morin has low toxicity and great tolerance, the exact molecular mechanisms of it are yet unknown and demand more in vitro and in vivo research. Establishing safe dosage, efficacy, and dose-response relationships requires clinical trials, which also help to open the path for morin's inclusion into dietary supplements and drug development for chronic diseases.

Keywords: Caspase activation, Flavonoid, Hepatoprotective, Morin, Reactive oxygen species.

INTRODUCTION

Pharmacological research has become more interested in natural compounds like flavonoids because of their low cost, widespread availability, and lack of side effects. The potent anti-inflammatory, anti-apoptotic, and other pharmacological characteristics of morin, a key bioflavonol, making it one of the most important bioflavonoids, particularly in the treatment of chronic diseases. [1]

Numerous health benefits have been demonstrated for morin, a naturally found polyphenol that is extracted from a variety of plants. It has anti-inflammatory, antihypertensive, anti-tumoral, antibacterial, neuroprotective, hypouricemic, antidiabetic, and antioxidant qualities by changing the activity of enzymes. Additionally, morin is well tolerated across time and has low toxicity, which suggests that it may be able to prevent a number of diseases[2]. Plant bioflavonoid morin hydrate has anti-inflammatory, anti-cancer, and anti-microbial qualities, among other health advantages. In addition to being a dietary supplement for better health and drug development, it also modifies cellular signaling pathways. However, to assure safety and dose-response interactions, specific clinical trials are required [3]. The morphology, kinetic, thermochemical, and electronic features of morin flavonoid in order to learn about its molecular features and its greatest radical scavenging activity. Morin showed the highest radical scavenging activity under excess free radical.

The structural organization is in accordance with the 3-O semiquinone. The predominant reactive sites were 3-OH, 2′-OH, and 4′-OH, and the first product was 3-O–2′-O quinone. Mendoza. [4] Morin has potent pharmacological effects against various cancers and has been studied as a natural dietary supplement to enhance the effects of other anticancer drugs [5]

MORIN

Morin is a yellow, crystalline flavonoid mainly in Moreasece family plants

PROPERTIES OF MORIN

Table 1: Properties of morin [6]

IUPAC Name	2-(2,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one
Molecular formula	$C_{15}H_{10}O_7$
Molecular Weight	302.23 g/mol
Physical properties	Solid
Melting Point	303 - 304 °C

MORIN HYDRATE CHEMISTRY

Morin's molecular formula is C15H10O7, and 2-(2,4-dihydroxyphenyl)- 3,5,7-trihydroxychromen-4-one is its IUPAC. Three additional hydroxy substituents are present at positions 2', 4', and 5 of the pentahydroxy flavone morin. The weight of the molecule is 302.23 g/mol. [6]

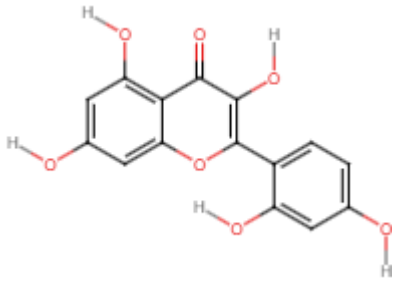

Figure 1: Chemical structure of morin (*2-(2,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one*)

PHARMACOLOGICAL ACTIVITY

Morin contains pharmacological characteristics such as anti-inflammatory and anti-apoptotic, shows promise for treating these conditions. This chapter reviews available research on morin's molecular mechanisms and its potential as a therapeutic agent.[7] By reducing reactive oxygen species (ROS) and blocking several targets, the bioflavonoid morin, which is well-known for its antioxidant qualities, has been acknowledged for its potential in both preventing and treating these conditions. It is anticipated that neurodegenerative diseases will overtake all other causes of death worldwide, placing a heavy financial strain on families and healthcare systems. Despite the lack of disease-modifying treatment strategies, oxidative stress is a key factor in many neurodegenerative disorders [8]

Anti-Inflammatory Activity: Morin showed anti-inflammatory properties during the acute stage of rat colitis caused by trinitrobenzene sulfonic acid. It facilitated tissue recovery, reduced myeloperoxidase activity, and enhanced oxidative stress in the colon, inhibiting the activity of colonic nitric oxide synthase. [9]

Anti- oxidant activity: The study investigates the antioxidant properties of flavonoids, specifically morin, from Moraceae plants. Morin showed strong scavenging effects against ABTS•+ radicals and reduced reactive oxygen species production and nuclear DNA damage caused by H2O2. It also restored cell viability by inhibiting mitochondrial dysfunction-mediated apoptosis. Morin also activated the Nrf2/HO-1 pathway and increased the expression of heme oxygenase-1, which is essential for reducing the harm that oxidative stress does to DNA. [10] Morin, when pre-treated with ISO, decreased lipid hydroperoxide, Catalase, glutathione peroxidase, superoxide dismutase, and reactive substances induced by thiobarbituric acid, and non - enzymatic antioxidants in rats, according to the study. [11]

Anti-diabetic activity: Type-2 diabetes is an insulin resistant disease with PTP1B as the chief negative regulator. Inhibiting or downregulating this enzyme enhances insulin sensitivity, making it a target for developing innovative anti-diabetic drugs. A research's found Morin to be a novel non-competitive small molecular the inhibitor of PTP1B, that functions as activator and sensitizer for insulin receptors, activating only metabolic pathways. Morin's cell action was tested on HepG2 cells and docking analysis was done [12]. In diabetic rats given Streptozotocin (STZ) and a high-fat diet (HFD), the study examines the synthesis, characterization, and assessment of a zinc-morin complex. The complex's oral administration significantly improved insulin resistance, glucose intolerance, hyperglycemia, and antioxidant competence, according to the results. According to the study's findings, the complex may have antioxidant, antidyslipidemic, and antidiabetic effects. [13]

Anti-cancer activity: The study investigates the ability to prevent cancer by mulberry flavonoid morin, which upregulates the Fas receptor and causes HCT-116 cells to produce caspase-8, -9, and -3. Morin turns on bid as well, and induces mitochondrial membrane potential loss. It also causes the production of ROS and suppresses anti-apoptotic proteins, such as Bcl-2 and cIAP-1. The study suggests that the crucial upstream signaling is Akt, regulating morin's apoptotic process. [14] Morin has anticancer properties, and was found to prevent the potential for breast cancer cells in humans to spread when endothelial growth factor is present. It inhibited the EGFR signaling pathway, which in turn suppressed MMP-9 activity and cell migration, causing DNA damage, and activating autophagy. Morin could be a potential therapeutic candidate for HER2 overexpressing breast cancer. [15]

In male Wistar rats, morin's protective effect on the liver against ethanol-induced biochemical alterations was assessed. After 60 days of ethanol use, oxidative stress increased and antioxidant levels decreased, resulting in liver and kidney damage. Morin may lessen alcohol-induced liver damage because it decreases the breakdown of lipids as well as repairs antioxidant, hepatic, along renal markers when taken orally [16]

Hepatoprotection: Three flavonoids—quercetin, silybin, and morin—are tested for their ability to shield mice from microcystin toxicity. Results show that these flavonoids can reverse the MC-LR's hepatotoxic effects in vivo, with no significant changes in serum alanine aminotransferase, catalase activity, or protein phosphatase activity [17]

Neuroprotection: Morin investigates the protective properties of natural flavonoid morin against arsenic and cadmium-induced neurotoxicity in PC12 cells. Results show that morin increases cell viability, decreases reactive oxygen species production, and reduces cleaved-caspase-3 levels, making it a promising treatment for these toxic metals [18]. A study on morin's preclinical bio-efficacy on focal ischemia in animals showed positive effects, including reduced neurological deficits, reduced MDA content, and increased antioxidant levels. Morin's neuroprotective effects may aid in ischemic stroke amelioration [19]

One study has discovered that a diet containing morin can safeguard against oxidative stress and neuroinflammation in PD-induced mice. The diet-maintained motor function against dysfunction and improved dopaminergic neuronal injury of the striatum and substantia nigra. Neuroinflammation was also minimized by morin, down-regulating glial activations of microglia and astrocytes. This has indicated that morin may act as a functional food component that can treat neurodegenerative diseases such as PD and other neurodegenerative disorders connected with neuroinflammation [20]

Cardio protection: The impact of natural flavanol morin on isolated heart tissue from rats and cardiac cells' myocardial ischemia-reperfusion injury (MIRI). The results indicate that morin treatment improves cardiac function, reduces infarct size, increases cell viability, and lowers LDH activity. Nevertheless, atractyloside treatment reverses these effects. [21]

Anti-Bacterial Activity: According to a study, the bioavailable flavonoid morin exhibits antibacterial properties against Vibrio cholerae. The bacterial divisome protein, VcFtsA, is bound by morin, which prevents its polymerization and ATPase activity. V. cholerae's cell division is impacted by this interaction, resulting in an elongated shape. Morin's low cytotoxicity to human cells makes it a useful therapeutic agent. This research may aid in the synthesis of new derivatives that more effectively target VcFtsA [22]

Antimicrobial Activity: A commonly occurring fungal infection, Candida albicans is made more pathogenic by virulence factors. Morin, a photo-bioactive compound, has been shown in a study to have strong inhibitory potential against virulence factors and biofilm formation. Morin has the potential to be a powerful therapeutic drug by successfully rescuing animals from candida infection and increasing their survival rate, according to in vivo studies conducted on zebrafish. [23]

Antiviral Activity: Dengue hemorrhagic fever is a severe disease caused by a dengue infection (DHF). Guava has been demonstrated to increase thrombocyte counts in patients due to its high tannin content and flavonoids, including guajavarin, quercetin, and morin. In order to determine how the morin compound impacted dengue virus replication, this study used the Viral ToxGlo assay. The Vero cell lines' CC50 was 12.46 µg/ml, whereas the dengue virus compounds' IC50 value was 9.42 µg/ml. [24]

Synergetic Activity

Antiviral & Anti-inflammatory effect: The research investigated the potential of morin hydrate, a flavonoid derived from Morus alba L., to combat the influenza A/Puerto Rico/8/1934 (A/PR/8; H1N1) virus, as well as a strain of the virus that has developed resistance to oseltamivir. According to the results, morin hydrate reduces chemokines and pro-inflammatory cytokines in infected mice, relieves symptoms, and lessens hemagglutination by A/PR/8. Co-administration of oseltamivir phosphate and morin hydrate reduces pulmonary inflammation and virus titers, suggesting antiviral activity. [25]

Anti-inflammatory & Neuroprotective: According to one study, in a mouse model of Parkinson's disease, a diet high in morin reduces dopaminergic neuronal damage and prevents motor dysfunction. By blocking the ERK–p65 pathway, morin inhibits glial activations, suggesting that it may have therapeutic value in the management of neurodegenerative diseases like Parkinson's disease. [26]

SUMMARY

Pharmacological Activity	Disease/Model Used	Experimental Outcome / Mechanism	References
Anti-inflammatory	TNBS-induced colitis in rats	↓ NOS, ↑ tissue repair, ↓ MPO activity	Gálvez et al., 2001
	PD-induced mice	↓ glial activation, ↓ ERK–p65 pathway	Hong et al., 2022
Anti- Oxidant	ABTS•+ and H_2O_2-induced damage	↑ Nrf2/HO-1, ↓ ROS, ↓ DNA damage, ↑ viability	Lee et al., 2017
	ISO-treated rats	↓ TBARS, ↑ antioxidant enzymes	Al-Numair et al., 2014
Antidiabetic	HepG2 cells, docking study	PTP1B inhibition, insulin sensitization	Paoli et al., 2013

	STZ + HFD rats (Zinc-morin complex)	↓ glucose, ↑ insulin sensitivity, ↑ antioxidant potential	Sendrayaperumal & Devaraj, 2010
Anti-Cancer	HCT-116 colon cancer cells	↑ Fas, caspase-8, -9, -3; ↓ Bcl-2, ↑ ROS	Hyun et al., 2015
	HER2+ breast cancer cells	↓ EGFR, ↓ MMP-9, ↑ DNA damage, autophagy activation	Lee et al., 2021
Hepatoprotective	Ethanol-treated Wistar rats	↓ lipid breakdown, ↑ hepatic & renal markers	Shankari et al., 2010
	Microcystin-LR exposure in mice	↓ ALT, normalized catalase and phosphatase activity	Jayaraj et al., 2007
Neuroprotective	PC12 cells (arsenic/cadmium neurotoxicity)	↓ ROS, ↑ viability, ↓ caspase-3	Banaeeyeh et al., 2024
	PD-induced mice	↓ neuroinflammation, ↑ dopaminergic neuron survival	Hong et al., 2022
	Ischemia model in animals	↓ MDA, ↓ deficits, ↑ antioxidant levels	Chen et al., 2017
Cardioprotective	Myocardial I/R injury in isolated rat hearts	↑ cell viability, ↓ infarct size, improved function	Liu et al., 2018

FUTURE ASPECTS

According to the various studies this article reviews, Morin Hydrate has proven helpful in the treatment of a variety of human illnesses. Even though in vitro and in vivo research has attempted to clarify the mechanisms of Morin Hydrate, more research is necessary to explain its molecular mechanism. Furthermore, clinical investigations are desperately needed to establish their potential utility of Morin.

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Conflict of Interest: The authors, Sampda Jain and Yogesh Yadav, declare that they have no known financial or personal relationships that could have appeared to influence the work reported in this paper. The research was conducted independently under the academic supervision of Prof. Manoj Sharma. All potential conflicts of interest have been disclosed.

Author Contributions: Sampda Jain and Yogesh Yadav conceptualized the review and designed its framework. Sampda Jain conducted the literature search and drafted the manuscript. Yogesh Yadav contributed to critical analysis of the literature and manuscript refinement. Prof. Manoj Sharma supervised the work and provided intellectual guidance and critical revisions. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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Data Availability Statement: The data supporting this paper are available in the cited references.

Ethical approval: Not applicable.

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