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Biological Properties of Morin: A review

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Abstract

Morin is a natural polyphenol, which is isolated of some plants from Moraceae family. Morin has various biological activities as antioxidant, antidiabetic, anti-inflammatory, antiulcer, antitumoral, antihypertensive, antibacterial, hypouricemic, and neuroprotective effects, by modulating the activity of many enzymes. In some cases, Morin showed a systemic protective action, reducing negative side effects of several drugs, without interfering with their functions. It showed a skin protection effect. In addition, in vitro and in vivo studies showed that morin has very low toxicity levels and its chronic administration is well tolerated. All these findings proved that Morin could be used, either alone or in combination with other drugs, to prevent many human pathologies.

Keywords: Morin, Chemical compounds, plants, bioactivities.

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1. Introduction

Plants are the major source of active chemical constituents against diseases [1]. Most of the world's population still relies on the folk medicines for the treatment of a large number of serious diseases. The biologically active principles of medicinal plants include flavonoids, phenolics, and polyphenols with promising anticancer and antioxidant activities [2]. Flavonoids, 2-phenylbenzo-γ-pyrone derivatives, are a broadly distributed class of naturally occurring pigments present in vascular plants, and are responsible for much of the coloring in nature. Some of them, for example quercetin, rutin and morin have antibacterial activity [3]. Morin is a yellow colour natural bioflavonoid abundantly available in different species of Moraceae family. Besides this, Morin is also harvested from several other sources like tea, coffee, cereals, fruits and red wine. Use of Morin has been found to be effective in a wide range of disease pathologies, which includes Alzheimer's disease (AD) [2,3], Parkinson's disease (PD) [4,5], ischemia [6,7], diabetes [8-10], cancer [11-13], cardiovascular anomalies [14,15], and renal complications [16]. Morin is considered as a potent therapeutic drug suggested for all those diseases, which are mainly affected by free radical vandalism [17]. Progressive research has showed that, administration of Morin has not associated with any adverse side effects [18]. Moreover, it is comparatively cost-effective and easily available [19]. The protective efficacy of Morin is mainly attributed by its anti-oxidant properties and also the unique structural feature that assists Morin to interact with nucleic acids, enzymes and proteins [20]. Besides well-known anti-oxidant property of Morin, it has recently been highlighted for the therapeutic benefits in neurological anomalies [8]. This review afforded the most biological activities of morin compound.

2. Biological Activities

2.1 Efficacy of morin in Alzheimer's disease

One of the potential contributions of Morin is the inhibition of glycogen synthase kinase-3β (GSK 3β), which is regarded the determining enzyme in the occurrence of AD pathology. It has been reported that inhibition of GSK 3β function can alter several crucial pathways in cellular

environment [23]. Alteration in choline metabolism and microtubule dynamics are notable among them [24]. Further, such inhibition has been seen to trigger apoptotic mechanism and impairs the axonal transport, which in terms of neurological spectrum is having utmost importance [25, 26]. In AD perspective, inhibition of GSK 3β has been reported to improve the cognitive condition among patients [27-29]. Morin at low concentration has showed (in vitro) remarkable inhibition of GSK 3β activity and thereby, reducing the pathogenic Aβ load in neuron, which further reduces the possibilities of Aβ-induced tau protein hyperphosphorylation [30].

2.2 Anti-cancer activity of Morin

Morin is found to be most promising, which showed profound anticancer activity by reducing DNA damage and modulating signalling pathways responsible for proliferation and differentiation [31, 32]. Morin is having the potency to inhibit carcinogenic activity of malformed cells and also has been reported to stop the tumor formation induced by carcinogenic chemical compounds. In rat model of carcinogenesis (induced by 7,12-dimethylbenz(a)-anthracene), Morin administration have showed reduced oxidative stress, decreased expression of tumor markers and inhibition of tumor growth [33]. Similar result has been found in another study, where carcinogenesis was induced by 12-O-tetradecanoyl-phorbol-13-acetate and after Morin treatment, restriction in carcinogenic transformation in liver cells was reported [34, 35].

2.3 Anti-gout effect of Morin

Morin efficiently reduces the serum level of Uric acid (UA) either by inhibiting xanthine oxidase or by inhibiting urate anion transporter-1 [36]. These pathways reduce the synthesis of UA and reabsorption of UA respectively. Further studies have showed that, Morin administration reduces plasma UA, without hampering the anti-oxidant balance in the cell [37, 38].

2.4 Protective effect of Morin against cardiovascular anomalies

Morin administration has been found to be effective as it expands the diameter of the blood vessel and effectively recapitulates the function of traditional drugs like Isoprenaline and Sodium nitroprusside [39]. In animal model of hypertension (induced by deoxycorticosterone acetate-salt), Morin treatment showed positive result and restored the psychomotor behaviors [40]. Similar studies also have established that, Morin significantly decreases the systolic and diastolic blood pressure in rodent model of hypertension [40]. In fructose diet induced hypertensive model, Morin treatment showed reduction of blood pressure, normalization of lipid profile and decreased endothelin-1 expression [41].

2.5 Protective effect of Morin in diabetic pathology

Several reports have documented the insulin mimetic effect of Morin, which also promotes the crucial influence in the normalization of blood glucose level . The effect of Morin has been found to be similar with the conventionally used antidiabetic drug- Glibenclamide, which shares common functional attributes in terms of rescuing pancreatic insulin-producing cells from cell death, sustaining insulin release, and by increasing the glycogen synthesis in liver [42]. Studies have shown that, Morin with zinc provides better functional attributes [43, 44]. In chronic spectrum, administration of Morin-Zinc complex showed decreased glucose level, improvement in insulin production, reduction in glycosylated hemoglobin content, and lipid profile [45, 46]. Depending upon the administration type (with or without Zinc), Morin enhances the insulin receptor mediated signaling and efficiently reduces the blood glucose levels [47].

2.6 Antibacterial activity of Morin

Morin inhibits that particular enzyme activity and thereby hindering in the establishment process of the bacteria. Further, Morin also inhibits the ATPase activity of DNA helicase RepA, which reduces the growth of the bacteria [48]. Morin derivatives and analogous structures also have showed better anti-bacterial activity in both cellular and rodent model system. Morin-3-O-arabinoside and Morin-3-O-lyxoside extracted from P. guajava have shown effective antibacterial effect in securing stored food quality by inhibiting the growth of *B. stearothermophilus*, *B. ther-mosphacta*, *E. coli*, *L. monocytogenes*, *P. fluorescens*, *enterica*, *S. aureus*, and *V. cholera* [49]. Depending upon available information it is presumable that, Morin is an effective antibacterial phytocomponent, which is having potential industrial efficacy to improve the shelf-life and the safety of foods, thereby preventing from food-borne diseases.

2.7 Antioxidant and cytoprotective effects of morin

Morin had strong scavenging effects against ABTS•+ radicals with enhanced SOD activity, which varied in a dose dependent manner. Morin was found to reduce H2O2-induced intracellular reactive oxygen species generation and nuclear DNA damage, and it recovered cell viability damaged by H2O2 via inhibition of mitochondrial dysfunction-mediated apoptosis. Notably, the treatment of V794 cells with morin markedly enhanced the expression of heme oxygenase1 but not quinone oxidoreductase, which was associated with the increased expression and phosphorylation of nuclear Factor erythroid 2 related factor 2 (Nrf2) and the down regulation of Kelch Like ECH associated protein expression. We conclude that morin effectively ameliorated oxidative stress induced DNA damage through intrinsic free radical scavenging activity.

3. Conclusion

This review showed the importance of Morin. Morin covers a large number of targets, which include oxidants, xenobiotics, excess of metals, radiations, pro-inflammatory factors. Morin could be a promising therapeutic agent against extended range of diseases and disorders, which includes cancer, cardiovascular diseases, neurological impairments, diabetes, toxin-induced liver and kidney damage, inflammation and oxidative radical-induced pathology.

References

[1]. Bako, S.P.; Bakfur, M.J.; John, I.; Bala, E.I. Ethno-medicinal and phytochemical profile of some savanna plant species in Nigeria. *Int. J. Bot.* 2005; 1: 147–150.

[2]. Williams, R.J.; Spencer, J.P.E.; Rice-Evans, C. Flavonoids: Antioxidants or signalling molecules. *Free Radic. Biol. Med.* 2004; 36: 838–849.

[3]. Bravo A, Anacona JR. Metal complexes of the flavonoid quercetin: antibacterial properties. *Transition Metal Chemistry*. 2001; 26(1):20-3.

[4]. Lemkul, J.A., and D.R. Bevan. Destabilizing Alzheimer's Aβ42 protofibrils with morin: Mechanistic insights from molecular dynamics simulations. *Biochemistry* 2010; 49 (18): 3935-46.

[5]. Noor, H. Morin hydrate inhibits amyloid formation by islet amyloid polypeptide and disaggregates amyloid fibers. *Protein Science* 2012; 21 (3): 373-82.

[6]. Caselli, A. Morin: A promising natural drug. *Current Medicinal Chemistry* 2016; 23(8) 2016: 774-91.

[7]. Caruana, M., Högen T. Inhibition and disaggregation of α-synuclein oligomers by natural polyphenolic compounds. FEBS Letters 2011; 585 (8): 1113-20.

[8]. Gottlieb, M. . Neuroprotection by two polyphenols following excitotoxicity and experimental ischemia. *Neurobiology of Disease* 2006; 23 (2): 374-86.

[9]. Al-Numair, K.S. Morin, a flavonoid, on lipid peroxidation and antioxidant status in experimental myocardial ischemic rats. *African Journal of Traditional, Complementary, and Alternative Medicines: AJTCAM/African Networks on Ethnomedicines* 2014; 11 (3): 14-20.

[10]. Ola, M.S. Flavonoid, morin inhibits oxidative stress, inflammation and enhances neurotrophic support in the brain of streptozotocin-induced diabetic rats. *Neurological Sciences* 2014; 35 (7) : 1003-08.

[11]. Paoli, P. The insulin-mimetic effect of morin: A promising molecule in diabetes treatment. *Biochimica et Biophysica Acta - General Subjects* 2013; 1830 (4): 3102-11.

[12]. Kapoor, R, and Kakkar P. Protective role of morin, a flavonoid, against high glucose induced oxidative stress mediated apoptosis in primary rat hepatocytes. *PLoS ONE*, 2012; 7 (8).

[13]. Birt, D. F., *et al*. Dietary agents in cancer prevention: Flavonoids and isoflavonoids. Pharmacology and Therapeutics, 2001; 90 (2-3) :157-77.

[14]. Zhang, S, and Morris, M.E. Effects of the flavonoids biochanin A, morin, phloretin, and silymarin on P-glycoprotein-mediated transport. *The Journal of Pharmacology and Experimental Therapeutics*, 2003; 304 (3):1258-67.

[15]. Zhang, S., Yang, X., and Morris. M.E. Flavonoids are inhibitors of breast cancer resistance protein (ABCG2)-mediated transport. *Molecular Pharmacology,* 2004; 65 (5): 1208-16.

[16]. García-Lafuente, A.. Flavonoids as anti-inflammatory agents: Implications in cancer and cardiovascular disease. *Inflammation Research*, 2009; 58 (9): 537-52.

[17]. Wu, T.W., Ling H.Z. Morin: A wood pigment that protects three types of human cells in the cardiovascular system against oxyradical damage. *Biochemical Pharmacology*, 1994; 47 (6):1099-103.

[18]. Prahalathan, P. Effect of morin, a flavonoid against DOCA-salt hypertensive rats: A dose dependent study. *Asian Pacific Journal of Tropical Biomedicine*, 2012; 2 (6): 443-48.

[19]. Chen Y. Flavonoids as superoxide scavengers and antioxidants. *Free Radical Biology and Medicine*, 1990; 9 (1): 19-21.

[20]. Choi, J. S., and Han, H. K. Pharmacokinetic interaction between diltiazem and morin, a flavonoid, in rats. *Pharmacological Research*, 2005; 52 (5): 386-91.

[21]. Milbury,P.E Determination of flavonoids and phenolics and their distribution in almonds. *Journal of Agricultural and Food Chemistry*, 2006; 54 (14): 5027-33.

[22]. Xie, M-X, Characterization of the interaction between human serum albumin and morin. *Biochimica et Biophysica Acta* 2006; 1760 (8):1184-91.

[23]. Hurtado, D.E. Selectively silencing GSK-3 isoforms reduces plaques and tangles in mouse models of Alzheimer's disease. *Journal of Neuroscience* 2012; 32 (21): 7392-402.

[24]. Glen, A. I. Choline uptake in patients with alzheimer pre-senile dementia'. Psychological Medicine 1981; 11 (0033-2917) :469-76.

[25]. Amor, S. Inflammation in neurodegenerative diseases. *Immunology* 2010; 129 (2):154-69.

[26]. Petit-Paitel, A. GSK-3beta: A central kinase for neurodegenerative diseases? *Med Sci* (Paris), 2010; 26 (5) :516-21.

[27]. Pei, J-J. Distribution of active glycogen synthase kinase 3β (GSK-3β) in brains staged for Alzheimer disease neurofibrillary changes. *Journal of Neuropathology and Experimental Neurology* 1999; 58 (9):1010-19.

[28]. Jo, J. Aβ1-42 Inhibition of LTP is mediated by a signaling pathway involving caspase-3, Akt1 and GSK-3β. *Nature Neuroscience* 2011; 14 (5) :545-47.

[29]. Llorens-Martín, M. GSK-3β overexpression causes reversible alterations on postsynaptic densities and dendritic morphology of hippocampal granule neurons in vivo. *Molecular Psychiatry* 2013; 18 (4): 451-60.

[30]. Madan Kumar, P. Morin ameliorates chemically induced liver fibrosis *in vivo* and inhibits stellate cell proliferation *in vitro* by suppressing Wnt/beta-catenin signaling. *Toxicology and Applied Pharmacology* 2014; 277 (2): 210-20.

[31]. Hyun, H.B. The flavonoid morin from moraceae induces apoptosis by modulation of Bcl-2 family members and Fas receptor in HCT 116 cells. *International Journal of Oncology* 2015; 46 (6): 2670-78.

[32]. Lee, J.H. Morin, a flavonoid from moraceae, inhibits cancer cell adhesion to endothelial cells and EMT by down-regulating VCAM-1 and N-cadherin. *Asian Pacific Journal of Cancer Prevention* 2016; 17 (7) : 3071-75.

[33]. Nandhakumar, R. Morin augments anticarcinogenic and antiproliferative efficacy against 7,12-dimethylbenz(a)-anthracene induced experimental mammary carcinogenesis. *Molecular and Cellular Biochemistry* 2012; 364 (1-2) : 79-92.

[34]. Hsiang, C-Y. Morin inhibits 12-O-tetradecanoylphorbol-13-acetate-induced hepatocellular transformation via activator protein 1 signaling pathway and cell cycle progression. *Biochemical Pharmacology* 2005; 69 (11) : 1603-11.

[35]. Sithara, Thomas. Morin inhibits proliferation of SW480 colorectal cancer cells by inducing apoptosis mediated by reactive oxygen species formation and uncoupling of Warburg effect. *Frontiers in Pharmacology* 2017; 8 (1) : 640.

[36]. Wang, C.P. Morin improves urate excretion and kidney function through regulation of renal organic ion transporters in hyperuricemic mice. *Journal of Pharmacy and Pharmaceutical Sciences* 2010; 13 (3) : 411-27.

[37]. Mo, S-F. Hypouricemic action of selected flavonoids in mice: Structure-activity relationships. *Biological & Pharmaceutical Bulletin* 2007; 30 (8) : 1551-56.

[38]. Santos, R., Fabiane, K.. Effect of flavonoids morin; quercetin and nicotinic acid on lipid metabolism of rats experimentally fed with triton. *Brazilian Archives of Biology and Technology* 2001; 44 (3) : 263-67.

[39]. Herrera, M.D., *et al*. Effects of flavonoids on rat aortic smooth muscle contractility: Structure-activity relationships. *General Pharmacology* 1996; 27 (2) : 273-77.

[40]. Prahalathan, Pi., Kumar, S. Morin attenuates blood pressure and oxidative stress in deoxycorticosterone acetate-salt hypertensive rats: A biochemical and histopathological evaluation. *Metabolism: Clinical and Experimental* 2012; 61 (8) : 1087-99.

[41]. Kang, D.G., *et al*. Effects of morin on blood pressure and metabolic changes in fructose-induced hypertensive rats. *Biological & Pharmaceutical Bulletin* 2004; 27 (11) : 1779-83.

[42]. Lin, M.H. Investigation of morin-induced insulin secretion in cultured pancreatic cells. *Clinical and Experimental Pharmacology and Physiology* 2017.

[43]. Nafisi, S. DNA adducts with antioxidant flavonoids: Morin, apigenin, and naringin. *DNA and Cell Biology* 27 (8) 2008: 433-42.

[44]. Nafisi, Sh. RNA binding to antioxidant flavonoids. *Journal of Photochemistry and Photobiology B: Biology* 2009; 94 (1) : 1-7.

[45]. Payán-Gómez, S.A. Computational molecular characterization of the flavonoid morin and its Pt(II), Pd(II) and Zn(II) complexes. *Journal of Molecular Modeling* 2011; 17 (5) : 979-85.

[46]. Selvaraj, S. 'Flavonoid-metal ion complexes: A novel class of therapeutic agents. *Medicinal Research Reviews* 2014; 34 (4) : 677-702.

[47]. Wei, Y, and Guo, M. Zinc-binding sites on selected flavonoids. *Biological Trace Element Research* 2014; 161 (2) : 223-30.

[48]. Xu, H. Flavones inhibit the hexameric replicative helicase RepA. *Nucleic Acids Research* 29 (24) 2001: 5058-66.

[49]. Arima, Hidetoshi, and Genichi Danno. Isolation of antimicrobial compounds from guava (*Psidium guajava* L.) and their structural elucidation. *Bioscience, Biotechnology, and Biochemistry* 2002; 66 (8) : 1727-30.

[50]. Moon Hee Lee, Hee-Jae Cha, Eun Ok Choi, Min Ho Han, Sung Ok Kim, Giyoung Kim, Su Hyun Hong, Cheol Park, Sungkwon Moon, Soonjeong Jeong, Moonjin Jeong, Wun-Jae Kim And Yung Hyun Cho. Antioxidant and cytoprotective effects of morin against hydrogen peroxide-induced oxidative stress are associated with the induction of Nrf-2-mediated HO-1 expression in V79-4 Chinese hamster lung fibroblasts. *International Journal of Molecular Medicine* 2017; 39: 672-680, .