ISSN: 0976-7126
Dwivedi & Shrivastava, 16(12):10-14, 2025

International Journal of Pharmacy & Life Sciences
Open Access to Researcher

Exploring the Therapeutic Potential of Naringin: Chemical Attributes and Pharmacological Evidence

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Article info

Received: 10/10/2025

Revised:15/11/2025

Accepted: 15/12/2025

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www.ijplsjournal.com

Abstract

Naringin is a naturally occurring flavanone glycoside predominantly found in citrus fruits, especially *Citrus paradisi* (grapefruit), and has gained considerable scientific interest due to its broad spectrum of pharmacological activities. Chemically, naringin consists of a flavanone nucleus conjugated with disaccharide moieties, conferring antioxidant and biological activity. Upon metabolism, naringin is converted into its aglycone naringenin, which plays a crucial role in mediating its therapeutic effects. Extensive preclinical studies have demonstrated that naringin exhibits antioxidant, anti-inflammatory, antimicrobial, anticancer, cardioprotective, hepatoprotective, neuroprotective, and antidiabetic activities through modulation of oxidative stress, inflammatory mediators, apoptosis pathways, and cellular signaling cascades. However, its poor aqueous solubility and limited oral bioavailability pose significant challenges for clinical translation. Recent advances in formulation strategies, particularly nano-based delivery systems, have shown promise in overcoming these limitations. This review provides a comprehensive overview of the chemical properties, metabolism, and diverse pharmacological activities of naringin, along with current challenges and future perspectives for its therapeutic application.

Keywords: Naringin, Flavonoid, Citrus bioactives, Pharmacological activities, Antioxidant

Introduction

Flavonoids are a major class of polyphenolic compounds widely distributed in fruits, vegetables, and medicinal plants, known for their significant health-promoting effects (Gupta et al., 2025). Among them, naringin has attracted growing attention due to its presence in citrus fruits and its extensive pharmacological profile. Naringin is responsible for the characteristic bitter taste of grapefruit and has been traditionally associated with digestive and metabolic health benefits (Li et al., 2014). In recent years, increasing evidence has highlighted the role of naringin as a multifunctional bioactive molecule capable of targeting multiple disease pathways simultaneously. Its ability to modulate oxidative stress, inflammation, microbial resistance, and metabolic dysregulation makes it a promising candidate for managing chronic and infectious diseases (Chen et al., 2016). This review focuses on the chemical nature, metabolic fate, and pharmacological potential of naringin, emphasizing its relevance in modern therapeutics.

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ISSN: 0976-7126
Dwivedi & Shrivastava, 16(12):10-14, 2025

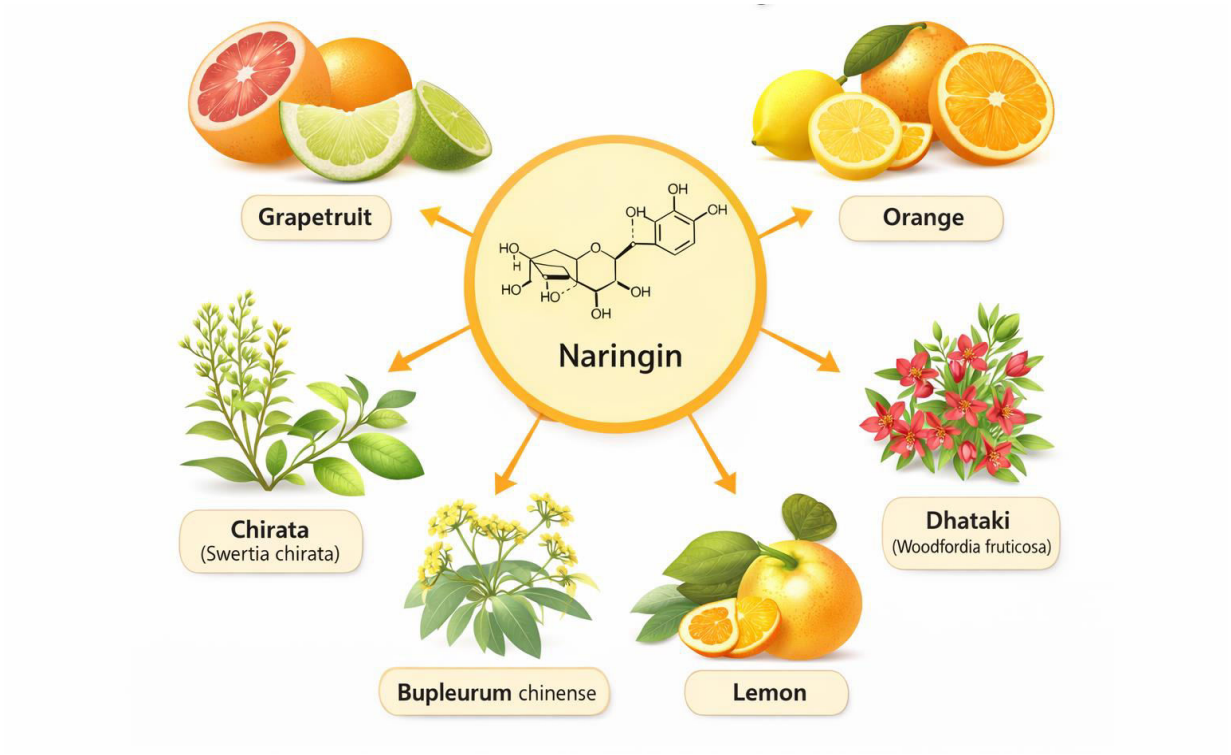

Fig. 1: Sources of Naringin

Chemical Structure and Physicochemical Properties

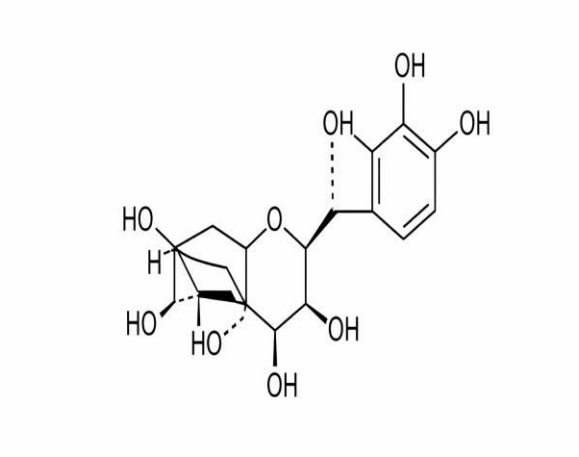

Fig. 2: Structure of Naringin

Naringin is chemically identified as 4′,5,7-trihydroxyflavanone-7-O-neohesperidoside, with a molecular formula of $C_{27}H_{32}O_{14}$. Structurally, it consists of a flavanone backbone linked to a disaccharide composed of rhamnose and glucose (Ross & Kasum, 2002). The presence of multiple hydroxyl groups contributes to its strong antioxidant capacity, while the glycosidic moiety influences solubility and absorption.

Despite its biological potency, naringin exhibits poor water solubility and limited permeability, which adversely affect its bioavailability. These physicochemical constraints necessitate the exploration of formulation approaches to enhance its therapeutic efficiency (Srinivasan et al., 2019).

Metabolism and Bioavailability

After oral administration, naringin undergoes enzymatic hydrolysis by intestinal microflora, converting it into its aglycone form, naringenin, which is more readily absorbed (Manach et al., 2005). Naringenin subsequently undergoes phase II metabolism, forming glucuronide and sulfate conjugates that circulate systemically.

Although metabolism enhances absorption, rapid biotransformation and first-pass metabolism significantly reduce systemic availability. These limitations have prompted the development of novel delivery systems such as nanoparticles,

liposomes, and solid dispersions to improve bioavailability and therapeutic outcomes (Jung et al., 2020).

Pharmacological Activities of Naringin

Antioxidant Activity

Naringin exhibits potent antioxidant activity by scavenging reactive oxygen species (ROS) and enhancing endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase (Kumar et al., 2010). By reducing oxidative stress, naringin protects cellular macromolecules from damage and plays a preventive role in oxidative stress-mediated diseases.

Anti-Inflammatory Activity

The anti-inflammatory effects of naringin are mediated through inhibition of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, as well as suppression of NF-κB and MAPK signaling pathways (Zhang et al., 2018). These properties make naringin a promising agent for managing inflammatory disorders, including arthritis and inflammatory bowel disease.

Antimicrobial and Anti-Resistance Potential

Several studies have demonstrated that naringin exhibits antibacterial and antifungal activity against both Gram-positive and Gram-negative pathogens. Additionally, it has shown potential in disrupting biofilm formation and enhancing the efficacy of conventional antibiotics, indicating its role as a resistance-modifying agent (Cushnie & Lamb, 2011).

Anticancer Activity

Naringin has been reported to inhibit cancer cell proliferation and induce apoptosis through modulation of mitochondrial pathways, caspase activation, and inhibition of angiogenesis (Patil et al., 2014). Its chemopreventive effects have been demonstrated in breast, colon, liver, and lung cancer models.

Cardioprotective and Hepatoprotective Effects

Naringin improves lipid metabolism, reduces oxidative damage, and attenuates inflammatory responses in cardiovascular and hepatic tissues. Experimental studies indicate its protective role against myocardial ischemia and chemically induced hepatotoxicity (Jeon et al., 2001).

Neuroprotective and Antidiabetic Effects

Neuroprotective effects of naringin are attributed to its ability to reduce neuroinflammation and oxidative stress, thereby improving cognitive function in neurodegenerative disease models (Golechha et al., 2014). Furthermore, naringin enhances insulin sensitivity and glucose uptake, supporting its antidiabetic potential (Alam et al., 2014).

Table 1: Important Pharmacological Activities of Naringin and Associated Animal Models

Pharmacological Activity	Animal Model Used	Experimental Induction / Method	Key Observations
Antioxidant activity	Rats / Mice	CCl_4-induced oxidative stress; H_2O_2 models	Reduced lipid peroxidation; increased SOD, CAT, GSH levels
Anti-inflammatory activity	Rats	Carrageenan-induced paw edema; CFA-induced arthritis	Inhibition of TNF-α, IL-1β, IL-6; suppression of NF-κB pathway
Anticancer activity	Mice	Xenograft tumor models; DMBA-induced carcinogenesis	Induction of apoptosis; inhibition of tumor growth and angiogenesis
Cardioprotective activity	Rats	Isoproterenol-induced myocardial infarction	Reduced myocardial injury markers; improved antioxidant status
Hepatoprotective activity	Rats	CCl_4- or paracetamol-induced hepatotoxicity	Decreased ALT, AST, ALP; protection of liver architecture
Neuroprotective activity	Rats	Kainic acid-induced epilepsy; cerebral ischemia models	Reduced neuroinflammation; improved cognitive and behavioral outcomes
Antidiabetic activity	Rats	Streptozotocin (STZ)-	Reduced blood glucose; improved

ISSN: 0976-7126
Dwivedi & Shrivastava, 16(12):10-14, 2025

		induced diabetes	insulin sensitivity
Anti-hyperlipidemic activity	Rabbits / Rats	High-fat diet-induced hyperlipidemia	Decreased total cholesterol, LDL, triglycerides
Antimicrobial activity	Mice	Systemic bacterial infection models	Reduced bacterial load; enhanced antibiotic efficacy
Anti-osteoporotic activity	Rats	Ovariectomy-induced osteoporosis	Increased bone mineral density; reduced bone loss
Gastroprotective activity	Rats	Ethanol- or NSAID-induced gastric ulcer	Reduced ulcer index; enhanced mucosal protection
Anti-atherosclerotic activity	Rabbits	Cholesterol-fed atherosclerosis model	Reduced plaque formation; improved lipid profile

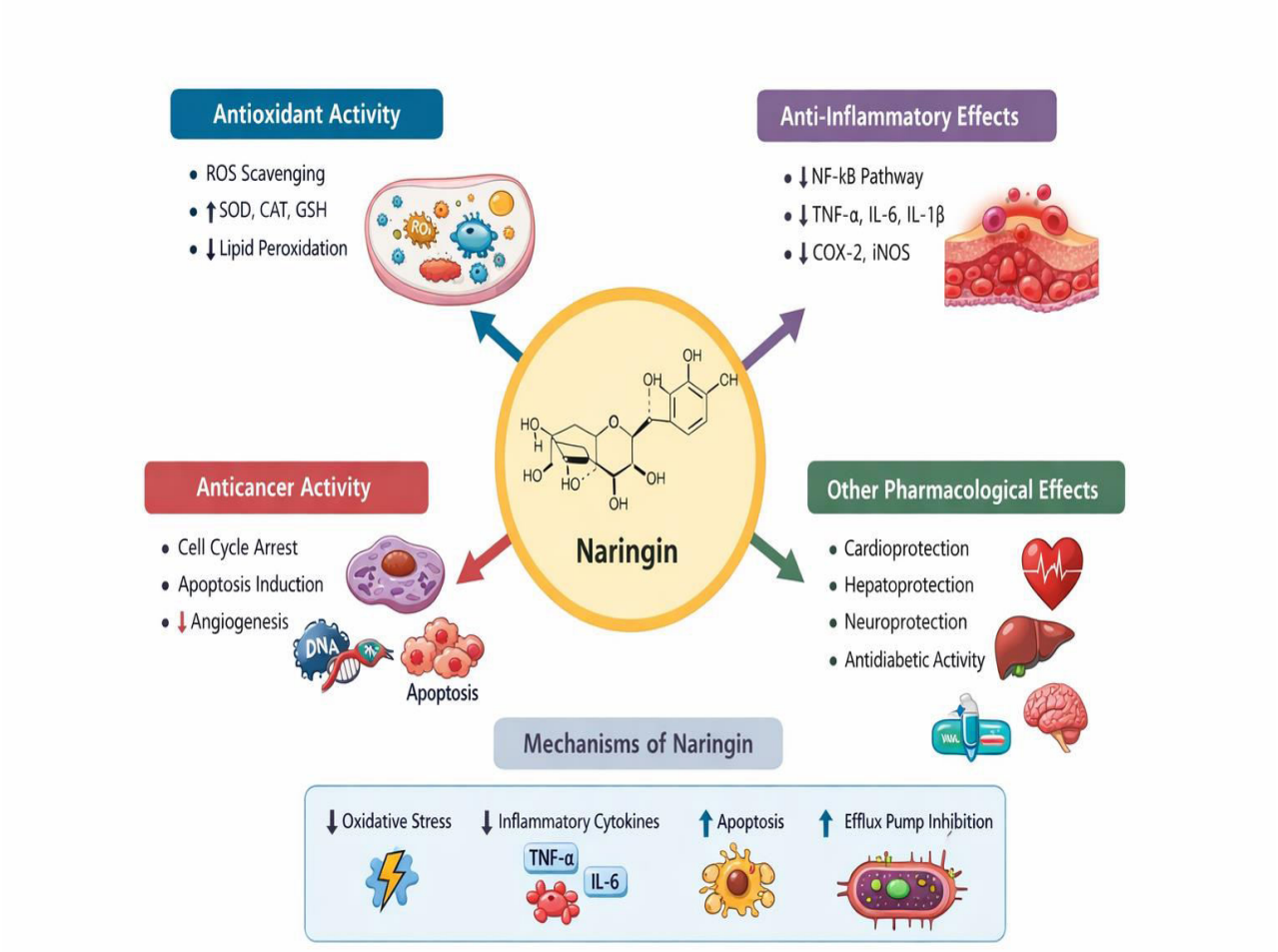

Fig. 3: Mechanism of Naringin

Challenges and Advanced Drug Delivery Approaches

Despite promising pharmacological properties, naringin's clinical use is restricted by poor solubility and rapid metabolism. Recent research has focused on nano-based delivery systems, including polymeric nanoparticles, lipid carriers, and nanoemulsions, which have demonstrated improved solubility, sustained release, and enhanced bioavailability (Sahu et al., 2021).

Conclusion

Naringin is a versatile bioactive flavonoid with significant therapeutic potential across a wide range of disease conditions. Its diverse pharmacological activities, combined with

advances in drug delivery technologies, position naringin as a promising candidate for future pharmaceutical development. Future research should focus on well-designed clinical trials to validate the therapeutic efficacy of naringin in humans. Integration of nanotechnology and targeted delivery systems may further expand its applicability in managing chronic diseases and antimicrobial resistance.

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Cite this article as:
Dwivedi S. and Shrivastava S. (2025). Exploring the Therapeutic Potential of Naringin: Chemical Attributes and Pharmacological Evidence. *Int. J. of Pharm. & Life Sci.,* 16(12):10-14.

Source of Support: Nil
Conflict of Interest: Not declared
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