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Mechanistic and Formulation Strategy Insights of Quercetin: Advances in Nano-Based Drug Delivery Systems – A Comprehensive Review

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ABSTRACT

Quercetin is a naturally occurring flavonoid extensively distributed in fruits, vegetables, medicinal plants, and beverages such as onions, apples, berries, grapes, and green tea (1). Owing to its broad spectrum of pharmacological activities, including antioxidant, anti-inflammatory, anticancer, antiviral, antimicrobial, cardioprotective, and neuroprotective properties, quercetin has gained significant attention in pharmaceutical and biomedical research. The therapeutic potential of quercetin is mainly attributed to its ability to regulate oxidative stress, inflammatory mediators, and multiple cellular signaling pathways including PI3K/Akt, MAPK, NF-κB, and apoptotic pathways. However, its clinical application is restricted due to poor aqueous solubility, rapid metabolism, low permeability, instability under physiological conditions, and limited oral bioavailability. Recent advancements in nanotechnology-based drug delivery systems have provided promising approaches to overcome these limitations. Various carrier systems such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanomicelles, nanoemulsions, dendrimers, and hydrogel-based systems have been extensively investigated to improve quercetin solubility, enhance stability, prolong systemic circulation, and achieve controlled as well as targeted drug delivery. These nanoformulations significantly improve therapeutic efficacy while minimizing systemic toxicity and adverse effects. The present review comprehensively summarizes the chemistry, sources, extraction methods, physicochemical characterization, pharmacological activities, molecular mechanisms, and limitations of quercetin. In addition, detailed emphasis is provided on advanced nanoformulation strategies, preparation techniques, comparative advantages, limitations, and recent research developments. The review further highlights future clinical perspectives and challenges associated with the successful translation of quercetin-based formulations into pharmaceutical applications.

Keywords: Quercetin, Flavonoid, Nanocarriers, Liposomes, Solid Lipid Nanoparticles, Polymeric Nanoparticles, Controlled Drug Delivery, Bioavailability Enhancement.

INTRODUCTION:

Flavonoids are naturally occurring polyphenolic compounds widely distributed in plants and are recognized for their remarkable therapeutic potential. Among them, quercetin is one of the most abundant and biologically active flavonol compounds found in fruits, vegetables, medicinal herbs, and beverages. Major dietary sources of quercetin include onions, apples, berries, broccoli, grapes, citrus fruits, tomatoes, tea, and red wine. Structurally, quercetin possesses five hydroxyl groups attached to its flavone backbone, which contribute significantly to its strong antioxidant and free radical scavenging activities (2) (3).

Oxidative stress is one of the major pathological factors involved in chronic diseases such as cancer, diabetes mellitus, cardiovascular disorders, inflammatory diseases, and neurodegenerative conditions. Quercetin exerts potent antioxidant effects by neutralizing reactive oxygen species (ROS), inhibiting lipid peroxidation, and enhancing endogenous antioxidant enzyme systems including superoxide dismutase (SOD), catalase, and glutathione peroxidase (4). In addition to antioxidant activity, quercetin demonstrates anti-inflammatory, anticancer, antiviral, antimicrobial, cardioprotective, hepatoprotective, and neuroprotective properties (5).

The anticancer activity of quercetin is associated with modulation of several molecular signaling pathways such as phosphoinositide 3-kinase/protein kinase B (PI3K/Akt), mitogen-activated protein kinase (MAPK), and nuclear factor kappa-B (NF-κB). Furthermore, quercetin induces apoptosis, inhibits angiogenesis, suppresses tumor proliferation, and arrests the cell cycle in various cancer models. Anti-inflammatory activity is mediated through inhibition of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β).

Despite its broad therapeutic potential, the clinical application of quercetin remains limited because of poor aqueous solubility, instability during storage, rapid metabolism, extensive first-pass elimination, and poor gastrointestinal absorption. These limitations result in low oral bioavailability and reduced therapeutic efficacy. Therefore, extensive research has focused on the development of advanced formulation strategies capable of improving the pharmacokinetic and pharmacodynamic profile of quercetin (6).

Nanotechnology-based drug delivery systems have emerged as highly promising approaches for enhancing quercetin delivery. Nanoformulations such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanomicelles, dendrimers, nanoemulsions, and hydrogels improve drug solubility, protect quercetin from degradation, provide sustained release, and facilitate targeted delivery to diseased tissues.

The purpose of this review is to critically discuss the physicochemical properties, extraction methods, therapeutic applications, molecular mechanisms, formulation challenges, and advanced nano-based delivery systems of quercetin with special emphasis on mechanistic insights, comparative evaluation of nanocarriers, and future clinical perspectives.

2.CHEMISTRY AND PHYSICOCHEMICAL PROPERTIES OF QUERCETIN

Quercetin belongs to the flavonol subclass of flavonoids and chemically exists as 3,3′,4′,5,7-pentahydroxyflavone. The molecular formula of quercetin is $C_{15}H_{10}O_7$ with a molecular weight of 302.24 g/mol.

2.1 Structural Features

The structure of quercetin contains:

- Two aromatic benzene rings (A and B rings)
- One heterocyclic pyrone ring (C ring)
- Five hydroxyl groups responsible for antioxidant activity

The hydroxyl substitutions contribute to:

- Free radical scavenging
- Metal ion chelation
- Hydrogen donation
- Anti-inflammatory activity

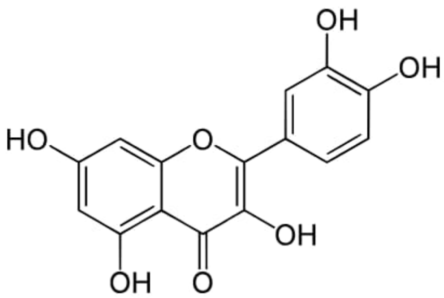


Figure 1. Chemical structure of quercetin

2.2 Physicochemical Characteristics

Property	Description
Molecular Formula	C15H10O7
Molecular Weight	302.24 g/mol
Appearance	Yellow crystalline powder
Solubility	Poorly soluble in water
Melting point	316-317*C
Stability	Sensitive to light
Nature	Lipophilic compound

3. EXTRACTION AND CHARACTERIZATION OF QUERCETIN

3.1 Extraction Methods

Quercetin is extracted from natural plant sources using different conventional and advanced extraction techniques.

3.1.1 Solvent Extraction

Conventional solvent extraction involves the use of ethanol, methanol, acetone, or hydroalcoholic mixtures for isolation of quercetin from plant materials.

Advantages:

- Simple procedure
- Cost-effective
- Easy scale-up

Limitations:

- Longer extraction time
- Lower selectivity
- Higher solvent consumption

3.1.2 Ultrasound-Assisted Extraction

Ultrasound waves improve solvent penetration and disrupt plant cell walls, thereby enhancing extraction efficiency (7)

Advantages:

- Improved yield
- Reduced extraction time
- Lower solvent requirement

3.1.3 Deep Eutectic Solvent Extraction

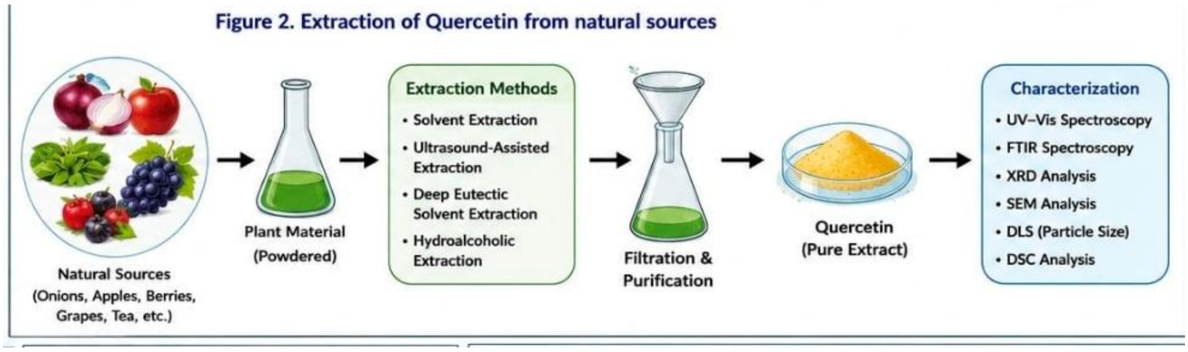


Figure 2. Schematic representation of quercetin extraction methods (7)

4. MECHANISMS OF PHARMACOLOGICAL ACTION

Quercetin exerts therapeutic effects through modulation of multiple signaling pathways and molecular targets.

4.1 Antioxidant Mechanism

Quercetin scavenges reactive oxygen species and prevents oxidative stress-induced cellular damage (1) (2).

Mechanisms include:

- Donation of hydrogen atoms
- Chelation of transition metal ions
- Inhibition of lipid peroxidation and
- Activation of antioxidant enzymes

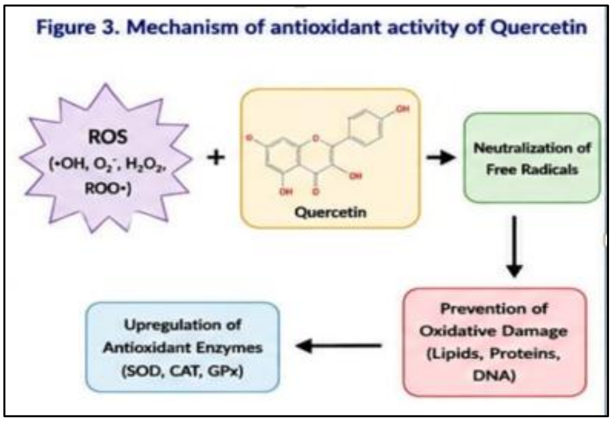


Figure 3. Mechanism of antioxidant activity of quercetin

4.2 Anti-inflammatory Mechanism

Quercetin inhibits inflammatory pathways by suppressing:

- NF-κB activation
- Cyclooxygenase (COX)

- Lipoxygenase (LOX)
- Pro-inflammatory cytokines

This results in reduced inflammation and tissue injury.

4.3 Anticancer Mechanism

Quercetin inhibits tumor progression through:

- Induction of apoptosis
- Cell cycle arrest
- Inhibition of angiogenesis
- Suppression of metastasis

It modulates signaling pathways such as:

- PI3K/Akt pathway
- MAPK pathway
- p53 pathway (9)

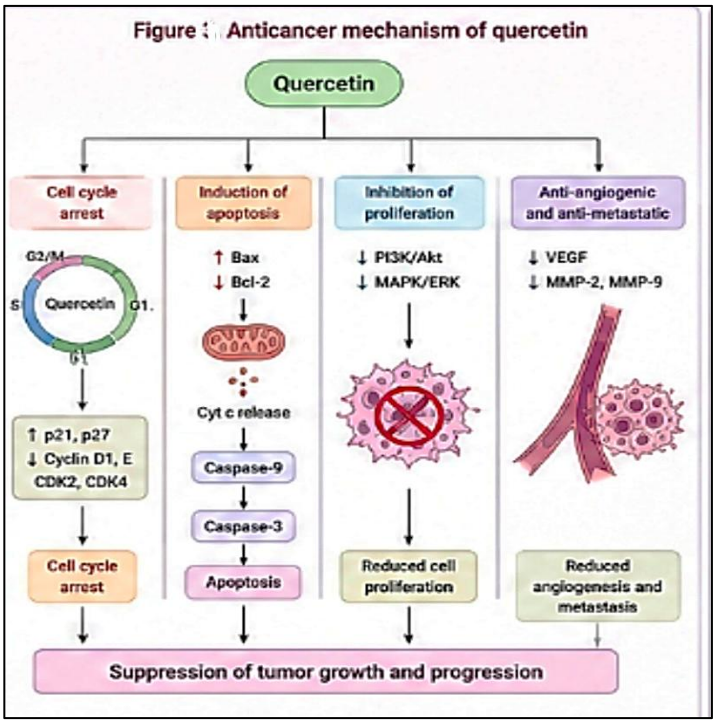


Figure 4. Molecular pathways involved in anticancer activity of quercetin

5. THERAPEUTIC APPLICATIONS OF QUERCETIN

5.1 Antioxidant Activity

Quercetin protects biomolecules such as DNA, proteins, and lipids against oxidative damage and reduces the risk of chronic diseases.

5.2 Anti-inflammatory Activity

It suppresses inflammatory mediators and decreases tissue inflammation in arthritis, inflammatory bowel disease, and respiratory disorders (10) (11).

5.3 Anticancer Activity

Quercetin demonstrates therapeutic potential against:

Breast cancer, Colon cancer, Lung cancer and Prostate cancer.

5.4 Antimicrobial Activity

Quercetin exhibits antibacterial activity against:

- Staphylococcus aureus
- Escherichia coli

It disrupts bacterial membranes and inhibits microbial enzymes (12).

5.5 Antiviral Activity

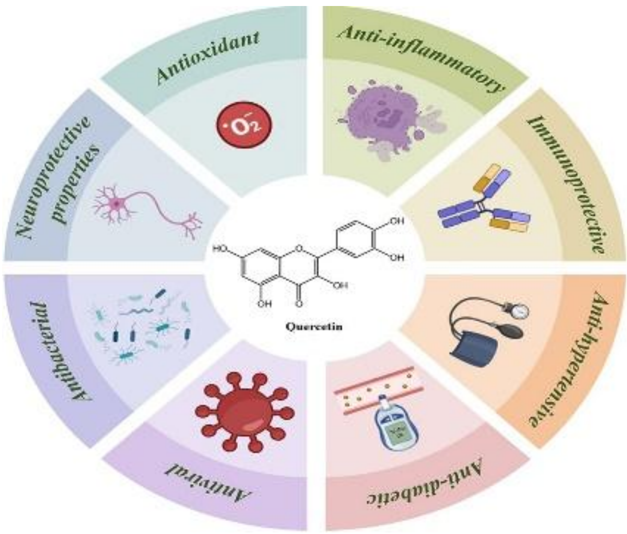
Quercetin inhibits viral replication and viral entry mechanisms against several viruses including dengue virus and influenza virus.

5.6 Neuroprotective Activity

Quercetin reduces neuroinflammation and oxidative neuronal damage associated with Alzheimer's and Parkinson's diseases (11).

5.7 Cardioprotective and Metabolic Effects

Quercetin improves endothelial function, reduces hypertension, regulates glucose metabolism, and exhibits anti-obesity effects (13).



6. LIMITATIONS OF QUERCETIN

Despite significant therapeutic potential, quercetin exhibits several formulation and pharmacokinetic limitations.

6.1 Poor Aqueous Solubility

Low water solubility limits dissolution and absorption after oral administration.

6.2 Low Bioavailability

Rapid metabolism and extensive first-pass elimination reduce systemic availability.

6.3 Instability

Quercetin undergoes degradation under:

- Light exposure
- Heat
- Oxidative conditions

6.4 Rapid Elimination

Short biological half-life reduces therapeutic concentration at target sites.

7. ADVANCED NANOFORMULATION STRATEGIES

Nanotechnology-based formulations improve the therapeutic performance of quercetin.

7.1 Liposomes

Liposomes are phospholipid vesicles capable of encapsulating hydrophilic and lipophilic drugs.

- Preparation Methods
- Thin film hydration
- Reverse phase evaporation
- Ethanol injection method

Advantages

- Biocompatibility
- Improved solubility
- Reduced toxicity
- Targeted delivery

Limitations

- Physical instability
- Drug leakage
- High production cost (14)

7.2 Solid Lipid Nanoparticles (SLNs)

SLNs consist of solid lipid matrices stabilized with surfactants.

Preparation Methods

- High-pressure homogenization

- Solvent emulsification
- Microemulsion technique

Advantages

- Sustained drug release
- Enhanced stability
- High drug loading
- Improved bioavailability

Limitations

- Limited drug incorporation
- Lipid crystallization (15)

7.3 Polymeric Nanoparticles

Polymeric nanoparticles are prepared using biodegradable polymers such as PLGA and chitosan.

- Preparation Methods
- Solvent evaporation
- Nanoprecipitation
- Ionic gelation

Advantages

- Controlled release
- Enhanced stability
- Site-specific delivery

Limitations

- Polymer toxicity concerns
- Complex manufacturing

7.4 Nanomicelles

Nanomicelles are self-assembled amphiphilic structures that improve solubility of hydrophobic drugs.

Advantages

- Small particle size
- Improved cellular uptake
- Enhanced permeability

Limitations

- Low physical stability
- Dilution-induced dissociation

7.5 Hydrogels

Hydrogels are three-dimensional polymeric networks capable of absorbing large amounts of water.

Advantages

•Localized delivery

•Controlled release

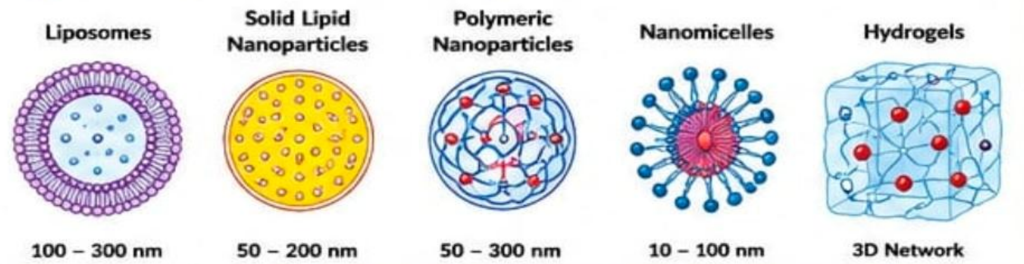
•Improved patient compliance

Limitations

•Poor mechanical strength

•Limited drug loading

Figure 5. Comparative overview of Quercetin nanoformulations



	Liposomes	Solid Lipid Nanoparticles	Polymeric Nanoparticles	Nanomicelles	Hydrogels
Composition	Phospholipids + Cholesterol	Solid Lipids + Surfactants	Biodegradable Polymers	Amphiphilic Surfactants	Hydrophilic Polymer Network
Advantages	Biocompatible, Targeted delivery	Sustained release, High stability	Controlled release, Site specific delivery	High solubility, Improved cellular uptake	Localized delivery, Patient compliance
Limitations	Leakage, Physical instability	Lipid crystallization, Limited loading	Complex preparation, Polymer toxicity	Dilution-induced dissociation, Low stability	Poor mechanical strength, Low drug loading
Key Benefits	Improved absorption & bioavailability	Enhanced bioavailability & sustained effect	Prolonged circulation & targeted action	Enhanced solubility & permeability	Controlled release & reduced side effects

8 .LITERATURE REVIEW

Recent studies have focused on improving the bioavailability and therapeutic efficacy of quercetin through advanced drug delivery systems. Liu et al. (2025) developed a phytosome-based hydrogel that significantly enhanced drug release and skin retention compared to formulations. Similarly, Mohamed et al. (2024) reported quercetin-loaded solid lipid nanoparticles with high entrapment efficiency and sustained release, showing improved anticancer activity.

Liu et al. (2023) formulated liposome-in-gel systems for topical delivery, which demonstrated conventional enhanced antioxidant activity and better skin permeability . In a clinical study, Riva et al. (2018) showed that phytosome formulations increased quercetin bioavailability up to 20-fold compared to free quercetin.

Additionally, Ahmad et al. (2016) reported that quercetin-loaded solid lipid nanoparticles significantly improved therapeutic outcomes in disease models compared to pure quercetin. Overall, these studies confirm that nanoformulation strategies effectively enhance quercetin's solubility, stability, and bioavailability, thereby improving its therapeutic potential.

9. FUTURE PROSPECTS

Future research should focus on:

1. Development of multifunctional nanocarriers
2. Ligand-mediated targeted delivery
3. Stimuli-responsive systems
4. Combination therapy approaches
5. Clinical translation and commercialization

Advanced nanotechnology and precision medicine approaches may significantly improve the therapeutic application of quercetin in the future.

10. CONCLUSION

Quercetin is a biologically active flavonoid possessing diverse pharmacological activities including antioxidant, anti-inflammatory, anticancer, antimicrobial, antiviral, cardioprotective, and neuroprotective effects. Its ability to regulate multiple signaling pathways makes it a promising therapeutic candidate for various chronic diseases. However, poor solubility, instability, rapid metabolism, and low oral bioavailability considerably restrict its clinical application.

Recent advances in nano-based drug delivery systems such as liposomes, solid lipid nanoparticles, polymeric nanoparticles, nanomicelles, and hydrogels have successfully addressed many of these challenges. These formulations improve solubility, enhance absorption, provide sustained release, protect quercetin from degradation, and enable targeted delivery to diseased tissues.

Among the available approaches, polymeric nanoparticles and lipid-based systems have shown particularly promising outcomes due to their enhanced stability, controlled release behavior, and improved therapeutic performance. Although substantial progress has been achieved, additional preclinical and clinical investigations are necessary to establish long-term safety, large-scale manufacturing feasibility, and regulatory acceptance.

Overall, the integration of quercetin with advanced nanotechnology-based delivery systems offers a promising strategy for improving therapeutic efficacy and facilitating future clinical translation.

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REFERENCES:

1.Boots AW, Haenen GRMM, Bast A. Health effects of quercetin: From antioxidant to nutraceutical. Eur J Pharmacol. 2008;585(2-3):325-37.
2.Hadidi M, Orellana-Palacios JC, Aghababaei F, Gonzalez-Serrano DJ, Moreno A, Lorenzo JM. Plant by-product antioxidants: Extraction, characterization, and applications. LWT. 2022;169:114003.
3.Zheng YZ, Deng G, Liang Q, Chen DF, Guo R, Lai RC. Antioxidant activity of quercetin and its derivatives. Sci Rep. 2017;7:7543.
4.Middleton E Jr, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: Implications for inflammation, heart disease, and cancer. Pharmacol Rev. 2000;52(4):673-751.
5.Rivera L, Morón R, Zarzuelo A, Galisteo M. Long-term resveratrol administration reduces metabolic disturbances and lowers blood pressure in obese Zucker rats. Obesity. 2008;16(9):2081-7.
6.Kandemir K, Tomas M, McClements DJ, Capanoglu E. Recent advances on the improvement of quercetin bioavailability. Food Chem. 2022;383:132336.
7.Mukhopadhyay P, Prajapati AK. Quercetin in anti-diabetic therapy and polymer-based delivery systems. RSC Adv. 2015;5:97547-68.
8.Ciardi MM, Ianni FF, Sardella R, Di Bona S, Cossignani L, Germani R, et al. Deep eutectic solvents for extraction of quercetin from plant materials. Materials (Basel). 2021;14(21):6465.

9.Xu F, Arumugasamy SK, Bors K, Ramasamy A, Jayaprakasha GK, Patil BS. Ultrasound-assisted extraction of quercetin from plant sources. Molecules. 2019;24(12):2300.
10.Lee M, Son M, Ryu E, Shin YS, Kim JG, Kang BW, et al. Quercetin induces apoptosis and inhibits proliferation in cancer cells. J Microbiol Biotechnol. 2015;25(9):1452-62.
11.Rogerio AP, Kanashiro A, Fontanari C, et al. Anti-inflammatory activity of quercetin and isoquercitrin in experimental murine allergic asthma. Inflamm Res. 2007;56(10):402-8.
12.Dias S, Victor J, Santos DO, et al. Antibacterial activity of quercetin against pathogenic microorganisms. Int J Environ Agric Biotechnol. 2018;3(6):1948-58.
13.Arts IC, Hollman PC, Bueno De Mesquita HB, et al. Dietary intake of flavonoids and quercetin bioavailability in humans. Br J Nutr. 2009;101(4):589-95.
14.Abd El-Rahman SN, et al. Liposomal drug delivery systems for flavonoids. Indian J Drugs. 2014;2(3):102-9.
15.Xu G, Li B, Wang T, Wan J, Zhang Y, Huang J, et al. Hydrogel-based quercetin delivery systems for controlled release applications. RSC Adv. 2018;8:21229-42.

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