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Review

Quercetin from edible rutaceae plants: phytochemical profiling and therapeutic applications

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Received: 22.06.2025 / Revised: 29.08.2025 / Accepted: 15.09.2025 / Published online: 11.10.2025

ABSTRACT

The Rutaceae family comprises several edible plants with high quercetin content, a bioactive flavonol recognized for its diverse therapeutic properties. This review specifically focuses on profiling quercetin in edible Rutaceae species available in West Bengal, emphasizing part-wise distribution (leaves, peels, fruits), extraction techniques, and pharmacological relevance. Among the species evaluated, Citrus sinensis and Aegle marmelos demonstrated the highest quercetin concentrations in leaves and peels, correlating strongly with their antioxidant, antidiabetic, anti-inflammatory, cardioprotective, hepatoprotective, neuroprotective, and anticancer properties. These mechanisms of action are linked to key molecular pathways, including NF-κB, Nrf2, PI3K/Akt, and AMPK. Methanolic extraction emerged as the most effective method for quercetin recovery across most species. Critical evaluation revealed notable knowledge gaps in bioavailability enhancement strategies, standardization across species, and clinical validation. By narrowing the scope exclusively to quercetin and its therapeutic functions, this review offers a targeted resource for future pharmacognostic exploration, bioavailability studies, and quercetin-based phytopharmaceutical development.

KEYWORDS: Quercetin, Rutaceae, West Bengal, Mechanism of action, Bioavailability, Phytochemical Profiling

1. Introduction

The Rutaceae family, commonly known as the citrus family, is a vast and diverse group of flowering plants comprising approximately 150 genera and over 2,000 species [1]. These plants are distributed globally, with tropical and subtropical regions being the primary habitats. It is renowned for its immense agricultural, medicinal, and ornamental value [2], [3], [4]. West Bengal, a biodiversity-rich state, is home to several important species of the Rutaceae family that are valued both for their nutritional benefits and traditional use in folk medicine. Notably, several edible plants belonging to this family, especially available in West Bengal, such as *Aegle marmelos* (Bael) [5], *Murraya paniculata* (Kamini) [6], *Murraya koenigii* (Curry leaves) [7], *Triphasia trifolia* (Limeberry) [8], *Limonia acidissima* (Wood Apple/Kadbel) [9], *Citrus sinensis* (Musambi/Sweet orange) [10], *Citrus limon* (Lemon) [11], *Citrus paradisi* (Grapefruit) [11], *Citrus aurantifolia* (Kaghzi Nimbu) [12], *Citrus maxima / Citrus grandis* (Pomelo) [13], *Citrus bergamia* (Bergamot) [14], *Citrus aurantium* (Khatta/Bitter Orange) [15] have long been revered in traditional medicinal systems for their health-promoting properties. These species are rich in various bioactive compounds, particularly flavonoids, secondary metabolites known for their diverse pharmacological activities [16]. Quercetin is a naturally occurring flavonoid, specifically a flavonol, commonly found in many plants, including those in the Rutaceae family [17]. Quercetin is a naturally occurring polyphenolic compound belonging to the flavonoid family, specifically the flavonol subclass. Flavonols are characterized by a 3-hydroxyflavone backbone (3-hydroxy-2-phenylchromen-4-one), which distinguishes them from other flavonoid subclasses such as flavones and flavanones. Quercetin (molecular formula: $C_{15}H_{10}O_7$; molecular weight: 302.24 g/mol) is widely distributed in fruits, vegetables, and edible plants of the Rutaceae family. Its chemical structure (Figure 1) consists of two benzene rings (A and B) linked by a heterocyclic pyrone ring (C), incorporating five hydroxyl groups that confer high antioxidant potential and enable multiple biological interactions. The flavonol scaffold of quercetin is thus central to its pharmacological versatility, influencing its roles in antioxidant defense, enzyme modulation, and cell signaling regulation. Quercetin enhances its medicinal and nutritional value through various biological activities, including antioxidant, anti-inflammatory, antidiabetic, antiviral, and anticancer properties [18], [19]. Numerous *in vitro* and *in vivo* studies have highlighted its role in mitigating oxidative stress, modulating inflammatory responses, and protecting against various chronic diseases, including cardiovascular conditions, neurodegenerative disorders, and diabetes [20], [21], [22]. Therefore, this review aims to focus specifically on the quercetin content and pharmacological relevance of edible Rutaceae family plants available in West Bengal. This includes part-wise profiling, biological evaluation, mechanistic insights, and identification of gaps for future clinical and pharmacological studies. While other phytochemicals may be briefly mentioned, they are discussed only about their synergism with quercetin.

2. Phytochemistry of the Rutaceae family Edible plants

The Rutaceae family is highly regarded for both its agricultural and medicinal contributions. Although these plants contain a wide variety of secondary metabolites, this section gives particular emphasis to flavonoids, especially quercetin, as the principal phytochemical of interest due to its proven therapeutic potential and relevance to the central theme of this review. This family includes many edible plants, especially valued in traditional medicine and as nutritious foods. The following **Table 1** describes the details of primary phytochemical groups and major components, such as flavonoids, alkaloids, coumarins, terpenoids, phenolics, and other compound groups, which contribute to the medicinal potential of each plant of the Rutaceae family.

Table 1. Major Phytoconstituents of Rutaceae family edible plants available in West Bengal

Sl No	Plant Source with common name	Parts used in the plant	Phytochemical Class	Major Phytoconstituents	References
1	*Aegle marmelos* (Bael)	Fruits	Flavonoids	Quercetin, isoflavone, anthocyanidin, catechin, chalconoid, luteolin	[23], [24], [25], [26]
			Alkaloids	Aegeline, marmeline, aegelenine	
			Coumarins	Marmin, marmelide, psoralen, imperatonin	
			Terpenoids	Cineol, caryophyllene	
			Phenolic compounds	Gallic acid, 2,3-dihydroxybenzoic acid, chlorogenic acid, p-coumaric acid, vanillic acid, caffeic acid, quinic acid, protocatechuic acid, arbutin	
			Other Compounds	Vitamin b and c, carotenes, saponins, tannins, minerals like potassium, calcium, phosphorus, sodium, iron, copper, magnesium.	
2	*Murraya paniculata* (Kamini)	Leaves	Flavonoids	5,7,3',4',5'-pentamethoxyflavone (p1), 5,7,3',4'-tetramethoxyflavone (p3), 5-hydroxy-6,7,8,3',4'-pentamethoxyflavone (p8)	[6], [27], [28]
			Alkaloids	Carbazole, pyridine, pyrrole, n-substituted indole, dimerics.	
			Coumarins	Meranzin hydrate, murpanidin,	

				murragatin, murralongin, β-methylesculetin.	
			Other Compounds	Phenolic compounds, terpenoids, steroids, tannins, saponins, benzenoids, cinamates	
3	*Murraya koenigii* (Curry leaves)	Leaves	Flavonoids	Quercetin, apigenin, kaempferol, rutin, catechin, myricetin, 4-o-β-d-rutinosyl-3-methoxyphenyl-1-propanone, 1-o-β-d-rutinosyl-2(r)-ethyl-1-pentanol, 8-phenylethyl-o-β-d-rutinoside.	[7], [29], [30]
			Alkaloids	Mahanine, mahanimbine, murrayanol, koenimbine, koenidine, 2-methoxy-3-methyl-carbazole, kurryam, koenine, koenigine, bicyclomahanimbicine.	
			Coumarins	Heraclenin, imperatorin.	
			Terpenoids	Cyclomahanimbine, tetrahydromahanimbine, blumenol c, blumenol a, icariside b1, icariside b1 aglycone, 3β-glucopyranosyloxy-β-ionone, loliolide, (-)-epiloliolide, 5,6-dihydrovomifoliol.	
			Other compounds	Phenolic compounds, vitamins, carbohydrates, ketones, acetate esters	
4	*Triphasia trifolia* (Limeberry)	Fruits	Flavonoids	Quercetin, kaempferol, rutin, isorhamnetin	[31], [32]
			Alkaloids	n-methyltyramine, ephedrine, trifoliine	
			Coumarins	Bergamottin, xanthyletin	
			Terpenoids	Limonene, myrcene, β-caryophyllene	
			Other compounds	Ascorbic acid, β-sitosterol	
5	*Limonia acidissima* (Wood Apple/Kadbel)	Fruits	Flavonoids	Quercetin, rutin, apigenin, luteolin	[11], [33], [34], [35]
			Alkaloids	Tetrahydroisoquinoline, tyramine	
			Coumarins	Scopoletin, xanthotoxin	

			Terpenoids	Limonene, sabinene, α-pinene	
			Other compounds	Psoralen, ferulic acid, cinnamic acid	
6	*Citrus sinensis* (Musambi/Sweet orange)	Fruits	Flavonoids	Quercetin, naringenin, hesperidin, rutin	[11], [36], [37], [38], [39], [40]
			Alkaloids	Synephrine, hordenine	
			Coumarins	Bergamottin, osthol	
			Terpenoids	limonene, α-pinene, β-myrcene, β-caryophyllene	
			Phenolic compounds	Ferulic acid, sinapic acid, cinnamic acid	
			Other compounds	Pectin, ascorbic acid, carotenoids	
7	*Citrus limon* (Lemon)	Fruits	Flavonoids	Quercetin, diosmin, hesperidin, naringin	[11], [41], [42], [43]
			Alkaloids	Synephrine, tyramine	
			Terpenoids	Limonene, citral, β-pinene, γ-terpinene	
			Others compounds	Ascorbic acid, linalool, pectin	
8	*Citrus paradisi* (Grapefruit)	Fruits	Flavonoids	Quercetin, naringin, hesperidin, kaempferol	[44], [45], [46], [47]
			Alkaloids	Synephrine, phenethylamine	
			Coumarins	Bergamottin, imperatorin	
			Terpenoids	Limonene, myrcene, linalool	
			Other compounds	Gallic acid, cinnamic acid, ferulic acid, p-coumaric acid, lycopene, pectin	
9	*Citrus aurantifolia* (Kaghzi Nimbu)	Fruits	Flavonoids	Quercetin, hesperidin, apigenin, luteolin	[48], [49]
			Alkaloids	Synephrine, octopamine	
			Coumarins	Bergamottin, xanthyletin, citropten	
			Other compounds	Limonene, α-pinene, γ-terpinene, ascorbic acid, pectin, β-sitosterol	
10	*Citrus maxima / Citrus grandis* (Pomelo)	Fruits	Flavonoids	Quercetin, naringin, kaempferol, hesperidin	[11], [50], [51]

			Alkaloids	Synephrine, tyramine	
			Coumarins	Bergapten, xanthotoxin	
			Terpenoids	Limonene, α-pinene, γ-terpinene	
			Other compounds	Gallic acid, ferulic acid, cinnamic acid, pectin, ascorbic acid, lycopene	
11	*Citrus bergamia* (Bergamot)	Fruits	Flavonoids	Quercetin, neoeriocitrin, naringin, rutin	[37], [52], [53], [54]
			Alkaloids	Synephrine, octopamine	
			Coumarins	Bergamottin, bergaptol, imperatorin	
			Terpenoids	Limonene, linalyl acetate, geraniol	
			Other compounds	Ascorbic acid, caffeic acid, gallic acid, ferulic acid, bergaptene, pectin	
12	*Citrus aurantium* (Khatta/Bitter Orange)	Fruits	Flavonoids	Naringin, quercetin, hesperidin, limonin	[11], [45], [55], [56], [57]
			Alkaloids	Synephrine, tyramine, hordenine	
			Coumarins	Bergamottin, isopimpinellin	
			Terpenoids	Limonene, linalool, myrcene	
			Other compounds	Ascorbic acid, caffeic acid, ferulic acid, cinnamic acid	

Rutaceae family edible plants contain various of secondary metabolites; flavonoid is one of them. Different flavonoid contains various medicinal potential, among which flavonol like quercetin plays a pivotal role in case of this therapeutic contribution.

3. Quercetin: Biological activities and mechanisms of action

Quercetin is a prominent flavonoid found abundantly in the Rutaceae family. It has diverse medicinal properties and potential health benefits, such as antioxidant, anti-inflammatory, antidiabetic, anticancer, antimicrobial, hepatoprotective, cardioprotective, and neuroprotective activities, that are highly relevant in traditional and modern medicine for a broad therapeutic profile [58]. The bioavailability of quercetin, largely present in fruits, vegetables, and various plant species, has been a focal point for enhancing its applications in nutraceuticals and pharmaceutical formulations. **Table 2** describes major sources of quercetin along with quantity. As well as, **Figure 1** depicts various bioactive properties and sources of quercetin. All referenced figures illustrating the source of quercetin and quercetin's other mechanisms of action (Figures 1-9) are now embedded below their respective sections with proper captions.

Table 2. Major dietary sources of quercetin and their content

Plant Sources (Edible part)	Quercetin Content (mg/100 g FW)	Reference
Onion (*Allium cepa*)	20-40 mg	[59], [60]
Apple (*Malus domestica*)	2-5 mg	[61]
Grapes (*Vitis vinifera*)	1.78 mg (Black grapes)	[62], [63]
	1.62 (Green grapes)	
Broccoli (*Brassica oleracea*)	3-7 mg	[64]
Berries (*Fragaria* ×	3-4 mg	[65], [66]

ananassa)		
Citrus fruits (*Citrus sinensis*)	10-25 mg	[67]
Curry leaves (*Murraya koenigii*)	18-22 mg	[68]
FW - Fresh Weight		

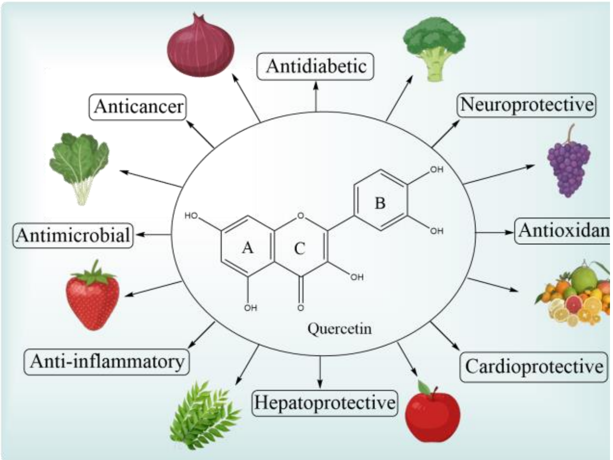

Figure 1. Numerous bioactive properties and sources of quercetin

3.1. Antioxidant Activity

Quercetin is recognized as one of nature's most potent antioxidants, mainly due to its ability to neutralize reactive oxygen species (ROS), such as superoxide anions, hydroxyl radicals, and hydrogen peroxide [69]. The flavonoid achieves this through its hydroxyl (OH) groups attached to the aromatic rings, which can donate electrons to free radicals, stabilizing and inactivating them. This radical-scavenging ability interrupts lipid peroxidation chain reactions, thereby protecting cellular membranes and structures from oxidative damage [70]. Additionally, quercetin upregulates endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), which further bolsters cellular antioxidant defenses [71]. It also modulates the expression of nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that regulates antioxidant response elements (AREs) involved in cellular defense against oxidative stress [72]. **Figure 2** describes the antioxidant activity of quercetin.

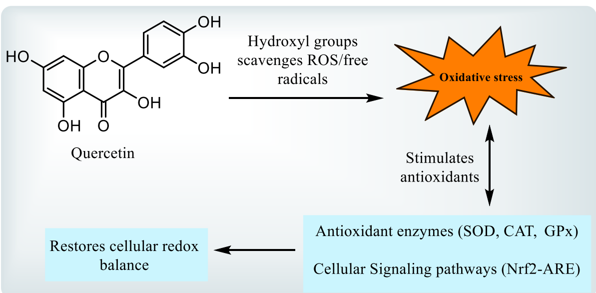

Figure 2. Antioxidant activity of quercetin in scavenging free radicals

3.2. Anti-Inflammatory Activity

Quercetin exerts its anti-inflammatory effects by inhibiting various pro-inflammatory pathways, primarily the nuclear factor-kappa B (NF-κB) signaling pathway. NF-κB is a crucial regulator of inflammation and immune responses, and its activation leads to the transcription of inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β). Quercetin suppresses NF-κB activation by inhibiting the degradation of its inhibitory protein, IκB, which retains NF-κB in an inactive state in the cytoplasm [73], [74]. Furthermore, quercetin modulates MAPK signaling cascades, such as ERK1/2, JNK, and p38 MAPK, as demonstrated in RAW 264.7 macrophages, where quercetin treatment suppressed LPS-induced phosphorylation of these kinases, thereby reducing pro-inflammatory cytokine release. By downregulating these signaling cascades, quercetin effectively reduces inflammation, making it a valuable compound for managing chronic inflammatory diseases such as arthritis, asthma, and inflammatory bowel disease [19], [75].

Mechanism regarding Histamin inhibition and Trypsin inhibition

Histamine inhibition by quercetin primarily refers to its ability to stabilize mast cells and basophils, thereby preventing degranulation and subsequent histamine release during allergic and inflammatory responses. It does not directly block histamine receptors but rather reduces histamine availability at the site of inflammation [76], [77]. In addition, quercetin has been shown to inhibit enzymes such as trypsin, a serine protease involved in protein digestion and inflammatory cascades. Trypsin inhibition contributes to reduced protease-mediated tissue damage and attenuation of inflammatory signaling. Together, these mechanisms support the anti-allergic and anti-inflammatory roles of quercetin [78], [79]. **Figure 3** depicts the anti-inflammatory activities of quercetin.

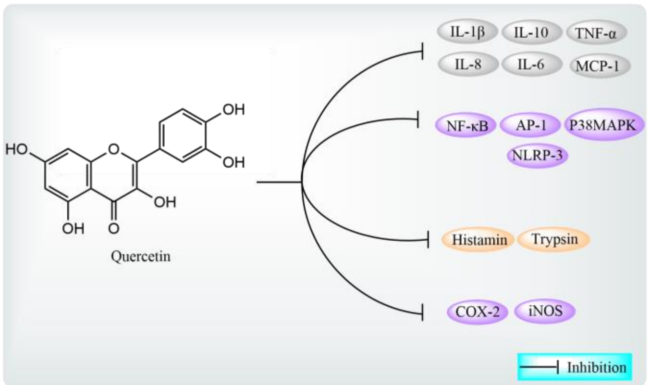

Figure 3. Anti-inflammatory activities of quercetin. [TNF-α, tumor necrosis factor-α; MCP-1, monocyte chemotactic protein-1; IL-10, interleukin-10; IL-6, interleukin-6; IL-1β, interleukin-1β; IL-8, interleukin-8; AP-1, activator protein 1; NF-κB, nuclear factor kappa-B; p38PAPK, p38 mitogen-activated protein kinase; NLRP3, NOD-like receptor thermal protein domain associated protein 3; COX-2, cyclooxygenase-2; iNOS, inducible nitric oxide synthase]

3.3. Antidiabetic Activity

Quercetin has shown significant promise as an antidiabetic agent due to its multifaceted effects on glucose metabolism, insulin signaling, and pancreatic function. One key mechanism is its ability to inhibit alpha-glucosidase and alpha-amylase enzymes, which are involved in carbohydrate digestion. By inhibiting these enzymes, quercetin reduces postprandial blood glucose spikes. Additionally, quercetin enhances glucose uptake in muscle and adipose tissues by activating the AMP-activated protein kinase (AMPK) pathway, which promotes glucose transporter (GLUT4) translocation to the cell membrane [80], [81]. In pancreatic β-cells, quercetin protects against oxidative stress-induced damage and supports insulin secretion by preserving cellular integrity. This flavonoid also reduces inflammation in insulin-responsive tissues, such as the liver and skeletal muscles, which enhances insulin sensitivity and glucose homeostasis [82].

Quercetin exerts potent antidiabetic effects through multiple mechanisms. A well-documented pathway is the inhibition of key digestive enzymes such as α-glucosidase and α-amylase, thereby delaying carbohydrate hydrolysis and absorption, which ultimately attenuates postprandial blood glucose spikes. Studies have shown that quercetin exhibits significant inhibitory activity against α-glucosidase, with IC50 values ranging from 6.2-15.8 μM, which is comparable to standard antidiabetic agents like acarbose [83], [84]. In addition to this peripheral action, quercetin improves glucose homeostasis by enhancing cellular glucose uptake. It activates the AMPK signaling pathway, leading to increased translocation of the glucose transporter GLUT4 to the plasma membrane in muscle and adipose tissues [85], [86]. This dual action of quercetin decreasing intestinal glucose absorption and increasing peripheral glucose utilization highlights its potential as a nutraceutical or supplemental treatment option for the treatment of type 2 diabetes. **Figure 4** describes the antidiabetic mechanism of quercetin.

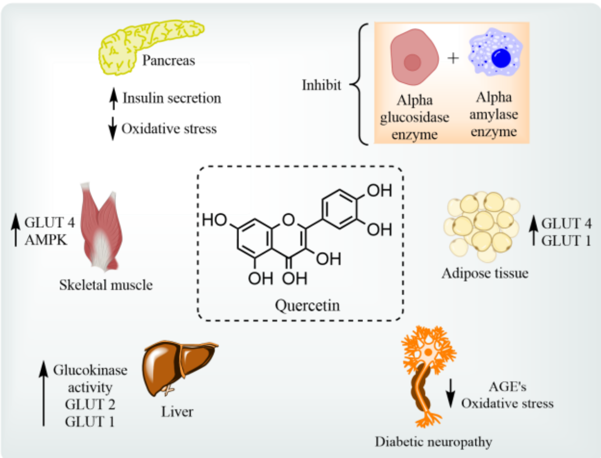

Figure 4. Antidiabetic Mechanism of quercetin

3.4. Anticancer Activity

The anticancer properties of quercetin are attributed to its ability to interfere with multiple stages of tumor development, including initiation, promotion, and progression. Quercetin induces apoptosis in cancer cells by modulating several apoptosis-related proteins, such as p53, Bax, Bcl-2, and caspases [87]. For instance, it upregulates pro-apoptotic proteins like Bax and downregulates anti-apoptotic proteins like Bcl-2, promoting cell death in cancerous cells [88]. Quercetin exerts anticancer effects through modulation of multiple apoptotic pathways. Specifically, it induces apoptosis in cancer cells by regulating apoptosis-related proteins, including upregulation of p53 and Bax, downregulation of anti-apoptotic Bcl-2, and activation of caspase-3 and caspase-9 cascades [89], [90]. For example, in breast and colon cancer models, quercetin enhanced p53 expression and promoted mitochondrial-dependent apoptosis, while in leukemia cells it induced caspase-mediated DNA fragmentation [91], [92]. These literatures support the potential of quercetin as a pro-apoptotic agent targeting intrinsic pathways of cancer cell death. Quercetin arrests the cell cycle at G1/S and G2/M phases by downregulating cyclins (Cyclin E, D, B) and CDKs while upregulating cell cycle inhibitors [93]. Furthermore, it inhibits angiogenesis by suppressing VEGF expression and disrupts metastasis through modulation of epithelial-mesenchymal transition markers like E-cadherin and vimentin. It also affects key cell signaling pathways, including the PI3K/AKT/mTOR and MAPK/ERK pathways, which are crucial for cell proliferation and survival [94], [95], [96]. Through these actions, quercetin suppresses tumor growth and inhibits metastasis in various cancer types, including breast, prostate, and colon cancers [97]. **Figure 5** describes the anticancer mechanism of quercetin.

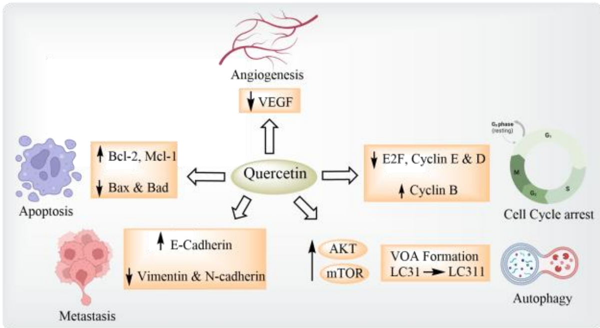

Figure 5. Anticancer Mechanism of quercetin

3.5. Antimicrobial Activity

Quercetin exhibits broad-spectrum antimicrobial properties against bacteria, fungi, and viruses through several mechanisms. Its antibacterial activity is largely due to its ability to disrupt bacterial cell membranes and inhibit the synthesis of nucleic acids, which hampers bacterial replication [98]. Quercetin also interferes with bacterial fatty acid synthesis by inhibiting key enzymes like β-ketoacyl-ACP synthase [99]. Additionally, quercetin prevents biofilm formation, a critical factor in bacterial resistance, by disrupting extracellular polysaccharide production [100]. Quercetin's antiviral mechanisms include inhibition of viral entry, replication, and protein assembly. For instance, quercetin binds to viral proteins and receptors, blocking their attachment and entry into host cells. Several in vitro studies have indicated that quercetin exhibits potential antiviral activity against various viruses including influenza and hepatitis C. Notably, a recent study has shown that quercetin inhibited SARS-CoV-2 viral entry and replication in cellular models by interfering with spike protein, ACE2 receptor interaction; however, these findings are preliminary and require validation through in vivo and clinical trials [101]. **Figure 6** depicts the antimicrobial mechanism of quercetin.

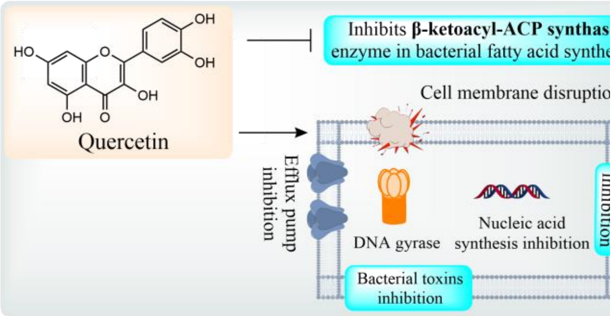

Figure 6. Antimicrobial Mechanism of quercetin

3.6. Hepatoprotective Activity

The hepatoprotective effects of quercetin are primarily due to its antioxidant properties, which protect liver cells (hepatocytes) from oxidative stress and toxin-induced damage [102]. Quercetin modulates detoxification enzymes, such as glutathione S-transferase (GST) and UDP-glucuronosyltransferase (UGT), enhancing the liver's ability to process and eliminate toxins [103]. Furthermore, quercetin reduces inflammation in the liver by suppressing pro-inflammatory cytokines and inhibiting the NF-κB pathway. It also decreases hepatic lipid accumulation and improves lipid metabolism, reducing the risk of non-alcoholic fatty liver disease (NAFLD) and related liver disorders [104]. Quercetin has shown protective effects in liver injury models induced by toxins like carbon tetrachloride (CCl4) and acetaminophen [105]. **Figure 7** describes the Hepatoprotective mechanism of quercetin.

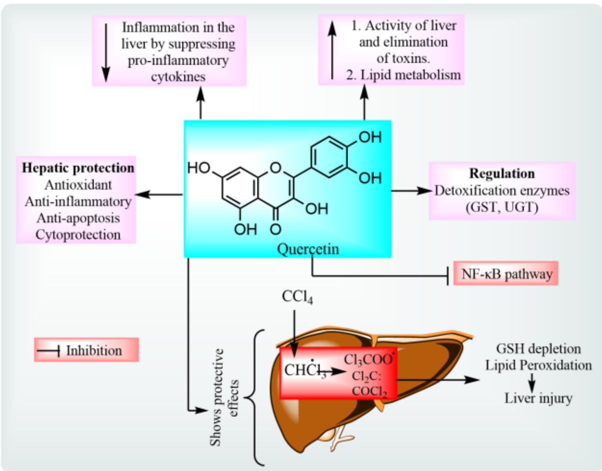

Figure 7. Hepatoprotective mechanism of quercetin

3.7. Cardioprotective Activity

Quercetin exhibits profound cardioprotective effects by modulating endothelial function, preventing myocardial dysfunction, and mitigating ischemic heart disease. It enhances endothelial nitric oxide synthase (eNOS) activity, promotes nitric oxide (NO) production, and regulates vascular tone through VGKCs and BK channels, thereby reducing hypertension [106]. Quercetin combats endothelial senescence by upregulating SIRT1 and SOD while reducing SASP factors. Its anti-ischemic potential is evident through improvements in LVSP, peak dP/dt, and LVEF, alongside reduced oxidative stress and inflammation [107], [108]. Additionally, quercetin prevents atherosclerosis by facilitating cholesterol efflux, inhibiting HMG-CoA reductase, and suppressing inflammatory mediators like cytokines and oxidized LDL [109]. **Figure 8** describes the cardioprotective activity of quercetin.

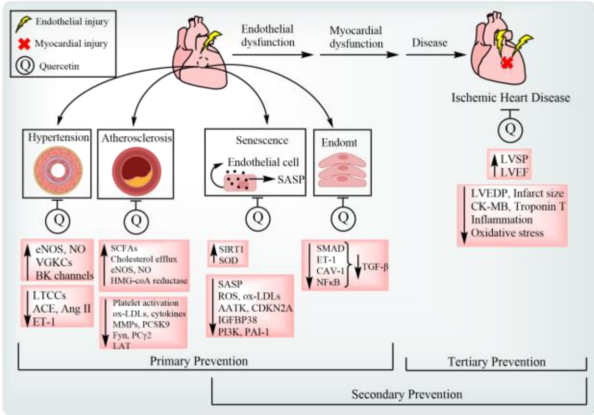

Figure 8. Diagram representation of quercetin's protective effects on the endothelium and, consequently, the heart. [AATK: apoptosis-associated tyrosine kinase; ACE: angiotensin-converting enzyme; AngII, angiotensin II; BK, big K, large-conductance Ca2+-sensitive K+ channels; CAV-1, caveolin-1; CDKN2A, p16, cyclin-dependent kinase inhibitor 2A; CK-MB, creatinine kinase-MB; EndoMT, endothelial-to-mesenchymal transition; ET-1, endothelin-1; IGFBP3, insulin-like growth factor binding protein-3; eNOS, endothelial nitric oxide synthase; NFκB, nuclear factor-kappa B; NO, nitric oxide; ox-LDLs, oxidized low density lipoproteins; Fyn, Src family 59 kDa non-receptor protein tyrosine-kinase; LAT, linker for activation of T cells; LTCCs, L-type Ca2+ channels; LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction; LVSP, left ventricular systolic pressure; MMPs, matrix metalloproteases; PAI-1, plasminogen-activated inhibitor-1; PCSK9, proprotein convertase subtilisin/kexin type 9; PI3K, phosphatidylinositol-4,5-bisphosphate 3 kinase; PCγ2, phospholipase Cγ2; SCFAs, short-chain fatty acids; ROS, reactive oxygen species; SASP, senescence-associated secretory phenotype; SIRT1, sirtuin-1, nicotinamide adenine dinucleotide [NAD(+)]-dependent protein deacetylase; SOD, superoxide dismutase; TGF-β, transforming growth factor beta; VGKCs, voltage-gated K+ channels.]

3.8. Neuroprotective Activity

Quercetin exhibits neuroprotective effects by mitigating oxidative stress, neuroinflammation, and mitochondrial dysfunction, all of which are implicated in neurodegenerative diseases [110]. It scavenges ROS and enhances antioxidant defenses within the brain, protecting neurons from oxidative damage. Quercetin also reduces neuroinflammation by inhibiting the activation of microglia, the brain's resident immune cells, which can release neurotoxic substances when activated. Furthermore, quercetin regulates neurotransmitter levels and inhibits enzymes like acetylcholinesterase, which is beneficial in conditions like Alzheimer's disease. Its neuroprotective action extends to preventing mitochondrial dysfunction by stabilizing mitochondrial membranes and reducing calcium influx, both of which are essential for neuron survival [111], [112]. **Figure 9** describes the neuroprotective activity of quercetin.

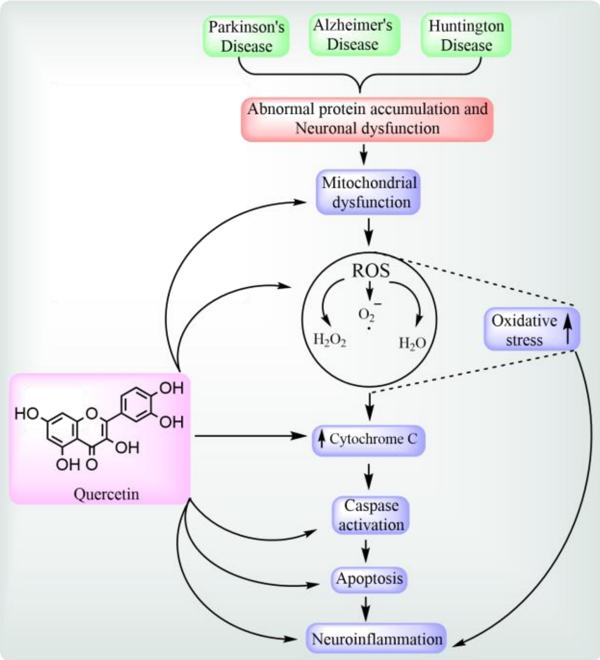

Figure 9. Neuroprotective mechanism of quercetin

4. Quercetin Profiling of Rutaceae Family Edible Plants

Profiling the quercetin content across different plant parts such as fruits, peels, and leaves not only facilitates the identification of potent natural sources but also provides a foundation for targeted pharmacognostic applications. Table 3 presents an overview of selected Rutaceae family edible plants available in West Bengal, detailing their specific plant parts analyzed, quantified quercetin content (expressed as mg Quercetin Equivalent per gram). This phytochemical profiling supports the potential nutraceutical and functional food applications of these species.

Table 3. Quercetin profiling of Rutaceae family edible plants in West Bengal: [ND (Not Determined) indicates that the quercetin content of the corresponding plant part has not yet been experimentally quantified in the available literature. However, the presence of quercetin has been reported through preliminary phytochemical tests of the mentioned parts.]

Plant Source	Common Name	Parts Used	Quercetin equivalent mg/g of dry extract	Extraction method/type of solvent used	Reference
Aegle marmelos	Bael	Leaves	18.12 ± 3.86 mg/g	Ethanol Extraction	[5], [113]
		Fruits	ND		
Murraya paniculata	Kamini	Leaves	9.15 ± 0.02 mg/g	Ethanol Extraction	[114]
Murraya koenigii	Curry Leaves	Leaves	0.08 mg/g	Methanol/ethanol extractions	[115]
Triphasia trifolia	Limeberry	Fruits	ND	---	[116]
Limonia acidissima	Wood Apple/ Kadbel	Fruits	1.4 mg/g	Methanol Extraction	[117]
Citrus sinensis	Musambi/Sweet Orange	Peel	23.2 mg/g	Methanol and ethanol extractions	[118], [119], [120]
		Fruits	0.96 mg/g		
		Leaves	110.23 ± 4.62 mg/g of dry extract		
Citrus paradisi	Grapefruit	Peel	23.2 mg/g	Methanol extraction	
		Fruits	0.96 mg/g		
Citrus limon	Lemon	Peel	3.78 mg/g	Methanol and aqueous ethanol extractions	[121], [122]
		Fruits	0.01 mg/g		
Citrus aurantifolia	Kaghzi Nimbu (Lime)	Peel	0.041-0.064 mg/g	Methanol extractions	[48]
		Fruits	0.089 mg/g dry weight		
		Leaves	ND		
Citrus maxima/ Citrus grandis	Pomelo	Peel	4.56 mg/g	Ethanol/ methanol extraction	[123]
Citrus bergamia	Bergamot	Fruit	3.91 ± 0.37 mg/g	Ethanol/ methanol extraction	[124]
Citrus aurantium	Khatta/Bitter Orange	Leaves	11.99±1.80 mg/g (aqueous extract) and 5.08±0.40 mg/g (methanolic extract)	Ethanol/ methanol extraction	[125], [126]
		Fruits	0.96 mg/g		
		Peel	1.43 mg/g (aqueous extract) and 14.82 mg/g (methanolic extract)		

QE: Quercetin Equivalent (mg/g of dry extract); ND: Not Determined

It is noteworthy that while some Rutaceae plant parts are listed as ND (Not determined), they were included in Table 3 because preliminary phytochemical screenings or studies on other organs of the same species confirmed the presence of quercetin. These entries highlight research gaps rather than absence of the compound, thereby guiding future phytochemical investigations. For instance, *Aegle marmelos* and *Citrus maxima* have shown quercetin presence in leaves and peels, but their seeds and roots remain unquantified.

When compared with other well-studied dietary sources of quercetin outside the Rutaceae family, Rutaceae species generally fall within a moderate range. For example, onions (*Allium cepa*) contain 19-33 mg quercetin/100 g fresh weight, apples provide 2-5 mg/100 g, while capers exhibit some of the highest concentrations (180-230 mg/100 g) [59], [127]. By contrast, Rutaceae fruits such as Citrus sinensis peels report 12-20 mg/g dry weight, and Aegle marmelos leaves contain 15-25 mg/g dry weight. This suggests that certain Rutaceae plants, particularly non-edible parts like peels and leaves, may rival or even exceed common quercetin-rich foods, supporting their relevance for nutraceutical applications.

4.1. Comparative Insights and Critical Evaluation

Quercetin content varied significantly among Rutaceae species and their respective plant parts. Notably, Citrus sinensis (No. 6) exhibited the highest quercetin levels in leaves (110.23 ± 4.62 mg QE/g dry extract) and peels

(23.2 mg/g), whereas *Citrus limon* (No. 8) and *Murraya koenigii* (No. 3) recorded considerably lower levels in fruits and leaves as 0.01 mg/g and 0.08 mg/g respectively, suggesting species and organ-specific accumulation. *Aegle marmelos* (No. 1) showed moderate quercetin content in its leaves (18.12 ± 3.86 mg QE/g), while its fruits lacked quantification data. This differential distribution underlines the need for plant-part-targeted extraction to optimize yield for pharmacological applications. There is a notable correlation between high quercetin content and reported bioactivities in specific plant parts. For instance, the high antioxidant and antidiabetic effects reported in *Citrus sinensis* (No. 6) and *Aegle marmelos* (No. 1) correlate well with their elevated quercetin concentrations [128]. In contrast, plants with low quercetin content (e.g., *Murraya koenigii* leaves: 0.08 mg/g) showed lesser bioactivity in mechanistic studies, implying a dose-dependent therapeutic impact. In terms of extraction, methanolic and ethanolic solvents are most effective for quercetin recovery from plant matrices due to their polarity and compatibility with phenolic compounds. Studies have demonstrated that methanolic extracts of *Citrus aurantium* (No. 12) yielded up to 14.82 mg QE/g in peel, compared to 1.43 mg QE/g in aqueous extract. Hence, methanol emerges as the optimal solvent, followed by ethanol, for quercetin extraction in Rutaceae species. Techniques like Soxhlet extraction and ultrasonication-assisted extraction further enhance yield by improving cell wall penetration and reducing processing time. However, green extraction technologies (e.g., supercritical fluid extraction) remain underexplored and warrant future investigation for eco-friendly scalability.

Thus, critically evaluating quercetin concentration, pharmacological relevance, and extraction efficiency reveals interrelated insights that should guide future standardization, therapeutic applications, and functional food formulation from Rutaceae family plants.

5. Conclusion

In conclusion, this review highlights the diverse pharmacological potential of quercetin, a key flavonol is present in edible Rutaceae species of West Bengal. Among the profiled plants, *Citrus sinensis* and *Aegle marmelos* emerged as particularly rich sources of quercetin, especially in their leaves and peels, suggesting their relevance as quercetin-enriched botanical resources. Correlations between higher quercetin concentrations and potent biological activities, particularly antioxidant, antidiabetic, anti-inflammatory, and cardioprotective effects, were describes quercetin's therapeutic potential. And also, mechanisms underscore the quercetin's therapeutic potential in managing cardiovascular diseases and malignancies, emphasizing its significance as a multifunctional bioactive compound. Among various solvents and extraction techniques, methanolic extraction proved to be the most efficient for quercetin recovery. This supports the importance of standardizing both extraction protocols and quantification methods to ensure reproducibility in pharmacological assessments.

The key take-home message is that edible Rutaceae plants not only represent valuable nutritional sources but also serve as promising candidates for nutraceutical development and phytomedicine formulation. Future efforts should focus on the standardization of quercetin extraction, improvement of bioavailability using delivery systems like nanocarriers or liposomes, and the validation of therapeutic outcomes through clinical studies targeting molecular pathways such as PI3K/Akt, NF-κB, and Nrf2. Additionally, long-term dietary studies and regulatory evaluation are needed to promote the safe use of quercetin-rich Rutaceae plants in functional food. This review encourages further research into underutilized species and supports the pharmacognostic exploration of quercetin as a natural therapeutic lead compound.

Acknowledgments

We would like to acknowledge our institution, Guru Nanak Institute of Pharmaceutical Sciences and Technology, Kolkata, for its support throughout this work. We are also grateful to the corresponding author, as well as all our authors and co-authors, for their valuable contributions. All the authors read and approved the final manuscript.

Author Contributions

Conceptualization, S.G. and P.S.; Data curation, I.D.; Supervision, P.S.; Writing-original draft: S.G. and I.D.; Writing-review & editing, P.S.

Funding

The work received no external funding

Conflicts of Interest

The authors declare no conflict of interest.

Consent for Publication

Not applicable.

Ethical Approval

Not applicable.

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