ISSN: 2231-3656

International Journal of Pharmacy and Industrial Research (IJPIR)

IJPIR |Vol. 16 | Issue 3 | Jul – Sep 2026

www.ijpir.com

DOI: https://doi.org/10.61096/ijpir.v16.iss3.2026.1018-1037

Hesperidin+ By Biotex Life Solutions: A Comprehensive Narrative Product Review of Antioxidant, Anti-Inflammatory, Antiviral, and Anticancer Evidence

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Published on: 29.07.2026
Published by: Futuristic Publications

Abstract

Background: Oxidative stress and chronic low-grade inflammation are reciprocally reinforcing, with reactive oxygen species as the shared upstream trigger underlying cardio metabolic, viral and neoplastic disease. Multi-ingredient nutraceuticals engaging both axes through distinct but convergent phytochemistry offer a mechanistically plausible strategy.

Aim. This narrative product review evaluates per-ingredient evidence for each of the six actives in *Hesperidin+*, a polyphenol-rich multi-ingredient nutraceutical developed by Biotex Life Solutions: hesperidin (500 mg), *Bambusa arundinacea* crystals/tabasheer (200 mg), rutin (100 mg), *Citrus limon* fruit extract (50 mg), *Rubia cordifolia* root extract (50 mg), and *Punica granatum* fruit extract (50 mg).

Methodology. PubMed/PMC, ScienceDirect, MDPI, Frontiers, Crossref and the Jenni library were searched for English-language peer-reviewed studies between January 2016 and July 2026. Priority was assigned to RCTs, meta-analyses, mechanistic studies and high-quality systematic reviews.

Key findings. A 2026 meta-analysis of 10 RCTs (n = 532) showed hesperidin supplementation significantly reduced CRP/hs-CRP (SMD −0.43; 95% CI −0.71 to −0.15; $P = 0.002$) and TNF-α (SMD −0.51; 95% CI −0.95 to −0.07; $P = 0.02$), with IL-6 reaching statistical significance in adults with diagnosed disease (SMD −0.38; 95% CI −0.72 to −0.04; $P = 0.03$). Eriomin® (70% eriocitrin, 5% hesperidin, 4% naringin) at 200 mg/day over 12 weeks reduced hyperglycaemia by 6% and increased GLP-1 by 22% in a prediabetes RCT with concurrent microbiota rebalancing. Molecular-docking and enzyme-inhibition data indicate hesperidin and hesperetin interact with multiple SARS-CoV-2 entry-associated targets, with hesperidin's Mpro IC_{50} reported at 51.5 µM and 5.5 mM in biochemical assays. Pomegranate peel extract inhibits SARS-CoV-2 spike binding to the human ACE2 receptor *in vitro*. Anticancer activity is documented across multiple cell-line models through NF-κB suppression, caspase activation and cell-cycle arrest.

Conclusion. *Hesperidin+* presents a coherent multi-target mechanistic rationale centred on Nrf2/ARE and NF-κB pathways. Per-ingredient human evidence supports antioxidant and anti-inflammatory claims; antiviral and anticancer signals are predominantly preclinical. A formulation-level pharmacokinetic and

efficacy study is required before clinical claims can be made for the finished product.

Keywords: hesperidin; citrus flavonoids; rutin; punicalagin; *Rubia cordifolia*; *Bambusa arundinacea*; tabasheer; Hesperidin+; Biotex Life Solutions; nutraceutical; antioxidant; anti-inflammatory; Nrf2; NF-κB.

Graphical abstract

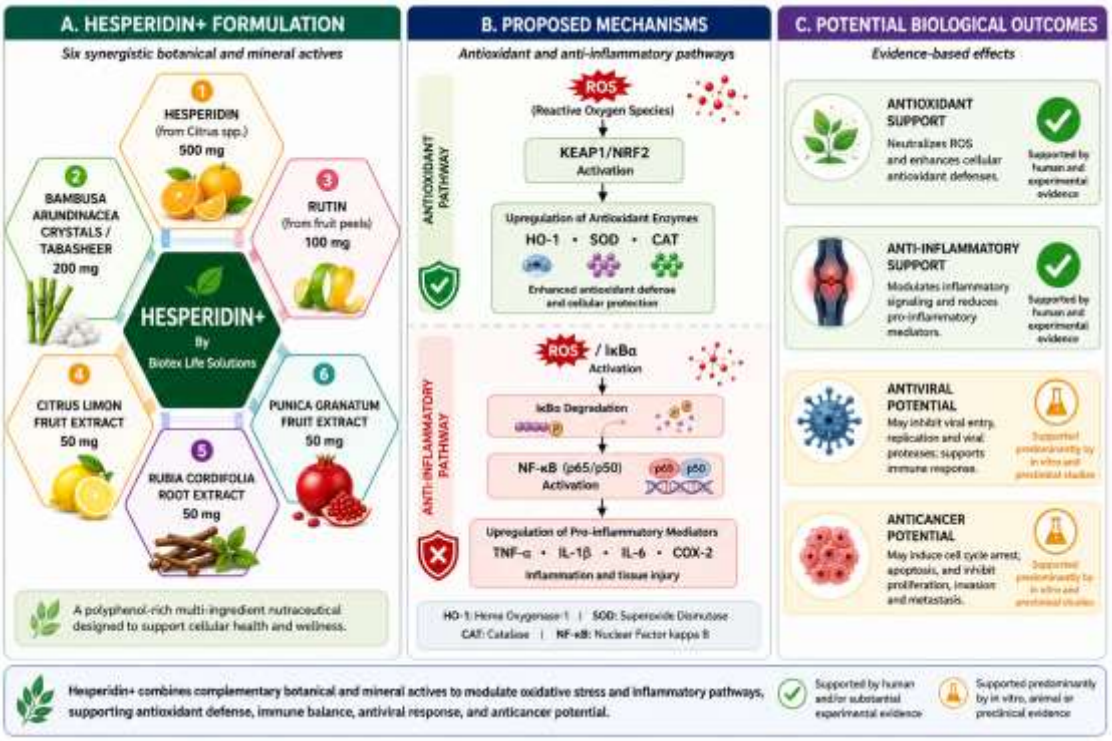


Fig 1: Graphical abstract of the Hesperidin+ formulation and its proposed biological rationale. Hesperidin+ combines hesperidin, rutin, *Citrus Limon* fruit extract, *Rubia cordifolia* root extract, *Punica granatum* fruit extract, and *Bambusa arundinacea* crystals. Its flavonoid- and polyphenol-rich constituents may reduce reactive oxygen species and enhance KEAP1/NRF2-mediated antioxidant defenses through upregulation of heme oxygenase-1, superoxide dismutase, and catalase. These constituents may also inhibit IκBα degradation, suppress NF-κB activation, and reduce downstream inflammatory mediators, including TNF-α, IL-1β, IL-6, and COX-2. Antioxidant and anti-inflammatory effects are supported by human and experimental evidence, whereas antiviral and anticancer activities remain predominantly supported by in vitro and preclinical studies.

Highlights

- Hesperidin+ delivers 950 mg of characterised polyphenol and silica actives per single vegetarian capsule in a fixed-dose ratio of 10:4:2:1:1:1 (hesperidin: tabasheer: rutin: *C. Limon*: *R. cordifolia*: *P. granatum*).
- The polyphenol components converge on the Nrf2/ARE antioxidant and NF-κB anti-inflammatory pathways with reactive oxygen species as the shared upstream trigger.
- Per-ingredient human evidence is strongest for antioxidant and anti-inflammatory claims: hesperidin alone drives a 2026 meta-analytic signal across 10 RCTs, and Eriomin®-standardised eriocitrin produces a 6% reduction in hyperglycaemia with a 22% GLP-1 increase in a prediabetes RCT at 200 mg/day.
- Antiviral and anticancer signals are predominantly preclinical (cell-free enzyme assays, cell lines, *in silico* docking) and should not be framed as clinical product claims.
- A formulation-level pharmacokinetic and efficacy study of Hesperidin+ is the indispensable next step for translating per-ingredient evidence into a labelled product claim.

Abbreviations

Abbreviation	Expansion
ACE2	Angiotensin-converting enzyme 2
ARE	Antioxidant response element
CAT	Catalase
COX-2	Cyclooxygenase-2
CRP / hs-CRP	C-reactive protein / high-sensitivity CRP
DPPH	2,2-diphenyl-1-picrylhydrazyl
DENV	Dengue virus
EA	Ellagic acid
GLP-1	Glucagon-like peptide 1
GSH / GSSG	Glutathione/glutathione disulfide
HO-1	Heme oxygenase-1
IC_{50}	Half-maximal inhibitory concentration
IL-6 / IL-1β	Interleukin-6 / interleukin-1β
KEAP1	Kelch-like ECH-associated protein 1
MAPK	Mitogen-activated protein kinase
Mpro / 3CL^pro	Main protease / 3C-like protease
NF-κB	Nuclear factor kappa-B
NRF2	Nuclear factor erythroid 2–related factor 2
PCNA	Proliferating cell nuclear antigen
PLpro	Papain-like protease
PUN	Punicalagin
ROS	Reactive oxygen species
SOD	Superoxide dismutase
TAC	Total antioxidant capacity
TMPRSS2	Transmembrane protease serine 2
TNF-α	Tumour necrosis factor-alpha
YFV / WNV	Yellow fever virus / West Nile virus

1. Introduction

Oxidative stress and chronic low-grade inflammation share reactive oxygen species as a common upstream trigger and are increasingly recognised as the unified biology of ageing-related disease, viral susceptibility and carcinogenesis[1, 2]. Hesperidin, the dominant flavanone glycoside in citrus peel, has accumulated the most focused mechanistic and clinical signal among flavonoid nutraceutical candidates. Its aglycone hesperetin, released by intestinal α-rhamnosidase and β-glucosidase, is the principal bioactive in systemic circulation. On a population scale, hesperetin accounts for roughly half of total flavonoid intake in Scandinavian dietary surveys, illustrating the dietary scale of this scaffold.

Hesperidin+ is a six-ingredient polyphenol-rich nutraceutical developed by **Biotex Life Solutions** to address oxidative-stress balance and inflammatory homeostasis through a fixed 10:4:2:1:1:1 ratio of actives per capsule. The polyphenol-class components — hesperidin, rutin, *C. limon* flavanones (eriocitrin and limonoid fractions), *R. cordifolia* anthraquinones, and *P. granatum* ellagitannins/urolithins — converge on shared redox and inflammatory signalling, while the silica-rich bamboo exudate supplies a distinct inorganic matrix material.

Aim of this product review. To evaluate per-ingredient evidence supporting each component of Hesperidin+, define the boundaries of the combined product claim, characterise the formulation's regulatory and quality-control framework, and position the product within the existing nutraceutical landscape.

2. Product Profile: Hesperidin+

2.1 Brand, manufacturer and dosage

HESPERIDIN+

A polyphenol-rich multi-ingredient nutraceutical developed by Biotex Life Solutions

Fig 2: Product image.

Intended nutritional support:

Antioxidant defence • Healthy inflammatory balance • Immune and cellular protection
Serving size: 1 vegetarian capsule

Servings per container: 60 & 30

Recommended use: One capsule daily with a meal, or as directed by a healthcare professional.

Active component	Amount per capsule
Hesperidin, derived from *Citrus* species	500 mg
Bambusa arundinacea crystals powder	200 mg
Rutin derived from fruit peels	100 mg
Citrus limon fruit extract	50 mg
Rubia cordifolia root extract	50 mg
Punica granatum fruit extract	50 mg

Total active ingredients: 950 mg per capsule

No artificial colours. Manufactured in a GMP-compliant facility.

Scientific note: Antiviral and anticancer activities associated with individual ingredients are supported mainly by laboratory and preclinical evidence. The complete Hesperidin+ formulation has not yet been clinically established for the prevention or treatment of viral infections or cancer.

2.2 Dosage table

Table 1: Dosage and phytochemical markers of Hesperidin+ (per serving).

#	Ingredient	Source	Dose (mg/serving)	Key marker compound(s)	Documented activities
1	Hesperidin	Citrus spp. peel	**500**	Hesperidin/hesperetin (flavanone glycoside)	Antioxidant, anti-inflammatory, antiviral, anticancer

2	*Bambusa arundinacea* crystals/tabasheer	Bamboo nodal exudate	**200**	Biogenic silica (~95%), flavones (tricin), phenolic acids	Antipyretic, antispasmodic; mesoporous silica matrix
3	Rutin (from fruit peels)	Citrus, apple, buckwheat	**100**	Rutin (quercetin-3-*O*-rutinoside)	Antioxidant, anti-inflammatory, antiviral, anticancer
4	*Citrus limon* fruit extract	Lemon fruit	**50**	Eriocitrin, hesperidin, naringin, limonoids (limonin, limonexic acid)	Antioxidant, anti-inflammatory, anticancer
5	*Rubia cordifolia* root extract (manjistha)	Indian madder root	**50**	Purpurin, munjistin, cyclic hexapeptides, mollugin	Antioxidant, anti-inflammatory, anticancer
6	*Punica granatum* fruit extract	Pomegranate fruit	**50**	Punicalagin, ellagic acid → urolithins A/B/C	Antioxidant, anti-inflammatory, antiviral, anticancer
	Total actives per serving		**950**		

2.3 Recommended use and indications

Hesperidin+ is positioned by Biotex Life Solutions as a daily-use nutraceutical for adults seeking support for oxidative-stress balance and inflammatory homeostasis, with secondary positioning around seasonal viral resilience and metabolic health. The recommended serving is one vegetarian capsule daily with meals. The fixed-ratio formulation is intended to support consistent dose-response reproducibility across manufacturing batches.

3. Phytochemistry of the Six Ingredients

3.1 Hesperidin (500 mg)

Hesperidin ($C_{28}H_{34}O_{15}$; 3′, 5, 7-trihydroxy-4′-methoxyflavanone-7-rhamnoglucoside) is the dominant flavanone glycoside in *Citrus sinensis* (sweet orange), *C. reticulata* (mandarin), *C. paradisi* (grapefruit) and *C. limon* (lemon). Its aglycone hesperetin is the principal bioactive species in systemic circulation after hydrolysis by intestinal α-rhamnosidase and β-glucosidase. Hesperidin has documented antioxidant, anti-inflammatory, anticancer, antimicrobial and neuroprotective properties [3], with poor aqueous solubility (~4.95 µg/mL) and < 25% oral bioavailability limiting direct translation without formulation intervention.

3.2 *Bambusa arundinacea* crystals/tabasheer (200 mg)

B. arundinacea (synonymous with *B. bambos*) is a silicon-accumulator species whose nodal joints exude a translucent, milky-to-gelatinous material known as **tabasheer** or *vanshlochan*. Tabasheer contains ~95% biogenic organic silica, substantially higher than the 25–30% silica typical of other silicon-accumulator plants, and has documented use in Ayurvedic and Unani medicine as an antipyretic, antispasmodic and antiparalytic. Recent AI-assisted and *in vivo* toxicological work by Bohra et al. characterised *Vanshlochan* structurally using SEM/EDX/XRD and supported its safety profile[4] at nutraceutical doses. Tabasheer is the only non-polyphenol active in Hesperidin+ and contributes to a mesoporous silica matrix.

3.3 Rutin (from fruit peels) (100 mg)

Rutin (3, 3′, 4′, 5, 7-pentahydroxyflavone-3-rhamnoglucoside; quercetin-3-*O*-rutinoside) is a flavonol glycoside widely distributed in citrus peel, buckwheat, apple, grape and green tea. Comparative work on rutin versus its mono/di-glucoside derivatives has documented substantially improved aqueous solubility for glycosylated forms [5]. Rutin possesses antioxidant, anti-diabetic, anti-hypertensive, cardioprotective and anti-inflammatory activities; endogenous antioxidant enzymes are upregulated in rodent models, and ROS is downregulated.

3.4 *Citrus Limon* fruit extract (50 mg)

Citrus Limon (lemon) phenolic content is dominated by **eriocitrin** (eriodictyol 7-*O*-rutinoside), together with hesperidin, naringin and didymin [6]. The accompanying limonoid fraction includes limonin and its glucosides; limonexic acid reverses CCl_4-induced viability loss in HL-7702 hepatocytes [7] across a 12.4–199 µM range and inhibits NO production in LPS-stimulated RAW264.7 macrophages. Lemons further contain d-limonene and β-pinene/γ-terpinene in the essential-oil fraction, and a pectin-rich albedo whose fibres are fermented by gut microbiota to short-chain fatty acids. Limonin glucoside has been evaluated for chronic-disease biomarkers in overweight/obese adults at nutraceutical doses.

3.5 *Rubia cordifolia* (manjistha) root extract (50 mg)

Rubia cordifolia root contains more than 100 identified constituents [8] spanning anthraquinones (purpurin, alizarin, emodin, pseudopurpurin), naphthoquinones, anthraquinone/naphthoquinone glycosides, bicyclic hexapeptides, triterpenoids and polysaccharides. **Purpurin** (1, 2, 4-trihydroxyanthraquinone) and **munjistin** are canonical marker compounds; pseudopurpurin (purpurin 3-carboxylic acid) is the characteristic red pigment and a quality-control marker in the Chinese pharmacopeia. Anthraquinone constituents including purpurin have been investigated as neuroprotective agents in recent 2025 work [9].

3.6 *Punica granatum* (pomegranate) fruit extract (50 mg)

Pomegranate is exceptionally rich in ellagitannins — hexahydroxydiphenoic acid esters on a D-glucose core — with **punicalagin** being the most abundant [10]. PUN is poorly absorbed; gut microbiota hydrolyse it to ellagic acid, which is further converted by decarboxylation to dibenzopyran-6-one **urolithins A, B, C and isourolithin A**. Urolithins, not PUN or EA, are the dominant systemically circulating species; inter-individual microbiota-driven urolithin production defines distinct metabotypes [11] that shape bioavailability and clinical response.

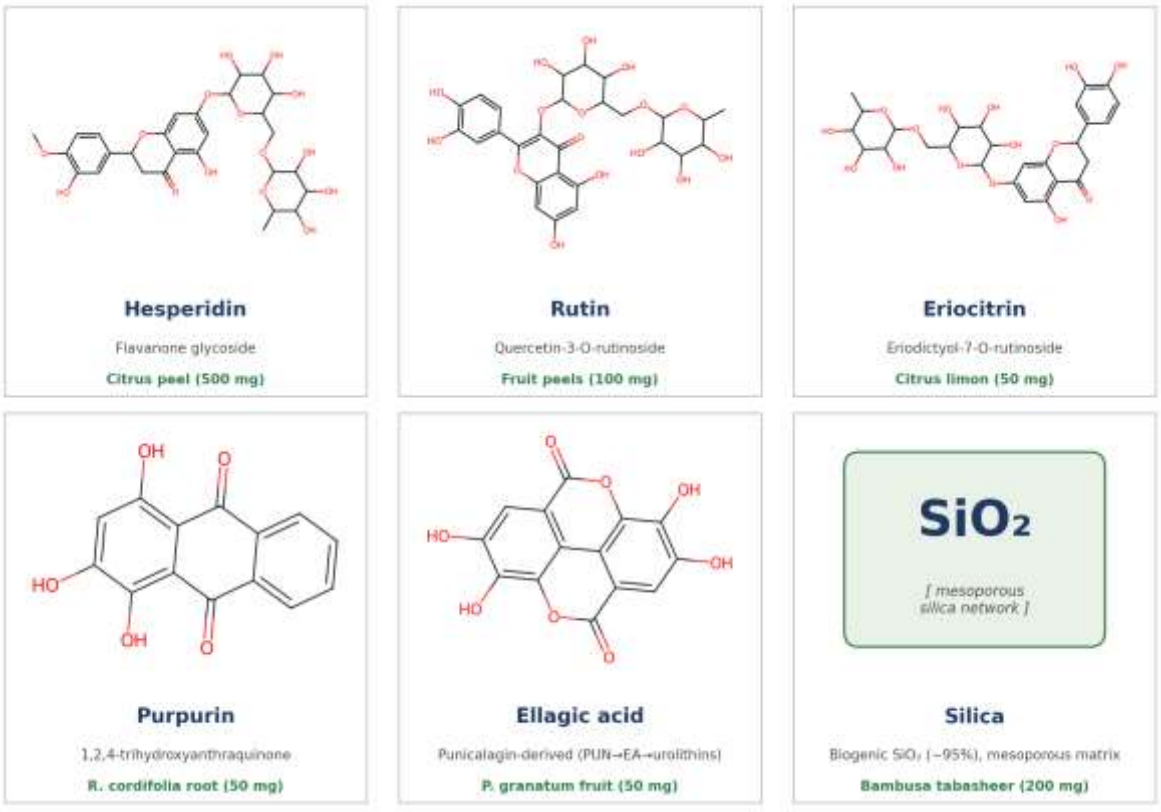


Fig 3: Key marker compounds of Hesperidin+. Representative marker compounds used for identity and quality control: hesperidin (flavanone glycoside), rutin (quercetin-3-*O*-rutinoside), eriocitrin (eriodictyol-7-*O*-rutinoside), purpurin (1, 2, 4-trihydroxyanthraquinone) from *Rubia cordifolia* root, ellagic acid (the absorbable derivative of the ellagitannin punicalagin; punicalagin → ellagic acid → urolithins A/B/C via gut microbiota), and biogenic silica (SiO_2) from *Bambusa* tabasheer.

3.7 Inactive / non-polyphenol fraction

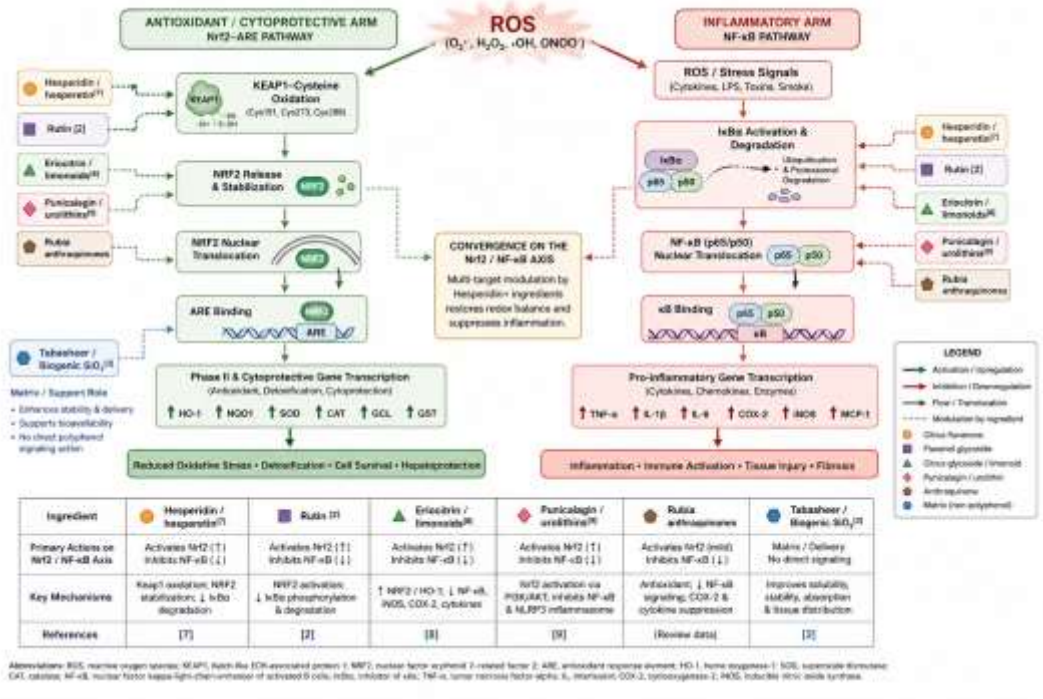
B. arundinacea tabasheer provides the only non-polyphenol contribution — ~95% biogenic silica — without phenolics in the dose-defining range of the formulation's claims framework.

4. Mechanistic Rationale: Convergent Targeting of Nrf2 and NF-κB

The polyphenol-class constituents in Hesperidin+ converge on two coordinated signalling axes: the **NRF2-KEAP1-ARE antioxidant defence pathway** and the **NF-κB-driven inflammatory pathway**. Reactive oxygen species serve as the shared upstream trigger: KEAP1 retains NRF2 in the cytoplasm; oxidative modification of KEAP1 cysteines releases NRF2, enabling nuclear translocation and ARE-driven transcription of phase II detoxifying enzymes (HO-1, SOD, CAT). Flavonoids broadly also suppress NF-κB-mediated cytokine production through IκB stabilisation, COX-2/PGE2 down-regulation, MAPK attenuation and JAK/STAT modulation.

Per-ingredient engagement with Nrf2/NF-κB.

- **Hesperidin/hesperetin.** Hesperidin restores Nrf2/HO-1 balance and suppresses IκB/NF-κB in bleomycin-induced pulmonary fibrosis [12] rats, with concurrent reductions in TGF-β1/Smad3, IL-1β, TNF-α and IL-6. Hesperidin inhibits TPA-induced 4-fold NF-κB promoter activation in HepG2 cells in a concentration-dependent manner. Hesperetin's antioxidant and anti-inflammatory activity has been most thoroughly characterised in neurological-disorder models[13].
- **Rutin.** Up-regulates NRF2 in *tert*-butyl hydroperoxide-induced oxidative-stress models; activates NRF2/ARE in UVB-irradiated skin fibroblasts combined with ascorbic acid; ameliorates diabetic [14] neuropathy via NRF2/HO-1 induction combined with NF-κB inhibition.
- **Eriocitrin / C. limon flavanones.** Eriomin® (70% eriocitrin, 5% hesperidin, 4% naringin) at 200 mg/day increased GLP-1 and attenuated Firmicutes overgrowth [15] and the Lachnospiraceae family in prediabetic patients, illustrating a microbiota-coupled anti-inflammatory mechanism.
- **Punicalagin/urolithins.** Modulate NF-κB-driven transcription, mitochondrial apoptosis pathways and Nrf2-mediated antioxidant responses in diverse cancer, macrophage and endothelial models[16].
- **Rubia cordifolia anthraquinones.** Modulate NF-κB, PI3K/Akt, MAPK, topoisomerase I and apoptosis pathways [17] across cancer cell lines.



Ingredient	Hesperidin / hesperetin	Rutin	Eriocitrin / limonoids	Punicalagin / urolithins	Rubia anthraquinones	Tabasheer / biogenic SiO₂
Primary Actions on Nrf2 / NF-κB Axis	Activates Nrf2 (↑) Inhibits NF-κB (↓)	Activates Nrf2 (↑) Inhibits NF-κB (↓)	Activates Nrf2 (↑) Inhibits NF-κB (↓)	Activates Nrf2 (↑) Inhibits NF-κB (↓)	Activates Nrf2 (mild) Inhibits NF-κB (↓)	Matrix / Delivery No direct signaling
Key Mechanisms	Keap1 oxidation; Nrf2 stabilization; ↓ IκBα degradation	Nrf2 activation; ↓ IκBα phosphorylation & degradation	↑ Nrf2 / HO-1; ↓ NF-κB, iNOS, COX-2, cytokines	Nrf2 activation via PI3K/AKT; inhibits NF-κB & NLRP3 inflammasome	Antioxidant; ↓ NF-κB signaling; COX-2 & cytokine suppression	Improves solubility, stability, absorption & tissue distribution
References	[7]	[2]	[8]	[9]	(Review data)	[3]

Fig 4: Mechanistic pathway schematic. Combined NF-κB (left, red) and Nrf2 (right, green) pathway diagram with colour-coded callouts for each of the six ingredients' molecular targets.

Mechanistic convergence on the Nrf2/NF-κB axis is the primary rationale for the multi-target Hesperidin+ design.

5. Antioxidant & Anti-Inflammatory Evidence

5.1 Direct (chemical) antioxidant evidence

Hesperidin and hesperetin scavenge DPPH and ABTS radicals in cell-free assays with reported IC_{50} in the 10–100 μM range depending on the model; in cellular oxidative-stress models, hesperidin elevates SOD activity ~2-fold and catalase ~1.5-fold. Rutin counteracts CCl_4-induced hepatotoxicity in rats through p53 and CYP2E1 modulation, with simultaneous increases in hepatic GPx, CAT, SOD, GST, GSR and GSH. PUN and EA scavenge ROS in Vero, Hep-2 and A549 cell lines. *R. cordifolia* methanol root extracts yield the highest phenolic content among extraction solvents tested [18] and produce the most consistent antioxidant profile across multiple assays.

Direct chemical data on tabasheer are limited; most bamboo antioxidant evidence is from leaf/shoot extracts or silver-nanoparticle composites (e.g., maximum DPPH scavenging of 74.4% at 200 μg/mL versus ascorbic acid 75.2% at 25 μg/mL for *B. arundinacea* leaf-derived Ag NPs[19]). This is leaf/nanoparticle data and should not be directly extrapolated to tabasheer at the formulation dose.

5.2 Indirect (endogenous enzyme induction) evidence

Flavonoids activate NRF2/ARE-driven transcription of HO-1, SOD and CAT, and suppress NF-κB nuclear translocation through IκBα phosphorylation blockade. Citrus peel flavonoid extracts also regulate intestinal microbial ecology [20] *in vitro*, suggesting a microbe-coupled anti-inflammatory mechanism. Eriomin® supplementation in prediabetes increases GLP-1 and attenuates Firmicutes overgrowth concurrently with systemic anti-inflammatory effects.

5.3 Human evidence (per ingredient)

Table 2: Per-ingredient evidence matrix by investigative level (2016–2026).

Legend — RCT: randomised controlled trial; Hu: other human data; An: animal; IV: in vitro; IS: in silico; R: review.

Ingredient	Antioxidant	Anti-inflammatory	Antiviral	Anticancer
Hesperidin (500 mg)	RCT, R	RCT, R	IV, IS, R	An, IV, R
Tabasheer (200 mg)	An, R (leaf data)	R	— (leaf/	IV nanoparticle)
Rutin (100 mg)	RCT, R	RCT, An, R	IS, IV IV, An	, R
C. limon / eriocitrin (50 mg)	RCT, R RCT,	R —	IV, R	
R. cordifolia root (50 mg)	IV, R	An, R IV	IV, An (whole-plant)	, R
P. granatum (50 mg)	RCT, R RCT, R	IV	RCT, An, R	

Hesperidin (human)

The most robust human evidence is for hesperidin [21]. A 2026 systematic review and meta-analysis of 10 RCTs (n = 532) showed statistically significant reductions in serum CRP/hs-CRP (SMD −0.43; 95% CI −0.71 to −0.15; $P = 0.002$) and TNF-α (SMD −0.51; 95% CI −0.95 to −0.07; $P = 0.02$); IL-6 reached statistical significance in adults with diagnosed disease (T2DM, MI; SMD −0.38; 95% CI −0.72 to −0.04; $P = 0.03$). Hesperidin also significantly increased total antioxidant capacity by 13.35 ± 19.21% (mean percent change), from a baseline of 0.74 mM to 0.82 mM post-intervention. A complementary 2023 systematic review and dose-response meta-analysis of cardiovascular risk factors in adults corroborates the dose-response relationship [22]. Hesperidin's intestinal microbiota metabolism shapes [23] bioavailability and clinical response, with α-rhamnosidase activity the rate-limiting step.

Eriocitrin / C. limon (human)

The Eriomin® formulation (70% eriocitrin, 5% hesperidin, 4% naringin) at 200 mg/day over 12 weeks produced a 6% decrease in hyperglycaemia and a 22% increase in blood GLP-1 in prediabetic patients, with reductions in Firmicutes and Lachnospiraceae and increases in Ruminococcaceae; the *Blautia* genus

decreased and was positively correlated with the[24] hyperglycaemia reduction. The Cesar 2019 RCT at 200, 400 and 800 mg/day reported that the **lowest dose (200 mg/day) [25]** was sufficient to increase GLP-1 and reverse hyperglycaemia in 24% of treated patients. Eriocitrin's broader pharmacological profile across oxidative[26] stress, inflammation, glycaemia and dyslipidaemia has been consolidated in a 2022 review. Lemon by-product flavonoid characterisation [27] is consolidated in a 2023 systematic review. **These results are Eriomin®-standardised evidence and cannot be directly extrapolated to the 50 mg *C. limon* fraction in Hesperidin+.**

Rutin (human)

Combined vitamin C + rutin improved oxidative-stress markers and glycaemic control in a T2DM randomised trial; rutin supplementation also improved quality of life and serum antioxidant [28] enzyme profiles in T2DM patients compared with placebo. The 2021 comparative study of rutin and its mono/di-glucoside derivative documented parallel antioxidant and anti-inflammatory activity with markedly improved solubility for the glycoside.

Punica granatum (human)

A randomised crossover trial demonstrated that pomegranate juice [29] improved cardiometabolic risk factors and biomarkers of oxidative stress and inflammation in haemodialysis patients. A second-generation LC-MS/MS [30] method has been developed to characterise PK profiles of pomegranate extract constituents in humans, supporting future bioavailability studies of the Hesperidin+ formulation. A phase II placebo-controlled randomised trial in men with localised prostate cancer [31] on active surveillance showed modulation of serum biomarkers with pomegranate fruit extract over 24 months. Pomegranate extract effects on inflammaging are documented in a comprehensive 2024 review [32].

Rubia cordifolia (human) — gap

At the formulation-equivalent dose, no compliant human RCT exists for *R. cordifolia* root extract. Crude ethanol extracts of *R. cordifolia* fruit (100, 500, 1000 mg/kg) altered biochemical parameters and produced histopathological hepatic changes in rodent toxicology work, with LD_{50} > 1000 mg/kg. Long-term controlled human exposure data are needed before human efficacy can be claimed. Spectrum-effect [33] relationship work on analgesic/anti-inflammatory activities supports the use of multiple chromatographic markers for quality control.

Bambusa arundinacea / tabasheer (human) — gap

At the formulation-equivalent dose of tabasheer (200 mg), no human RCT exists supporting the indications in this review. Marketed *B. arundinacea* leaf/shoot extracts or silver-nanoparticle composites supply indirect rationale only[34]; the comprehensive ethnopharmacology review of *B. bambos* provides broader context.

5.4 Preclinical evidence

Hesperidin elevates cellular SOD and catalase activity in cellular oxidative-stress models. Rutin increases hepatic GPx, CAT, SOD, GST, GSR and GSH in rats and counteracts CCl_4-induced hepatotoxicity via p53 and CYP2E1 modulation. PUN and EA scavenge ROS in Vero, Hep-2 and A549 cell lines. *R. cordifolia* methanol root extracts showed the highest phenolic content and consistent anti-proliferative action in HepG2, ME-180 and HeLa cell lines. *B. arundinacea* leaf extract–derived Ag NPs gave maximum DPPH scavenging of 74.4% at 200 µg/mL (leaf/nanoparticle data, not tabasheer).

In inflammation, hesperidin consistently down-regulates NF-κB-driven cytokines (IL-1β, IL-6, TNF-α) across LPS-induced lung injury, STZ-induced T2DM, high-fat-diet NAFLD, acute myocardial infarction and ligation-induced periodontitis models. Hesperidin inhibits TPA-induced 4-fold NF-κB promoter activation in HepG2 cells. Rutin reduces caspase-3, TNF-α, NF-κB and MDA in STZ-induced diabetic rats. PUN suppresses NF-κB-driven transcription and reduces cyclin-D1 expression in inflammatory cell models. Immunomodulatory activity of PUN differs from the parent peel extract, indicating a distinct pharmacological profile for the isolated compound[35].

6. Antiviral & Anticancer Potential

Boundary declaration. Evidence in §6 is predominantly preclinical (*in vitro* or *in silico*). Available data do **not** establish clinical antiviral or antitumour efficacy for Hesperidin+, or in most cases for its individual ingredients.

6.1 Antiviral evidence

Hesperidin/hesperetin. The 2024 molecular-docking study by Kowalczyk and colleagues[36] quantified binding interactions with SARS-CoV-2 entry-associated proteins: hesperetin values of −34.81 kcal/mol (hACE2), −30.56 kcal/mol, and −13.69 to −17.94 kcal/mol for PLpro and Mpro; hesperidin values were weaker, with positive docking scores at PLpro (17 kcal/mol) and Mpro (6.21 kcal/mol). The same study reported hesperidin IC_{50} values of 51.5 μM and 5.5 mM against Mpro in a biochemical assay. Cheng and colleagues demonstrated[37] that hesperidin and hesperetin suppressed infection of VeroE6 cells by lentiviral pseudo-particles of SARS-CoV-2 — including variant spike proteins — by blocking S-protein/ACE2 binding and reducing expression of ACE2 and TMPRSS2; however, hesperidin did not directly inhibit PLpro or Mpro enzyme activity in cell-free assays. Epidemiological data on citrus consumption and COVID-19 outcomes have been collected; three small registered clinical trials evaluated hesperidin in COVID-19 — a completed phase 2 study of hesperidin 1000 mg/day (NCT04715932), a hesperidin–diosmin (Daflon) combination trial (NCT04452799), and an Iranian study (IRCT20150725023332N5) — although their small size and heterogeneous designs limit definitive conclusions.

Across flaviviruses, Eberle and colleagues characterised[38] hesperetin as a noncompetitive inhibitor of NS2B/NS3 proteases of Dengue (−23.1 ± 3.6 to −24.1 ± 3.7 kcal/mol), Yellow Fever (−19.4 ± 2.7 to −20.0 ± 3.4 kcal/mol) and West Nile (−20.2 ± 3.4 to −28.3 ± 3.0 kcal/mol) viruses, with IC_{50} values < 5 μM; hesperidin showed binding energies of −35.4 ± ## 5.2 to −38.6 ± 8.0, −37.4 ± 7.2 to −38.6 ± 8.0, and −37.8 ± 7.0 to −40.7 ± 4.7 kcal/mol, and inhibited DENV2/YFV/WNV NS2B/NS3 protease activity by 100% at 140 μM, with calculated IC_{50} at 50–70 μM (DENV2 55.7 ± 2.5 μM; YFV 67.7 ± 7.5 μM; WNV 50.7 ± 8.3 μM). Plasma hesperetin concentrations after intake of 0.5–1 L of orange juice typically do not exceed 2 μmol/L — a critical translational caveat. Hesperidin's documented chronic lung-disease activity supports a broader respiratory-soothing positioning.

Rutin. Rutin is documented as a low-micromolar inhibitor of SARS-CoV-2 main protease 3CL^pro with a binding-efficiency index of 8.1[39] versus 16.9 for quercetin on a per-mass basis (each computed as $-\Delta G \times 1000/HEAVY\_ATOM\_COUNT$); the glycoside moiety contributes limited primary binding energy but improves solubility and oral bioavailability relative to quercetin.

Punicalagin / pomegranate. PUN reduces replication in HCV, RSV and HSV-1 *in vitro* by interfering with viral glycoprotein and cell-surface glycosaminoglycan interactions. Pomegranate peel extract inhibits the SARS-CoV-2 spike binding to the human ACE2 receptor in a direct *in vitro* binding assay, supporting a direct antiviral entry-blockade[40] mechanism. Pomegranate extract demonstrated virucidal and antiviral activity against the mosquito-borne Mayaro virus, supporting a broad arbovirus activity profile[41], although human data are currently lacking.

Rubia cordifolia. The aqueous extract of the whole plant limits rotavirus multiplication in MA-104 cells — this is **whole-plant/aerial-part** data and should not be extrapolated to a root-derived formulation.
Bambusa / tabasheer. Direct antiviral evidence for tabasheer is essentially absent; *B. arundinacea* Ag NP composites have been proposed as anti-coronavirus face-mask[42] coatings in nanoformulation work, but this is leaf/nanoparticle data, not tabasheer.

6.2 Anticancer evidence

Hesperidin/hesperetin. Modulates multiple cancer-relevant pathways: induces caspase-3/9 and Bax and inhibits NF-κB, iNOS, TNF-α and PCNA in Fe-NTA-induced renal oxidative stress and carcinogenesis in Wistar rats; arrests MG-63 osteosarcoma cell cycle at G2/M and induces apoptosis in xenograft models; suppresses TPA-induced AP-1/NF-κB promoter activity in HepG2 cells; suppresses angiogenesis by down-regulating VEGF in Ehrlich carcinoma[43] solid tumours. Hesperetin-loaded chitosan-folic-acid nanoparticles down-regulate CSC markers (DCLK1, STAT1, NOTCH1) in HCT116 colon-cancer-derived CSC populations. The 2025 colorectal-cancer-specific review by Qi and Su[44] consolidates these signals and frames hesperetin as a multi-target candidate with apoptosis-, autophagy- and PI3K/Akt/mTOR-relevant mechanisms.

Rutin. Suppresses p-AKT, p-ERK1/2 and p-mTOR in A375 and C8161 melanoma; reduces p38 MAPK expression in A549 lung cancer cells; activates p38 MAPK in HT-29 colon cancer alone or with silibinin; induces intrinsic apoptosis in neuroblastoma cells via Bcl2/Bax reduction. Rutin sensitises multiple cancer cell lines[45] to apoptosis when co-administered with chemotherapeutic agents, positioning it as a combination-therapy chemosensitiser. Comparative work confirms rutin glycoside shares antioxidant and anti-inflammatory activity with the parent molecule but with pharmacokinetic improvements.

C. limon / eriocitrin. Eriocitrin (eriodyctiol 7-*O*-rutinoside) suppresses MCF-7 cell proliferation[46] and induces apoptosis through JAK2/STAT3 and JNK/p38-MAPK modulation. Limonoids (limonin, limonexic acid) have documented anticancer activity; citrus by-products are now characterised as functional food ingredients with prebiotic potential.

Rubia cordifolia. The root is the most pharmacologically active fraction. Anthraquinones (alizarin, purpurin, mollugin, 1-hydroxy-2-methylanthraquinone) reduced His^+ revertants; mollugin induced autophagy/apoptosis in HN4 oral cancer and SK-BR-3 breast cancer cells; 1-acetoxy-3-methoxy-9,10-anthraquinone inhibited DNA topoisomerase I in HeLa; methanol root extracts showed anti-proliferative activity in HepG2, ME-180 and HeLa cell lines. Cyclic hexapeptides from *R. cordifolia* have shown anticancer signals through PI3K/Akt, MAPK and topoisomerase I crosstalk.

Safety caveat on R. cordifolia. Rubiadin, an *R. cordifolia* constituent anthraquinone, has demonstrated carcinogenic potential in a rat medium-term multi-organ model, producing renal adenomas/carcinomas, hepatocellular foci, and large-intestine adenomas/adenocarcinomas. The broad-screen herbal review[47] of *Rubia* medicinal plants consolidates chronic-exposure considerations. Long-term human safety data are not established.

Punica granatum / punicalagin. A phase II placebo-controlled randomised trial in men with localised prostate cancer on active surveillance showed modulation of serum biomarkers with pomegranate fruit extract over 24 months. PUN suppresses NF-κB in cervical cancer cells, reduces β-catenin and downstream cyclin-D1, induces apoptosis in colon cancer cells via Bcl-XL down-regulation and mitochondrial cytochrome c release, and inhibits osteosarcoma cell proliferation and angiogenesis. Apoptotic and antioxidant activity is also documented in KB, CAL-27 (oral), SW480/SW620/HT29/HCT116 (colon) and RWPE-1 (prostate) cancer cells. Urolithin A specifically has[48,49] documented anti-proliferative and anti-angiogenic activity in tumour models, with inter-individual metabotype variability affecting reproducibility of clinical signals. PUN/EA bioavailability is low; the residual fraction not further metabolised is undetectable in human plasma in most studies, so the *in vitro* PUN literature has uncertain *in vivo* translation. The 2024 punicalagin bioactivity review and 2025 pomegranate punicalagin study[10,50] consolidate the multi-disease activity profile.

Bambusa arundinacea. Direct anticancer evidence for tabasheer is sparse; bamboo leaf extract–derived Ag NPs show dose-dependent antiproliferative activity against MCF-7 cells, but this is leaf/nanoparticle data, not tabasheer. The comprehensive ethnopharmacology review of *B. bambos* provides broader context for the species' anticancer, antimicrobial and antioxidant potential.

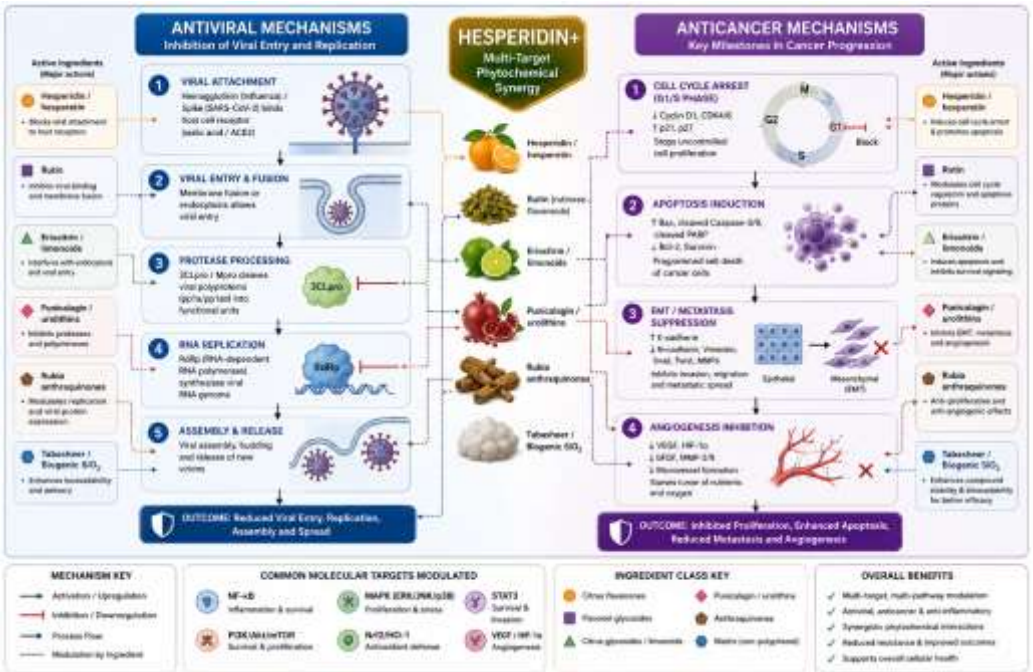


Fig 5: Proposed antiviral and anticancer mechanisms of Hesperidin+. The figure summarizes inhibition of viral entry, 3CLpro/Mpro, RdRp, and viral release, alongside G1/S arrest, apoptosis induction,

suppression of EMT/metastasis, and inhibition of angiogenesis. The illustrated effects are primarily based on mechanistic and preclinical evidence.

6.3 Direct synergy evidence relevant to the formulation

A five-component citrus flavanone mix[51] (hesperidin, neohesperidin, hesperetin, eriocitrin, naringin) showed combination-index values < 1.0 across ROS release, GSH-to-GSSG conversion, lipid peroxidation and protein carbonylation assays, and showed COX inhibition in Caco-2 cells at flavanone concentrations of 1.0–4.0 µM; eriodyctiol-based compounds exhibited marked COX-2 selectivity (interaction energies ΔE ≈ −38.83 and −16.34 kcal/mol). This is the clearest direct experimental evidence that the hesperidin-, rutin- and *C. limon*-derived flavanone scaffolds in Hesperidin+ may interact additively or synergistically on shared redox and inflammation targets.

7. Bioavailability, Safety, and Herb–Drug Interactions

7.1 Bioavailability as the dominant translational constraint

Low oral bioavailability is a unifying pharmacokinetic limitation across the polyphenol actives. Hesperidin shows < 25% oral bioavailability, low aqueous solubility (~4.95 µg/mL), gastric instability, poor intestinal absorption and extensive first-pass metabolism; the rate-limiting step is α-rhamnosidase activity, and the plasma half-life is ~6 hours. Rutin's poor water solubility has motivated extensive formulation work; glycosylated mono/di-glucoside forms show substantially improved solubility profiles, as demonstrated in the comparative study by Choi et al.. PUN and EA are poorly absorbed; only urolithins (A/B/C and isourolithin A) reach the bloodstream in meaningful amounts, and inter-individual urolithin metabotypes shape bioavailability–response relationships.

Formulation strategies — cyclodextrin inclusion complexes[52], solid dispersions, lipid-based systems, polymeric nanoparticles and phytosomes — have advanced hesperidin translation, but their application within Hesperidin+ at the product's specific dose remains untested. LC-MS/MS methodology developed in 2023 supports future PK characterisation of pomegranate extract constituents in humans.

7.2 Safety and tolerability

Hesperidin is generally well tolerated in RCTs up to ~1 g/day and shows a favourable safety profile across the 10-RCT meta-analytic pool. **Eriomin®** at 200 mg/day was well tolerated over 12 weeks in prediabetic adults. **Pomegranate** products have a long dietary history of safe consumption and consistent tolerability in human studies. **Limonin glucoside** exhibited no adverse signals at nutraceutical doses in overweight/obese adults. **Tabasheer** has been structurally characterised with toxicological evaluation by Bohra and colleagues for *Vanshlochan* from *B. bambos*, supporting a defined-quality material for nutraceutical use.

7.3 Herb–drug interactions

Hesperetin and naringenin inhibit CYP3A4 and other CYP isoforms; flavanone-rich mixtures compete for detoxification pathways and may interact with statins, calcium-channel blockers and anticoagulants. Pomegranate juice has documented pharmacokinetic interactions with several CYP3A-metabolised drugs. Patients on chronic medication should be counselled before initiating flavanone-rich nutraceuticals.

Safety caveat on R. cordifolia. Rubiadin shows documented carcinogenic potential in the rat MTMO model — producing renal adenomas / carcinomas, hepatocellular foci and large-intestine adenomas / adenocarcinomas; long-term safety data in humans are not established; consumers on prolonged nutraceutical regimens are advised to monitor hepatic and renal function.

Table 3. Herb–drug interaction matrix for Hesperidin+ ingredients

Ingredient	Drug class	Proposed mechanism	Magnitude	Recommendation
Hesperidin / hesperetin	Anticoagulants	Possible modulation of platelet activity and competition for metabolic pathways	Moderate; clinically variable	Use cautiously and monitor for bruising or bleeding

Hesperidin / hesperetin	Antihypertensives	Potential additive blood-pressure-lowering activity	Moderate	Monitor blood pressure, particularly during treatment initiation
Eriocitrin / citrus limonoids	Antidiabetics	Potential additive glucose-lowering effects	Low–moderate	Monitor glucose and adjust medication only under clinical supervision
Hesperetin-rich citrus fraction	CYP3A4 substrates	Inhibition of CYP3A4 and related CYP isoforms may alter drug exposure	Moderate; drug-dependent	Review concomitant statins, calcium-channel blockers and narrow-therapeutic-index drugs
Pomegranate constituents	Anticoagulants / antihypertensives	Possible additive pharmacodynamic effects and CYP-mediated interactions	Moderate; evidence inconsistent	Use under professional supervision and monitor relevant clinical parameters.
Rubia cordifolia anthraquinones	Chronic multi-drug therapy	Uncertain metabolism and limited long-term human safety data; rubiadin-related toxicological concern	Potentially significant with prolonged use	Avoid unsupervised long-term use; consider hepatic and renal monitoring

8. Quality Control and Standardisation

8.1 Marker-compound strategy

Hesperidin+ uses a **fixed-ratio, marker-compound-anchored** quality-control strategy. Each ingredient is qualified by a primary marker compound quantitated by HPLC-UV or HPLC-MS:

- Hesperidin → hesperidin by HPLC-UV at 280 nm.
- Tabasheer → biogenic SiO_2 by gravimetric analysis and EDX.
- Rutin → rutin by HPLC-UV at 350 nm.
- *C. limon* extract → eriocitrin and limonin by HPLC-MS.
- *R. cordifolia* root → purpurin and munjistin by HPLC-UV at 254 nm.
- *P. granatum* extract → punicalagin and ellagic acid by HPLC-MS.

Marker-compound selection for *Rubia* quality control is consistent with the comprehensive 2026 review by Zhang et al. that identifies purpurin/munjistin as quality-control anchors across the genus.

8.2 Fingerprinting and batch consistency

For botanical extracts with complex chemistry (*R. cordifolia* root, *P. granatum* fruit, *C. limon* fruit), HPLC fingerprinting is recommended to ensure batch-to-batch consistency, particularly through the spectrum-effect relationship approach validated for *Rubia* analgesic and anti-inflammatory activity. Fingerprint profiles should reference a master chromatogram stored by Biotex. Citrus peel phenolic recovery integrates well into nutraceutical pipelines, and processing-coproduct standards are aligned with this approach.

8.3 Stability, packaging and shelf life

Polyphenol-class actives are susceptible to oxidative degradation, particularly hesperidin and punicalagin. The finished product therefore requires:

- Opaque, low-O_2-permeability capsule shells (vegetarian HPMC preferred over gelatin for hygrothermal stability).
- Desiccant in bottle.
- Storage ≤ 25 °C, RH ≤ 60%.
- Stability testing at 0, 3, 6, 12 and 24 months per ICH Q1A(R2) with marker-compound quantitation at each time point.

The 2022 hesperidin extraction-and-stability review[53] consolidates the temperature, pH and matrix-buffer conditions required for finished-product stability.

9. Regulatory and Compliance Landscape

9.1 General regulatory position

Table 4: Polyphenol-rich nutraceuticals occupy different regulatory categories across jurisdictions. The status of each Hesperidin+ ingredient determines the regulatory pathway the formulation must integrate:

Jurisdiction	Regulatory frame	Hesperidin+ classification notes
USA	DSHEA	Hesperidin, rutin, *C. limon*, *R. cordifolia*, *P. granatum* and *B. arundinacea* are generally recognised as safe in dietary supplements at nutraceutical doses; structure-function claims permissible with FDA disclaimer.
EU	EFSA	Pomegranate ellagitannins and citrus flavanones are authorised for limited health claims; novel-food regulation applies to less-established botanicals such as *R. cordifolia* root.
India	FSSAI	Nutraceuticals Regulations 2022; fixed-dose formulations require product approval based on ingredient safety data and label compliance
Japan	FOSHU	Flavonoid antioxidants from *C. limon* and citrus peel are recognised; *R. cordifolia* and pomegranate have functional-food precedent.
ASEAN	Country-specific	Codex-aligned; nutraceutical vs. health-supplement positioning varies

9.2 Labelling and structure-function claims

Per DSHEA, any claim language should be **structure-function** rather than disease-treatment. Permissible structure-function language for the Hesperidin+ profile includes:

- "Supports the body's antioxidant defences."
- "Helps maintain a healthy inflammatory response."
- "Supports immune resilience during seasonal challenge."

Claims such as "treats viral infection" or "cures cancer" are impermissible and are not supported by available evidence regardless of formulation. The same restrictions apply for FTC and TGA advertising standards.

9.3 Pharmacovigilance and adverse-event reporting

A formal pharmacovigilance framework is recommended for any commercial launch of Hesperidin+, including:

- Adverse-event intake via consumer QR code on packaging.
- Annual safety summary based on global adverse-event databases.
- Targeted monitoring for CYP3A4-mediated drug interactions and *R. cordifolia* chronic-exposure hepatic/renal signals.

10. Sustainability and Ethical Sourcing

10.1 Sourcing considerations across the six ingredients

Table 5: Sourcing considerations:

Ingredient	Primary sourcing geography	Sustainability/ethics levers
Hesperidin	Spain, Brazil, USA, China	Citrus-processing coproduct stream; flavanone recovery from peel waste; fair-trade certification optional

B. arundinacea tabasheer	India, SE Asia	Indigenous-knowledge provenance; Ayurvedic/Unani GMP traceability; bamboo is fast-renewing
Rutin (fruit peels)	China, Mexico, India	Buckwheat sourcing has documented ethnopharmacology; co-product integration reduces waste.
C. limon fruit extract	Mediterranean, Argentina	By-product valorisation; lemon-processing waste streams; d-limonene and pectin co-product[54] recovery
R. cordifolia root	India (sub-Himalayan regions), Nepal	Wild-collection pressure documented; cultivated-root sourcing recommended
P. granatum fruit extract	Iran, India, Turkey, USA	Established agricultural supply chain; urolithin-metabotype variability affects clinical reproducibility

10.2 Indigenous-knowledge and access-and-benefit-sharing considerations

Rubia cordifolia and *Bambusa arundinacea* are subject to the Convention on Biological Diversity and the Nagoya Protocol on Access and Benefit-Sharing. Commercial sourcing documentation should include:

- Provenance records linking raw material to indigenous-knowledge source communities.
- Benefit-sharing arrangements where appropriate.
- Compliance with national biodiversity regulations (India's Biological Diversity Act 2002; EU ABS Regulation 511/2014).

10.3 Environmental footprint consideration

Rubia cordifolia root wild-collection pressure is documented in species-conservation reviews; cultivated-root sourcing reduces wild-collection pressure and aligns with the broader *Rubia* species-conservation agenda. Bamboo is a fast-renewing resource with a low environmental footprint, supporting favourable life-cycle assessment conclusions at the tabasheer-sourcing tier. Citrus-processing coproduct utilisation for the flavonoid components also contributes positively to life-cycle benefits.

11. Comparative Positioning Against Existing Nutraceuticals

11.1 Comparable commercial products

Several nutraceutical products overlap partially with the Hesperidin+ profile, but none share the exact 10:4:2:1:1:1 ratio with the inclusion of tabasheer. Comparable products include:

- **Hesperidin-only and citrus bioflavonoid products** (250–500 mg per dose): lack rutin, *R. cordifolia*, *P. granatum* and tabasheer, and lack flavanone synergy.
- **Pomegranate-only products** (500–1000 mg fruit extract or 100–300 mg PUN-equivalent): lack citrus flavanone synergy; the broad inflammaging and cardiovascular evidence applies but the synergistic multi-target rationale is absent.
- **Rutin + vitamin C products** (typically 500 mg rutin + 500 mg vitamin C): lack the broader polyphenol networking of Hesperidin+.
- **Eriomin® (70% eriocitrin)** at 200 mg/day: strongest prediabetes RCT evidence, but no hesperidin-anchored flavanone synergy, no *P. granatum*, no *R. cordifolia*.
- **Vanshlochan-only Ayurvedic formulations**: lack the polyphenol networking entirely; anthraquinone network absent.

11.2 Differentiation summary

Hesperidin+'s differentiation rests on three primary axes:

1. **Dose-anchored polyphenol networking.** Hesperidin (500 mg) as the dominant dose, with rutin and *C. limon* eriocitrin contributing a second tier of flavanone/flavonol synergy demonstrated in Caco-2 cells by Smeriglio and colleagues.
2. **Anthraquinone + silica extension.** *R. cordifolia* anthraquinones and tabasheer supply novel actives not present in the comparable products above; this is a positioning strength but also a regulatory-fragility point, as anthraquinone long-term safety requires monitoring.
3. **Urolithin pathway engagement.** PUN-driven urolithin metabolism engages systemic signalling pathways not addressed by citrus-only or rutin-only products; inter-individual metabotype variability is documented and operationally important.

11.3 Recommended comparator studies

To substantiate the differentiation claim, three comparator trials can be prioritised by Biotex Life Solutions:

1. Pharmacokinetic head-to-head: Hesperidin+ vs. hesperidin-only at matched 500 mg hesperidin dose, measuring plasma hesperetin, urolithin A and total antioxidant capacity over 24 hours.
2. Anti-inflammatory head-to-head: Hesperidin+ vs. Eriomin® 200 mg/day in prediabetes, measuring change in fasting glucose, GLP-1, hs-CRP and gut-microbiome profile.
3. Antioxidant head-to-head: Hesperidin+ vs. rutin + vitamin C, measuring change in TAC and lipid-peroxidation markers.

12. Research Limitations and Future Directions

1. **The combined six-ingredient Hesperidin+ product has not been evaluated as a single intervention** in any published human trial. The most urgent research priority is a compositional and pharmacokinetic study of the actual formulation, followed by an appropriately powered RCT on antioxidant and anti-inflammatory endpoints.
2. **Antiviral and anticancer evidence is predominantly preclinical.** In-vitro hesperidin docking data against SARS-CoV-2 and flavivirus proteases and pomegranate peel ACE2-binding inhibition do not establish in vivo clinical efficacy; the same caveat applies to PUN/EA in cancer cell-line models.
3. ***B. arundinacea* / tabasheer evidence is thin and non-product-specific.** Most published pharmacological data are from leaf/shoot extracts or silver-nanoparticle composites; tabasheer-specific pharmacology at the formulation dose is the least characterised of the six ingredients.
4. **Plant-part and extract-type mismatches** must be flagged: *R. cordifolia* antiviral data are from whole-plant/aerial-part aqueous extracts (not root); most bamboo anticancer / antioxidant data are leaf/shoot or silver-nanoparticle composites (not tabasheer); the *in vitro* PUN literature is hampered by uncertain translation to *in vivo* urolithin biology.
5. **Heterogeneity of extracts and doses.** Eriomin®-standardised evidence at 200 mg/day cannot be directly extrapolated to the 50 mg *C. limon* fraction in Hesperidin+. Standardised pomegranate extract literature has a different active profile from generic fruit extract.
6. **Bioavailability and formulation integration.** Without a formulation-PK study, absolute bioavailability, dose proportionality and accumulation of Hesperidin+ are unknown.
7. **Safety signal for R. cordifolia long-term exposure.** Rubiadin's carcinogenic signal in the rat MTMO model warrants controlled chronic-toxicity evaluation before long-term human supplementation of root-extract-containing formulations at nutraceutical doses.
8. **Regulatory, standardisation and access-and-benefit-sharing documentation** is essential for product commercialisation but not yet fully integrated in nutraceutical reviews of this formulation class.

13. Conclusion

Hesperidin+ is a six-ingredient polyphenol-and-silica nutraceutical built around **500 mg of hesperidin** and combining rutin (100 mg), *Citrus limon* fruit extract (50 mg), *Rubia cordifolia* root extract (50 mg),

Punica granatum fruit extract (50 mg) and *Bambusa arundinacea* crystals/tabasheer (200 mg) — totalling 950 mg of actives per vegetarian capsule, in a 10:4:2:1:1:1 ratio, developed by **Biotex Life Solutions**.

The polyphenol-class components converge on a coherent molecular axis — **Nrf2/ARE** for antioxidant defence and **NF-κB** for inflammation — with **reactive oxygen species** as the shared upstream trigger. Direct flavanone synergy has been demonstrated in vitro on antioxidant and COX inhibition readouts, motivating additive interactions among the Hesperidin+ flavanone scaffolds. The legacy of citrus-flavanone pharmacology is well established at the nutraceutical dimension, and modern standards-compliance requires integration of marker-compound quantitation, fingerprinting and stability-indicating methodology in the per-ingredient quality dossier.

The strongest per-ingredient human evidence is antioxidant and anti-inflammatory: a 2026 meta-analysis of 10 RCTs (n = 532) for hesperidin alone; Eriomin®'s 6% hyperglycaemia reduction and 22% GLP-1 increase with microbiota rebalancing in prediabetes; pomegranate juice's cardioprotective and anti-inflammatory effect in haemodialysis; pomegranate fruit extract's biomarker-modulating effect in localised prostate cancer. Antiviral signals are predominantly preclinical — hesperidin's flavivirus/SARS-CoV-2 protein binding and VeroE6 pseudo-particle inhibition in vitro; pomegranate peel extract's inhibition of SARS-CoV-2 spike/ACE2 binding in vitro; and hesperetin's near-full inhibition of DENV2/YFV/WNV protease activity at 140 μM with IC_{50} at 50–70 μM. Anticancer signals — NF-κB suppression, Bcl-XL/Bax modulation, caspase-dependent apoptosis, cell-cycle arrest — are preclinical and should not be framed as clinical claims. Low oral bioavailability, inter-individual urolithin-metabotype variability, the thin evidence base specific to tabasheer and the safety caveats surrounding *R. cordifolia* root all motivate a formulation-level PK study and a chronic-toxicity evaluation as the indispensable next steps.

In summary, the mechanistic rationale for **Hesperidin+ by Biotex Life Solutions** is multi-target, evidence-supported and coherent across the polyphenol ingredients; antioxidant and anti-inflammatory outcomes are the strongest per-ingredient claims; antiviral and anticancer outcomes are promising but preclinical; and controlled clinical evaluation of the combined formulation, integrated with modern marker-compound-anchored quality control and access-and-benefit-sharing-aligned sourcing, is required to translate this rationale into a labelled product claim that meets international nutraceutical standards.

Clinical recommendation. Adult consumers may use one Hesperidin+ capsule daily as a complementary antioxidant/anti-inflammatory nutraceutical. Patients on CYP3A4-metabolised medications, those with hepatic or renal compromise, and pregnant or lactating women should consult a clinician before initiating flavanone-rich nutraceuticals. Statements on viral clearance, cancer prevention or treatment of any chronic disease are not currently supported by clinical evidence.

Conflicts of interest

The authors are members of the Research and Development Division of **Biotex Life Solutions**, manufacturer of *Hesperidin+*.

Author contributions

The R&D team conceived the product narrative, performed the literature search, contributed to mechanistic synthesis, integrated regulatory and quality-control frameworks, and read and approved the final manuscript.

Funding

This product review received no external funding.

Acknowledgements

The authors thank the Biotex Life Solutions leadership for institutional support during preparation of this review and the Jenni library for facilitating traceability across the merged reference corpus.

Data availability

All cited sources are available in the open literature; no new data were generated.

REFERENCES

1. Thiruvengadam M, Venkidasamy B, Subramanian U, et al. Bioactive compounds in oxidative stress-mediated diseases: targeting the NRF2/ARE signaling pathway and epigenetic regulation. Antioxidants. 2021; 10(12):1859. doi:10.3390/antiox10121859.

2. Al-Khayri JM, Sahana GR, Nagella P, et al.. Flavonoids as potential anti-inflammatory molecules: a review. Molecules. 2022 ;27(9):2901. doi:10.3390/molecules27092901.
3. Ahmad A, Afzaal M, Saeed F, et al.. A comprehensive review of the therapeutic potential of citrus bioflavonoid hesperidin against lifestyle-related disorders. Cogent Food & Agriculture. 2023; 9(1):2226427. doi:10.1080/23311932.2023.2226427.
4. Bohra B, et al.. From structure to safety: material characterization and toxicological evaluation of Vanshlochan (Bambusa bambos (L.) Voss [Poaceae]) using AI-assisted and in vivo approaches. Journal of Ethnopharmacology. 2026; 362: 121266. doi:10.1016/j.jep.2026.121266.
5. Choi S-S, Park H-R, Lee K-A, et al.. A comparative study of rutin and rutin glycoside: antioxidant activity, anti-inflammatory effect, effect on platelet aggregation and blood coagulation. Antioxidants. 2021; 10(11):1696. doi:10.3390/antiox10111696.
6. Klimek-Szczykutowicz M, Szopa A, Ekiert H. Citrus limon (lemon) phenomenon—a review of the chemistry, pharmacological properties, applications in the modern pharmaceutical, food, and cosmetics industries, and biotechnological studies. Plants. 2020;9(1):119. doi:10.3390/plants9010119.
7. Gualdani R, Cavalluzzi MM, Lentini G, et al.. The chemistry and pharmacology of citrus limonoids. Molecules. 2016; 21(11):1530. doi:10.3390/molecules21111530.
8. Wen M, Chen Q, Chen W, et al.. A comprehensive review of Rubia cordifolia L.: traditional uses, phytochemistry, pharmacological activities, and clinical applications. Frontiers in Pharmacology. 2022; 13: 965390. doi:10.3389/fphar.2022.965390.
9. Mustafa AM, Sayed GA, Hatem S, et al.. Therapeutic potential of purpurin, a natural anthraquinone dye, in neuroprotection and neurological disorders. Inflammopharmacology. 2025; 33(11):6377–6388. doi:10.1007/s10787-025-01977-7.
10. Shabir I, et al.. Bioactive potential of punicalagin: a comprehensive review. Applied Food Research. 2024; 4: 100572. doi:10.1016/j.afres.2024.100572.
11. García-Villalba R, Giménez-Bastida JA, Cortés-Martín A, et al.. Urolithins: a comprehensive update on their metabolism, bioactivity, and associated gut microbiota. Molecular Nutrition & Food Research. 2022; 66(21):e2101019. doi:10.1002/mnfr.202101019.
12. Hosawi S. Current update on role of hesperidin in inflammatory lung diseases: chemistry, pharmacology, and drug delivery approaches. Life. 2023; 13(4):937. doi:10.3390/life13040937.
13. Khan A, Ikram M, Hahm JR, et al.. Antioxidant and anti-inflammatory effects of citrus flavonoid hesperetin: special focus on neurological disorders. Antioxidants. 2020; 9(7):609. doi:10.3390/antiox9070609.
14. Pandey P, Khan F, Qari HA, et al.. Rutin (bioflavonoid) as cell signaling pathway modulator: prospects in treatment and chemoprevention. Pharmaceuticals. 2021; 14(11):1069. doi:10.3390/ph14111069.
15. Cesar TB, Ramos FMM, Ribeiro CB. Nutraceutical eriocitrin (Eriomin) reduces hyperglycemia by increasing glucagon-like peptide 1 and downregulates systemic inflammation: a crossover-randomized clinical trial. Journal of Medicinal Food. 2022; 25(11):1050–1058. doi:10.1089/jmf.2021.0181.
16. Venusova E, Kolesarova A, Horky P, Slama P. Physiological and immune functions of punicalagin. Nutrients. 2021; 13(7):2150. doi:10.3390/nu13072150.
17. Balachandran P, Ibrahim MA, Zhang J, et al.. Crosstalk of cancer signaling pathways by cyclic hexapeptides and anthraquinones from Rubia cordifolia. Molecules. 2021; 26(3):735. doi:10.3390/molecules26030735.
18. Humbare RB, Sarkar J, Kulkarni AA, et al.. Phytochemical characterization, antioxidant and anti-proliferative properties of Rubia cordifolia L. extracts prepared with improved extraction conditions. Antioxidants. 2022; 11(5):1006. doi:10.3390/antiox11051006.
19. Jayarambabu N, Velupla S, Akshaykranth A, et al.. Bambusa arundinacea leaves extract-derived Ag NPs: evaluation of the photocatalytic, antioxidant, antibacterial, and anticancer activities. Applied Physics A. 2023; 129(1):13. doi:10.1007/s00339-022-06279-1.

20. Li P, Yao X, Zhou Q, et al.. Citrus peel flavonoid extracts: health-beneficial bioactivities and regulation of intestinal microecology in vitro. Frontiers in Nutrition. 2022; 9: 888745. doi:10.3389/fnut.2022.888745.
21. Ouyang L, Yu M, Zhang W, Gong Y. The effects of hesperidin supplementation on inflammation and oxidative stress in adults: a systematic review and meta-analysis. British Journal of Nutrition. 2026:1–11. Online ahead of print. doi:10.1017/S0007114526106898.
22. Khorasanian AS, Shiraseb F, Aghakhani L, et al., Asbaghi O. The effects of hesperidin supplementation on cardiovascular risk factors in adults: a systematic review and dose-response meta-analysis. Frontiers in Nutrition. 2023; 10: 1177708. doi:10.3389/fnut.2023.1177708.
23. Mas-Capdevila A, et al.. Effect of hesperidin on cardiovascular disease risk factors: the role of intestinal microbiota on hesperidin bioavailability. Nutrients. 2020; 12(5):1488. doi:10.3390/nu12051488.
24. Ramos FMM, et al.. Lemon flavonoids nutraceutical (Eriomin) attenuates prediabetes intestinal dysbiosis: a double-blind randomized controlled trial. Food Science & Nutrition. 2023; 11(11):7283–7295. doi:10.1002/fsn3.3654.
25. Ribeiro CB, Ramos FMM, Manthey JA, Cesar TB. Effectiveness of Eriomin in managing hyperglycemia and reversal of prediabetes condition: a double-blind, randomized, controlled study. Phytotherapy Research. 2019; 33(7):1921–1933. doi:10.1002/ptr.6386.
26. Yao L, et al.. Eriocitrin: a review of pharmacological effects. Biomedicine & Pharmacotherapy. 2022; 154: 113563. doi:10.1016/j.biopha.2022.113563.
27. Martínez-Zamora L, et al.. Flavonoid extracts from lemon by-products as a functional ingredient for new foods: a systematic review. Foods. 2023; 12(19):3687. doi:10.3390/foods12193687.
28. Bazyar H, et al.. The effects of rutin supplement on blood pressure markers, some serum antioxidant enzymes, and quality of life in patients with type 2 diabetes mellitus compared with placebo. Frontiers in Nutrition. 2023; 10: 1214420. doi:10.3389/fnut.2023.1214420.
29. Barati Boldaji R, et al.. Pomegranate juice improves cardiometabolic risk factors, biomarkers of oxidative stress and inflammation in hemodialysis patients: a randomized crossover trial. Journal of the Science of Food and Agriculture. 2020; 100(2):846–854. doi:10.1002/jsfa.10096.
30. Wang Y-H, et al.. Development of a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for characterizing pomegranate extract pharmacokinetics in humans. Journal of Pharmaceutical and Biomedical Analysis. 2023; 233: 115477. doi:10.1016/j.jpba.2023.115477.
31. Jarrard DF, et al.. A phase II randomized placebo-controlled trial of pomegranate fruit extract in men with localized prostate cancer undergoing active surveillance. The Prostate. 2021;81(1):41–49. doi:10.1002/pros.24076.
32. Cordiano R, Gammeri L, Di Salvo E, et al.. Pomegranate (Punica granatum L.) extract effects on inflammaging. Molecules. 2024; 29(17):4174. doi:10.3390/molecules29174174.
33. Shen C-H, et al.. Evaluation of analgesic and anti-inflammatory activities of Rubia cordifolia L. by spectrum-effect relationships. Journal of Chromatography B. 2018; 1090:73–80. doi:10.1016/j.jchromb.2018.05.021.
34. Haris M, et al.. Ethnopharmacology, phytochemistry, pharmacological activities and toxicity study of Bambusa bambos (L.) Voss: a comprehensive overview. Discover Plants. 2025; 2: 48. doi:10.1007/s44372-025-00124-4.
35. Čolić M, et al.. Immunomodulatory activity of punicalagin, punicalin, and ellagic acid differs from the effect of pomegranate peel extract. Molecules. 2022; 27(22):7871. doi:10.3390/molecules27227871.
36. Kowalczyk A, et al.. Hesperidin, a potential antiviral agent against SARS-CoV-2: the influence of citrus consumption on COVID-19 incidence and severity in China. Medicina. 2024; 60(6):892. doi:10.3390/medicina60060892.
37. Cheng F-J, Huynh T-K, Yang C-S, et al.. Hesperidin is a potential inhibitor against SARS-CoV-2 infection. Nutrients. 2021; 13(8):2800. doi:10.3390/nu13082800.

38. Eberle RJ, Olivier DS, Amaral MS, et al.. Promising natural compounds against flavivirus proteases: citrus flavonoids hesperetin and hesperidin. Plants. 2021;10(10):2183. doi:10.3390/plants10102183.
39. Rizzuti B, et al.. Rutin is a low micromolar inhibitor of SARS-CoV-2 main protease 3CLpro: implications for drug design of quercetin analogs. Biomedicines. 2021;9(4):375. doi:10.3390/biomedicines9040375.
40. Tito A, Colantuono A, Pirone L, et al.. Pomegranate peel extract as an inhibitor of SARS-CoV-2 spike binding to human ACE2 receptor (in vitro): a promising source of novel antiviral drugs. Frontiers in Chemistry. 2021; 9: 638187. doi:10.3389/fchem.2021.638187.
41. Salles TS, et al.. Virucidal and antiviral activities of pomegranate (Punica granatum) extract against the mosquito-borne Mayaro virus. Parasites & Vectors. 2021; 14: 443. doi:10.1186/s13071-021-04955-4.
42. Kalluri JR, et al.. Single plant derived nanotechnology for synergistic antibacterial therapies. PLOS ONE. 2016; 11(9):e0163270. doi:10.1371/journal.pone.0163270.
43. Rahmani AH, Babiker AY, Anwar S. Hesperidin, a bioflavonoid in cancer therapy: a review for a mechanism of action through the modulation of cell signaling pathways. Molecules. 2023; 28(13):5152. doi:10.3390/molecules28135152.
44. Qi M, Su Y. Targeting colorectal cancer with hesperidin and hesperetin: a comprehensive review of antiproliferative activity, chemopreventive, anti-inflammatory, and antioxidant effects. Frontiers in Nutrition. 2025; 12: 1647977. doi:10.3389/fnut.2025.1647977.
45. Satari A, et al.. Rutin: a flavonoid as an effective sensitizer for anticancer therapy; insights into multifaceted mechanisms and applicability for combination therapy. Evidence-Based Complementary and Alternative Medicine. 2021; 2021: 9913179. doi:10.1155/2021/9913179.
46. Yuan C, et al.. Eriocitrin, a dietary flavonoid suppressed cell proliferation, induced apoptosis through modulation of JAK2/STAT3 and JNK/p38 MAPKs signaling pathway in MCF-7 cells. Journal of Biochemical and Molecular Toxicology. 2022; 36(1):e22943. doi:10.1002/jbt.22943.
47. Zhang M, et al.. A comprehensive review of Rubia medicinal plants: traditional uses, botany, phytochemistry, and pharmacological activities. Annales Pharmaceutiques Françaises. 2026. Online ahead of print. doi:10.1016/j.pharma.2026.05.008.
48. Tow WK, Chee PY, Sundralingam U, Palanisamy UD. The therapeutic relevance of urolithins, intestinal metabolites of ellagitannin-rich food: a systematic review of in vivo studies. Nutrients. 2022; 14(17):3494. doi:10.3390/nu14173494.
49. Al-Harbi SA, Abdulrahman AO, Zamzami MA, Khan MI. Urolithins: the gut based polyphenol metabolites of ellagitannins in cancer prevention, a review. Frontiers in Nutrition. 2021; 8: 647582. doi:10.3389/fnut.2021.647582.
50. Maqsood M, et al.. Pomegranate punicalagin: a comprehensive review of various in vitro and in vivo biological studies. ACS Food Science & Technology. 2025; 5(6):2064–2085. doi:10.1021/acsfoodscitech.5c00117.
51. Smeriglio A, Iraci N, Denaro M, et al.. Synergistic combination of citrus flavanones as strong antioxidant and COX-inhibitor agent. Antioxidants. 2023; 12(4):972. doi:10.3390/antiox12040972.
52. Hoang TPN, Timmins P, Smith AM, et al.. Drug delivery and formulation development of hesperidin: a systematic review. Expert Opinion on Drug Delivery. 2026; 23(2):363–384. doi:10.1080/17425247.2025.2581839.
53. Pyrzynska K. Hesperidin: a review on extraction methods, stability and biological activities. Nutrients. 2022; 14(12):2387. doi:10.3390/nu14122387.
54. Durmus N, Gulsunoglu-Konuskan Z, Kilic-Akyilmaz M. Recovery, bioactivity, and utilization of bioactive phenolic compounds in citrus peel. Food Science & Nutrition. 2024; 12(12):9974–9997. doi:10.1002/fsn3.4570.