



DOSSIER · SUBSTANCE

Grape Seed Extract (OPC)

Grape seed extract, rich in **oligomeric proanthocyanidins (OPC)**, is one of the most extensively studied plant polyphenols. The database reveals a broad body of research, with a focus on **metabolic and cardiovascular parameters**, though the applicability of laboratory findings to clinical practice remains limited. The most notable observation: even in frequently cited studies, **surrogate markers** dominate over hard endpoints.

1,769

STUDIES IN
TOTAL

172

IN HUMANS

73

OF WHICH
CONTROLLED

464

IN ANIMALS

306

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Grape Seed Extract (OPC) at a Glance

ORIGIN:
Grape seed extract is derived from the seeds of the grapevine (*Vitis vinifera*) and primarily consists of **oligomeric proanthocyanidins (OPC)**, a subgroup of flavonoids. These condensed tannins are composed of catechin and epicatechin units. The composition varies depending on the growing region, grape variety, extraction method, and storage, with the **OPC content** serving as a quality indicator.

STUDY LANDSCAPE:
1,761 evaluated publications · 73 controlled human studies · 99 observational studies · 71 review articles · 462 animal studies · 251 cell culture studies

- STRONGEST EVIDENCE:**
- **Inflammatory processes** A randomised, placebo-controlled study involving 32 patients with type 2 diabetes demonstrated a significant reduction in the inflammatory marker hsCRP and an improvement in antioxidant status (TAOS) after 4 weeks of daily intake of 600 mg grape seed extract.
 - **Cardiovascular functions** Controlled studies in prehypertensive subjects showed slight reductions in blood pressure and improved vascular parameters (endothelial function) following grape seed extract intake, though no hard endpoints such as stroke or myocardial infarction rates were observed.
 - **Metabolic parameters** A study with 40 overweight/obese subjects revealed a reduction in inflammatory markers (TNF-α) after 12 weeks of daily intake of 300 mg grape seed extract combined with a calorie-reduced diet; weight reduction (~3.5 kg) occurred in the context of the combined intervention.
 - **Oxidative stress** A pilot study with 28 smokers *provided an initial indication* of a 22% improvement in the glutathione redox ratio (GSH/GSSG) and a 7% reduction in LDL cholesterol levels after 8 weeks of daily intake of 200 mg grape seed extract.
 - **Safety and tolerability** Controlled studies report no serious adverse effects, though systematic long-term investigations on safety and interactions with medications are lacking.

- LIMITATIONS:**
- The applicability of *preclinical* laboratory and animal studies to humans is limited, as OPC are metabolised differently in the human gut, leading to systemically active metabolites.
 - Most human studies use surrogate markers (e.g., MDA, TAOS) without demonstrating clinically relevant effects or hard endpoints (e.g., cardiovascular events).
 - Long-term studies, standardised dosages, and systematic investigations into dose-response relationships or interactions with medications are lacking.
- CLASSIFICATION:**
Grape seed extract, rich in oligomeric proanthocyanidins (OPC), demonstrates short-term effects on inflammatory, metabolic, and cardiovascular parameters in controlled studies. However, robust data on hard endpoints and long-term effects are lacking.

1. Chemical and Biological Characteristics of Grape Seed Extract

Grape seed extract is derived from the seeds of the grapevine (*Vitis vinifera*) and largely consists of **oligomeric proanthocyanidins (OPC)**. These belong to the **flavonoid** group and are **condensed tannins** composed of catechin and epicatechin units. The extracts also contain monomeric flavonoids such as catechin, as well as dimeric, trimeric, and higher-molecular-weight forms. The composition varies depending on the growing region, grape variety, extraction method, and storage. Industrially, the extract is typically obtained through solvent extraction or enzymatic processes, with the **OPC content** serving as a quality indicator.

Critical for research is the **bioavailability** of the polyphenols present. OPC are only partially absorbed in the gut; a large proportion reaches the colon unchanged, where they are metabolised by the **gut microbiota**. The resulting metabolites—such as phenolic acids—may exert systemic effects but are chemically distinct from the parent compounds. This complicates the attribution of effects to specific constituents. Additionally, studies often use **standardised extracts**, the composition of which does not always align with commercially available preparations. Measuring OPC or their metabolites in blood or urine is methodologically challenging and not uniformly standardised.

2. What the Studies Show in Detail

The pivotal human studies and key reviews — by application area, including population, duration, preparation, measured parameters, and results, as reported in the original publications. Numbers are included only where provided in the study.

Distribution of controlled human studies by application area — the numbers are not additive, as a single study may be assigned to multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Metabolism	24
Oxidative stress	23
Cardiovascular system	22
Inflammatory processes	22
Fatigue and stress	16

APPLICATION AREA	CONTROLLED STUDIES
Safety and tolerability	16
Gut and microbiome	10
Oncology	8

Inflammatory Processes

In a randomised, double-blind, placebo-controlled crossover study involving 32 patients with type 2 diabetes (16 men, 16 women; mean age 61.8 ± 6.36 years; BMI 30.2 ± 5.92 kg/m²; diabetes duration 5.9 ± 2.14 years), the effect of grape seed extract (600 mg/day) over 4 weeks was investigated. Endothelial function (photoplethysmography), oxidative stress (total antioxidant status [TAOS], glutathione redox ratio [GSH/GSSG]), inflammatory markers (high-sensitivity C-reactive protein [hsCRP], urinary albumin-to-creatinine ratio), insulin resistance (HOMA-IR), and metabolic parameters (fructosamine, lipid profile) were measured. Grape seed extract resulted in a significant reduction in hsCRP (inflammatory marker) and an improvement in TAOS (oxidative stress), whereas placebo produced no changes. However, the study was limited by its short duration and specific population, precluding conclusions about long-term effects or generalisability to other patient groups ¹.

A randomised, controlled crossover study involving 40 overweight or obese participants (BMI 25.3 ± 3.7 kg/m²; age 51 ± 11 years) examined the effect of grape seed extract (300 mg/day) combined with a calorie-restricted diet over 12 weeks. Anthropometric parameters, inflammatory markers (tumour necrosis factor-α [TNF-α], hsCRP), and neuropeptide Y were measured. Compared with the placebo group, significant reductions in body weight (-3.5 kg vs. -0.3 kg) and inflammatory markers were observed. The study suggests potential anti-inflammatory effects of the combination but does not allow conclusions about the isolated effect of grape seed extract on these parameters ⁹.

A randomised, double-blind pilot study involving 28 male smokers investigated the effect of monomeric and oligomeric flavanols from grape seeds (200 mg/day) over 8 weeks. Macro- and microvascular function, as well as biomarkers for oxidative stress (glutathione redox ratio [GSH/GSSG]), inflammation, and lipid metabolism, were measured. In participants with elevated baseline values, total cholesterol decreased by 5% and LDL cholesterol by 7%. The GSH/GSSG ratio increased by 22% (P < 0.05). Additionally, an ex vivo anti-inflammatory effect against added bacterial endotoxin was observed. The study was small and limited to smokers, so the results are not generalisable.

HYPOTHESIS The available studies suggest that grape seed extract (OPC) exerts anti-inflammatory effects via a reduction in pro-inflammatory markers (hsCRP, TNF-α) and an improvement in antioxidant status (TAOS, GSH/GSSG). Possible mechanisms include inhibition of NF-κB signalling pathways and modulation of endothelial function. However, long-term studies with larger, more heterogeneous populations and systematic investigation of the dose-response relationship are lacking. Furthermore, it remains unclear whether the observed effects are attributable to the specific proanthocyanidins or other accompanying compounds in the extract.

Systematic investigations into the long-term anti-inflammatory effects of grape seed extract in various populations are lacking, as are studies that elucidate the underlying molecular mechanisms in detail.

Overall Picture

OPC as an antioxidant: Mechanism vs. clinical evidence

Grape seed extract is often described in the literature as a **'POTENT ANTIOXIDANT'**, based on in vitro studies demonstrating the **free radical-scavenging function** of its constituent polyphenols. However, these findings **cannot be directly extrapolated to the human body**. In vivo, OPCs are scarcely absorbed in their original form but are instead metabolised by the gut microbiota into smaller metabolites. While these metabolites may also exert antioxidant effects, they reach significantly lower concentrations than in cell cultures. Moreover, the **antioxidant capacity** in blood plasma following OPC intake is often only transient and not clinically detectable.

Most human studies measure **INDIRECT MARKERS**, such as **total antioxidant capacity (TAC)** or **malondialdehyde (MDA)**, without establishing a causal link to disease progression. Even if these markers are altered in the short term, it remains unclear whether this has **clinically meaningful effects**. Critically, many studies **lack placebo controls** or **blinding**. The frequently cited assumption that OPCs 'reduce oxidative stress' is therefore **mechanistically plausible but not sufficiently supported by clinical evidence**.

3. How Robust Is the Research?

The research landscape on grape seed extract is **heavily focused on basic science**: The majority of studies involve cell cultures, animal models, or biochemical investigations. Controlled studies have been conducted in humans. The applications examined in controlled studies centre on **metabolic parameters** (e.g., lipid and glucose metabolism), **antioxidant markers**, **cardiovascular functions** (primarily blood pressure and vascular elasticity), and **inflammatory processes**. Less frequently investigated are **oncological questions**, **gut health**, or **fatigue syndromes**. The most cited controlled studies date from 2009–2020 and predominantly assessed **surrogate parameters** such as vascular function or oxidative stress markers.

The methodological quality of human studies is **heterogeneous**. Many studies are small, of short duration, and employ varying extract forms or dosages across the investigated areas. A central issue is the **lack of standardisation** in measurement methods: Antioxidant effects are often assessed via indirect markers such as **MDA** or **TEAC**, whose clinical relevance is debated. Furthermore, long-term studies with **hard endpoints** (e.g., cardiovascular events) are

lacking. The applicability of animal and cell culture studies is limited, as the **metabolism** of OPC differs in humans. Review articles frequently highlight **plausible biochemical mechanisms** without consistent confirmation in clinical studies.

4. Common Claims and the Supporting Data

STATEMENT	EVIDENCE BASE
Grape seed extract has been studied for lowering blood pressure; controlled results are inconsistent	Controlled studies demonstrate slightly altered vascular parameters (e.g., endothelial function) and modest reductions in blood pressure in prehypertensive c
OPC has been investigated for improving skin ageing; the evidence is limited	There are no controlled long-term studies in humans. Laboratory findings on collagen stabilisation or UV protection are not transferable to clinical applications.
Grape seed extract has been examined for anti-inflammatory effects; the results are inconsistent	In vitro and animal studies demonstrate inhibition of inflammatory markers (e.g., NF-κB, COX-2). Human studies typically measure surrogate parameters such
OPC has been studied for supporting cancer prevention; the evidence is insufficient	The available data are limited to cell culture and animal models . Controlled human studies are lacking. Observational studies show no consistent associations

5. The Most Robust Studies

Ranked by strength of evidence, not by prominence. The full evaluation includes many more studies; only the most reliable are listed here.

Controlled Human Studies

- ¹ Effects of grape seed extract in Type 2 diabetic subjects at high cardiovascular risk: a double blind randomized placebo controlled trial examining me (2009)
- ² Effect of grape seed extract on blood pressure in subjects with the metabolic syndrome (2009)
- ³ Effects of grape seed proanthocyanidin extract on menopausal symptoms, body composition, and cardiovascular parameters in middle-aged women: a randomi (2014)
- Two apples a day lower serum cholesterol and improve cardiometabolic biomarkers in mildly hypercholesterolemic adults: a randomized, controlled, cross (2020)
- ⁴ Effects of Grape Seed Proanthocyanidin Extract on Vascular Endothelial Function in Participants with Prehypertension: A Randomized, Double-Blind, Plac (2019)
- ⁵ Effect of polyphenol-rich grape seed extract on ambulatory blood pressure in subjects with pre- and stage I hypertension (2013)
- Pleiotropic benefits of monomeric and oligomeric flavanols on vascular health: A randomised controlled clinical pilot study (2011)
- Impact of cranberries on gut microbiota and cardiometabolic health: Proceedings of the Cranberry Health Research Conference 2015 (2016)
- Analysis of the response to two pharmacological protocols in patients with oral lichen planus: A randomised clinical trial (2023)
- Efficacy and safety of Gelsectan in diarrhoea-predominant irritable bowel syndrome: A randomised, crossover clinical trial (2019)

- ⁶ Double-blind, placebo-controlled, randomised phase II trial of IH636 grape seed proanthocyanidin extract (GSPE) in patients with radiation-induced breast oedema (2006)
- ⁷ Effect of oligomeric proanthocyanidin on antioxidant status and lung function in patients with chronic obstructive pulmonary disease (2018)
- ⁸ The effect of red grape seed extract on serum paraoxonase activity in patients with mild to moderate hyperlipidaemia (2016)
- ⁹ The effects of grape seed extract (*Vitis vinifera*) supplementation on inflammatory markers, neuropeptide Y, anthropometric measures, and appetite in obese individuals (2020)
- ¹⁰ The impact of grape seed extract treatment on blood pressure changes: A meta-analysis of 16 randomised controlled trials (2016)
- ¹¹ Effect of grape seed proanthocyanidin extract on hard exudates in patients with non-proliferative diabetic retinopathy (2019)
- Suppression of *Helicobacter pylori* infection by daily cranberry intake: A double-blind, randomised, placebo-controlled trial (2021)
- Pine bark (*Pinus* spp.) extract for treating chronic disorders (2020)
- ¹² Comparative effect of grape seed extract (*Vitis vinifera*) and ascorbic acid in oxidative stress induced by on-pump coronary artery bypass surgery (2017)
- ¹³ Grape Seed Extract Positively Modulates Blood Pressure and Perceived Stress: A Randomised, Double-Blind, Placebo-Controlled Study in Healthy Volunteers (2021)
- A double-blind, randomised clinical trial of dietary supplementation on cognitive and immune functioning in healthy older adults (2014)
- ¹⁴ Grape Seed Extract Supplementation and the Effects on Biomarkers of Oxidative Stress and Metabolic Profiles in Female Volleyball Players: A Randomised Study (2016)
- Potential benefits of 4 weeks of flavonoid supplementation on impairment of endothelial function after a high-fat meal (2011)
- ¹⁵ Two-year clinical evaluation of a proanthocyanidin-based primer in non-carcinous cervical lesions: A double-blind randomised clinical trial (2020)

6. Summary

Grape seed extract, rich in oligomeric proanthocyanidins (OPC), has been primarily investigated in controlled human studies for its effects on metabolic, cardiovascular, and inflammatory parameters. The most robust findings demonstrate short-term improvements in surrogate markers such as hsCRP (inflammation), TAOS (antioxidant status), or endothelial function, particularly in specific populations (e.g., individuals with type 2 diabetes, overweight individuals, smokers). Minor reductions in blood pressure and positive effects on lipid profiles have also been documented, though always in small, heterogeneous studies of short duration. The clinical relevance of these results remains unclear, as no studies with hard endpoints (e.g., cardiovascular events) or long-term data are available. Furthermore, the bioavailability of OPC is limited, as they are only partially absorbed in the gut and metabolised by the gut microbiota into metabolites whose systemic effects are not identical to those of the parent compounds.

HYPOTHESIS The observed effects of grape seed extract may stem from modulation of inflammatory and oxidative stress pathways, such as inhibition of the NF-κB signalling pathway or improvement of endothelial function. However, since most studies rely on surrogate markers, it remains unclear whether these mechanisms translate into clinically meaningful outcomes. Additionally, it is uncertain whether the effects are attributable to the OPC themselves or to accompanying substances in the extract. A saturation effect at higher doses is conceivable but has not been systematically investigated. **Hypothesis:** If the anti-inflammatory and antioxidant effects are confirmed in larger, longer-term studies, grape seed extract could play a supportive role in managing metabolic or cardiovascular risk factors—though only with consideration of its limited bioavailability and the need for standardised extracts.

To clarify the clinical relevance of grape seed extract, long-term studies involving large, heterogeneous populations and hard endpoints (e.g., cardiovascular events) would be required. Furthermore, systematic dose-response investigations should be conducted to identify optimal dosages and potential saturation effects. The role of the gut microbiota in the metabolism of OPC and the systemic effects of the resulting metabolites should be analysed in detail. Finally, studies on interactions with medications (e.g., anticoagulants) and long-term safety aspects are lacking. Only on this basis could it be determined whether grape seed extract shows effects beyond surrogate markers.

7. Unresolved Questions

- **Long-term effects:** There are no studies examining the use of grape seed extract over several years—neither regarding efficacy nor safety.
- **Dose-response relationship:** Unclear whether higher doses produce stronger effects or whether a **saturation effect** occurs. Standardised dosages are lacking.
- **Drug interactions:** Possible interactions with **anticoagulants** or **chemotherapeutic agents** have not been systematically investigated.

Frequently Asked Questions

Can grape seed extract be used for metabolic syndrome?

Controlled studies demonstrate **slight improvements** in surrogate parameters such as fasting glucose, insulin resistance, or lipid profiles. However, these effects are **not clinically relevant** and do not compare to those of established therapies. Furthermore, studies on **hard endpoints**, such as diabetes incidence or cardiovascular events, are lacking. The evidence does **not support a therapeutic recommendation**.

How reliable are antioxidant markers following OPC intake?

The measurement of antioxidant markers such as **TEAC** or **MDA** is **methodologically contentious**. Even if these markers are altered in the short term, it remains unclear whether this is **biologically meaningful**. Many studies use different assays, limiting comparability. Moreover, these markers **do not correlate with clinical outcomes**.

Are there differences between grape seed extract and other polyphenol sources?

Grape seed extract contains **high-molecular-weight proanthocyanidins**, which differ in bioavailability and metabolism from other polyphenol sources (e.g., green tea extract, resveratrol). However, direct comparative studies are lacking. The **gut microbiota** plays a central role in metabolism, meaning effects cannot be universally extrapolated. Standardised extracts are **not comparable to natural foods**.

Sources

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Kar P, Laight D, Rooprai HK, Shaw KM, Cummings M · 2009
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Taghizadeh M, Malekian E, Memarzadeh MR, Mohammadi AA, Asemi Z · 2016
- 15 Two-year clinical evaluation of a proanthocyanidins-based primer in non-carious cervical lesions: A double-blind randomized clinical trial
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International Health Research

Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
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