# Background literature data on the development of L-Blend technology: complex of wine and alfa-cyclodextrin (α-CD)

A comprehensive review of peer-reviewed literature examining the innovative combination of wine compounds with alpha-cyclodextrin for enhanced health benefits and sensory characteristics.

# Role of oxidative stress, chronic inflammation, and platelet aggregation

Natural products with antioxidant, anti-inflammatory, and anti-platelet aggregation activities play a crucial role in the prevention of cardiovascular diseases and other chronic disorders, as demonstrated by numerous peer-reviewed studies(1).

## Antioxidant Protection

Antioxidants scavenge reactive oxygen and nitrogen species, preventing oxidative stress, which is a key driver of atherosclerosis, diabetes, cancer, and neurodegenerative disease(2). Clinical trials confirm that natural antioxidants—such as those in soursop, beetroot, garlic, almond, green tea, and wine—offer protective effects against cardiovascular diseases via reduction in blood pressure, lipid improvement, and direct mitigation of vascular oxidative injury(3).

## Anti-Inflammatory Action

Chronic inflammation underlies not only cardiovascular disease but also diabetes, cancer, neurodegeneration, atherosclerosis, and autoimmune conditions(4). The search for safe anti-inflammatory agents in nature addresses the risks and side effects of long-term non-steroidal or steroidal drug use, as plant-derived compounds offer multi-targeted and low-toxicity approaches for managing chronic inflammation(5).

## Platelet Aggregation Control

Platelet aggregation is a critical factor in the formation of blood clots that lead to heart attacks and strokes; its inhibition is central to cardiovascular protection. Phytoceuticals could have a potential effect on the primary prevention of atherothrombotic events at an appropriate dosage, but not as a replacement for the current treatment(5).

# Comprehensive Meta-Analysis Evidence on Red Wine Benefits

Several large-scale meta-analyses demonstrated that moderate red wine consumption exerts cardio and vasoprotective effects through antioxidant, anti-inflammatory, and antiplatelet mechanisms.

| Study (Year) | Studies (n) | Key Findings | Mechanisms |
|---|---|---|---|
| Lucerón-Lucas-Torres et al. (2023) | 25 | Moderate red wine consumption reduces overall cardiovascular risk markers, including improved lipid profiles and reduced arterial stiffness. | Antioxidant, anti-inflammatory |
| Wojtowicz et al. (2023) | 18 | Consistent evidence for reduced incidence of coronary heart disease and stroke with light to moderate red wine intake. | Anti-inflammatory, anti-platelet |
| Zhong et al. (2022) | 32 | Reduces risk of type 2 diabetes and improves insulin sensitivity in non-diabetic individuals. | Antioxidant, metabolic regulation |
| Lucerón-Lucas-Torres et al. (2025) | 28 | Further confirms the beneficial effects on endothelial function and blood pressure regulation. | Antioxidant, vasodilation enhancement |
| Sheng et al. (2024) | 22 | Demonstrates a protective effect against certain cancers, specifically colon and prostate cancer, attributed to polyphenol content. | Antioxidant, anti-proliferative |
| Arranz et al. (2012) | 15 | Highlights the role of red wine in improving gut microbiota composition, contributing to overall health. | Prebiotic effect, anti-inflammatory |

This comprehensive overview underscores the consistent scientific support for moderate red wine consumption as a beneficial component of a healthy lifestyle, particularly regarding cardiovascular and metabolic health.

# No safe level of regular alcohol consumption

**Critical Health Warning:** Contemporary high-quality evidence challenges previous assumptions about alcohol safety.

Despite earlier meta-analytic claims of cardioprotective effects from red wine, contemporary high-quality evidence indicates that no level of alcohol consumption is safe:

01

## Bias Correction Reveals Truth

When common biases (e.g., sick-quitter, misclassification, residual confounding) are addressed, the apparent mortality benefit of moderate drinking disappears and even low intake is associated with increased cancer risk(12).

02

## WHO Official Position

The World Health Organization likewise concludes that any amount of alcohol is harmful and elevates cancer risk (WHO Europe, 2023).

03

## Large-Scale Evidence

A large pooled analysis of 599,912 current drinkers demonstrates rising all-cause and several cardiovascular mortality risks with increasing consumption and no threshold below which alcohol is risk-free, particularly for cancer(13).

# Pros and cons of non-alcoholic wine from the health benefits standpoint

## Potential Benefits

Non-alcoholic (dealcoholized) wine can deliver some cardiometabolic effects via grape polyphenols—e.g., a randomized crossover trial in high-risk men found that dealcoholized red wine lowered systolic/diastolic blood pressure and increased plasma nitric oxide, implicating the non-alcoholic fraction as active(11). Because it contains little or no ethanol, it also avoids the alcohol-associated increase in cancer risk observed even at low intakes.

### ⚠ The Matrix Effect Challenge

However, the wine "matrix effect" matters: ethanol in the hydroalcoholic matrix acts as a vehicle that can enhance the bioavailability of lipophilic phenols such as tyrosol, hydroxytyrosol, and resveratrol; underestimating this matrix/vehicle effect can yield misleading results when alcohol is removed or when single compounds are used instead of the phytocomplex(14).

### Clinical Study Limitations

Some clinical studies show muted effects of dealcoholized wine (e.g., underwhelming outcomes in post-menopausal women(15) and no improvement in flow-mediated dilation when compared with red wine(16)), and grape juice(17) proved an ineffective matrix for quercetin/resveratrol absorption unless ethanol was added.

### Processing Challenges

Beyond pharmacokinetics, dealcoholization methods themselves can diminish health-relevant constituents and sensory quality: membrane and thermal techniques frequently reduce desirable volatile esters and can alter phenolics(18).

### Sugar Addition Trade-offs

Producers also often add substantial sugar to restore body, with consumer acceptability in a fully dealcoholized Chardonnay reached only at ~40 g/L added sugar—an obvious nutritional trade-off(19).

# Rationale to use alfa-cyclodextrin to improve health and taste benefits

Using alpha-cyclodextrin (α-CD) in non-alcoholic wine formulations can substantially enhance both health and sensory qualities, based on recent peer-reviewed literature.

### Molecular Enhancement

α-CD forms inclusion complexes with wine compounds, improving stability and bioavailability of beneficial polyphenols.

### Sensory Improvement

Enhanced color stability, improved aroma profiles, and better mouthfeel characteristics in non-alcoholic wine products.

### Health Benefits

Additional health properties from α-CD itself, including prebiotic effects and metabolic benefits.

# α-CD Health Benefits and Sensory Improvements

## α-CD adds on to health benefits

### Prebiotic Effects

Alpha-cyclodextrin acts as a soluble dietary fiber that is not digested in the small intestine but is instead fermented by gut microbiota, leading to beneficial shifts in microbial composition and increased production of short-chain fatty acids(20).

### Glucose Control

α-CD has proven effects on reducing postprandial glucose excursions(21), the ability to bind dietary fats and inhibit their absorption(22),(23), and even decreasing atherosclerosis progression in animal models(24).

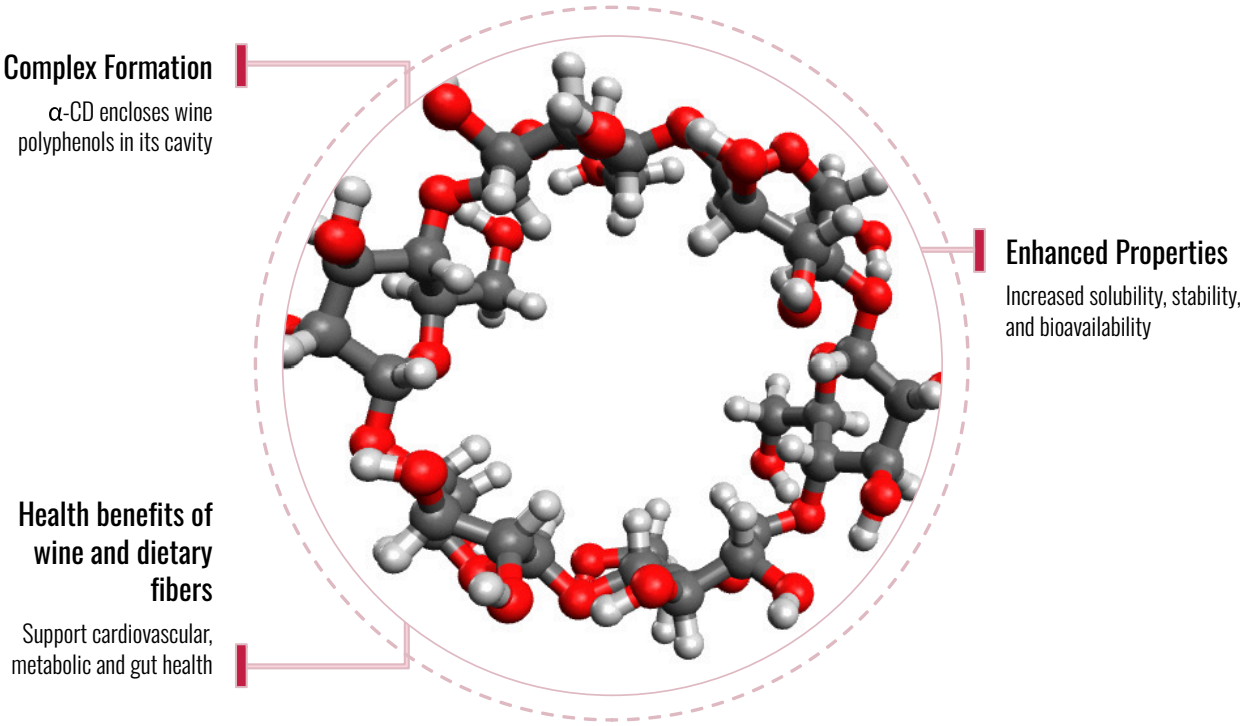
### Performance Enhancement

Recent research indicates that α-CD supplementation improves endurance exercise performance and reduces post-exercise fatigue, likely through increased availability of energy substrates and modulation of inflammatory responses post-exercise(25).

## Sensory and Stability Improvements

In winemaking, α-CD improves color stability, enhances floral and fruity aromas, and delivers a more harmonious and pleasant taste profile, as highlighted by sensory panel research. It achieves these effects through copigmentation: α-CD interacts with grape phenolics and anthocyanins, preserving vibrant color and reducing bitterness or astringency—common shortcomings of non-alcoholic wines. Studies show enhanced visual appeal and ester preservation, leading to richer, more authentic wine-like aromas and mouthfeel(26),(27).

# Hypothesis of α-CD – wine micronutrients complexes activity




## Hypothesis

We assume that α-CD forms inclusion complexes with polyphenols and volatile aroma compounds, improving their water solubility, stability, and bioavailability. We hypothesize that these complexes will enhance wine micronutrient activity towards key mechanisms supporting cardiovascular health: antioxidant effects, chronic inflammation, and thrombocyte aggregation.

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