World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 4
Page: 909-922

ETHNOPHARMACOLOGICAL AND PHARMACOLOGICAL INSIGHTS INTO VITIS VINIFERA (GRAPE): A PLANT WITH MULTIFUNCTIONAL THERAPEUTIC POTENTIAL

Chandrabhushan Singh*, Jitendra Kumar Malik, Gyan Singh, Vivek Gupta

Research Scholar, Faculty of Pharmacy, PK University, Thanra - 473665, Madhya Pradesh, India.

Article Received: 1 March 2026 | | Article Revised: 23 March 2026 | | Article Accepted: 12 April 2026

***Corresponding Author: Chandrabhushan Singh**
Research Scholar, Faculty of Pharmacy, PK University, Thanra - 473665, Madhya Pradesh, India.
DOI: https://doi.org/10.5281/zenodo.19593415

How to cite this Article: Chandrabhushan Singh, Jitendra Kumar Malik, Gyan Singh, Vivek Gupta (2026) ETHNOPHARMACOLOGICAL AND PHARMACOLOGICAL INSIGHTS INTO VITIS VINIFERA (GRAPE): A PLANT WITH MULTIFUNCTIONAL THERAPEUTIC POTENTIAL. World Journal of Pharmaceutical Science and Research, 5(4), 909-922.

ABSTRACT

Vitis vinifera (Vitaceae), commonly known as grape, represents a dynamic interface between traditional medicine, functional nutrition, and modern molecular pharmacology. Historically valued in Ayurveda, Unani, and Mediterranean healing systems as a cardiotonic and rejuvenating fruit, it has gained renewed scientific interest due to its dense and diverse polyphenolic composition. Grapes contain bioactive constituents including resveratrol, proanthocyanidins, catechins, quercetin, anthocyanins, tannins, and phenolic acids, which collectively contribute to broad-spectrum biological activities. Rather than functioning solely as radical scavengers, these phytochemicals act as modulators of cellular signaling networks. Experimental and clinical studies indicate that grape-derived compounds exert cardioprotective, antidiabetic, neuroprotective, hepatoprotective, anticancer, and anti-aging effects. Mechanistically, these benefits are mediated through activation of Nrf2-dependent antioxidant responses, inhibition of NF-κB-driven inflammation, regulation of mitochondrial integrity, modulation of PI3K/Akt and MAPK pathways, enhancement of endothelial nitric oxide bioavailability, and control of apoptosis-related proteins. Such multitarget interactions position Vitis vinifera within the framework of systems and network pharmacology, addressing interconnected oxidative, inflammatory, and metabolic disturbances underlying chronic diseases. Recent advances in formulation science, including standardized grape seed extracts, nanoencapsulated resveratrol, phytosome complexes, and functional nutraceutical platforms, have improved stability, absorption, and translational relevance. However, challenges persist in extract standardization, pharmacokinetic optimization, dose harmonization, and large-scale clinical validation. This review integrates ethnopharmacological insights with contemporary molecular evidence to highlight Vitis vinifera as a multifunctional, mechanism-driven botanical candidate with promising potential in integrative and preventive healthcare strategies worldwide, particularly for chronic inflammatory and metabolic disorders.

KEYWORDS: Vitis vinifera; Grapes; Resveratrol; Polyphenols; Antioxidant; Cardioprotective; Anticancer; Ethnopharmacology.

1. INTRODUCTION

Cardiovascular disorders, diabetes mellitus, neurodegenerative, cancer, and metabolic syndrome are some of the chronic diseases that pose a major health issue in the world and are the major causes of morbidity and death in the world. Accumulated evidence suggests that enduring oxidative stress, chronic low-grade inflammation, mitochondrial dysfunction and metabolic imbalance are the key processes involved in pathogenesis and progression of the disorders.[1]

Despite the development of the conventional pharmacotherapies, issues of safety in the long term, drug resistance, high costs of treatment, and failure to deliver total therapeutic effects have stimulated the use of the bioactive compounds of plants as complementary and preventive approaches.[2] In that way, the polyphenol-containing natural products have received considerable interest because of their ability to regulate the redox homeostasis, inflammatory cascades, cellular signaling, and gene expression patterns connected with the development of chronic diseases.[3]

One of the oldest and most popular fruit crops still studied today and used in traditional medical systems like Ayurveda, Unani or Mediterranean folk medicine is vitis vinifera, or grape as it is more commonly known.[4] The different parts of the plant such as fruits, seeds, skins and leaves are traditionally considered as a cardiotonic, hepatoprotective, nutritive and rejuvenating agent and have been used in treatment of digestive disturbances, inflammatory disorder, fatigue and age-related ailments.[5] Most of these ethnomedicinal assertions have now been confirmed by modern scientific studies and its extensive therapeutic properties have been attributed to a multifaceted phytochemical repertoire of resveratrol, proanthocyanidins, flavonoids, anthocyanins, tannins, and other phenolic molecules.[6]

The objective of this review is to critically and exhaustively assess the ethnopharmacological relevance, phytochemical composition, pharmacological actions, molecular mechanisms of action, formulation developments, safety issues, and the clinical prospects of Vitis vinifera thus bringing out its potential in the area of multifunctional therapeutic candidates in the modern integrative and preventive medicine.[7]

2. Literature Search Methodology

An in-depth and well-organized literature review was done to obtain pertinent scientific information about the ethnopharmacology, phytochemistry, pharmacological interactions, mechanism of action, formulations, and clinical significance of Vitis vinifera. Large electronic databases such as PubMed, ScienceDirect, SpringerLink, Scopus and Google Scholar were searched in order to provide a wide range of peer-reviewed articles.[8]

The keywords were chosen to include traditional and modern scientific approaches and contained both combinations of such terms like: Vitis vinifera, grape polyphenols, resveratrol, grape seed extract, antioxidant activity, cardioprotective activity, anticancer activity, antidiabetic activity, neuroprotective effect, ethnopharmacology. Search results were narrowed down and optimized using Boolean operators (AND, OR). Manual screening was also done to select relevant studies that were included in reference lists of the selected articles.[9]

The inclusion criteria included original in vitro studies, in vivo experimental studies, clinical trials, systematic reviews, and formulation-based research on grape-derived extracts or isolated phytoconstituents. Publications written in English and containing a clear experimental methodology and finding measures were deemed eligible. Articles that were not sufficiently experimentally validated, provided incomplete methodological information or were not scientifically based were filtered out to preserve reliability and scientific rigor of the review.[10]

The literature retrieved was systematically analyzed critically and sorted based on thematic relevancy and classified to give a structured and evidence-based summary of the existing evidence on Vitis vinifera.[11]

3. Botanical Description and Ethnomedicinal Uses

Vitis vinifera is a perennial, deciduous, woody climbing vine with a family of Vitaceae and is one of the oldest domesticated fruit crops in human civilization. Archeobotanical data indicate that it was cultivated more than 6,000-8,000 years ago, especially in the Mediterranean basin and Western Asia.[12] Nowadays, it has been widely cultivated in temperate and subtropical areas all over the world, such as Europe, Asia, North and South America, Africa and Australia, and has been a major source of global food, nutrition as well as wine production. The high adaptability to a variety of soils and various climatic parameters contributed to the creation of a vast number of cultivars that differ in morphological and phytochemical features.[13]

Vitis vinifera is botanically vigorous, and the stems are long and flexible and grow in the form of bifid tendrils that are located opposite the leaves. The leaves are alternate showing a large cordate, palmately lobed, and serrated leaf, with a characteristic reticulate venation. It has flowers that are small, greenish in color and inconspicuous, and they occur in compound panicles mostly self-pollinating.[14] The fruit is an actual berry which is clustered together in compact clusters, differing in size, shape and color- green and golden-yellow, red, purple and deep black- depending on the cultivar and anthocyanin content. Mesocarp fleshy is a good source of glucose, fructose, organic acids, vitamins and phenolic compounds and the seeds are especially good sources of proanthocyanidins and catechins, which are potent antioxidants and source of many therapeutic effects.[15]

Vitis vinifera has taken a leading role in Ayurveda, the Unani, Persian, Greek and the Mediterranean traditional medicine ethnomedically. The fruits have been taken as mild laxative, digestive stimulant and nutritive tonic in fighting weakness and tiredness. Grape preparations have been suggested to be used by traditional practitioners due to its cardiovascular strengthening properties, improvement of blood circulation, palpitations treatment, and conditions that resemble high blood pressure.[16] The plant was also considered as a hepatoprotective drug and taken in the treatment of jaundice and liver diseases. More so, the grape derivatives have been used in inflammatory disease, respiratory problems, and convalescence treatment. Grape pulp and seed preparations have been used in old cosmetology as a skin rejuvenator, wound healer aid, and visible aging delayer, and indeed, is well-trusted as an agent to help people look younger, healthier and more energetic.[17]

Table 1: Taxonomical Classification and Ethnomedicinal Uses of Vitis vinifera[18]

S. No.	Parameter	Description
1	Kingdom	Plantae
2	Subkingdom	Tracheobionta (Vascular plants)
3	Division	Magnoliophyta (Angiosperms)
4	Class	Magnoliopsida (Dicotyledons)
5	Subclass	Rosidae
6	Order	Vitales
7	Family	Vitaceae
8	Genus	Vitis
9	Species	Vitis vinifera L.
10	Common Names	Grape (English), Angoor (Hindi), Anab (Unani)
11	Plant Parts Used	Fruits, seeds, skin, leaves
12	Ethnomedicinal Uses	Laxative, cardiotonic, hepatoprotective, anti-inflammatory, rejuvenative tonic, skin revitalizer

4. Phytochemical Profile

It is a highly sophisticated and biologically active phytochemical composition, and this is the molecular framework of its broad-based therapeutic potential. These constituents are distributed qualitatively and quantitatively and depend on cultivar, geographic area, soil type, climatic and ripening status and method of extraction.[19] The levels of phytochemicals in different parts of the plants differ as grape seed, grape skin is the most concentrated source of phenolic compounds and the pulp is the source of the majority of nutritional components, including sugars, organic acids, and vitamins.[20]

Vitis vinifera is a plant with both primary metabolites that are important in the physiology of plants and secondary metabolites that cause pharmacological activity. The major products of metabolism are carbohydrates (glucose and fructose), organic acids (tartaric, malic, and citric acids), amino acids, and vitamins. Nevertheless, the therapeutic value of the plant is mainly explained by the wide range of secondary metabolites, especially phenolic compounds with antioxidant and signaling-modulatory action.[21]

4.1 Major Phytochemical Classes

The largest and most widely studied family of phytochemicals in Vitis vinifera are polyphenols, which are used as strong free radical scavengers and regulators of redox-responsive pathways.

The flavonoids, i.e., flavonols, flavan-3-ols and flavones, serve as contributing factors against inflammatory effects, vasoprotective and cardioprotective actions. The phytoalexin known as stilbenes and especially resveratrol in particular is made due to environmental stress and is also linked to anti-aging, anticancer and metabolic regulation. Strong anti-inflammatory and antioxidant effects are exhibited by anthocyanins which are the sources of red and purple hue in grape skin.[22] The proanthocyanidins and condensed tannin, abundant in seeds, have been identified to possess excellent antioxidant activity and endothelial protective power. Phenolic acids also add up to anti-inflammatory and antimicrobial effects.[23]

4.2 Key Bioactive Compounds

The most well-known bioactive substances that have been extracted out of Vitis vinifera are resveratrol, quercetin, catechin, epicatechin, gallic acid, and oligomeric proanthocyanidins. The application of resveratrol in the regulation of antioxidant defense mechanisms and regulation of inflammatory mediators has been widely researched. Both quercetin and catechins have high radical-scavenging and anti-inflammatory properties.[24] Epicatechin enhances vascular and metabolic functions whereas gallic acid provides antimicrobial and cytoprotective properties. Proanthocyanidins, which are mostly high in grape seeds, exhibit synergistic antioxidant, cardioprotective and tissue-protective activity.[25]

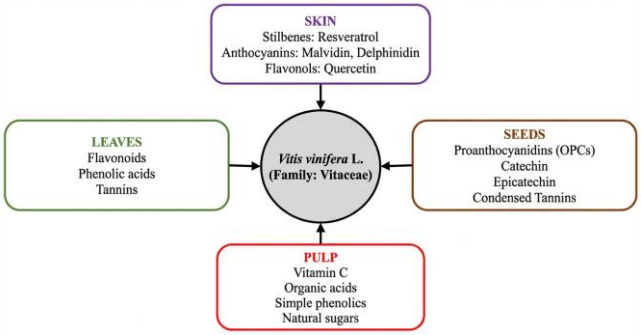

Figure 1: Distribution of Major Phytochemicals in Different Parts of Vitis vinifera.[26]

Table 2: Major Phytochemical Constituents of Vitis vinifera[27]

S. No.	Phytochemical Class	Major Compound	Plant Part Predominantly Found	Reported Biological Activity
1	Stilbene	Resveratrol	Skin	Antioxidant, cardioprotective, anticancer
2	Flavonol	Quercetin	Skin, leaves	Anti-inflammatory, vasoprotective
3	Flavan-3-ol	Catechin	Seeds	Antioxidant, cardioprotective
4	Flavan-3-ol	Epicatechin	Seeds	Endothelial protection, metabolic regulation
5	Proanthocyanidin	Oligomeric proanthocyanidins (OPCs)	Seeds	Strong antioxidant, vascular protection
6	Anthocyanin	Malvidin	Red/purple skin	Free radical scavenging, anti-aging
7	Anthocyanin	Delphinidin	Red/purple skin	Anti-inflammatory, anticancer
8	Phenolic acid	Gallic acid	Seeds, skin	Antimicrobial, antioxidant
9	Phenolic acid	Caffeic acid	Pulp, skin	Anti-inflammatory, antioxidant
10	Tannin	Condensed tannins	Seeds	Astringent, antioxidant
11	Vitamin	Vitamin C (Ascorbic acid)	Pulp	Immune support, antioxidant
12	Vitamin	Vitamin E (Tocopherol)	Seeds	Lipid peroxidation inhibition

5. Pharmacological Activities

The broad array of pharmacological actions that Vitis vinifera shows can simply be explained by the high levels of polyphenols, flavonoids, stilbenes, and proanthocyanidins. These bioactive compounds communicate with a number of molecular targets and signaling pathways, which allow the plant to display protective actions on a variety of organ systems. Its multifunctional therapeutic profile is supported by both in vitro and in vivo studies in addition to the emerging clinical evidence.[28]

5.1 Antioxidant Activity

Vitis vinifera is widely recognized for its potent antioxidant properties. The antioxidant potential of grape extracts and isolated compounds has been extensively evaluated using standard in vitro assays such as DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2-azinobis-3-ethylbenzothiazoline-6-sulfonic acid), and FRAP (ferric reducing antioxidant power).[29] These assays consistently demonstrate high radical scavenging capacity, particularly in seed and skin extracts rich in proanthocyanidins and resveratrol. In biological systems, grape polyphenols reduce lipid peroxidation, enhance endogenous antioxidant enzyme activity (such as superoxide dismutase and catalase), and maintain redox homeostasis, thereby protecting cells from oxidative damage.[30]

5.2 Cardioprotective Activity

Phytochemicals present in the grape have great cardioprotective activity in various ways. Research has indicated that there is enhancement of lipid profiles such as a decrease in total cholesterol levels, low-density lipoprotein (LDL), and triglyceride levels and an increase in the amount of high-density lipoprotein (HDL). One of the most important protective mechanisms is inhibition of LDL oxidation since oxidized LDL is at the center of the atherosclerosis development. Also, the grape polyphenols are known to improve the endothelial functionality through providing better bioavailability of nitric oxide and lessening vascular inflammation, which contributes to better vascular tone and circulation.[31]

5.3 Anticancer Activity

Vitis vinifera has shown promising anticancer properties in numerous experimental cancer systems. Grape polyphenols, especially resveratrol and quercetin, are reported to cause apoptosis by turning on caspases and by regulating pro- and anti-apoptotic proteins. They also induce cell cycle arrest at particular stages and thus prevent unregulated cell proliferation. Also, anti-angiogenic effects have been observed, which restricts the vascularization and metastasis of tumors. The mediating activities include the modulation of signaling pathways, including NF-KB, PI3K/Akt and MAPK.[32]

5.4 Antidiabetic Activity

Antidiabetic properties of Vitis vinifera are associated with the fact that this plant can help in enhancing insulin sensitivity and glucose metabolism. Experimental studies show a decrease in the level of fasting blood glucose, and an increase in glucose tolerance. The effect of grape polyphenols on carbohydrate metabolism is based on the increase in insulin signaling pathways, the decrease in oxidative stress in pancreatic 8-cells, and the regulation of several important enzymes that regulate the process of glucose homeostasis. All of these measures will lead to improved glycemic regulation.[33]

5.5 Neuroprotective Activity

Grape phytochemicals are neuroprotective in neurodegenerative disease and oxidative neuronal injury models. Grape-derived compounds prevent the oxidative damage of neurons and neuronal apoptosis by scavenging reactive oxygen species and inhibiting neuroinflammatory mediators. Resveratrol and its analogs have been reported to regulate signaling pathways that control neuronal survival, synaptic plasticity and mitochondrial activity which sustain cognitive health.[34]

5.6 Hepatoprotective Activity

Vitis vinifera has hepatoprotective properties against chemically induced liver toxicity and oxidative stress. Grape extracts lower high liver enzymes, lower lipid peroxidation, and raise antioxidant defense systems in the hepatic tissue. The prevention of toxin-induced liver damage is linked to hepatocyte membrane stabilization and inhibition of inflammatory reactions. Such results indicate its possible use as a liver health supportive agent.[35]

Table 3: Summary of Pharmacological Activities of Vitis vinifera.[36]

S. No.	Pharmacological Activity	Extract/Compound	Experimental Model	Key Findings
1	Antioxidant	Grape seed extract	DPPH, ABTS, FRAP assays	Strong free radical scavenging activity
2	Antioxidant	Proanthocyanidins	In vivo oxidative stress models	Reduced lipid peroxidation
3	Cardioprotective	Resveratrol	Animal models	Improved lipid profile and reduced LDL
4	Cardioprotective	Polyphenol-rich extract	Atherosclerosis models	Inhibited LDL oxidation and plaque formation
5	Anticancer	Resveratrol	Cancer cell lines	Induced apoptosis and caspase activation
6	Anticancer	Grape skin extract	Tumor models	Cell cycle arrest and anti-angiogenic effects
7	Antidiabetic	Polyphenol extract	Diabetic animal models	Reduced fasting blood glucose
8	Antidiabetic	Catechin/Epicatechin	Insulin resistance models	Improved insulin sensitivity

9	Neuroprotective	Resveratrol	Neurotoxicity models	Protected neurons from oxidative damage
10	Neuroprotective	Grape seed extract	Cognitive impairment models	Reduced neuroinflammation
11	Hepatoprotective	Grape extract	Hepatotoxicity models	Decreased liver enzyme levels
12	Anti-inflammatory	Quercetin-rich extract	Inflammatory models	Suppressed pro-inflammatory cytokines

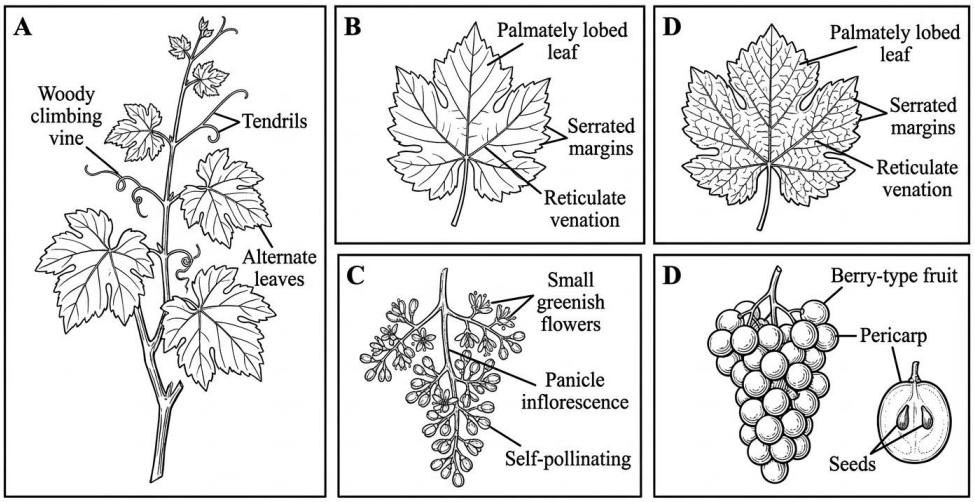

Figure 2: Botanical Morphology of Vitis vinifera.[37]

6. Mechanisms of Action

Vitis vinifera has a wide pharmacological spectrum, which is mediated by a complex of interconnected molecular processes that address oxidative stress, inflammation, apoptosis, and vascular dysfunction. The bioactive constituents of the plant include: resveratrol, proanthocyanidins, quercetin, catechins, anthocyanins, which are not just antioxidants, but intracellular signaling cascade modulators and transcriptional regulators. The therapeutic flexibility of this interaction is based on its multitarget interaction.[38]

One of the key processes is the scavenging of reactive oxygen species (ROS), superoxide anions, hydroxyl radicals, and peroxynitrite. Overproduction of ROS causes cellular membranes, proteins, and DNA damage that enhances the development of the disease. Grape polyphenols directly counteract these reactive species and disrupt the chains of lipid peroxidation, consequently providing the protection against the cellular structures and maintaining the redox balance.[39]

In addition to direct antioxidant effect, Vitis vinifera suppresses nuclear factor kappa B (NF-KB) signaling an important mediator of inflammation. Inhibition of the NF-ckB activation blocks the pro-inflammatory genes and mediators' transcription, and decreases the responses to chronic inflammatory events and conditions. This is along with a modulation of inflammatory cytokines like tumor necrosis factor-alpha (TNF- 6) and interleukin-6 (IL- 6), which have a central role to play in metabolic and cardiovascular disorders.[40]

The other important mechanism is the activation of endogenous antioxidant defense systems. Grape compounds stimulate the activity and expression of antioxidant enzymes such as superoxide dismutase (SOD), catalase and glutathione peroxidase which enhance intrinsic cellular resistance to oxidative damage.[41]

Apoptotic pathways can also be regulated, which also plays a part in the therapeutic effect. The constituents of vitis vinifera affect mitochondrial integrity and alter the expression of the Bcl-2 family protein and caspases and, thus, regulate the programmed cell death in cancerous and damaged cells. Also, endothelial nitric oxide bioavailability can be improved, which leads to relaxation of the vascular system, inhibits platelet formation, and has cardiovascular protective effects, including the improvement of endothelial activity and vascular inflammation.[42]

7. Formulation Approaches and Bioavailability Enhancement

Therapeutic potential of Vitis vinifera has in turn prompted the formulation of different formulations strategies to enhance stability, absorption and clinical effects of its bioactive components. Grape-derived phytochemicals have demonstrated good pharmacological effects in experimental animal models and yet, in most instances, their clinical realization is hindered by low solubility in aqueous solution, rapid clearance and low bioavailability in the bloodstream especially resveratrol.[43]

Dietary supplements are being widely promoted in the market as conventional dosage forms based on its standardized levels of proanthocyanidins and antioxidant compounds like grape seed extract in capsule forms. The uses of these formulations are usually associated with cardiovascular support, anti-aging effects and metabolic health. On the same note, resveratrol pills, tablets, and capsules have been formulated to provide amounts of concentrated doses of the stilbene compound; nevertheless, the metabolism by the hepatic system and poor oral bioavailability decrease its systemic exposure.[44]

In order to eliminate such shortcomings, sophisticated methods of drug delivery have been sought. Nanoemulsions improve ability to be absorbed through the gastrointestinal tract and solubility by minimizing particle size and maximizing surface area increasing bioavailability. We can find liposomal formulations that entrap bioactive compounds in the phospholipid bilayers, which inhibit the degradation of bioactive compounds and enhance targeted delivery. These types of nanocarrier-mediated strategies have revealed better pharmacokinetics and therapeutic assistances in preclinical trials.[45]

Also, the use of grape polyphenols in the functional foods and nutraceutical products, including fortified drinks, yogurts, and dietary supplements, can be regarded as a potential approach towards preventive healthcare. Although these advances have been made, there are issues that remain such as low oral bioavailability of resveratrol, short half-life phase II metabolism, inconsistent extraction standardization, and the necessity of optimal dosing regimen with clinical validation on a large scale.[46]

8. Safety Profile and Toxicological Aspects

The consumption of vitis vinifera and its products in the diet or in a standardized supply within recommended doses are normally considered to be safe (GRAS). Grapes and grape preparations have been used longer without much toxicity being reported and preclinical toxicology data have shown that grape seed extracts and polyphenol-containing formulations have a broad margin of safety. Experimental models of acute and sub-chronic toxicity usually indicate the absence of significant adverse effects in therapeutic dosage levels.[47]

Nevertheless, there are slight adverse effects that are experienced at an increased dosage of supplements especially gastroinstestinal distress which manifests as nausea, bloating, diarrhea or a headache. These are normally short-lasting

and dose-related. High doses of resveratrol supplementation have sometimes been linked with slight digestive symptoms because of the high metabolism and poor absorption in the system.[48]

The possibility of drug-herb interactions is another fact that should be taken into account. The anticoagulant and antiplatelet effects of grape polyphenols, particularly resveratrol, are not very strong, and may be beneficial to the action of blood-thinning drugs like warfarin, aspirin, or other anticoagulants. Precaution is thus recommended in those who are on antithrombotic therapy or are having bleeding disorders. Also, there have been recommendations on the modulation of cytochrome P450 enzymes, which implies that prescription drugs may interact.[49]

In spite of positive safety data, clinical safety of high dose over the long term is not adequately defined. Randomized controlled trials of large scale are required to determine optimal dosing schedules, long-term tolerability, and safety profile in different patient groups such as older individuals and chronic disease patients.[50]

9. Future Perspectives

The growing scientific concern of Vitis vinifera is an indication of the necessity of strategic developments that will ensure that Vitis vinifera is no longer used traditionally or experimentally to validate its efficacy, but rather used as an evidence-based therapeutic agent. Despite the fact that there is substantial preclinical evidence of its multifunctional therapeutic potential, there are research gaps that need to be filled to ensure that the translational reliability and regulatory acceptance is enhanced.[51]

Standardization of extracts is one of the main priorities. Diversity of cultivar type, geographical origin, harvesting conditions and extraction methods play a greater role in determining phytochemical composition. Standard preparation procedures that entail specific concentrations of the major bioactive compounds will contribute to reproducibility, consistency of batch to batch, and predictability of treatment.[52]

The other important direction is identification and validation of bioactive markers. Although resveratrol and proanthocyanidin are commonly researched, there is a need to conduct extensive profiling of synergistic phytoconstituents and pharmacodynamic interplay. Standardization through biomarker may also be used to facilitate regulatory approval and optimization of clinical dose. Another area that is likely to be transformative is the progress that has been made on the systems of delivery in enhancing bioavailability and treatment efficiency. Nanocarriers, phytosome complexes, sustained-release preparations, and targeted delivery systems could help address shortcomings related with solubility, rapid metabolism, and unfortunate absorption systemically.[53]

Besides, to validate efficacy in various disease conditions and populations, large-scale, randomized, placebo-controlled clinical trials will be required. The systemic assessment of long-term safety data, dose-response, and pharmacokinetic harmonization needs to be performed. Lastly, customized nutraceutical applications, along with the assistance of genomic, metabolomic, and lifestyle profiling, can allow the use of Vitis vinifera in prevention and adjunctive healthcare to be precise.[54]

10. CONCLUSION

Vitis vinifera stands at the intersection of tradition, nutrition, and molecular therapeutics, embodying the evolving paradigm of food as medicine. From its longstanding ethnomedicinal applications to its scientifically validated pharmacological profile, Vitis vinifera has emerged as a multifunctional botanical with systemic therapeutic relevance.

Its dense polyphenolic matrix—encompassing resveratrol, proanthocyanidins, flavonoids, anthocyanins, and phenolic acids—functions beyond simple antioxidant activity, orchestrating complex cellular signaling networks that regulate oxidative stress, inflammation, apoptosis, metabolic homeostasis, and endothelial function.

The breadth of evidence supporting its antioxidant, cardioprotective, anticancer, antidiabetic, neuroprotective, and hepatoprotective activities positions Vitis vinifera as a prototype of network pharmacology in plant-based medicine. Unlike single-target synthetic drugs, grape-derived phytochemicals act synergistically across interconnected biological pathways, offering a systems-level approach to chronic disease prevention and management. Emerging formulation innovations, including standardized extracts and advanced delivery platforms, further enhance its translational and clinical applicability. Nevertheless, to fully unlock its therapeutic promise, future efforts must prioritize extract standardization, bioavailability optimization, mechanistic precision, and robust, large-scale clinical validation.

Integrating phytochemical research with omics technologies and personalized healthcare strategies may redefine its role in preventive and integrative medicine.

In summary, Vitis vinifera represents more than a dietary fruit—it is a scientifically compelling, mechanism-driven botanical candidate with significant potential to contribute to next-generation, evidence-based therapeutic strategies worldwide.

Acknowledgement: Nil

Conflict of Interest: Nil

REFERENCES

1. Balakumar P, Maung-U K, Jagadeesh G. Prevalence and prevention of cardiovascular disease and diabetes mellitus. Pharmacological research, 2016 Nov 1; 113: 600-9.
2. Baryakova TH, Pogostin BH, Langer R, McHugh KJ. Overcoming barriers to patient adherence: the case for developing innovative drug delivery systems. Nature reviews Drug discovery, 2023 May; 22(5): 387-409.
3. Rudrapal M, Khairnar SJ, Khan J, Dukhyil AB, Ansari MA, Alomary MN, Alshabrmi FM, Palai S, Deb PK, Devi R. Dietary polyphenols and their role in oxidative stress-induced human diseases: Insights into protective effects, antioxidant potentials and mechanism (s) of action. Frontiers in pharmacology, 2022 Feb 14; 13: 806470.
4. Urbi Z, Hossain MS, Rahman KH, Zayed TM. Grape: A medicinal fruit species in the holy Qur'an and its ethnomedicinal importance. World Applied Sciences Journal, 2014; 30(3): 253-65.
5. Shah SM, Akram M, Riaz M, Munir N, Rasool G. Cardioprotective potential of plant-derived molecules: a scientific and medicinal approach. Dose-response, 2019 May 24; 17(2): 1559325819852243.
6. Pattaluchetty P, Soundaryashree NR, Chandan RS. Phytochemicals as Therapeutic Agents: A Comprehensive Review on Their Role in Disease Prevention and Health Promotion. Biopress Journal of Computational Life Sciences (BJCLS), 2025 Aug 31; 1(05): 23-43.
7. Pareek A, Pant M, Gupta MM, Kashania P, Ratan Y, Jain V, Pareek A, Chuturgoon AA. Moringa oleifera: an updated comprehensive review of its pharmacological activities, ethnomedicinal, phytopharmaceutical formulation, clinical, phytochemical, and toxicological aspects. International journal of molecular sciences, 2023 Jan 20; 24(3): 2098.

8. Bagul VS, Bafna PS, Patil DM, Mutha RE. Classification of Crude Drugs of Natural Origin. Pharmacognosy and Phytochemistry: Principles, Techniques, and Clinical Applications, 2025 Mar 13: 17-44.
9. Nassiri-Asl M, Hosseinzadeh H. Review of the pharmacological effects of Vitis vinifera (Grape) and its bioactive constituents: an update. Phytotherapy research, 2016 Sep; 30(9): 1392-403.
10. Smith JD. Single-case experimental designs: a systematic review of published research and current standards. Psychological methods, 2012 Dec; 17(4): 510.
11. Xiong W, Risse J, Berke L, Zhao T, Van de Geest H, Oplaat C, Busscher M, Ferreira de Carvalho J, Van Der Meer IM, Verhoeven KJ, Schranz ME. Phylogenomic analysis provides insights into MADS-box and TCP gene diversification and floral development of the Asteraceae, supported by de novo genome and transcriptome sequences from dandelion (Taraxacum officinale). Frontiers in plant science, 2023 Jun 21; 14: 1198909.
12. Bates J. Vitis sp., Vitaceae and viticulture in the Indus Civilization, South Asia ca. 3200–1500 BC: a critical review. Vegetation History and Archaeobotany, 2022 Apr; 31(2): 205-20.
13. Mathew I, Shimelis H. Genetic analyses of root traits: Implications for environmental adaptation and new variety development: A review. Plant Breeding, 2022 Dec; 141(6): 695-718.
14. Vasconcelos MC, Greven M, Winefield CS, Trought MC, Raw V. The flowering process of Vitis vinifera: a review. American journal of enology and viticulture, 2009 Dec 1; 60(4): 411-34.
15. Shahidi F, Varatharajan V, Oh WY, Peng HJ. Phenolic compounds in agri-food by-products, their bioavailability and health effects. Food Bioact, 2019 Mar 31; 5(1): 57-119.
16. Saeed M, Ali D, Anees A. Grapes as a medicine in the light of Prophetic & Unani medicine: A comprehensive review. Int J Unani Integr Med, 2024; 8: 35-8.
17. Al-Asmari AK, Al-Elaiwi AM, Athar MT, Tariq M, Al Eid A, Al-Asmary SM. A review of hepatoprotective plants used in Saudi traditional medicine. Evidence-Based Complementary and Alternative Medicine, 2014; 2014(1): 890842.
18. Gavídia Valencia JG, Venegas Casanova EA, Hajdu Z, Gonzáles Pósito GS, Sopán Benaut CN, Aro Díaz RJ, Castro Gálvez KA, Amaya Lau LO, Cerna Reyes FT, Rengifo Penadillos RA, Rubio López FR. A recent review on the traditional use, phytochemical constituents, and pharmacological activity of Vitis vinifera L.(Vitaceae). JOURNAL OF APPLIED BIOLOGY AND BIOTECHNOLOGY, 2025; 13(6): 5-20.
19. Bandaranayake WM. Quality control, screening, toxicity, and regulation of herbal drugs. Modern phytomedicine: turning medicinal plants into drugs, 2006 Sep 20: 25-57.
20. Radulescu C, Buruleanu LC, Nicolescu CM, Olteanu RL, Bumbac M, Holban GC, Simal-Gandara J. Phytochemical profiles, antioxidant and antibacterial activities of grape (Vitis vinifera L.) seeds and skin from organic and conventional vineyards. Plants, 2020 Oct 30; 9(11): 1470.
21. Goufo P, Singh RK, Cortez I. A reference list of phenolic compounds (including stilbenes) in grapevine (Vitis vinifera L.) roots, woods, canes, stems, and leaves. Antioxidants, 2020 May 8; 9(5): 398.
22. Ciumărnean L, Milaciu MV, Runcan O, Vesa ȘC, Răchișan AL, Negrean V, Perné MG, Donca VI, Alexescu TG, Para I, Dogaru G. The effects of flavonoids in cardiovascular diseases. Molecules, 2020 Sep 21; 25(18): 4320.
23. Oluwole O, Fernando WB, Lumanlan J, Ademuyiwa O, Jayasena V. Role of phenolic acid, tannins, stilbenes, lignans and flavonoids in human health–a review. International Journal of Food Science and Technology, 2022 Oct; 57(10): 6326-35.

24. Simonetti G, Brasili E, Pasqua G. Antifungal activity of phenolic and polyphenolic compounds from different matrices of Vitis vinifera L. against human pathogens. Molecules, 2020 Aug 17; 25(16): 3748.
25. Nawrot-Hadzik I, Matkowski A, Hadzik J, Dobrowolska-Czopor B, Olchowy C, Dominiak M, Kubasiewicz-Ross P. Proanthocyanidins and flavan-3-ols in the prevention and treatment of periodontitis—Antibacterial effects. Nutrients, 2021 Jan 7; 13(1): 165.
26. Moldovan ML, Carpa R, Fizeșan I, Vlase L, Bogdan C, Iurian SM, Benedec D, Pop A. Phytochemical profile and biological activities of tendrils and leaves extracts from a variety of Vitis vinifera L. Antioxidants, 2020 Apr 30; 9(5): 373.
27. Dwibedi V, Saxena S. Diversity and phylogeny of resveratrol-producing culturable endophytic fungi from Vitis species in India. 3 Biotech, 2019 May; 9(5): 182.
28. Flamini R, Mattivi F, De Rosso M, Arapitsas P, Bavaresco L. Advanced knowledge of three important classes of grape phenolics: anthocyanins, stilbenes and flavonols. International journal of molecular sciences, 2013 Sep 27; 14(10): 19651-69.
29. Sy B, Krisa S, Richard T, Courtois A. Resveratrol, ε-viniferin, and vitisin B from vine: Comparison of their in vitro antioxidant activities and study of their interactions. Molecules, 2023 Nov 10; 28(22): 7521.
30. Bagchi D, Bagchi M, Stohs SJ, Das DK, Ray SD, Kuszynski CA, Joshi SS, Pruess HG. Free radicals and grape seed proanthocyanidin extract: importance in human health and disease prevention. Toxicology, 2000 Aug 7; 148(2-3): 187-97.
31. Pagliaro B, Santolamazza C, Simonelli F, Rubattu S. Phytochemical compounds and protection from cardiovascular diseases: a state of the art. BioMed Research International, 2015; 2015(1): 918069.
32. Bose S, Chatterjee S, Mazumder S, Ghosh S, Dhar AK, Singh N. Investigating Preventive and Therapeutic Anti-cancer Potential of Grapes and their Bioactive Constituents. The Natural Products Journal., 2025 Oct; 15(7): E22103155323035.
33. Orhan N, Aslan M, Orhan DD, Ergun F, Yeşilada E. In-vivo assessment of antidiabetic and antioxidant activities of grapevine leaves (Vitis vinifera) in diabetic rats. Journal of ethnopharmacology, 2006 Nov 24; 108(2): 280-6.
34. Herman F, Westfall S, Brathwaite J, Pasinetti GM. Suppression of presymptomatic oxidative stress and inflammation in neurodegeneration by grape-derived polyphenols. Frontiers in pharmacology, 2018 Aug 28; 9: 867.
35. Tabeshpour J, Mehri S, Shaebani Behbahani F, Hosseinzadeh H. Protective effects of Vitis vinifera (grapes) and one of its biologically active constituents, resveratrol, against natural and chemical toxicities: A comprehensive review. Phytotherapy research, 2018 Nov; 32(11): 2164-90.
36. Nassiri-Asl M, Hosseinzadeh H. Review of the pharmacological effects of Vitis vinifera (Grape) and its bioactive compounds. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives, 2009 Sep; 23(9): 1197-204.
37. Najmaddin C, Hussin K, Maideen H. Comparative study on the anatomy and palynology of the three variety of Vitis vinifera varity (family Vitaceae). African Journal of Biotechnology, 2011; 10(74): 16849-53.
38. Mohammed SA, Saad HM, Esmail KA, Eliwa D, Rohiem AH, Awad AA, El-Adawy SA, Amer SS, Abdelhiee EY. Protection by Vitis vinifera L. Against Cisplatin-Induced Testicular Injury: Oxidative Stress, Inflammation, and Ferroptosis. Pharmaceuticals, 2026 Jan 20; 19(1): 178.

39. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Valko M. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Archives of toxicology, 2023 Oct; 97(10): 2499-574.
40. Dinh W, Füth R, Nickl W, Krahn T, Ellinghaus P, Scheffold T, Bansemir L, Bufe A, Barroso MC, Lankisch M. Elevated plasma levels of TNF-alpha and interleukin-6 in patients with diastolic dysfunction and glucose metabolism disorders. Cardiovascular Diabetology, 2009 Nov 12; 8(1): 58.
41. Masella R, Di Benedetto R, Varì R, Filesi C, Giovannini C. Novel mechanisms of natural antioxidant compounds in biological systems: involvement of glutathione and glutathione-related enzymes. The Journal of nutritional biochemistry, 2005 Oct 1; 16(10): 577-86.
42. Mastellone G, Gennaro G, Marengo A, Sgorbini B, Larrea V, Cirrincione S, Lamberti C, Hernando I, Gai F, Rubiolo P, Cagliero C. Evaluating the effect of in vitro digestion on the total polyphenol content of Vitis vinifera L. by-products. InLibro degli abstract, 2023; (pp. 154-154).
43. Bogdan C, Pop A, Iurian SM, Benedec D, Moldovan ML. Research advances in the use of bioactive compounds from vitis vinifera by-products in oral care. Antioxidants, 2020 Jun 8; 9(6): 502.
44. Lyu W, Rodriguez D, Ferruzzi MG, Pasinetti GM, Murrough JW, Simon JE, Wu Q. Chemical, manufacturing, and standardization controls of grape polyphenol dietary supplements in support of a clinical study: mass uniformity, polyphenol dosage, and profiles. Frontiers in Nutrition, 2021 Dec 16; 8: 780226.
45. Salvia-Trujillo L, Martín-Belloso O, McClements DJ. Excipient nanoemulsions for improving oral bioavailability of bioactives. Nanomaterials, 2016 Jan 14; 6(1): 17.
46. Kurćubić VS, Stanišić N, Stajić SB, Dmitrić M, Živković S, Kurćubić LV, Živković V, Jakovljević V, Mašković PZ, Mašković J. Valorizing grape pomace: A review of applications, nutritional benefits, and potential in functional food development. Foods, 2024 Dec 23; 13(24): 4169.
47. Downs J, Zoltowska A, Hackney T, Gardner DS, Ashmore A, Brennan ML. Scoping review exploring the evidence base on Vitis vinifera toxicity in dogs after ingestion: Clinical effects, treatments and types of V. vinifera. Veterinary Record, 2024 Oct 5; 195(7): no-.
48. Ronis MJ, Pedersen KB, Watt J. Adverse effects of nutraceuticals and dietary supplements. Annual review of pharmacology and toxicology, 2018 Jan 6; 58: 583-601.
49. Talasaz AH, McGonagle B, HajiQasemi M, Ghelichkhan ZA, Sadeghipour P, Rashedi S, Cuker A, Lech T, Goldhaber SZ, Jennings DL, Piazza G. Pharmacokinetic and pharmacodynamic interactions between food or herbal products and oral anticoagulants: evidence review, practical recommendations, and knowledge gaps. InSeminars in Thrombosis and Hemostasis, 2024 Sep 17. Thieme Medical Publishers, Inc..
50. Yuan Y, Zhou H, Liu S. Statistical and practical considerations in planning and conduct of dose-optimization trials. Clinical Trials, 2024 Jun; 21(3): 273-86.
51. Lippi P, Eichmeier A, Puccioni S, Mattii GB, Cataldo E. Essential Oils Usage on Vitis vinifera L., from the Vineyard to Post-Harvest: Advantages, Limitations, and Future Perspectives. Phyton-International Journal of Experimental Botany, 2025: 0-.
52. Manganaris GA, Goulas V, Mellidou I, Drogoudi P. Antioxidant phytochemicals in fresh produce: exploitation of genotype variation and advancements in analytical protocols. Frontiers in Chemistry, 2018 Feb 6; 5: 95.

53. Mubeen B, Hasnain A, Atif S, Hakim F, Sheharyar S, Hassan M, Iqbal M, Moustafa M, Alshaharni M, Duan M. Phytochemicals as multi-target therapeutic agents for oxidative stress-driven pathologies: mechanisms, synergies, and clinical prospects. Phyton, 2025; 94(7): 1941.
54. Krueger JG, Ferris LK, Menter A, Wagner F, White A, Visvanathan S, Lalovic B, Aslanyan S, Wang EE, Hall D, Solinger A. Anti–IL-23A mAb BI 655066 for treatment of moderate-to-severe psoriasis: Safety, efficacy, pharmacokinetics, and biomarker results of a single-rising-dose, randomized, double-blind, placebo-controlled trial. Journal of Allergy and Clinical Immunology, 2015 Jul 1; 136(1): 116-24.