

**EVALUATION OF GRAPES STEM-DERIVED PHYTOCHEMICALS FOR
PHARMACOLOGICAL EFFICACY AND COSMECEUTICAL FORMULATION****Sarfaraj S. K.*, Anisha Shakil Akhter, Sukesh Kumar Mehta, Himanshu Singh, Dipanshu Kumar, Ms. Soma Ghosh**

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ABSTRACT

While the phytochemical profile of *Vitis vinifera* is well documented, the stems produced as waste product during wine and juice processing are relatively under-utilised despite being a rich source of phenols. In this work, extracts collected from grape stems were evaluated for their chemical profile and biological properties with a special emphasis on antioxidant, antimicrobial, anti-inflammatory and tyrosinase-inhibitory action. The extract was rich in polyphenols, comprising tannins, flavonoids phenolic acids and stilbenes such as resveratrol that are responsible for its prominent free radical scavenging potential. Biological studies demonstrated (anti)bacterial activity to skin-associated bacteria and facilitated wound healing, indicating potential dermatological use. As a result of these results, a topical formulation containing standardized grape stem extract was developed and evaluated with respect to its physicochemical stability, safety profile, and in vivo activity. Conclusively, the results suggest that grape stems are a potential and eco-friendly natural matrix of bioactive molecules which can be used in cosmeceutics and pharmaceutical applications.

KEYWORDS: Grape stem extract, Phytochemicals, Pharmacological activity, Cosmeceutical formulation.**1. INTRODUCTION**

Grapes are members of the Vitaceae family and genus *Vitis*, which are botanical berry-type fruits. Grapes are non-climacteric fruits borne in panicles (grape-like clusters) and come in many colours of which the most common ranges from light yellow (green), amber, red, to black (purple, blue, dark purple). "White grapes" are actually green in color, and are derived from the purple grape. It is believed that grapes have been cultivated in Asia for a few thousand years and with good reason; Greece was only one of many countries grateful for the agricultural and cultural benefits of growing these unique berries. The earliest introduction of one of the principal economic contributors was around 1600 when wheat began to be planted. Grape production, however, was not introduced until later in the colonial period.^[1]

Table 1: Plant Profile.

Category	Description
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Vitales
Family	Vitaceae
Genus	<i>Vitis</i> L.

When ripe the berries are black and succulent, and make a good wine: common species found near the sea are "fox grape" (*Vitis vulpina*), snow sweet-leaf (*Sapoum palustre*), firefly berry, of which great quantities do well in all parts; river-bank grape follows the course of streams for hundreds of miles, ever luxuriant as it goes: bird gravery holds like gallinaceous birds. *Vitis vinifera* the grapevine species most commonly cultivated today-evolved from hybridisation of wild *Vitis* lines.^[2] Optimal grape growing conditions are usually found in warm-temperate areas, between 30 and 50°N or S of the

equator. Grapes are grown on a large scale around the world in terrestrial agriculture and contribute tens of millions of tonnes to the global fruit supply every year. Grapes are used for winemaking in addition to fresh and dried consumption and according to FAO report, widespread extensive specialized areas produce a variety of grape (p. 96). 71% as wine, 27% fresh fruit and 2% dried.^[3] The area of vineyard land is still increasing, growing by about 2% annually. The world's largest producer is still Italy with 8.3 million tonnes, followed by France (6.7 million tonnes) and the United States (6.2 million tonnes). By continent, production was in 2015: Europe (40%), Asia (31%) and the Americas (20%).^[4]

1.1. Properties of the Grape Plant

The grape plant (*Vitis vinifera*) contains a large profile of biologically active chemicals, comprising polyphenols, flavonoids, anthocyanins, proanthocyanidins and resveratrol among its most important molecules responsible for the pharmacological properties described over centuries and confirmed by;

1.2. Essential Pharmacological Characteristics

1.2.1. Antioxidant Activity

Grape seed and skin extracts are powerful antioxidants — resveratrol, and proanthocyanidins being the most potent ones which counterattack these free radicals that cause oxidative stress, the underlying source of cellular aging and degenerative diseases.^[5]

1.2.2. Anti-inflammatory Activity

Polyphenols in grapes inhibit inflammatory factors, such as COX-2, IL-6 and TNF- α , that can reduce chronic inflammation and subsequent tissue damage.

1.2.3. Cardioprotective Effects

Polyphenols also have the capacity to enhance vascular function and lipid profiles and lower blood pressure, thereby preventing the risk for CVD.

1.2.4. Neuroprotective Activity

Resveratrol is able to penetrate the blood-brain barrier and lower amyloid plaque formation, while increasing neuron survival indicating an advantage in neurodegeneration.

1.2.5. Anticancer Properties

Several active compounds function by inducing apoptosis and suppression of proliferation in cancer cell lines such as breast, colon and prostate cancer.

1.2.6. Hepatoprotective and Antimicrobial Effects

Studies Anitiday et al showed that grape extracts suppress growth of microorganisms and protect liver cell from toxin-induced damage and fibrosis.

1.2.7. Anti-Aging Mechanisms

Resveratrol can activate SIRT1 to increase mitochondrial functions, decrease cell aging and senescence level as well as protect telomeres etc., which together results in an effective anti-aging effect including skin tightening, (hydration/water retention) and revitalize.^[6]

Table 2: Phyto-Constituents of Grape Plant.

Chemical Constituent	Percentage
Carbohydrates	12-18%
Protein	0.5-0.6%
Fat	0.3-0.4%
Calcium	0.01-0.02%
Phosphorus	0.01-0.08%
Potassium	0.1-0.2%
Vitamin C	0.01-0.02%
Vitamin A	0.001-0.0015%

Table 3: Bioactive Constituents of Grape Plant Parts And Their Applications.

Plant Part	Main Bioactive Constituent	Application In Disease Treatment	Refrence
Grape Skin	Resveratrol, Anthocyanins, Flavonoids	Antioxidant, Cardioprotective, Anticancer, Neuroprotective	[7]
Grape Seed	Proanthocyanidins, Flavan-3-ols (Catechin, Epicatechin)	Anti-inflammatory, Anti-obesity, Antidiabetic, Cardiovascular protection	[8]
Grape Pulp	Organic acids, Sugars, Vitamins (C, E), Phenolics	Energy source, Antioxidant, Immune support	[9]
Grape Leaf	Flavonoids (Quercetin, Kaempferol), Phenolic acids	Anti-inflammatory, Antimicrobial, Anti-ulcer, Wound healing	[10]
Grape Stalk	Stilbenes (Resveratrol, Piceid), Tannins	Antioxidant, Anticancer, Antimicrobial	[11]
Grape Root/Bark	Stilbenoids, Phenolic acids, Triterpenes	Antimicrobial, Anticancer, Hepatoprotective	[12]

2. Antioxidant Activity & Cardioprotective Mechanisms

2.1. Antioxidant Activity

The active components derived from *Vitis vinifera* are a wide range of compounds, including flavonoids,

anthocyanins, catechins, phenolic acids tannins proanthocyanidin and stilbenes whereby resveratrol being the most frequently reported. They are present in the skin, seeds, stems, and leaves of grapes and have powerful free radical scavenging effects resulting in wide

ranging therapeutic interventions such as cardioprotective, neuroprotective, anti-aging, and anticancer properties.^[13]

Grape-derived compounds have drawn attention because of its strong antioxidant capacity and it has potential uses, such as pharmaceutical development, nutraceuticals formulations, functional foods fortification and topical dermatology. The majority of their biological effects can be attributed to the elimination of oxidative stress.^[14]

2.2. Cardioprotective Activity

It has been reported that resveratrol, quercetin, catechins and proanthocyanidins could protect cardiovascular diseases in multiple biochemical pathways. These substances affect cardiovascular health through regulation of oxidative stress, lipid metabolism, inflammatory pathways, and vascular function.^[15]

2.3. Mechanisms of Action

2.3.1. Antioxidant Activity

One proposed mechanism involves neutralizing reactive oxygen species (ROS), which helps limit oxidative modification of LDL cholesterol, a recognized factor in the development of atherosclerosis.^[16]

2.3.2. Endothelial Protection

Resveratrol, as well as other flavonoids, normalizes nitric oxide (NO) bioavailability in the endothelium, contributing to increased vasodilation and vascular compliance.

2.3.3. Anti-inflammatory Effects

Available experimental data demonstrated that these polyphenols can suppress NF- κ B transactivation and down-regulate the expression of COX-2, IL-6, TNF- α and other inflammatory mediators.^[17]

2.3.4. Antiplatelet & Antithrombotic Actions

Resveratrol also suppresses platelet aggregation, which can reduce the possibility of thrombosis by regulating the AA-TXA₂ pathway and balance between prostacyclin.^[18]

2.3.5. Lipid & Glucose Regulation

Grape Polyphenols and Lipid Profiles The reasons why grape poly phenols footholds in lipid profiles are mentioned: 5 a.

- Increasing HDL
- Decreasing LDL
- Reducing triglycerides

They also boost insulin sensitivity, indirectly benefiting the cardiovascular system.^[18]

2.4. Anticancer Activity

Grapes are high on the anticancer phytochemicals, including resveratrol, quercetin, anthocyanins and proanthocyanidins. They affect the molecular pathways

involved in cancer by apoptosis, proliferation, anti-angiogenesis and tumor progression.^[19]

Mechanisms include

- ROS reduction
- Mitochondrial apoptotic activation
- Cell-cycle arrest
- Reduced metastatic potential

Resveratrol has been described to reduce the resistance of tumour cells to some anticancer drugs in certain cancer models.^[20]

2.5. Neuroprotective Activity

Polyphenols derived from *Vitis vinifera* show potent neuroprotective effects through their abilities to suppress oxidative stress, inflammation, apoptosis and amyloid- β aggregation. These are among the advantages that extend also to neurodegenerative disorders such as AD, PD, and stroke.^[21]

3. Mechanisms of Action

3.1. Antioxidant Action

- Scavenges ROS/RNS
- Increases the levels of endogenous antioxidant enzymes (SOD, catalase, GPx)

3.2. Anti-Inflammatory Action

- Inhibits NF- κ B
- Reduces microglial activation

3.3. Anti-Apoptotic Action

- Regulates Bcl-2/Bax
- Inhibits caspase-3 pathways

3.4. Amyloid-Beta and Tau Modulation

- Prevents A β aggregation
- Reduces tau hyperphosphorylation

3.5. Mitochondrial Protection

- Restores ATP synthesis
- Prevents mitochondrial dysfunction

3.6. Neurotransmission Enhancement

- Increases acetylcholine levels
- Improves synaptic plasticity^[22]

3.7. Anti-Inflammatory Activity

Resveratrol, quercetin, anthocyanins and proanthocyanidins of *Vitis vinifera* have strong anti-inflammatory effect. They decrease the oxidative stress, block release of interferon as well as other inflammatory mediators and protect tissue from damages associated with chronic inflammation.^[23]

Mechanisms

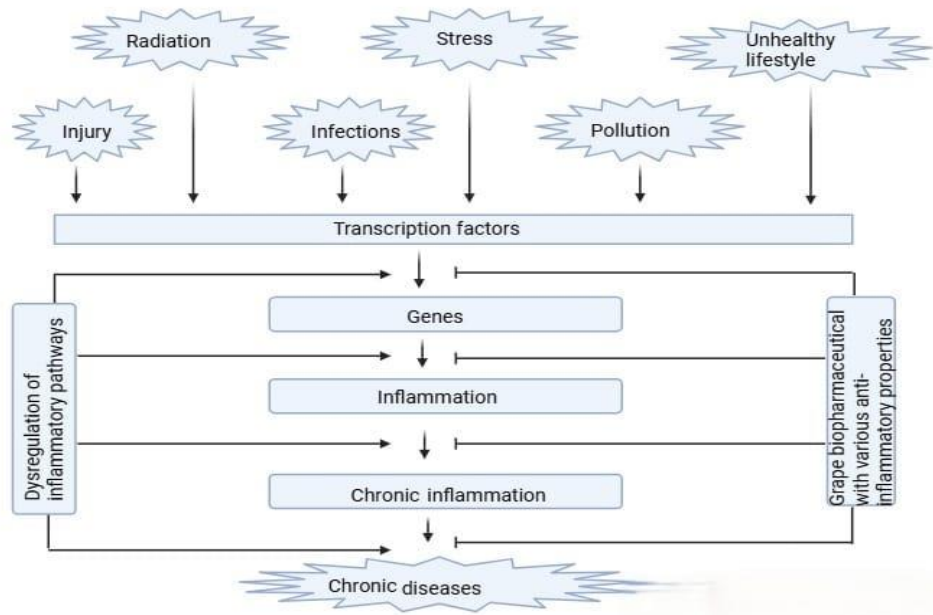


Figure 1: Mechanism of Anti-Inflammatory Activity.

3.8. Anti-Obesity Activity

Anti-obesity effects of grape polyphenols including resveratrol, quercetin, catechins and anthocyanins have

been observed. They mediate the process of adipogenesis, lipid metabolism, thermogenesis and inflammatory responses in obesity.^[23]

Mechanisms include

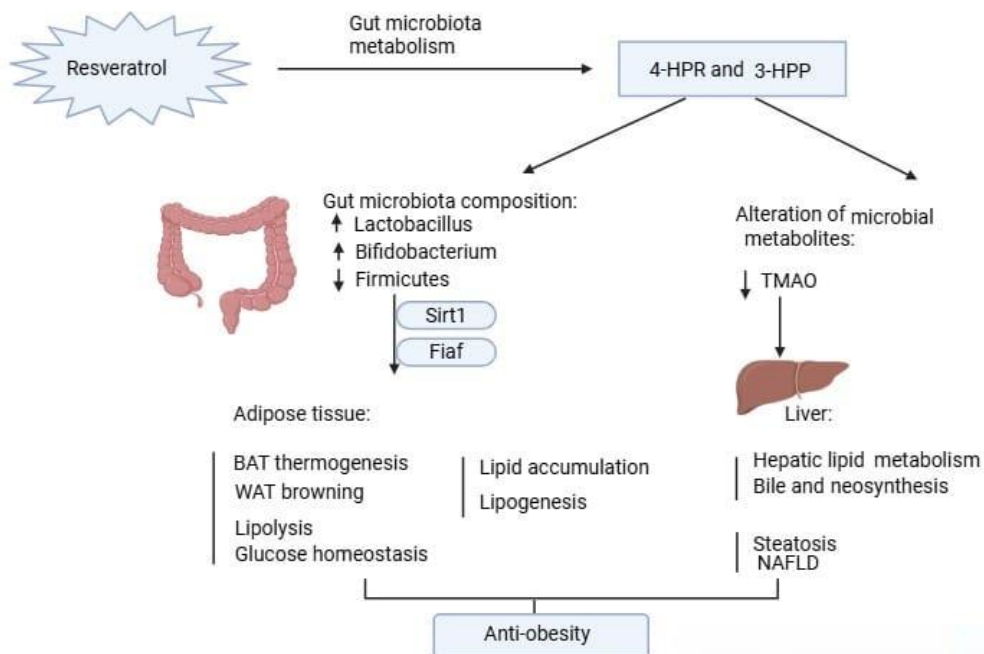


Figure 2; Mechanism of Anti-Obesity Activity.

3.9. Anti-Diabetic Activity

Polyphenolic compounds in *Vitis vinifera* have marked anti-diabetic effects via regulation of glucose metabolism, insulin signaling and oxidative homeostasis.^[24]

Mechanisms

- Activation of SIRT1/AMPK
- Increased GLUT4 translocation
- Inhibition of α -glucosidase and α -amylase
- Protection of pancreatic β -cells

- Reduced inflammatory cytokines
- Improved lipid metabolism

Cumulatively, these biologic effects could potentially benefit glucose tolerance and prevent long-term complications of diabetes.^[24]

3.10. Antimicrobial Activity

Phytochemicals, such as resveratrol, quercetin, catechins, anthocyanins and tannins present in grapes are well known for their antimicrobial activity against bacteria, fungi and certain viruses.

Mechanisms

- Cell-wall disruption
- Inhibition of microbial enzymes
- Interference with nucleic acid synthesis
- Inhibition of biofilm formation

Although there are differences between types of plant parts, extracts from grape seeds and skins show more powerful antimicrobial activities in comparative studies.^[25]

3.11. Anti-Ulcer Activity

Resveratrol, catechins, anthocyanins and proanthocyanidins play a promising role in gastroprotection.

Mechanisms

- ROS neutralization
- Increased mucus & bicarbonate secretion
- Inhibition of gastric acid production by H⁺/K⁺-ATPase regulation
- NF-κB pathway inhibition
- Anti-H. pylori activity

By these actions the extract seems to promote healing of the gastric tissue and mucosal protection.^[25]

3.12. Wound-Healing Activity

Time to heal Adjuvant substances like resveratrol, quercetin, proanthocyanidins, tannins and anthocyanins facilitate the rate of wound healing through;

- Reducing oxidative stress
- Promoting fibroblast proliferation
- Enhancing collagen deposition
- Improving angiogenesis
- Preventing infection

The liver is shielded by grape polyphenols against injury from metabolic overload, oxidative stress, alcohol and toxins.^[26]

Mechanisms include

- ROS/RNS scavenging
- Increased antioxidant enzymes
- NF-κB suppression
- Membrane stabilization
- Inhibition of stellate cell activation in the liver
- Enhanced detoxification pathways

These actions are beneficial for liver health and might prevent NAFLD.^[27]

4. Cosmetic Formulations With Grape Stem Extracts

Grape stem extracts contain numerous actives such as resveratrol, flavonoids, tannins, anthocyanins and other polyphenols that are excellent candidates for topical formulations in dermatology and cosmetics. These substances provide wide range of antioxidant, anti-inflammatory, anti-aging, antimicrobial and photoprotective effects in creams/lotions/sunscreens/gels/serums/shampoos/skin-brightening agents and are featured by solids scientific evidence.^[28]

4.1. Anti-Aging Creams and Serums

Grape stem extracts including resveratrol and proanthocyanidins increase collagen synthesis, promote dermal structure and inhibit oxidative stress, so it is best for anti-aging.^{[28][29]}

Benefits

- Lines & wrinkles reduction
- Improved elasticity
- Prevention of premature aging
- Enhanced hydration

Color, odor, and photostability are major formulation challenges, which can be overcome by means of encapsulation technologies (e.g. nanoemulsions/liposomes/dendrimers).

4.2. Moisturizing Lotions

In addition, ARA prevents against TEWL (Transepidermal water loss), increases hydration and strengthens the skin barrier.^[30]

Benefits

- Smoother, softer skin
- Improved moisture retention

4.3. Sunscreens & Photoprotective Formulations

Stilbenes in general and resveratrol, scavenge UV-induced free radicals and suppress lipid peroxidation thus constituting useful supplements to UV filters.

They potentiate the activities of inorganic and organic sunscreens, augmenting photoprotection and delaying photoaging.

Key considerations

- Evaluation of radiation protective UV filters: Applicability of the ISO 24444 & ISO 24443 methods
- Resveratrol's photolability improved with encapsulation

4.4. Anti-Acne Gels and Creams

Flavonoids and tannins in grape stems have antimicrobial effects on *Propionibacterium acnes* in addition to anti-inflammatory activity.

Benefits

- Reduces acne-causing bacteria

- Minimizes inflammation
- Prevents scarring

4.5. Skin-Brightening & Anti-Hyperpigmentation Formulations

Tyrosinase, the key enzyme for melanogenesis, is suppressed by grape polyphenols.^{[31][32]}

Benefits

- Reduced pigmentation
- Decreased dark spots
- Improved skin tone

Resveratrol also prevents the oxidative stress that promotes hyperpigmentation.^[26]

4.6. Haircare: Shampoos & Serums

Antioxidants on the other hand shield hair follicles from oxidative stress and environmental pollutants they also promote scalp health while strengthening to naturally improve your hairs condition.

Benefits

- Improved shine
- Stronger shafts
- Reduced breakage

The formulating performance is depended on the surfactant system, solid content, pH value and foam stability.^{[33][34]}

5. Characterization and Evaluation of Formulations

Quality assurance, safety, stability and the efficacy of formulations with grape stem extracts are guaranteed by product characterization.

5.1. Characterization of Creams & Serums

5.1.1. Physical & Organoleptic Evaluation

Appearance, color, and olfact are visual characteristics which influence the stability as well as consumer acceptance of a product.

5.1.2. pH Measurement

Best range : 4.5-6.5 to mimic skin's natural pH level and prevent irritation, fitting individual skin type as well.

5.1.3. Viscosity & Rheology

Measured via rotational viscometry. Creams exhibit shear-thinning behavior, which is crucial for spreadability and tactility.^[35]

5.1.4. Droplet Size & Emulsion Stability

Quality of emulsion is monitored through microscopy analysis or particle size measurement, where smaller droplets are desired as it improves stability and active availability bioactive.

5.1.5. Chemical Analysis

- HPLC for resveratrol and polyphenols
- Total phenolic content via Folin–Ciocalteu
- Antioxidant assays such as DPPH/ABTS.^{[36][37]}

5.2. Evaluation of Creams & Serums

5.2.1. Stability Studies

Performed at fast and real times by monitoring pH, viscosity, color, odor and separation phase.^[38]

5.2.2. Functional Testing

- SPF & UVA sunscreens testing (ISO 24444, 24443)^[39]
- antioxidant activity (DPPH, ABTS)

5.2.3. In-Vitro Dermal Delivery

Release and skin penetration are measured using Franz diffusion cells.^[40]

5.2.4. Microbiological Assessment

Viable count and pathogen exclusion: E. coli, S. aureus, P. aeruginosa, C. albicans included. RichTextBox: The following list of pathogens are to be used in the development of test organisms for this characteristic if needed : E. coli, S. aureus, P. aeruginosa, C.albicans.^[41]

5.2.5. Safety Evaluation

Patch tests and RhE (reconstructed human epidermis) models identify irritant or sensitizing properties.

Characterization of Lotions

- Lotions have a lower viscosity than a cream and are used:
- Organoleptic stability testing
- pH and conductivity testing
- Microscopic droplet evaluation

Bioactive composition is confirmed by chemical and antioxidant assays.

6. Evaluation of Lotions

6.1. Stability Testing

The stability is verified in both normal and accelerated conditions for long-term behavior. Parameters such as pH, color, odor, viscosity and phase separation are observed. Techniques such as centrifugation and freeze–thaw assure formulation stability.

6.2. Microbial Quality

Micro testing to make sure there are no harmful pathogens present. Total microbial content is determined and the absence of E. coli, Staphylococcus aureus and Pseudomonas aeruginosa must be confirmed according to pharmacopeial standards.

6.3. Skin Penetration

Penetration studies indicate how well active substances penetrate into the skin. Tape stripping and Franz diffusion cells are widely used methods.

6.4. Functional Performance

Product efficacy is assessed by hydration studies with the Corneometer or TEWL. It is also possible to conduct in vitro measurements of antioxidant activity or SPF if applicable.

6.5. Safety Evaluation

Its safety is based on skin irritation and sensitivity tests. Reconstructed human epidermis (RhE) models and volunteer patch tests are conducted to confirm skin compatibility.

6.6. Consumer Acceptability

The spreadability, texture, smell, absorption and skin feeling of the product are tested from sensory point of view so as to guarantee pleasant product and user experience.

Characterization of Sunscreens

Includes

- Appearance and spreadability
- pH & viscosity
- UV filter quantification via HPLC/LC-MS
- Photostability under solar simulation

The size of particles is of importance for ZnO/TiO₂ filters.^[42]

6.7. Evaluation of Sunscreens

- **In-vitro assay:** UV absorbance is quantified with a spectrophotometer to determine SPF. UVA protection can be tested through processes such as PPD or critical wavelength.
- **In-vivo experiments:** SPF is demonstrated on human skin by determining minimal erythema doses following UV irradiation. Water-resistance is also tested following activities such as immersion or sweating.
- **Photostability:** The product is irradiated with simulated sunlight to find out whether the UV filters degrade or stop working.
- **Safety:** Irritation, Sensitization and Cytotoxicity Tests are conducted. Nanoparticle sunscreens should be further investigated for skin permeation.
- **Consumer acceptance:** User evaluation for spreadability, skin feel, greasiness, whitening effect and overall comfortness on application.

Characterization of Gels

Gels require

- Clarity, homogeneity
- pH stability
- Rheology and viscosity (Brookfield testing)
- Swelling index
- Drug content uniformity

In vitro release studies with Franz cells.^[43]

6.8. Evaluation of Gels

- **In vitro release:** Franz diffusion cells are employed to investigate the drug's permeation through a suitable membrane.
- **Ex-vivo Permeation:** The rating of the ability of a drug to permeate through biological tissue from human or animal skin.

- **Stability studies:** The pH, viscosity and drug content were determined over a period of time according to ICH guidelines.
- **Bioactivity assays:** If the gel contains active extracts, antioxidant or antimicrobial activities can be determined using techniques such as DPPH or agar diffusion.
- **Skin irritation:** Safety can be evaluated by irritation studies (animals or human patch testing).^[44]

Characterization of Skin-Brightening Formulations

Key assessments

- Drug content via HPLC/UV
 - Globule size
 - Spreadability
 - Tyrosinase inhibition tests
 - In-vitro and ex-vivo permeation
- Long-term stability per ICH guidelines.

6.9. Evaluation of Skin Brightening Formulations

- **In vitro release:** The release of active materials through artificial semipermeable or synthetic membrane is studied by using Franz diffusion cells.
- **Ex-vivo permeation:** The process is conducted using human or animal skin to determine if the ingredient, such as arbutin or vitamin C, can penetrate and deposit on the skin.
- **Melanin effects:** Experiments on melanocyte cell lines (such as B16F10), allow the measurement of tyrosinase in vitro inhibition and a decrease in melanin biosynthesis.
- **Antioxidant activity:** can be checked through methods involving DPPH, ABTS or FRAP since oxidative stress is involved in pigmentation.
- **Safety and irritation testing:** Human or animal patch tests (Draize technique) assure the product is safe and nontoxic.
- **Stability studies:** Performed according to ICH guidelines at different temperatures, light and humidity for pH, drug content, viscosity changes or change in appearance.
- **Clinical SEL:** Volunteer studies with a chromameter or melanin index help demonstrate the brightening effect in clinical conditions and the reduction of dark spot.^[21]

Characterization of Shampoos

Includes

- Organoleptic parameters
- pH (5–7)
- Viscosity
- Surface tension
- Foam stability
- Wetting time
- Active-ingredient assay

The performance was compared with cleaning, conditioning effect and irritation test as well as a consumer study.

6.10. Evaluation of Shampoo

- **Cleaning efficacy:** In vitro test where artificial sebum is applied to hair tresses and the performance of the shampoo in removing it compared to a standard.
- **Conditioning ability:** Measured by such means as wet combing, slip tests or tensile strength, to determine how easy it is to detangle and smooth hair after washing.
- **Surface Tension Test:** To test the activity of surfactants, as low surface tension means better cleaning.
- **Irritation testing:** Heigheralive Mildness assessed with a human patch test or zein protein tests, where lower numbers indicate increased irritation.
- **Microbes protection:** Prevents product from microbial contamination over its shelf life.
- **Consumer Review:** Volunteers provide feedback for factors such as lather, shine, smoothness, after-feel and ease of combing.^[45]

7. Grape Stems as a Source for the Recovery of Resveratrol: Formulation Considerations

Researches prove that grape stems, an important viticultural by-product, are rich in trans-resveratrol and stilbenes as well as their synergistic antioxidants.

Extraction methods such as:

- Ethanol extraction
- Solid-liquid extraction
- Green extraction technologies have demonstrated high efficiency and bioactive polyphenols yield.

The selection of the extraction techniques influences

- Extract purity
- Color and odor
- Stability in the final formulation
- Residual matrix components
- Co-antioxidants present, occasionally stabilizing

Crude extracts may need to be further treated (i.e. decolorized, microencapsulated) for cosmetic acceptability.

7.1. Physicochemical Characteristics of Formulations

7.1.1. pH

Topical resveratrol products usually have a pH range of 4.5 to 6.5, which is most compatible with counteracting skin's barrier and reducing irritation.

pH drift may occur due to

- Hydrolysis of polyphenols
- Presence of acidic fractions
- Thermal/oxidative instability.

7.1.2. Viscosity & Rheology

The majority of creams are non-Newtonian, shear-thinning which is important for:

- Spreadability
- Sensory feel
- Stability

Viscosity is influenced by

- Emulsifier type
 - Oil phase proportion
 - Thickeners (carbomers/xanthan)
 - Solubilization or precipitation of resveratrol
- Nanoencapsulation effectively stabilizes the rheology and prevents the formation of particles.^[46]

7.1.3. Spreadability

Proper spreadability ensures uniform dosing. Resveratrol nanocapsule or solubilized formulations display better spreadability than crystalline suspensions.

7.1.4. Appearance & Homogeneity

Crude grape-stem extracts can introduce:

- Dark coloration
- Particulate precipitation
- Stability issues

Improved homogeneity is achieved using:

- Lipid nanocarriers
- Dendrimers
- Nanoemulsions
- Solvent optimization

7.2. Chemical Stability (Antioxidant, Thermal and Photo stability)

Resveratrol undergoes degradation through;

- Oxidation
- UV-induced isomerization (trans → cis)
- Heat sensitivity

Powerless without protective systems, resveratrol degrades very quickly in potency.

Encapsulating agents therapeutic A variety of encapsulation technologies, such as liposomes, NLCs and dendrimers increase the stability of by a number of nanoemulsions means:

- Reducing photodegradation
- Limiting oxygen exposure
- Improving shelf-life

7.2.1. In Vitro Antioxidant Activity and Anti-Aging Correlation

Grape-stem-derived resveratrol formulations show:

- Strong DPPH/ABTS radical scavenging
- Cognis decreased oxidative stress indicators in cell models

But in vitro ≠ the clinical results you are hoping for.

Bioavailability depends on:

- Delivery system
- Solubility
- Penetration depth

7.2.2. Cliniscal™ Effectiveness, Safety & Irritation Profile

Human patch tests result in little to no irritation for formulations of 0.5-1% resveratrol that are adequately stabilized.

Risk factors include

- Tannin-induced irritation
- Residual pesticides
- Improper pH
- Microbial contamination

Therefore, extract characterization is necessary prior to its use in cosmetic.

Formulation Strategy Impact (Evidence Synthesis) 木 oriasis: Evidence) 作り木汀 Formulation Strategy Impact- Around this time the Japanese learned to make and use celluloid a film made from cellulose.

7.3. Resveratrol O/W Creams Free

Pros: Simple, low-cost formulation.

Cons: Low photostability, short half-life, risk of precipitation.

- High initial antioxidant activity
- Rapid decline under accelerated conditions
- Visible crystals if undissolved

7.4. Encapsulated/Nanoformulated Resveratrol

Forms of nanoparticles: liposomes, nanoemulsions, dendrimers, NLCs and invasomes.

Benefits:

- Superior stability
- Improved penetration
- Sustained release
- Enhanced in vivo performance

7.5. Purified Grape Stem Extract vs. Crude Extracts

Purified:

- Higher potency
- Reduced color
- Lower tannins
- Requires stabilization

Crude

- Contain synergistic antioxidants
- Stronger initial antioxidant activity
- More color/odor
- Regulatory challenges

7.6. Typical Reported Values (Literature)

- **pH:** 4.5–6.5 for minimal irritation
- **Rheology:** shear-thinning, non-Newtonian
- **Spreadability:** better in nanoformulations

- **Stability**

- Encapsulated → months of stability

- Free → weeks hypodilution, or significant reduction in week of stress

- **Total antioxidant capacity:** >50% of scavenging activity depending on tested concentration

Overall Conclusion

Grape stem extracts rich in resveratrol as a high potential sustainable actives for anti-age topical products because of;

- Strong antioxidant effect
- Collagen protection
- Anti-inflammatory action
- Photoprotection

But, their effectiveness is primarily related to formulation science such as:

- Encapsulation
- pH control
- Extract purity
- Stability testing
- Bioavailability assessment

Standardized extraction and validated skin-uptake studies are warranted in the future to relate in vitro data with clinical efficacy.^[47]

8. CONCLUSION

The present study highlights the significant yet underutilized potential of grape stem biomass as a sustainable source of bioactive phytochemicals with wide-ranging pharmacological and cosmeceutical applications. Comprehensive analysis reveals that grape stems, often discarded as agro-industrial waste, are rich in polyphenolic compounds such as resveratrol, flavonoids, tannins, and phenolic acids, which collectively contribute to strong antioxidant, anti-inflammatory, antimicrobial, and anti-aging activities. These bioactivities are primarily mediated through mechanisms involving reactive oxygen species scavenging, modulation of inflammatory pathways, enhancement of cellular defense systems, and regulation of key metabolic and signaling pathways. Furthermore, the study demonstrates that grape stem extracts exhibit promising therapeutic effects, including cardioprotective, neuroprotective, anticancer, and wound-healing properties, thereby reinforcing their relevance in both pharmaceutical and dermatological domains. The incorporation of these extracts into topical formulations such as creams, gels, serums, and sunscreens shows encouraging results in terms of stability, safety, and functional efficacy. However, the effectiveness of these formulations is highly dependent on factors such as extraction methods, standardization of bioactive content, formulation design, and stability optimization. The challenges related to photostability, bioavailability, and physicochemical instability of key compounds like resveratrol necessitate advanced delivery approaches, including nanoencapsulation and lipid-based carriers, to enhance therapeutic performance and shelf life. In addition, rigorous evaluation protocols, including

physicochemical characterization, microbiological assessment, and in vitro/in vivo testing, are essential to ensure product quality and consumer safety. Grape stem-derived phytochemicals represent a promising, eco-friendly alternative for the development of innovative cosmeceutical and pharmaceutical products. Future research should focus on large-scale extraction standardization, clinical validation, and advanced formulation strategies to fully translate these findings into commercially viable and therapeutically effective applications.

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