

BIORICH

INSIGHTS

PHARMACEUTICAL INGREDIENTS,
HEALTH SOLUTIONS & INNOVATION

TOPICAL DRUG DELIVERY SYSTEMS

FROM FOUNDATIONAL INGREDIENTS TO
ADVANCED TOPICAL DELIVERY SYSTEMS

Explore the role of pharmaceutical
ingredients in designing transdermal
patches and optimizing formulation



STRUCTURE AND FUNCTION

Overview of ingredients and their
roles in transdermal patches



CONTROLLED DRUG RELEASE

Polymers and excipients for
transdermal delivery.



VERSATILE INGREDIENTS

Excipients, polymers, actives and
botanical extracts.



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KNOWLEDGE FOR IMPROVED HEALTH

Delivering comprehensive expertise in raw materials and solutions for the pharmaceutical sector.

SCIENCE FOR HEALTH QUALITY FOR LIFE

 is a business operating in the field of supplying raw materials and biotechnology solutions to various industries.

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Building sustainable value through superior and reliable raw material products.



TRANSDERMAL PATCH

COMPOSITION & FUNCTION

Structure, classification, and function of materials in transdermal drug delivery systems.



STRUCTURE

Main layers of the transdermal patch



CLASSIFICATION

Transdermal drug delivery systems



FUNCTION

Controlled release, maintaining adhesion

MINOR PATCH —————
A BRIGHTER FUTURE



TRANSDERMAL
MEDICATION
ADMINISTRATION

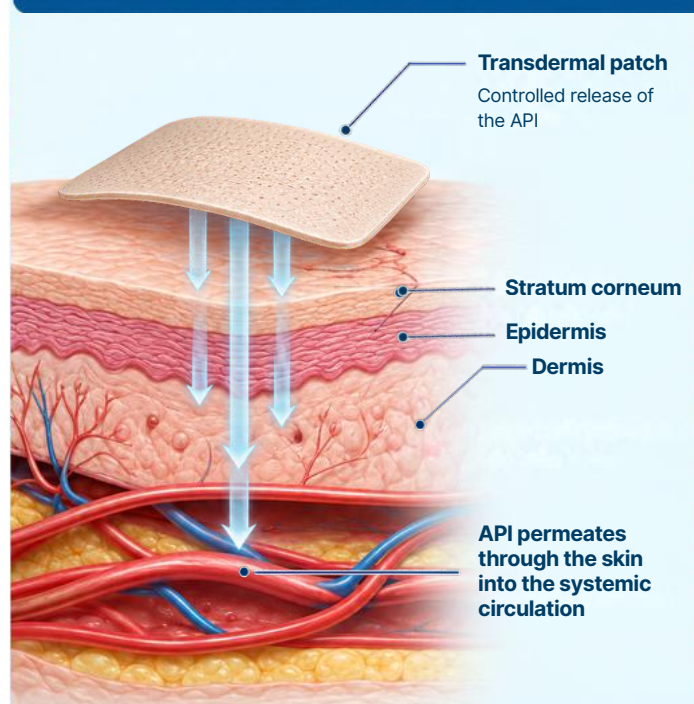
1 INTRODUCTION TO TRANSDERMAL PATCHES

Transdermal patches are formulations applied to intact skin, allowing the active pharmaceutical ingredient to be released and absorbed through the skin barrier to achieve a systemic effect. An adhesive system ensures contact with the skin, while the formulation regulates the release and absorption of the active pharmaceutical ingredient throughout the duration of use.

Transdermal patches represent a distinctive dosage form of transdermal therapeutic systems (TTS) or transdermal drug delivery systems (TDDS). TTS are engineered to administer active pharmaceutical ingredients into the bloodstream in a **continuous** and in a **controlled manner**, thereby ensuring a stable supply of the medication throughout the treatment duration.

The advancement of TTS aims to overcome certain limitations of oral administration, specifically **first-pass metabolism** and **the effects of the gastrointestinal environment**, while harnessing the potential for controlled and sustained drug release.

MECHANISM OF ACTION OF TRANSDERMAL PATCHES.



CONTINUOUS

CONTROLLED

PROLONGED

"Transdermal therapeutic systems open up a novel approach in the development of highly efficient drug delivery systems while reducing side effects for patients"

2 CLASSIFICATION OF TRANSDERMAL THERAPEUTIC SYSTEMS

Based on the physical distribution of the API within the structural layers of the patch, TTS can be divided into 3 main types:

01 LIQUID RESERVOIR SYSTEM (Drug in reservoir – DIR)



- Backing layer
- API-containing layer
- Rate-controlling membrane
- Adhesive layer
- Release liner

Liquid reservoir system

The API is dissolved in liquid or gel form and contained within a distinct "reservoir," separated from the skin by a rate-controlling membrane and an adhesive layer.

02 POLYMER MATRIX SYSTEM (Drug in polymer matrix)



- Backing layer
- API-containing layer
- Adhesive layer
- Release liner

Polymer matrix system

The API is dispersed or dissolved within a polymer matrix; the release rate depends on the properties of the matrix and the drug diffusion process.

03 DRUG-IN-ADHESIVE SYSTEM (Drug in adhesive – DIA)



- Backing layer
- Drug/Adhesive-containing layer
- Release liner

Drug-in-adhesive system

The API is dissolved or dispersed directly into the pressure-sensitive adhesive layer. This adhesive layer serves a dual purpose: adhering to the skin and acting as the reservoir for drug release.



3 FUNDAMENTAL COMPOSITION OF ADHESIVE PATCHES

Transdermal patches are multilayer systems in which each layer plays a distinct role and works synergistically to control the **rate and extent of drug release and permeation** over the application period.

Their basic structure comprises a backing layer, drug-containing layer (reservoir/matrix), rate-controlling membrane, pressure-sensitive adhesive layer and release liner.

“The multilayer structural design enables the transdermal patch to maintain stability, control active ingredient release, and ensure effective skin contact throughout the application period



A BACKING LAYER



► Role

The backing layer is the outermost layer of the TTS system, protecting the inner layers from external physical and chemical influences. Its material must be flexible and pliable, with suitable barrier properties to limit the diffusion of the active pharmaceutical ingredient (API) and excipients. It must also be compatible with the API and excipients, while providing adequate oxygen transmission and a high moisture vapor transmission rate.

● Frequently utilized substances

Polyvinyl, polyethylene, polyester, aluminum, and polyolefin.

B DRUG-CONTAINING LAYER



► Role

It is a reservoir that contains the API intended for transdermal delivery. The active ingredient may be dissolved or dispersed within a polymeric network. It can exist in liquid or gel form within a separate reservoir or be uniformly dissolved and dispersed directly within the polymer matrix or adhesive layer.

► It typically includes:

- API
- Matrix-forming polymers (Natural polymers, synthetic polymers, pressure-sensitive adhesives [in DIA systems])
- Permeation enhancers
- Other excipients (humectants, preservatives, antioxidants, pH modifiers)

C PRESSURE-SENSITIVE ADHESIVE LAYER



► Role

Pressure-sensitive adhesives maintain adhesion between the patch and the skin, offering immediate and prolonged tack throughout use. They require excellent biocompatibility causing no skin irritation or sensitization and complete chemical compatibility with the drug and excipients.

● Frequently utilized substances

Polyisobutylene (PIB), polydimethylsiloxane (PDMS), acrylic adhesives, and natural plastics.

D RATE-CONTROLLING MEMBRANE



► Role

Commonly used in reservoir systems to control skin diffusion rates according to specific kinetics.

● Frequently utilized substances

Ethylene vinyl acetate, silicone resins, polyurethane, polyisobutylene, polyacrylates, and pressure-sensitive adhesives.

F RELEASE LINER



► Role

Acts as primary packaging in direct contact with the drug and formulation layers, requiring complete chemical inertness.

● Frequently utilized substances

Non-woven paper, polyethylene, and polyvinyl fabrics are treated with a fine layer of silicone, Teflon, or metallic film.

4 QUALITY STANDARDS FOR TTS

In addition to **standard quality tests**, including **identity, assay, impurities, uniformity, drug release, and irritation**. TTS during research and development requires complete adhesion performance evaluation.

GENERAL QUALITY METRICS

Description

The product must be uniform, possess appropriate tackiness (easy to adhere and peel off), and cause no skin irritation.

Identification & Assay

According to the specifications in the individual monograph.

Content uniformity

Average content of 10 units tested within the range of 90 – 110%.

Mass uniformity of drug-containing layer

Not more than 2 units exceed $\pm 5\%$ of the average mass, and no unit exceeds $\pm 10\%$ of the average mass.

Uniformity of area

Not more than 2 units exceed $\pm 5\%$ of the average mass, and no unit exceeds $\pm 10\%$ of the average mass.

Irritation

Evaluate results by observing and recording differences between control and test skin areas at 1h, 24h, 48h, and 72h post-cleansing on rabbit skin.

EVALUATION IN RESEARCH

Adhesion evaluation

Stable skin adhesion throughout the treatment period is critical to TTS efficacy. Adhesion performance is evaluated via **peel adhesion, release liner peel, tack, shear, and cold flow tests**.

01
PEEL ADHESION TEST

Measure the force necessary to peel the patch from a standard test

02
RELEASE LINER PEEL TEST

Measure the force necessary to remove the release liner from the adhesive layer prior to application.

03
TACK TEST

Measures the immediate adhesion capacity of the adhesive upon brief contact with a surface.

04
SHEAR TEST

Measures the cohesive strength of the adhesive matrix under the influence of a shear load.

05
COLD FLOW TEST

Evaluates the oozing or migration of adhesive beyond the backing edges or through the release liner during storage.

OVERVIEW OF DOSAGE FORM

CREAM

From emulsion to cream formulations
stable and suitable for topical use



OIL PHASE

An essential
phase in emulsion
formation.



EMULSIFIER

Stabilizes the
emulsion
structure.

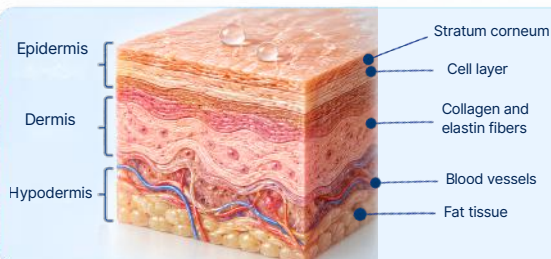


AQUEOUS PHASE

An essential
phase in emulsion
formation.



1 GENERAL INTRODUCTION



SKIN - A PROTECTIVE BARRIER/ DRUG DELIVERY ROUTE

The skin is an **essential organ** of the body, serving as a protective barrier against external hazards while also playing a role in **regulating body temperature** and **storing energy**. Furthermore, the skin is a key pathway for targeted drug delivery.

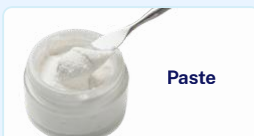
Topical semisolid preparations are designed for local action or drug delivery through the skin. Depending on the API properties and therapeutic objectives, they include **ointments, creams, pastes, and gels**.



Ointment



Cream



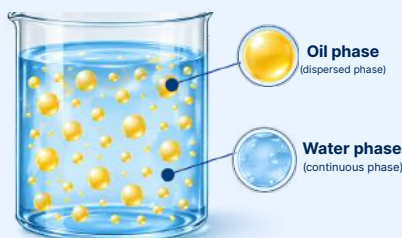
Paste



Gel

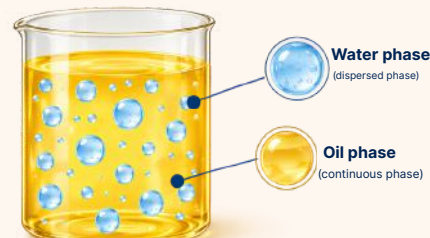
TWO TYPES OF EMULSION SYSTEMS FOR CREAM FORMULATIONS

OIL IN WATER (O/W)



Oil in water (O/W): Oil is the dispersed phase; water is the continuous phase.

WATER IN OIL (W/O)



Water in oil (W/O): Water is the dispersed phase; oil is the continuous phase.



CREAM OR TOPICAL CREAM

Creams, or topical creams, are a category of soft drugs **frequently used in topical formulations**. According to the Vietnamese Pharmacopoeia V, creams are multiphase dispersion preparations characterized by a notably soft and smooth texture, comprising an oil phase, an aqueous phase, and an emulsifier. Based on the continuous and dispersed phases, creams are categorized into two primary emulsion systems.

2 INGREDIENTS IN THE FORMULATION

*Quality arises from
exacting standards.*

A topical cream formulation generally comprises four primary components: **the active ingredient**, **the aqueous phase**, **the oil phase**, and **the emulsifier**. These ingredients collaborate to establish a stable emulsion system, thereby ensuring therapeutic efficacy and safety during application.

A AQUEOUS PHASE

It serves as a solvent to dissolve hydrophilic active ingredients while delivering initial moisture to the skin.

Purified water	Serves as the main vehicle in the system, dissolving components in the aqueous phase.
Humectants	Glycerin, propylene glycol, and sorbitol retain moisture and prevent skin dryness.
Suspending agent	Alginate, cellulose derivatives, and carbomer increase aqueous-phase viscosity.
Preservative	Methylparaben, propylparaben, and benzoic acid inhibit microbial growth.
Chelating agent	EDTA sodium binds metal ions to reduce compound degradation.
Solubilizer	Alcohol, propylene glycol, and surfactants improve solubility, permeability, and active ingredient absorption.

B OIL PHASE

It contributes to the dissolution of the components in the oil, resulting in a smooth and soft texture for the product.

Solvent	Vegetable oil, petrolatum, and liquid paraffin dissolve oil-phase components.
Emollient	Paraffin, cetyl alcohol, and stearyl alcohol contribute to a soft and smooth skin texture.
Antioxidant	BHT and BHA assist in curbing oxidation and preserving the stability of the active components.
Thickener	Cetyl alcohol, stearyl alcohol, and beeswax are significant excipients that influence the viscosity of creams, their adhesive characteristics, and the release of the active ingredient.



**Mixing
precaution**

The aqueous phase temperature should be
2-5°C higher than the oil phase

C ACTIVE INGREDIENT

It is the primary component responsible for generating the therapeutic effect of the formulation. Depending on the treatment objective, the active ingredient may fall into various categories, including corticosteroids, antifungals, antihistamines, antibiotics, antivirals, and others.

SOME PREVALENT CATEGORIES OF ACTIVE INGREDIENTS



Corticoid



Antifungal



Antihistamine



Antibiotic



Antiviral

D EMULSIFIER

Emulsifiers are an essential component in cream formulations, contributing to the physical stability of the emulsion system throughout the product's shelf life. Depending on the HLB value (hydrophilic-lipophilic balance) of the emulsifier, can be categorized into two groups:

W/O EMULSIFIER Low HLB (3-6)

It is a non-polar or oil soluble emulsifier, ideal for water in oil (W/O) emulsions.

Ex: lanolin, cetostearyl alcohol, cetyl alcohol, poloxamer, calcium oleate, sorbitan monooleate (span 80)

O/W EMULSIFIER High HLB (8 – 18)

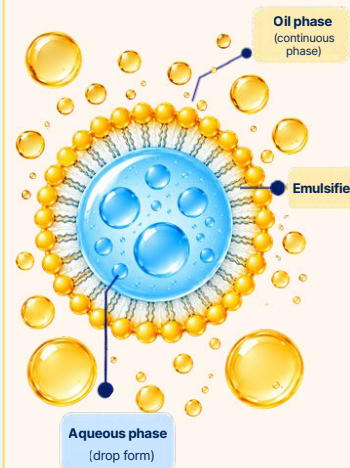
As a hydrophilic or polar emulsifier, it is appropriate for oil in water (O/W) emulsions.

Ex: sodium stearate, polyoxyl 20 cetostearyl ether, polyethylene glycol 40 stearate, polysorbate 80

O/W emulsion



W/O emulsion



3 PACKAGING THAT HOLDS CREAM

The containers containing the cream medication must be sterilized prior to use, either through heat sterilization or immersion sterilization.

WIDELY UTILIZED CREAM PACKAGING



Glass jar



Ceramic jar



Aluminum tubes



Plastic tubes

4 QUALITY STANDARDS FOR CREAM FORMULATIONS

REQUIRED SPECIFICATIONS FOR TOPICAL CREAMS

Description	White to off-white, homogeneous cream.
Identification & Assay	Tested according to individual monograph specifications.
Homogeneity	Visually observe the smear with the naked eye (at a distance of approximately 30 cm); no particles are visible in 3 out of 4 test specimens.
Uniformity of mass	Not more than 1 unit out of 10 units lies outside the limit of ± 5% of the average mass.
Microbial limit	Total aerobic microbial count (TAMC) < 10 ² CFU/g Total combined yeasts/moulds count (TYMC) < 10 ² CFU/g Absence of <i>Staphylococcus aureus</i> in 1 g Absence of <i>Pseudomonas aeruginosa</i> in 1 g



OTHER QUALITY EVALUATION SPECIFICATIONS

Viscosity	Evaluates the consistency and rheological behavior of the formulation.
Penetration	Based on measuring the depth of penetration of a probe (typically a cone-shaped object) into the semisolid matrix using a penetrometer under defined conditions.
Adhesion	Measures the time required to separate two solid surfaces (typically glass plates) with an intermediate semisolid layer under a specified weight.
pH	Topical creams should have a pH close to that of the skin while ensuring optimal emulsion stability, as well as compatibility of excipients, active ingredients, and preservatives.
Spreadability	Measures the spread area under the influence of a specified weight.
Extrudability	This property should be considered and evaluated during the early stages of topical cream research and development.
In vitro drug release testing	The two commonly applied in vitro methods are the membrane diffusion method and the gel diffusion method.

POLYVINYL ALCOHOL

MATRIX-FORMING POLYMERS FOR TOPICAL SYSTEMS

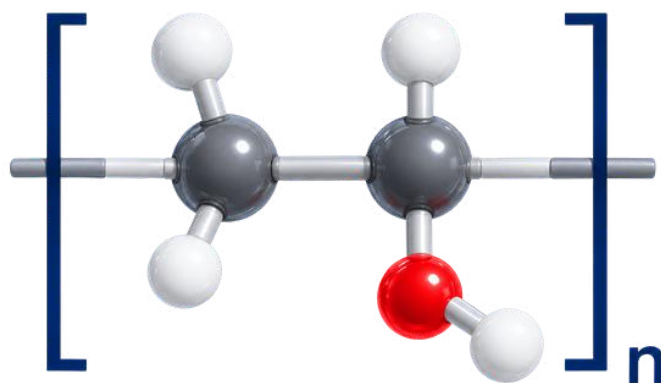
Controlling structure, viscosity, and
mechanical properties for topical formulations



1 GENERAL INTRODUCTION

In formulations such as transdermal patches, film-coated tablets, eye drops, and microemulsions, PVA serves various functions depending on the specific objectives of the formulation. In medicated plaster, PVA may be incorporated into the drug-containing layer, backing layer, release control membrane, or pressure-sensitive adhesive layer; thus, its role must be evaluated based on its precise location and function.

Thanks to its capacity to hydrate and facilitate interactions among polymer chains, PVA plays a significant role in the formation of polymer structures, influencing viscosity, rheology, mechanical properties, and adhesion. Consequently, the value of PVA in adhesive plasters extends beyond its viscosity-enhancing capabilities; it also encompasses its ability to modify the structure and mechanical properties of the product.



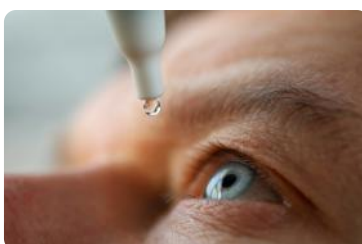
**3D structure of
Polyvinyl Alcohol**



Medicated plaster



Film-coated tablets



Ophthalmic drops



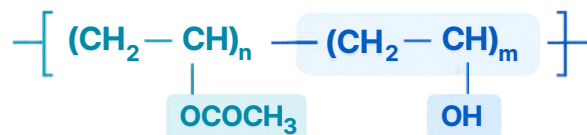
Microemulsion system

2 WHAT IS PVA?

Polyvinyl alcohol (PVA) is a water-soluble synthetic polymer produced from polyvinyl acetate (PVAc) via hydrolysis. The characteristics of PVA are significantly influenced by its degree of polymerization and the degree of hydrolysis: the degree of polymerization affects viscosity and film strength, whereas the level of hydrolysis affects hydrophilicity, water resistance, and gas barrier properties.

The variations in these two parameters give rise to the unique characteristics of PVA grades available in the market:

Polyvinyl Alcohol



Hydrophobic unit

Hydrophilic unit

01 DEGREE OF POLYMERIZATION

Reflects polymer chain length

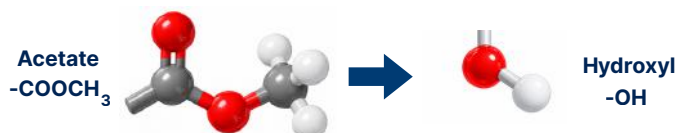
- Higher degree of polymerization, longer polymer chains, increasing chain interactions and entanglement, thereby increasing PVA solution viscosity and film-forming ability.
- In practice, commercially available PVA grades are frequently categorized by viscosity, an empirical parameter indicative of the polymer chain length.

Viscosity (4% solution)	Low (4 – 20 mPa·s)	Average (20 – 60 mPa·s)	High (> 60 mPa·s)
Degree of polymerization	~500	~3250	~5000
Molecular mass	~20,000 Da	~130,000 Da	~200,000 Da

02 DEGREE OF HYDROLYSIS

Reflects the conversion ratio of Acetate to Hydroxyl groups

- The greater the degree of hydrolysis, the more hydroxyl groups are present on the polymer chain, enhancing the polymer's hydrophilicity, water resistance, and gas barrier properties.
- In practice, PVA grades available in the market are categorized by varying degrees of hydrolysis, including low hydrolysis (< 80%), medium hydrolysis (85 - 89%), and complete hydrolysis (> 98%).



Degree of hydrolysis	Low (<80%)	Average (85-89%)	Completely (> 98%)
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 Variations in the degree of polymerization and degree of hydrolysis lead to distinct differences in the physical properties of PVA, including viscosity, film strength, water solubility, and water resistance

3 APPLICATIONS OF POLYVINYL ALCOHOL

Classify	Role	Describe	Dosage form
	Film formation	Forms a continuous polymer film, maintaining structural integrity and mechanical strength of the system.	Coated tablets, orally disintegrating films (ODFs)
	Matrix formation	Forms a drug-containing matrix, controlling drug properties and release.	Transdermal patches, medicated plaster (matrix system)
	Viscosity enhancement	Increases aqueous-phase viscosity, adjusting formulation consistency and rheology.	Topical emulsions, lotions, eye drops
	Hydrogel formation	Forms a water-retaining polymer network, providing a gel structure and a hydrated drug environment.	Transdermal patches, medicated plaster (DIR)
	Adhesion support	Incorporated into the PSA layer, enhancing skin adhesion with suitable polymers	Transdermal patches, medicated plaster (PSA)

PRACTICAL APPLICATIONS IN MEDICATED PLASTER



**ZEPOLAS PAP
40 MG**

Flurbiprofen – 40 mg



**RAPYDAN
70 MG/70 MG**

Lidocaine / Tetracaine
70 mg / 70 mg



**LIDOCAINE
LIBRA-PHARM**

Lidocaine – 700 mg

PARTIALLY NEUTRALIZED

POLYACRYLATE

**Gel-forming polymers
establish the structural foundation
for topical formulations**

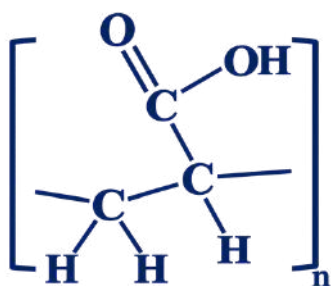


1 INTRODUCTION TO PNP

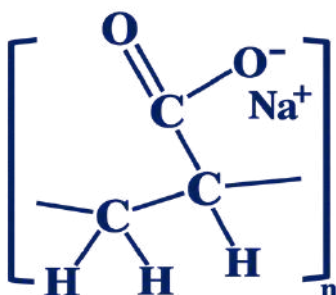
Partially Neutralized Polyacrylate (PNP) is a polymer synthesized through the polymerization of acrylic acid, wherein a segment of the carboxylic acid group ($-\text{COOH}$) is converted into a carboxylate group ($-\text{COO}^-$), typically as a sodium salt. Consequently, both $-\text{COOH}$ and $-\text{COO}^-$ are present along the polymer chain, with the proportion of each form contingent upon the degree of neutralization.

THE STRUCTURE OF PNP

Polyacrylic acid



Sodium polyacrylate



Degree of neutralization

- This percentage (%) represents the carboxyl groups ($-\text{COOH}$) on the polymer chain that have been neutralized into sodium salts ($-\text{COO}^- \text{Na}^+$).
- In pharmaceutical and cosmetic applications, the degree of neutralization of PNP must be chosen to align with product specifications to attain the desired properties, including:



Viscosity



Water absorption & swelling capacity



pH



Gel strength



SUMMARY OF TYPICAL NEUTRALIZATION DEGREES IN COMMERCIAL RAW MATERIALS

DEGREE OF NEUTRALIZATION	Degree of neutralization 35%	Degree of neutralization 50%	Degree of neutralization 70%
 Viscosity (mPa·s)	450 – 600	500 – 650	500 – 650
 pH	5,5 – 6,1	6,2 – 6,8	7,0 – 7,4
 Acrylic acid (%)	65%	50%	30%
 Sodium acrylate (%)	35%	50%	70%

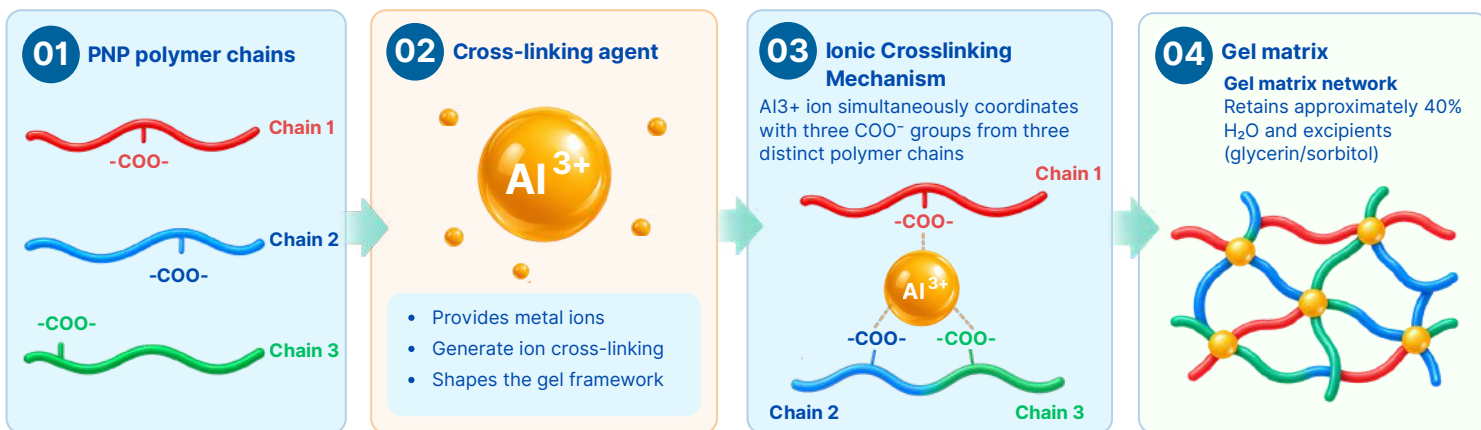


2 THE ROLE OF PNP IN THE FORMULATION

In gel formulations, PNP not only **enhances viscosity** but also actively participates in **hydrogel network formation**. Upon interaction with water, the polymer chains hydrate and swell; a process dictated by **polymer concentration** and **the degree of neutralization**.

When a portion of the **-COOH groups is converted into -COO⁻** carboxylate ions, these groups can interact with **polyvalent cations (such as Al³⁺)** to form interchain cross-links, establishing a **cross-linked polymer network**. This network entraps water and yields a continuous gel matrix, serving as the essential foundation for PNP's structural role in hydrogel systems

MECHANISM OF PNP GEL MATRIX FORMATION



3 APPLICATION

In gel formulations, PNP not only enhance the structure but also impart significant functional properties to the gel system:

01 ENHANCING SKIN ADHESION Enables the gel system to adhere to the skin surface and maintain contact throughout application.	02 MAINTAINING GEL SHAPE Provides structural framework and mechanical strength, preserving gel shape and resisting deformation.	03 WATER AND SOLVENT RETENTION Retains water or solvents within the polymer network, maintaining structural stability and gel state.
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COMMERCIAL PRODUCTS THAT EMPLOY PNPs

VERSATIS



Versatis 700 mg medicated plaster (UK)

Lidocaine **700** mg

FLECTOR TISSUGEL



Flector Tissugel medicated plaster (UK)

Diclofenac Sodium **140** mg

OLFEN



Olfen 140 mg medicated plaster (PT)

Diclofenac Sodium **140** mg

ECOSIP - KETO



Ecosip-Keto medicated plaster

Ketoprofen **30** mg

CETYL ALCOHOL & STEARYL ALCOHOL

DIFFERENCES

IN STRUCTURE, FUNCTION & APPLICATIONS



1 GENERAL INTRODUCTION

Fatty alcohols are a group of lipophilic excipients, typically isolated from waxes and mostly existing in a solid state at room temperature. They are miscible with many other lipophilic excipients such as vegetable oils, liquid paraffin, petrolatum, and lanolin. Furthermore, they exhibit **relative stability against acids, alkalis, light, and atmospheric oxygen, making them less prone to oxidation during storage.**

In emulsion systems, fatty alcohols have a **relatively weak emulsifying capacity in water-in-oil (W/O) emulsions**, but they can **enhance the emulsifying efficiency of other emulsifiers-especially hydrophilic ones**-thereby improving the stability and structure of the emulsion system. Consequently, they are widely used in semi-solid preparations and topical emulsions.

Cetyl alcohol and stearyl alcohol are two common fatty alcohols utilized as excipients in pharmaceutical formulations.



VARIED
APPLICATIONS



Semi-solid
preparation



Topical
emulsion



Texture & stability
adjustment
systems

FATTY ALCOHOLS

IDENTICAL GROUP OF EXCIPIENTS



C16

CETYL ALCOHOL



C18

STEARYL ALCOHOL

IDENTICAL GROUP OF EXCIPIENTS

STRUCTURAL DISTINCTIONS

VARIATIONS IN ATTRIBUTES

2 COMPARISON OF CETYL ALCOHOL AND STEARYL ALCOHOL

PARAMETER	CETYL ALCOHOL (C16)	STEARYL ALCOHOL (C18)
INCI name	Cetyl Alcohol	Stearyl Alcohol
IUPAC name	Hexadecan-1-ol	Octadecan-1-ol
Chemical formula	$C_{16}H_{33}OH$	$C_{18}H_{37}OH$
Molecular mass	242.44 g/mol	270.48 g/mol
Melting point	46 – 52°C	57 – 60°C
HLB	~ 15,5	~ 15,5
Crystal hardness	Medium	High



THERMODYNAMICS
Thermodynamic differences

CETYL ALCOHOL (C16)

- Formations of a highly ordered and uniform crystal network upon cooling, contributing to stable gel matrix formation and viscosity enhancement.
- Crystal structure may alter during storage, impacting overall system stability.



Ordered crystal network

STEARYL ALCOHOL (C18)

- Longer carbon chain exhibits higher hydrophobicity and lower hydration/ water-retention capacity compared to Cetyl Alcohol.
- Stearyl Alcohol's thermodynamically stable crystal structure preserves the gel framework and long term viscosity while minimizing room temperature polymorphism.



More stable crystal structure



IMPACT ON THE SKIN
Differences in sensory experience

CETYL ALCOHOL (C16)

- Lower melting point and less densely packed crystal network allow quick structure collapse upon skin contact.
- Easily releases the aqueous phase during application, creating a lightweight, non-greasy feel ideal for lotions or daily light creams.



Lightweight skin feel

STEARYL ALCOHOL (C18)

- Higher melting point and stronger interchain alkyl interactions create a denser, more resilient structure.
- Imparts opacity, a rich cushiony feel, prolonged skin residence time, and a soft protective barrier.



Rich & Long-lasting feel

3 APPLICATIONS OF CETYL ALCOHOL AND STEARYL ALCOHOL



CETYL ALCOHOL (C16)

Suitable for lightweight formulations with easy spreading and a smooth, non-greasy finish, such as light creams, gels, and lotions. Controlled heating and cooling are essential to maintain structure and viscosity during storage.



STEARYL ALCOHOL (C18)

Suitable for formulations requiring a thicker consistency, greater mechanical strength, and better retention of the product layer on the skin. Applications may include rich creams, ointments, and cosmetic products such as lipsticks and night creams.

COMMERCIAL INCLUDE CETYL/STEARYL ALCOHOL.

Lamisil AT Cream  Terbinafine hydrochloride 1 mg/g Contains cetyl alcohol C16	AFusic Cream  Fusidic acid 2 mg/g Contains cetyl alcohol C16	Zyclara Cream  Imiquimod 3.75 mg/g Contains stearyl and cetyl alcohol C16 C18	Zolcream Cream  Clotrimazole 1 mg/g Contains stearyl and cetyl alcohol C16 C18
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METHYL SALICYLATE

A multi-mechanism
active ingredient
in topical analgesics



SOURCE

Essential oil of
Gaultheria procumbens L.



CHEMICAL FORMULA

C₈H₈O₃



MOLECULAR MASS

152.15 g/mol



DOSAGE FORM

Creams - Onitments
- Medicated plaster

1 GENERAL INTRODUCTION

Methyl salicylate (methyl 2-hydroxybenzoate) is a methyl ester of salicylic acid, classified within the salicylate group of compounds, and serves as the primary constituent of wintergreen oil - *Gaultheria procumbens* L.

Methyl salicylate is utilized in formulations such as creams, ointments, and medicated plasters as a local analgesic, offering temporary relief from muscle and joint pain. This effect is associated with its local sensory influence and modulation of the pain response, thus aiding in the reduction of pain perception in the application area. The concentration of methyl salicylate is modified according to the dosage form and treatment objective.



Extracted from
wintergreen essential oil

Gaultheria procumbens L.
wintergreen essential oil

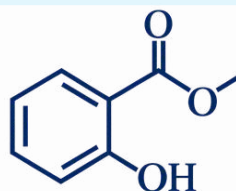
2 PROPERTIES OF METHYL SALICYLATE



CHEMICAL FORMULA



STRUCTURAL FORMULA



MOLECULAR MASS

152.15

PARAMETER	VALUE
 Physical State	Colorless to pale yellow liquid at ambient conditions, with a characteristic odor.
 Solubility	Very slightly soluble in water; miscible with ethanol (96%), fixed oils, and essential oils.
 Freezing Point	-8 to -9°C
 Boiling point	220 to 224°C
 log K_{ow}	2,55
 Density (at 20 °C)	1.18 – 1.19 g/ml
 Volatility	Volatile at room temperature.
 Transdermal permeability	Skin penetration of Methyl Salicylate is facilitated by its lipophilicity and small molecular size , enabling distribution into the stratum corneum and diffusion into underlying subcutaneous tissues.

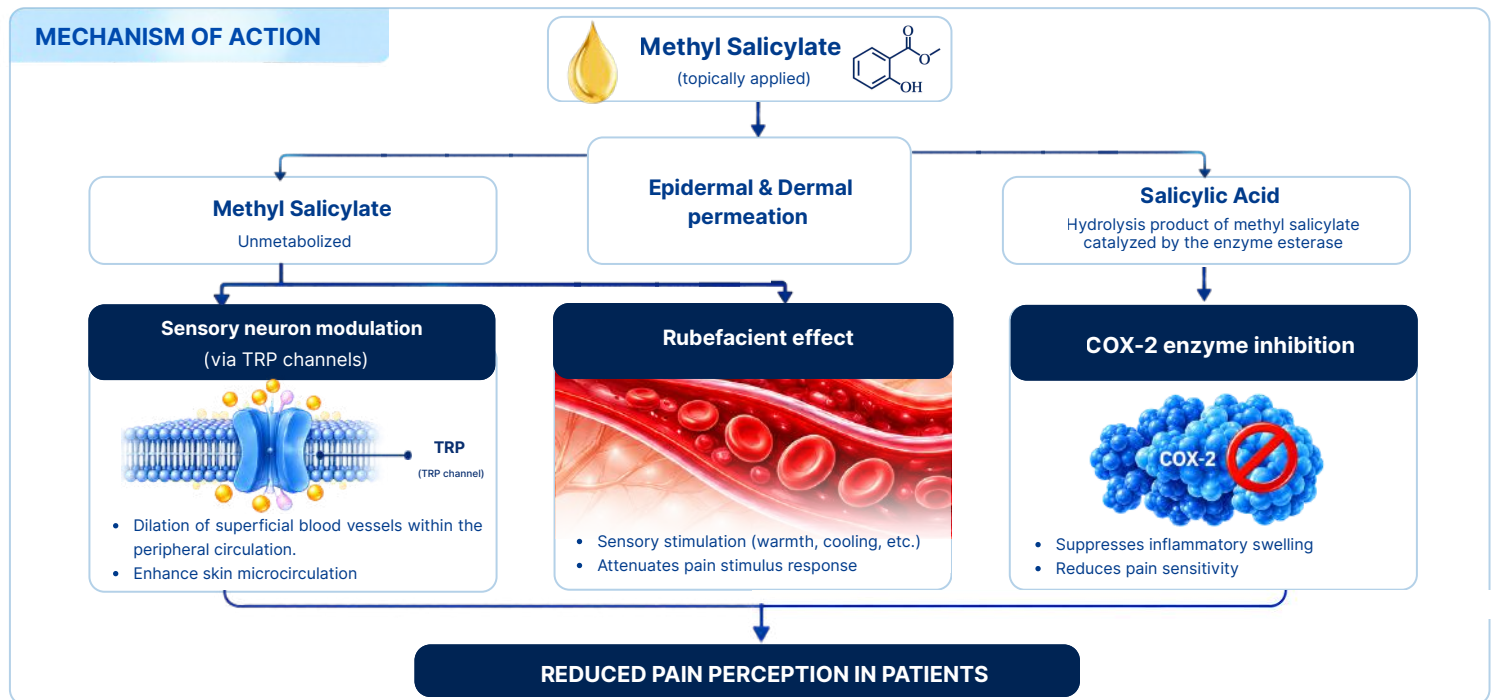


Methyl salicylate – from skin penetration to multimodal mechanisms of action, expanding its potential in topical analgesic development.



3 MECHANISM OF ACTION OF METHYL SALICYLATE

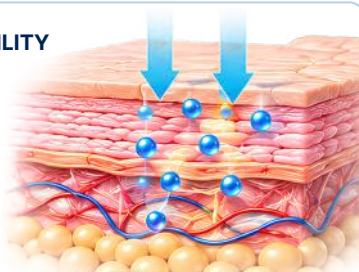
Methyl Salicylate produces topical analgesic effects by **modulating the activity of peripheral sensory neurons**, with **TRPV1** being an important ion channel involved in this mechanism. It also induces local responses, such as **vasodilation and changes in thermal sensation**. As it penetrates the epidermis and dermis, a portion of Methyl Salicylate is **hydrolyzed into Salicylic Acid** by endogenous skin esterases, and this metabolite may also contribute to the local effects.



4 ADVANTAGES OF METHYL SALICYLATE

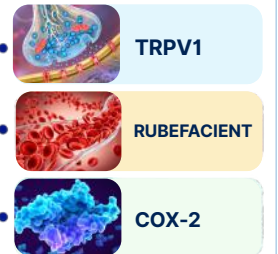
01 EXCELLENT SKIN PERMEABILITY

Methyl Salicylate possesses moderate lipophilicity and a small molecular size, allowing the active ingredient to access underlying tissues and sensory neurons, aligning with **localized target action at the application site**.



02 VARIED MECHANISMS OF ACTION

Methyl Salicylate exerts direct **activity on sensory neuronal systems**, induces **localized physiological skin responses**, and hydrolyzes into salicylic acid to **inhibit COX-2** → reducing patient pain perception.



03 RAPID LOCALIZED ONSET

Transdermal permeation and direct target-tissue action enable Methyl Salicylate to elicit a rapid localized response shortly after application.



04 FORMULATION FLEXIBILITY

It can be combined with **Menthol**, **Camphor**, and other topical active ingredients and is available in various formulations, including creams, ointments, and medicated plasters.



5 APPLICATIONS OF METHYL SALICYLATE

Methyl salicylate serves as a topical analgesic in a range of formulations, including creams, ointments, and medicated plasters, with concentrations varying according to the specific formulation and recipe.

PREPARATIONS THAT INCLUDE METHYL SALICYLATE

Methyl Salicylate 25% Cream



Methyl salicylate **25%**

NeuroGestic Ointment



Methyl salicylate **15%**

Salonpas Medicated plaster



Methyl salicylate **10%**

CETOSTEARYL ALCOHOL

ROLE IN THE STRUCTURE AND STABILITY OF SEMISOLID FORMULATIONS

Cetyl Alcohol (C16) + Stearyl Alcohol (C18)



C16 : C18

50:50 • 30:70

Cream • Gel • Lotion • Ointment



1 INTRODUCTION TO CETOSTEARYL ALCOHOL

Cetostearyl alcohol, or Cetearyl alcohol, is a blend of two straight-chain fatty alcohols: **Cetyl alcohol (C16)** and **Stearyl alcohol (C18)**. The proportion of these components leads to variations in the physical properties and characteristics of the raw materials when integrated into formulations.

In pharmaceuticals, cetostearyl alcohol is extensively utilized in semi-solid topical formulations as a **viscosity enhancer**, **consistency modifier**, **emollient**, and **co-emulsifier**. It is typically available in two commercial ratios of cetyl alcohol to stearyl alcohol: 50:50 and 30:70.

STANDARD MARKET RATES

50:50

Cetyl Alcohol: Stearyl Alcohol

30:70

Cetyl Alcohol: Stearyl Alcohol



2 PROPERTIES OF CETOSTEARYL ALCOHOL

PROPERTY	INFORMATION
Physical state	White to cream-colored waxy solid, available in blocks, flakes, pellets, or granules, with a faint characteristic sweet odor.
Melting point	48 – 56°C
Solubility	Practically insoluble in water; soluble in ethanol (95%), ether, and oils.
Incompatibility	Incompatible with strong oxidizing agents and metallic salts.
Application	Utilized at concentrations ranging from 1% to 10% as a co-emulsifier in O/W emulsions and as an emulsifier in W/O emulsions.
Store	Store in a tightly closed container at temperatures between 15 to 25°C.

EFFECT OF C16 : C18 RATIO ON TEXTURE AND STABILITY

50:50

Cetyl Alcohol : Stearyl Alcohol



- Suitable for low viscosity emulsions.
- Delivers higher structural stability in O/W emulsion systems.
- Associated with the formation of a more stable lamellar gel network.

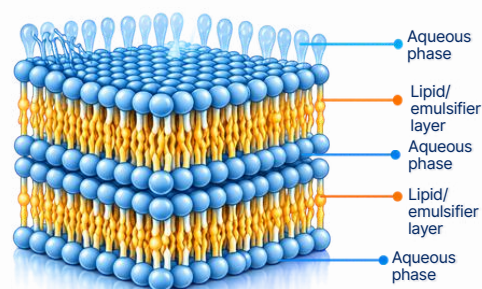
30:70

Cetyl Alcohol : Stearyl Alcohol



- Suitable for emulsions that necessitate increased viscosity.
- Exhibits lower structural stability compared to the 50:50 ratio in O/W emulsion studies

LAMELLAR GEL STRUCTURE



The lamellar gel network contributes to structure building and enhances the stability of O/W emulsion systems.

3 ADVANTAGES OF CETOSTEARYL ALCOHOL

A MULTIFUNCTIONALITY IN A SINGLE SYSTEM

Can simultaneously act as a **viscosity enhancer**, **emollient**, and **co-emulsifier**, thereby fulfilling multiple functional roles within a single formula simplifying the excipient system and streamlining formulation design.



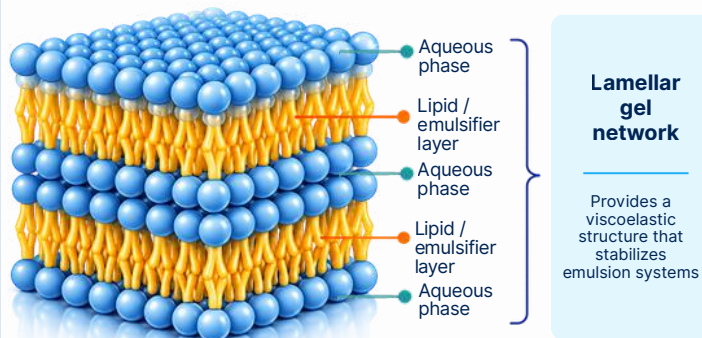
B TEXTURE CONTROL OF PREPARATIONS

Structure-building capability allows fine-tuning of consistency and rheology, thereby **creating optimal textures** for semi-solid preparations such as creams and lotions.



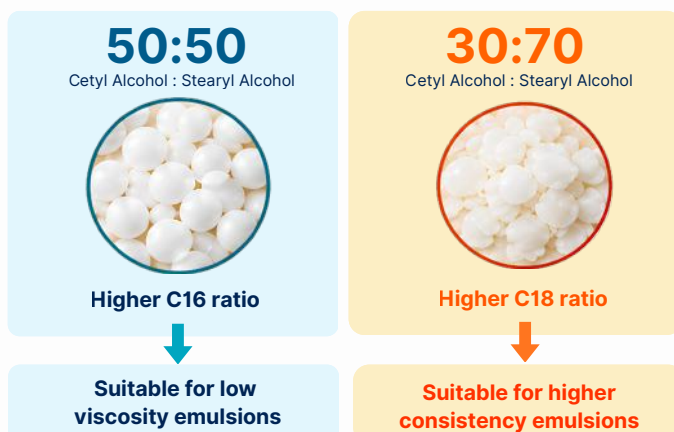
C EMULSION STABILIZATION SUPPORT

When combined with an O/W emulsifier, Cetostearyl Alcohol can contribute to the **formation of a lamellar gel phase**, creating a viscoelastic network in the continuous phase. This network **increases consistency** and **restricts the movement of formulation components**, thereby helping **maintain the physical stability** of creams, gels, lotions, and ointments.



D PHARMACEUTICAL DESIGN FLEXIBILITY

Variations in the Cetyl Alcohol (C16) to Stearyl Alcohol (C18) ratio across raw material grades allow precise selection **based on the targeted texture and rheological requirements** of the formulation.



4 APPLICATION

Due to its good skin tolerability, Cetostearyl Alcohol is widely used in creams, gels, lotions, and ointments as a consistency agent and co-emulsifier in both oil-in-water (O/W) and water-in-oil (W/O) emulsions. It also contributes to the softness and creamy texture of the formulation.

PRODUCTS CONTAINING CETOSTEARYL ALCOHOL



CLEOCIN

Dosage form

Cream



Clindamycin Phosphate

20 mg/g



AVEENO

Dosage form

Ointment



Glycerin

400 mg/g



CROTAN

Dosage form

Lotion



Crotamiton

100 mg/g

BILBERRY

DRY EXTRACT

ANTHOCYANIN-RICH BLUEBERRY EXTRACT

SUPPORTS EYE HEALTH

and visual function

HELPS PROTECT CELLS

against oxidative stress



1 GENERAL INTRODUCTION

Bilberry Dry Extract is a botanical ingredient derived from the fruits of *Vaccinium myrtillus L.*, known for its polyphenol content, particularly anthocyanins. These compounds are important bioactive constituents of bilberry and have been widely investigated for their **antioxidant activity and cell-protective effects**. Bilberry has also attracted research interest in eye health and is used in formulations designed to **support eye health and visual function**.

BILBERRY DRY EXTRACT IS UTILIZED IN FORMULATIONS TARGETING:

01



Supports eye health and visual function

02



Supports cellular protection against oxidative stress

03

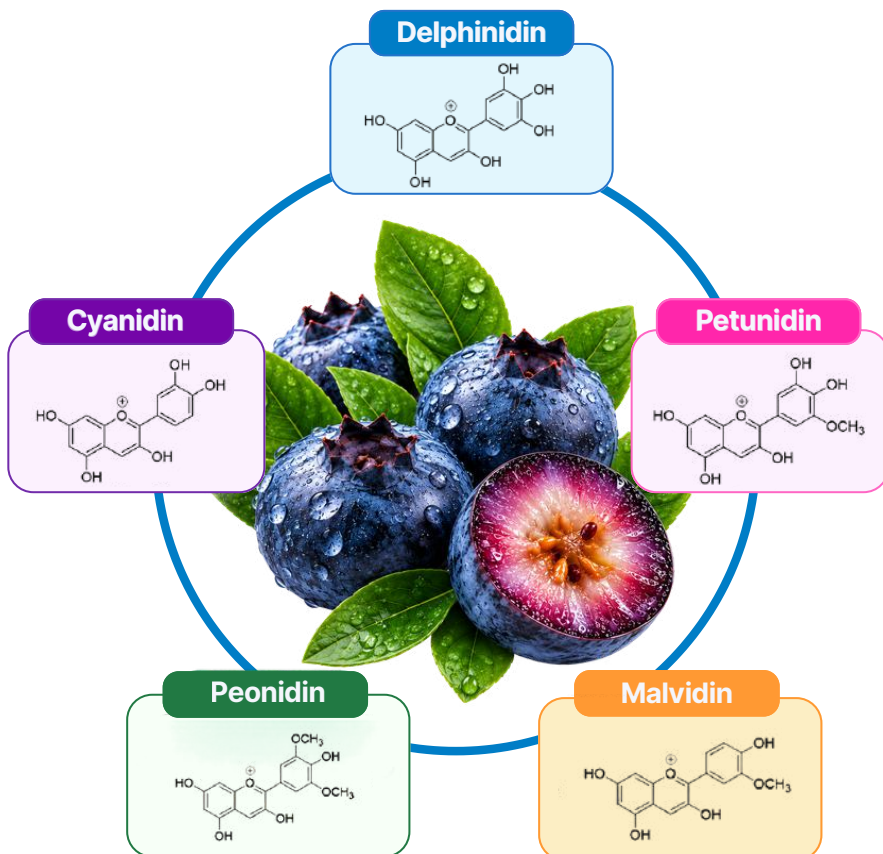


Helps reduce eye fatigue and digital eye strain



2 ACTIVE COMPONENT

Anthocyanins and anthocyanidins are related but distinct compounds. Anthocyanidins are the aglycone forms, whereas anthocyanins are formed when anthocyanidins are glycosylated with one or more sugar molecules.



CHARACTERISTICS OF BILBERRY ANTHOCYANINS

Bilberry is characterized by **15 anthocyanin derivatives**, formed by combining **5 main anthocyanidins** with 3 common sugars: glucose, galactose, and arabinose

5 ANTHOCYANIDIN (aglycone)

- Delphinidin
- Cyanidin
- Petunidin
- Peonidin
- Malvidin

THREE SUGAR (common)

- Glucose
- Galactose
- Arabinose

+



5 ANTHOCYANIDIN STRUCTURES × 3 TYPES OF SUGAR



15 ANTHOCYANIN DERIVATIVES

CHARACTERISTICS OF BILBERRY

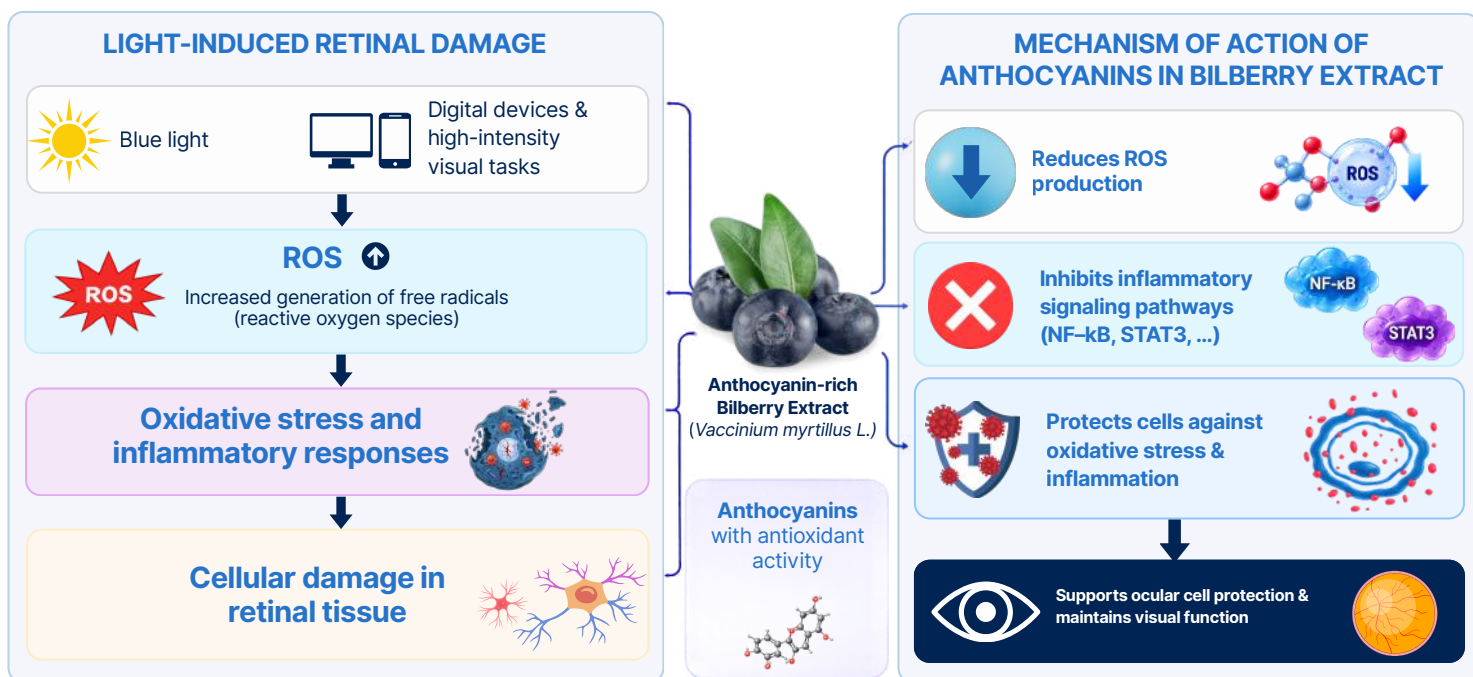
STRUCTURAL DIVERSITY

Anthocyanin derivatives arise from the combination of five anthocyanidin backbones with different sugar moieties, contributing to the characteristic chemical profile of *Vaccinium myrtillus L.*

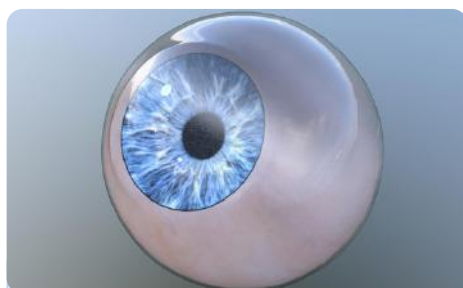


3 EYE PROTECTION MECHANISM

The eyes, particularly the retina, are continuously exposed to light, which can promote the generation of **reactive oxygen species (ROS)**. When ROS levels exceed the capacity of endogenous antioxidant defenses, **oxidative stress** may occur, contributing to **inflammatory responses and cellular damage**. Preclinical studies suggest that anthocyanins in bilberry extract may modulate these processes, potentially helping to **protect ocular cells** against oxidative stress and inflammation.

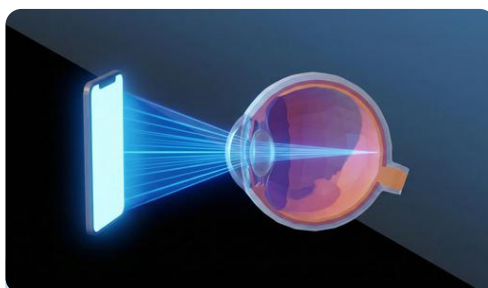


4 APPLICATIONS IN MARKETING PRODUCTS



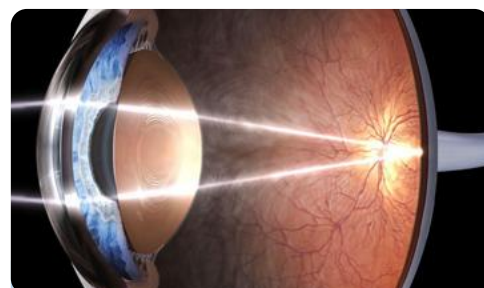
SUPPORT FOR EYE HEALTH AND VISUAL FUNCTION

Used in formulations designed to support eye health and maintain visual function. This is a prominent application of bilberry, making it suitable for daily eye health supplements.



RELIEF FROM EYE STRAIN

Used in formulations intended to help relieve eye strain, particularly in products for individuals with frequent visual demands, such as prolonged screen use or reading.



SUPPORT FOR OCULAR ACCOMMODATION

Used in formulations designed to support the eye's accommodative function, making it suitable for eye health products intended for individuals with high visual demands.

MARKETING PRODUCTS CONTAINING BILBERRY DRY EXTRACT



Blackmores Bilberry



Bilberry Extract & Lutein



Ultra Bilberry, Lutein & Zeaxanthin

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Biorich provides advanced raw material solutions, supporting formula optimization, enhancing efficacy, and ensuring quality for your pharmaceutical products.

CUSTOMERS REQUIRE

-  Raw material samples
-  COA/ Specification
-  R&D Support
-  Technical documentation
-  Suitable excipient solution
-  Detailed pricing

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-  Raw material sampling
-  Provide COA/ technical documentation
-  Formula and excipient advisory services
-  Optimizing formulations and manufacturing processes

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Meets
international
standards



CONSISTENT QUALITY

Complies with
stringent GMP
requirements



TECHNICAL SUPPORT

Dedicated &
in-depth
consultation



GLOBAL NETWORK

Connecting
reputable
worldwide
manufacturers

BIO RICH

INSIGHTS

**PHARMACEUTICAL INGREDIENTS,
HEALTH SOLUTIONS & INNOVATION**



NEW GENERATION EXCIPIENTS

Improve efficiency,
optimize formulas



PHARMACEUTICAL SOLUTIONS

Advanced technology for
superior performance



SUPERIOR QUALITY

Complies with stringent
international standards



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development



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