

BIORICH

INSIGHTS

PHARMACEUTICAL INGREDIENTS,
HEALTH SOLUTIONS & INNOVATION

PROTECT & EFFICIENCY

OPTIMIZING
PHARMACEUTICAL PRODUCTS

Advanced excipient technology helps protect active ingredients, optimize formulation efficiency, and improve patient treatment outcomes.



PROTECT THE ACTIVE INGREDIENT

Protect the active ingredient from harsh environments and degradation.



IMPROVE EFFICIENCY

Improve solubility, bioavailability, and process efficiency.



QUALITY & SAFETY ASSURANCE

Risk control, compliance with regulations, patient protection.



FUNCTIONAL COATING

Moisture-proof coatings, enteric-coated films, extended-release films

LINING


Increases the adhesion of the film coating, preventing interaction with the core.

HUMAN SERVING

Contains therapeutic active ingredients



SCIENCE FOR HEALTH QUALITY FOR LIFE

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

We offer a wide range of products such as **Active pharmaceutical ingredients (APIs), excipients, enzymes, vitamins,** and other biological components, serving the pharmaceutical, nutritional, healthcare, cosmetic, agricultural, and environmental industries.



PREMIUM QUALITY

We are committed to strict quality and safety standards for all our products.



SCIENCE-BASED SOLUTIONS

Driven by science and innovation to support pharmaceutical/food/cosmetic formulation for your business.



YOUR TRUSTED PARTNER

Building sustainable value through superior and reliable raw material products.



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ENTERIC COATED TABLET

AND THE POLYMERS USED



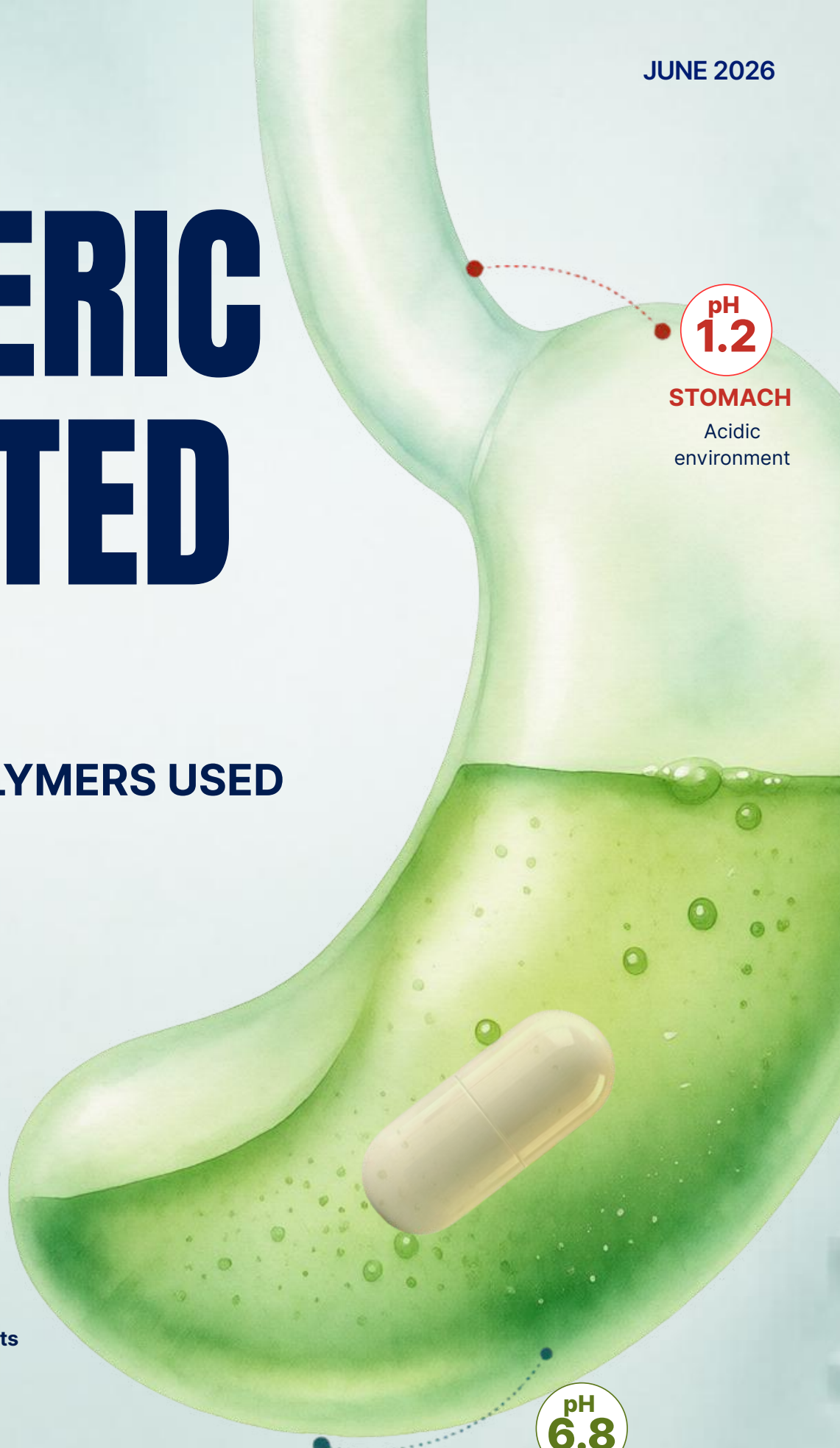
PROTECT
Sustained Gastric
Acid Resistance



RELEASE
Release in the
intestine (pH – 6.8)



EFFECTIVE
Increased
bioavailability,
reduced side effects



pH
1.2

STOMACH
Acidic
environment

pH
6.8

SMALL INTESTINE
Release of APIs



1 ENTERIC-COATED TABLETS

Enteric-coated tablets are film-coated tablets covered with a polymer coating that is resistant to gastric fluids and designed to release the API in the intestinal environment.

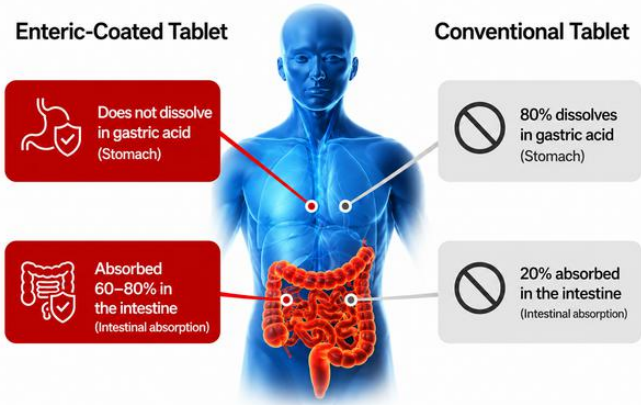
The acid-resistant coating protects the tablet from degradation in the acidic conditions of the stomach and subsequently dissolves in the intestine, allowing the API to be released at the desired site of action.

Due to their convenience, ease of manufacturing, and the absence of a requirement for expensive equipment, enteric-coated tablets have attracted considerable interest and are widely utilized in modern pharmaceutical technology.

OUTSTANDING ADVANTAGES

- ✓ Protect the from stomach acid.
- ✓ Control release site in the intestine.
- ✓ Increased bioavailability and therapeutic efficacy.
- ✓ Easy to formulate, suitable for industrial-scale production.
- ✓ Improve the stability and sensory properties of the tablets.

PURPOSE OF ENTERIC-COATED FILM



1

Reduce irritation or avoid nausea when the drug is released in the stomach.

2

Protecting the API from the effects of stomach acid (enzymes, antibiotics).

3

Enteral release helps maintain drug concentration, reducing first-pass metabolism in the liver.

4

Improved sensory appeal, a more attractive tablet surface, and masked unpleasant odors and tastes.

ENTERIC-COATED MEMBRANE PROPERTIES

1 ACID RESISTANCE
Resistant to stomach acid

- pH 1.2
- 2 hours
- The tablet is intact, not disintegrated

2 INTESTINAL RELEASE
Ensure release in the intestine

- pH 6.8
- 60 minutes
- Tablet disintegrates and releases API

3 WEIGHT GAIN
Weight gain of the film-coating layer

- 5 - 15%
- Typically 5 - 7%
- Ensuring efficiency and stability

2 THE APIS NEED TO BE COATED WITH AN ENTERIC-COATED FILM

GROUP OF APIS	SUBGROUP	FOR EXAMPLE	PURPOSE
EASILY DEGRADED BY GASTRIC FLUID	Digestive enzymes	Pancreatin, Trypsin	✓ Protection from stomach acid
	Antibiotic	Erythromycin, Penicillin	✓ Avoid degradation
	Proton pump inhibitors (PPIs)	Omeprazole, Esomeprazole, Lansoprazole, Rabeprazole	✓ Increased bioavailability
	Bioactive substances	Hormones, high doses of B vitamins	✓ Protecting activity
CAUSE IRRITATION OR DAMAGE TO THE STOMACH	NSAIDS	Aspirin, Diclofenac, Naproxen, Ibuprofen	✓ Reduce irritation
	Mineral salts and irritants	Potassium chloride iron supplement	✓ Reduce mucosal damage
	Corticosteroid	Prednisolone, Dexamethasone (high doses, long-term treatment)	✓ Increase feelings of well-being
LOCAL ACTION OR SITE-SPECIFIC ABSORPTION IN THE INTESTINE	Intestinal medication	Sulfosalazine, Mesalamine	✓ Area of effect
	Laxative	Bisacodyl	✓ Intestinal release
VEGETABLE OILS & SUPPLEMENTS	Omega-3	Fish oil, Omega-3	✓ Prevent acid reflux and heartburn

2 POLYMERS ARE COMMONLY USED FOR ENTERIC-COATED TABLETS

POLYMER GROUP	TYPICAL POLYMER	ILLUSTRATION	MAIN FEATURES	DISSOLUTION PH
CELLULOSE DERIVATIVES	<ul style="list-style-type: none"> Cellulose acetate phthalate (CAP) Hydroxypropyl ethylcellulose phthalate (HPECP) Hydroxypropyl methylcellulose phthalate (HPMCP) Hydroxypropyl methylcellulose acetate succinate (HPMCAS) 		<ul style="list-style-type: none"> ✓ Excellent film-forming ability, producing continuous and durable films. ✓ Commonly used in enteric-coated systems. ✓ Its flexible pH range allows for easy dissolution and suitability for multiple release sites in the intestine. 	4.5 – 6.8
VINYL ACETATE DERIVATIVES	<ul style="list-style-type: none"> Poly vinyl acetate phthalate (PVAP) 		<ul style="list-style-type: none"> ✓ It creates a stable film with good mechanical strength. ✓ It has good acid-resistant properties, protecting the APIs in the stomach. ✓ Compatible with many components in film coating formulations. 	5.0
METHACRYLIC ACID DERIVATIVES	<ul style="list-style-type: none"> Eudragit L100-55 Eudragit L30D-55 Eudragit L100 		<ul style="list-style-type: none"> ✓ Precise control of the release site. ✓ High repeatability between production batches. ✓ The pH range of dissolution is narrow, suitable for intestinal release requirements. 	5.5 – 6.0
NATURAL ORIGIN	<ul style="list-style-type: none"> Shellac Sodium alginate 		<ul style="list-style-type: none"> ✓ Naturally sourced, bio-safe. ✓ Applications include specialized formulations and health supplement products. 	5.0 – 7.0

IDEAL ENTERIC-COATED POLYMER

- ✓ It must have solubility at a pH suitable for the desired target of action (intestine, rectum, etc.).
- ✓ Compatibility with other components of the coating solution and with the API helps ensure the uniformity and effectiveness of the film-coated tablets.
- ✓ Ability to form a continuous coating
- ✓ Non-toxic
- ✓ Reasonable cost



Solubility suitable for intestinal pH



Good acid resistance



Continuous film formation capability



Compatibility with the API and excipients

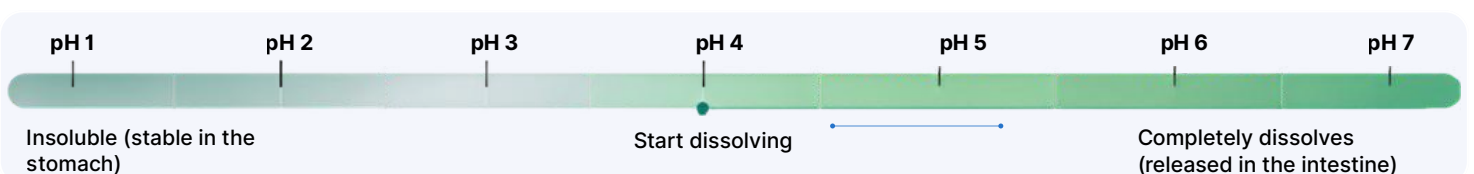


Safe and non-toxic



Reasonable cost, cost-effective

PH SCALE OF POLYMER DISSOLUTION



POLYOXYL CASTOR OIL

**SOLUBILIZER FOR
LIQUID AND SEMI-SOLID
DOSAGE FORMS**



EFFECTIVE SOLUBILIZER

Increase the solubility of poorly soluble drugs.



SUPERIOR EMULSIFIER

Stabilizing emulsions and suspensions



INCREASE PERMEABILITY

Improves absorption and bioavailability.



SAFE & STABLE

Colorless, odorless, and durable over time.

APPLICATIONS IN VARIOUS DOSAGE FORMS



Syrups & Oral Solutions



Oral suspension



Cream & Gel



Lotions & topical drugs



Injectable drugs



1 INTRODUCTION TO POLYOXYL CASTOR OIL

Polyoxyl castor oil is a class of excipients derived from polyoxyl ethylated castor oil, including non-ionic surfactants commonly used in pharmaceutical formulations to improve solubility, emulsification, permeability, and bioavailability of poorly water-soluble APIs, especially in liquid and semi-solid dosage forms.



COMMONLY USED POLYOXYL CASTOR OIL

POLYOXYL 40 HYDROGENATED CASTOR OIL (USP/NF)



POLYOXYL 40 HYDROGENATED CASTOR OIL (USP/NF) + PROPYLENE GLYCOL



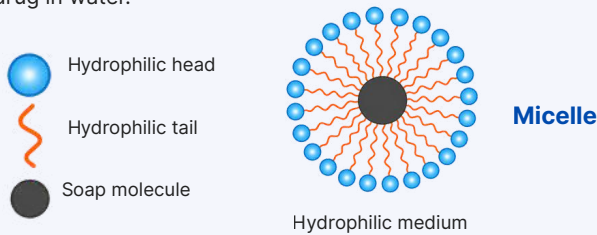
POLYOXYL 35 CASTOR OIL (USP/NF)



2 SOBILIZATION MECHANISM

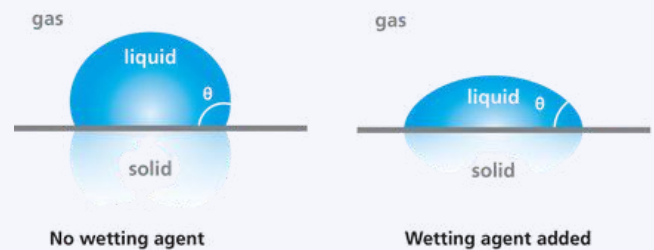
A CREATE MICELLES – MAIN SOLUBILIZATION MECHANISM

When dispersed in water at appropriate concentrations, surfactant molecules self-assemble to form micelles with a hydrophobic core inside and a hydrophilic outer shell. Drugs that are poorly soluble in water will be dissolved or trapped within this micelle core, increasing the apparent solubility of the drug in water.

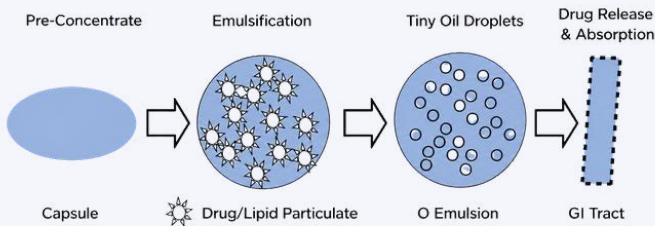


B REDUCE SURFACE TENSION

In addition to their micelle-forming mechanism, this group of excipients also helps reduce the surface tension between the drug substance and the dispersion medium (reducing the contact angle between the solute and the solvent), improving the wettability of the drug particles and promoting dispersion.



C CREATE A SELF-EMULSIFYING SYSTEM



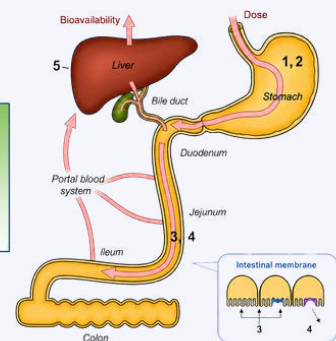
In self-emulsifying or microemulsifying systems, polyoxyl castor oil also helps form very small oil droplets, increasing the contact area of the drug with the dissolution medium and thus improving the dissolution rate and absorption of the drug.

D P-GLYCOPROTEIN INHIBITION

Human Intestinal Absorption (HIA)

- 1,2 – Stability + Solubility
- 3 – Passive + Active Tr.
- 4 – Pgp efflux + CYP 3A4

Oral Bioavailability (%F)



These excipients can also affect biological membrane permeability and inhibit P-glycoprotein, contributing to increased oral bioavailability of some poorly absorbed drugs.

3 ADVANTAGE



01 COLORLESS - ODORLESS

A white to pale yellow liquid, transparent or slightly cloudy, odorless and tasteless, and does not affect the taste of the formulation.



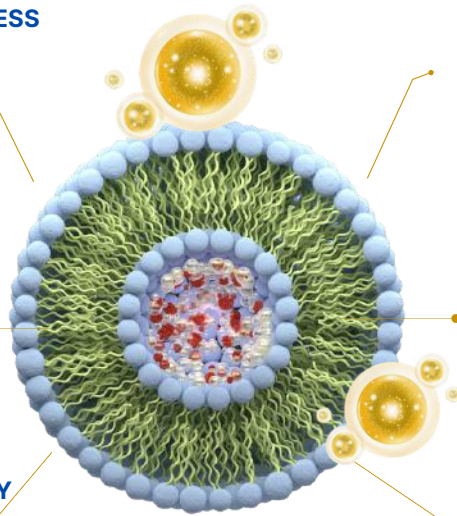
02 LOW VISCOSITY

Its very low viscosity poses little difficulty in the preparation process.



03 SUPERIOR SOLUBILITY

It dissolves very well in water, dissolves well in alcohol and ethyl acetate, but is insoluble in mineral oil.



04 HIGH STABILITY

Very durable and does not develop an odor under recommended storage conditions.



05 NO PRECIPITATION

Compatible with products containing electrolytes, salts, and acids.



06 HIGH HLB (14 - 17)

Ideal O/W emulsifier for poorly water-soluble APIs.

4 APPLICATIONS IN PHARMACEUTICAL FORMULATION

<p>A. SOLUBILIZER</p> <p>Improves the water solubility of the API that is poorly soluble in syrup, increasing solubility and bioavailability.</p>	<p>B. EMULSIFIER</p> <p>Hydrophobic substances in pharmaceutical emulsions (fatty acids/alcohols, mineral oils, etc.)</p>	<p>C. INCREASED PERMEABILITY</p> <p>Increase the permeability and dispersion of the API in pharmaceutical suspensions.</p>
<p>D. MASKING AGENT</p> <p>Helps mask the unpleasant taste of some APIs in oral liquid dosage forms.</p>	<p>E. SLOWS DOWN EVAPORATION</p> <p>Minimize alcohol or essential oil loss and reduce the risk of re-precipitation.</p>	<p>F. FILM FORMATION & ADHESION REDUCTION</p> <p>Increase film-forming ability, reduces adhesion and scaling properties, resulting a smoother product.</p>

COMMON DOSAGE FORMS



RECOMMENDED APIS

	Polyoxyl 40 Hydrogenated Castor Oil	Polyoxyl 40 Hydrogenated Castor Oil + Propylene Glycol	Polyoxyl 35 Castor Oil
RECOMMENDED APIS	<ul style="list-style-type: none"> Vitamin A Vitamin D Vitamin E 	<ul style="list-style-type: none"> Paracetamol Bromhexin HCl Ambroxol HCl Dextromethorphan HBr Ciproheptadine 	<ul style="list-style-type: none"> Vitamin A Vitamin D Vitamin E

METHACRYLIC ACID COPOLYMER

AND THE APPLICATION IN ENTERIC-COATED TABLETS



PROTECT THE API
in the stomach



COMPLETE DRUG RELEASE
in the duodenum/ small intestine



SOLUBLE AT PH > 5.5
suitable for enteric-coated application



COMPATIBILITY
with various organic solvents



CONSISTENT QUALITY
complies with USP/NF,
Ph. Eur standards.





1 INTRODUCTION TO METHACRYLIC ACID CO-POLYMER

Methacrylic acid copolymers are a general class of polymers derived from methacrylic acid, with their primary application in pharmaceutical formulation being film-forming agents for enteric coating.

Several derivatives of methacrylic acid are commonly used:

- ✓ **Methacrylic acid & Methyl methacrylate co-polymer**
- ✓ **Methacrylic acid & Ethyl acrylate co-polymer**

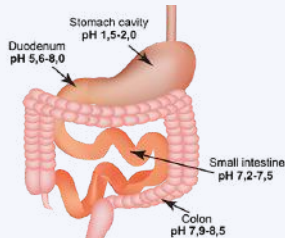
SUPPLY FORM

POWDER FORM	VS	PRE-MIXED SUSPENSION FORM
		
<ul style="list-style-type: none"> ✓ Convenient for storage. ✓ Easily adjust and change the formula. ✓ A broad selection of appropriate solvents. 		<ul style="list-style-type: none"> ✓ Optimizing the polymer dispersion process. ✓ Using water helps reduce the risk of residual solvent. ✓ Reduce the risk of fire and explosion during the production process.

2 PROPERTIES OF METHACRYLIC ACID DERIVATIVE EXCIPIENTS

SOLUBLE AT PH > 5.5

Suitable for enteric-coated tablets, ensuring the film layer remains intact at gastric pH and guaranteeing the release of the API when the tablet reaches the desired site of action, the duodenum/ small intestine.



WELL IN SOLVENTS

To create a stable solution or suspension, convenient for the film coating process.

- Alcohol,
- Methanol
- Isopropyl Alcohol
- Acetone









INSOLUBLE BUT WELL DISPERSED IN WATER

Forms a homogeneous, stable dispersion system, suitable for water-based coating formulations.



3 ADVANTAGES OF METHACRYLIC ACID DERIVATIVE EXCIPIENTS

ADVANTAGE	VALUE DELIVERED
 Superior enteric-coated efficacy	Optimal protection of the API in the stomach and release in the duodenum/ small intestine.
 Not rapidly hydrolyzed	More stable than some other ester polymers (e.g., cellulose acetate phthalate – CAP).
 Creates a film coating with an aesthetically pleasing appearance and good mechanical strength	Produces smooth, glossy, and firm film-coated tablets.
 The film coating formula can be easily adjusted	Flexibility in optimizing formulas to achieve desired results.
 Low viscosity	Convenient for the film coating process, reducing the risk of spray gun clogging.
 Included in the monographs of USP/NF, Ph. Eur	Convenient for the product registration process.

LUBRICANT GLIDANT IN TABLET PRODUCTION

THE ROLE OF LUBRICANTS,
ANTI-ADHERENTS, AND
GLIDANTS IN MODERN
TABLET FORMULATION



IMPROVE
FLOWABILITY



MINIMIZE
TABLET STICKING



OPTIMIZATION
THE TABLET
EJECTION

1 INTRODUCTION TO LUBRICANTS - GLIDANTS



ONE OF FOUR ESSENTIAL COMPONENTS

Lubricants - glidants are one of the four essential components in tablet formulations.



LOW CONCENTRATION - BIG IMPACT

Even when used in low concentrations, this group of excipients offers numerous benefits to the quality of finished tablets, the tablet compression process, and the lifespan of tablet compression machine.



MAKING THE RIGHT CHOICE IS KEY

Consider material properties, compatibility, and cost for formulation optimization.



Choosing the right lubricant and glidant optimizes the manufacturing process, improves product quality, and extends equipment lifespan.



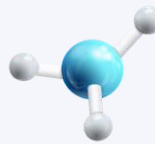
4 ESSENTIAL COMPONENTS IN THE TABLET FORMULA

Fillers



Ensure mass uniformity and modify powder properties.

Binders



Create bonds between powder particles.

Disintegrants



Ensure disintegration, dissolution, and bioavailability.

Lubricants/ Glidants



Improve tablet quality and equipment lifespan.

2 ROLE IN TABLET FORMULATION

In the tablet compression process, lubricant and glidants affect the following stages:

1



ARRANGE AND BIND POWDER PARTICLES



Firstly, glidants affect powder flow into the die cavity and influence the particle rearrangement and interparticle bonding within the powder bed under the applied compression force.

2



TABLET EJECTION



Subsequently, following tablet formation, lubricants influence the frictional interactions between the tablet and the punches and die, and facilitate tablet ejection from the die in the tablet press.

3



ENSURING TABLET QUALITY



Finally, in finished tablet formulations, lubricants significantly contribute to key tablet properties, including organoleptic characteristics, solubility, and disintegration behavior.

Although they are often collectively termed glidants and lubricants, these excipients can be further subdivided into groups based on their primary functions in tablet formulations:

GLIDANT



Their main function is to enhance the flowability of the powder blend, contributing to uniform tablet weight and consistent drug content.

ANTI-ADHERENT



Their main function is to prevent tablet adhesion to the punch faces and to minimize defects such as surface pitting.

LUBRICANT



Their main functions include reducing friction between the tablet and the die wall, enabling smooth tablet ejection from the die cavity, and enhancing the durability of punches, dies, and the tablet press. In addition, they improve tablet surface finish and help prevent defects such as lamination and edge chipping.

3 COMMON TYPES OF LUBRICANT AND GLIDANT

NAME OF EXCIPIENT	ROLE	PROPERTIES	CONCENTRATION
 SILICON DIOXIDE	Glidant	<ul style="list-style-type: none"> Hydrophilic, with various types differing in size and density 	1 – 2%
 MAGNESIUM STEARATE	Lubricant & anti-adherent	<ul style="list-style-type: none"> The most commonly used lubricant. High melting point (88–130°C). Hydrophobic and may affect tablet disintegration and dissolution. Prolonged mixing may negatively influence tablet hardness. Metallic taste. Incompatible with certain APIs, such as proton pump inhibitors (PPIs). 	0,5 – 1%
 SODIUM STEARYL FUMARATE	Lubricant & anti-adherent	<ul style="list-style-type: none"> Very high melting point (224–245°C). More hydrophilic and therefore has a reduced impact on tablet disintegration and drug dissolution. Has little effect on tablet hardness even when blending time is prolonged. Shows minimal to almost no incompatibility with APIs. 	0,5 – 1%
 STEARIC ACID	Lubricant & anti-adherent	<ul style="list-style-type: none"> Moderate melting point (67–72°C). Hydrophobic and may affect tablet disintegration and drug dissolution. Prolonged mixing may influence tablet hardness. 	0,5 – 3%
 GLYCERYL DIBEHENATE	Lubricant & anti-adherent	<ul style="list-style-type: none"> Low melting point (65 – 77°C) Belongs to the lipid excipient group and contributes to the production of tablets with a smooth and glossy appearance. 	1 – 3%
 HYDROGENATED CASTOR OIL	Lubricant & anti-adherent	<ul style="list-style-type: none"> Low melting point (65 – 77°C) Belongs to the lipid excipient group and contributes to the production of tablets with a smooth and glossy appearance. 	0,5 – 4%
 HYDROGENATED VEGETABLE OIL	Lubricant & anti-adherent	<ul style="list-style-type: none"> Low melting point (65 – 75°C) Belongs to the lipid excipient group and contributes to the production of tablets with a smooth and glossy appearance. High stability Tablet adhesion support 	0,5 – 4%
 PEG 4000/6000	Lubricant for effervescent tablets and ODTs	<ul style="list-style-type: none"> Hydrophilic lubricant. Does not create an oily film when effervescent tablets and ODTs dissolve. Does not affect the disintegration and dissolution of the tablet. 	1 – 3%

AVOCADOFLEX

AVOCADO SOYBEAN
UNSAPONIFIABLES (ASU)

SUPPORTS MOBILITY AND
JOINT HEALTH



JOINT FLEXIBILITY

Supports the natural inflammatory response.



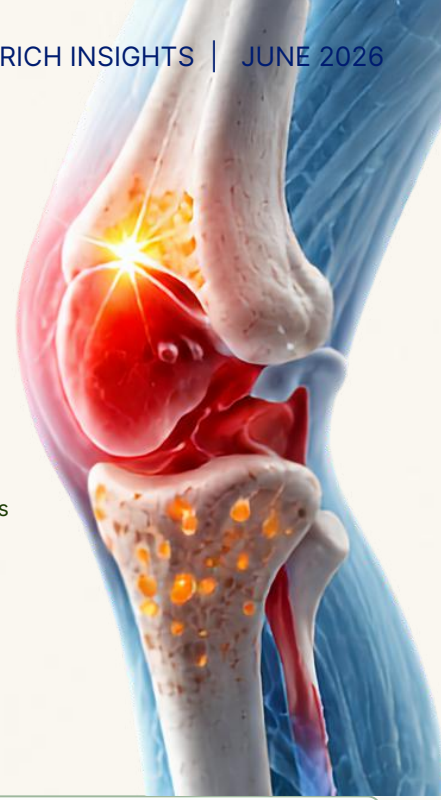
PROTECT CARTILAGE

Protect and maintain cartilage structure.



MOVE FREELY

Supports joint function and mobility.



AVOCADOFLEX

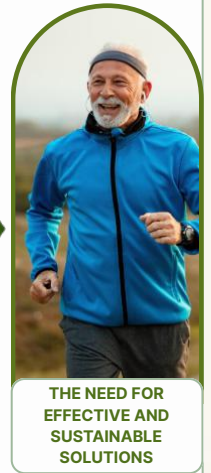
**IMPROVED NATURAL INGREDIENTS
FOR BONE & JOINT HEALTH AND
LONG-TERM MOBILITY.**

Avocadoflex® is a blend of non-saponifiable substances from avocados and soybeans, containing a minimum of 30% phytosterols. This product is designed to support joint comfort and mobility over time by supporting the body's natural inflammatory response.

1 WHY DOES THE MARKET NEED AVOCADOFLEX?

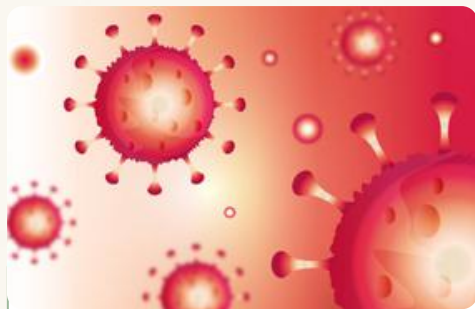
The demand for bone and joint care solutions is growing rapidly due to the aging population and the willingness to pay for healthcare products.

However, most traditional joint support products focus only on reducing pain and stiffness, rather than supporting joint structure restoration. Understanding this, Avocadoflex® was created to fill this gap.



COMPREHENSIVE SUPPORT MECHANISM

Thanks to its anti-inflammatory, antioxidant, and analgesic properties, Avocadoflex® is used to treat musculoskeletal problems.



01 REGULATING THE INFLAMMATORY RESPONSE

Regulate inflammatory cytokines, naturally reducing inflammation and improving pain.



02 PROTECTING CARTILAGE STRUCTURE

Helps protect joint cartilage from degeneration and harmful environmental factors causing inflammation.



03 SUPPORTS JOINT TISSUE REGENERATION.

Supports the regeneration and repair of cartilage tissue, maintaining a healthy joint structure in the long term.








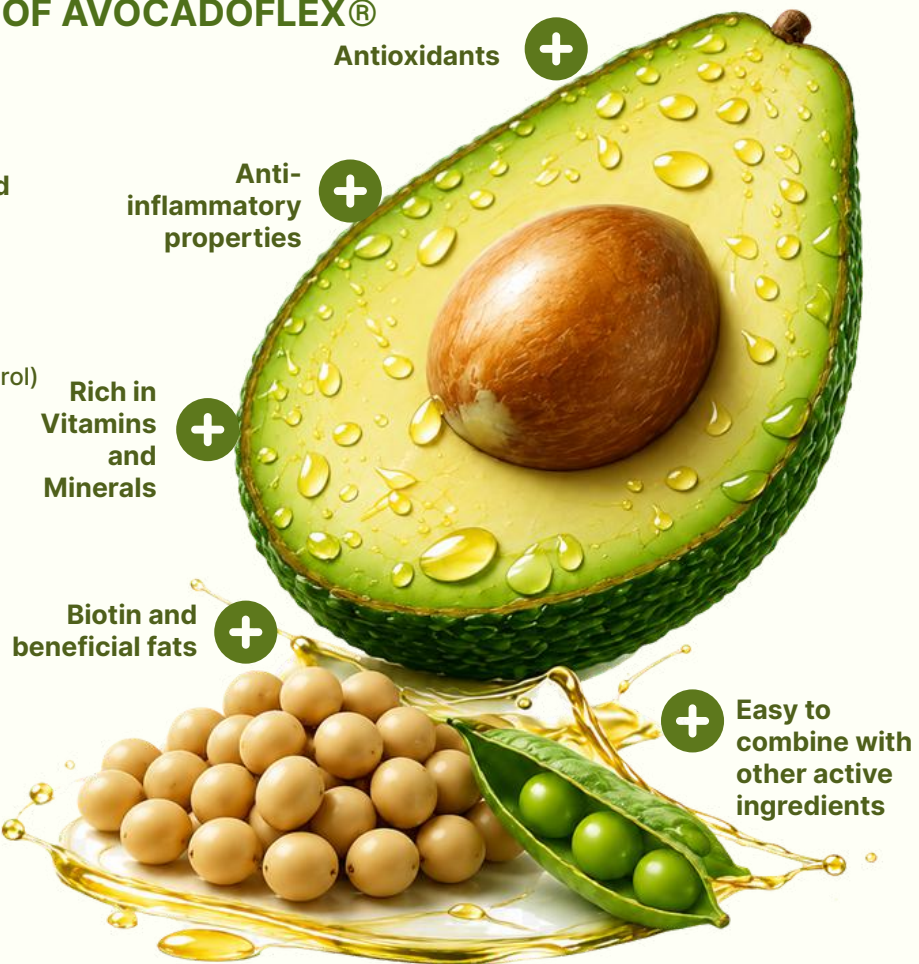
Unlike ingredients that only alleviate symptoms, Avocadoflex® directly targets the pathogenesis of osteoarthritis. Thanks to its root-cause mechanism, this ingredient allows manufacturers to develop products that not only reduce joint pain but also support long-term joint structure protection.

2 THE ACTIVE INGREDIENTS OF AVOCADOFLEX®

The main active ingredient of Avocadoflex® is **Avocado Soybean Unsaponifiables (ASU)** – Unsaponifiable substances from avocados and soybeans.

Avocadoflex® contains important bioactive compounds including:

-  Phytosterols (sitosterol, campesterol, stigmasterol)
-  Tocopherols – Natural Vitamin E
-  Squalene
-  Lipid-soluble antioxidants
-  Plant-derived bioactive lipid compounds



Of that, **phytosterols account for 30%**. This compound offers indirect benefits through its anti-inflammatory effects, regulating bone metabolism and supporting cartilage protection.

3 ADVANTAGES OF AVOCADOFLEX



HIGH PURITY AND STANDARDIZATION

Manufactured under strict GMP standards for consistent active content



PLANT-BASED ORIGIN, CLEAN LABEL TREND

Avocadoflex® is made entirely from plant extracts, aligning with the current trend of vegan functional foods.



OPTIMAL BIOAVAILABILITY

Enhanced absorption and joint tissue delivery for optimal efficacy.



STRONG COORDINATION AND COLLABORATION CAPABILITIES

Avocadoflex® easily combines with other common joint support ingredients to create superior joint support products through a multi-mechanism approach.

COMBINED WITH



GLUCOSAMINE



CHONDROITIN



COLLAGEN TYPE II




MSM



HYALURONIC ACID

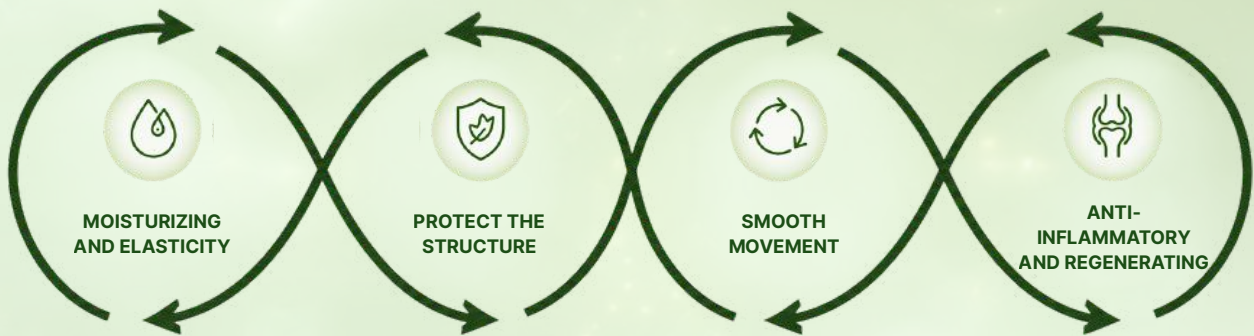
APPLICATION AVOCADOFLEX

Thanks to its multifaceted mechanism of action, Avocadoflex® is suitable for functional food products:

-  Supports the treatment of osteoarthritis
-  Joint care for the elderly
-  Increase physical activity for athletes
-  Long-term protection of joint cartilage

THE MULTI-DIMENSIONAL MECHANISM OF ACTION OF AVOCADOFLEX

Avocadoflex® supports bone and joint health through four main mechanisms:



DOSAGE FORM

Avocadoflex® is supplied in powder form, suitable for dosage forms such as:



TABLETS



HARD CAPSULES



POWDER



GRANULES

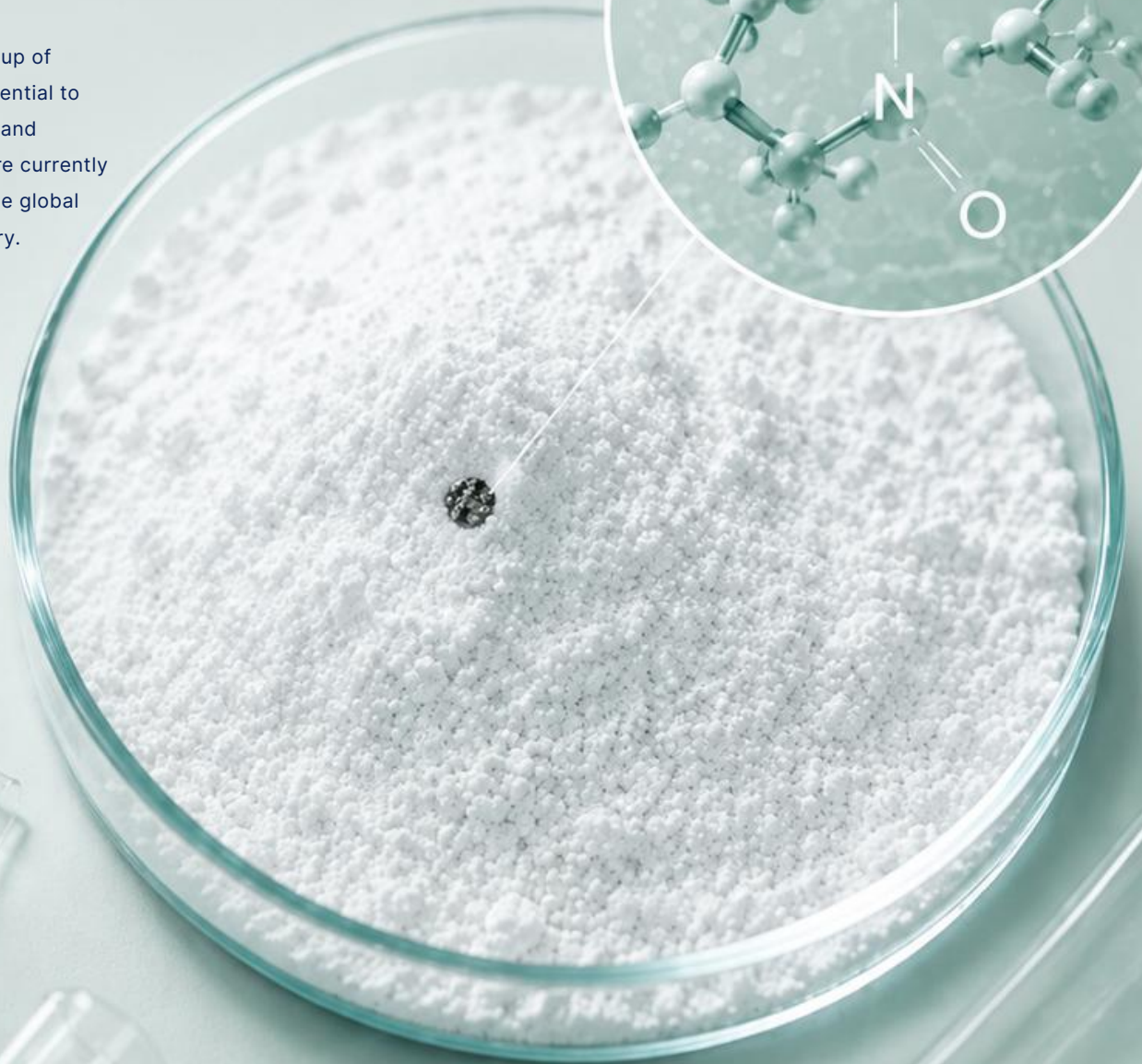
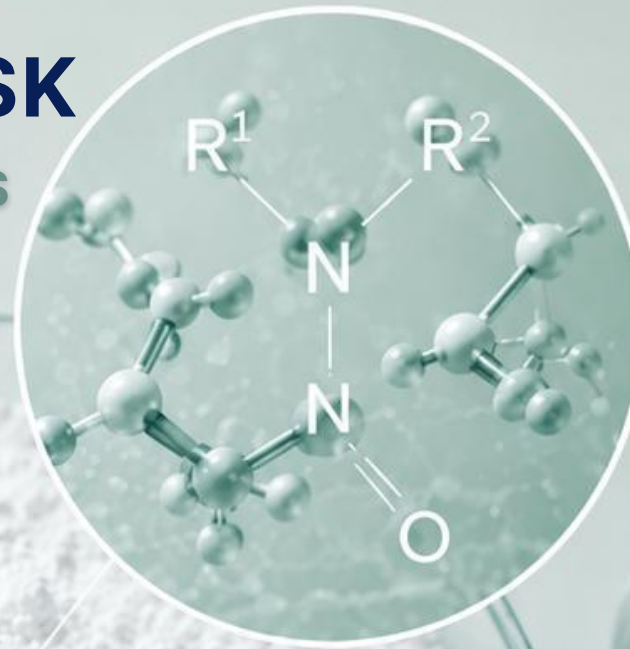


POWDER/GRANULES FOR SUSPENSION

NITROSAMINE

THE ASSOCIATED RISK IN PHARMACEUTICAL INGREDIENTS

Nitrosamines are a group of impurities with the potential to cause gene mutations and carcinogenicity, and are currently strictly controlled in the global pharmaceutical industry.



1 WHAT IS NITROSAMINE?

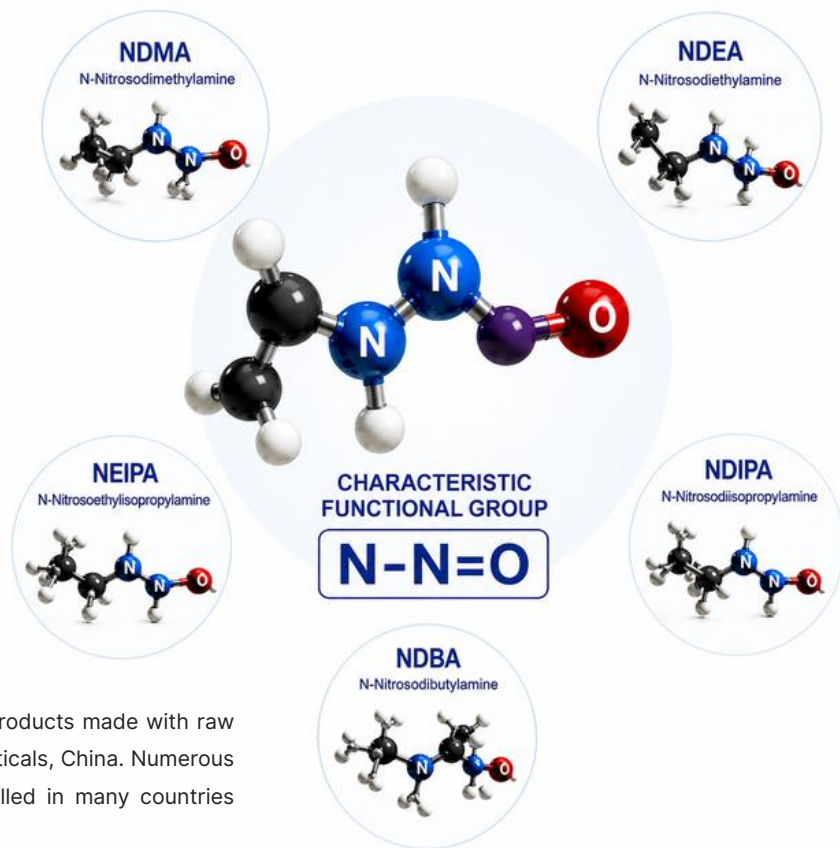
Nitrosamines are a group of organic compounds containing the N-nitroso (-N=O) functional group, usually formed from the reaction between amines and nitrate groups (often nitrites) in an acidic environment.

SOME NITROSAMINES THAT ARE OF COMMON CONCERN IN PHARMACEUTICALS INCLUDE:

- **N-Nitrosodimethylamine (NDMA)**
- **N-Nitrosodiethylamine (NDEA)**
- **N-Nitrosoisopropylamine (NEIPA)**
- **N-Nitrosodibutylamine (NDBA)**

These substances are considered mutagenic contaminants, and many of them are classified as potentially carcinogenic in humans or experimental animals.

This impurity was first detected in finished Valsartan products made with raw materials manufactured by Zhejiang Huahai Pharmaceuticals, China. Numerous batches of Valsartan produced there have been recalled in many countries worldwide, including Vietnam.



2 THE FORMATION PROCESS OF NITROSAMINES IN ACTIVE INGREDIENTS AND EXCIPIENTS

In pharmaceutical ingredients, nitrosamines are usually not intentionally added but are unintentionally formed during manufacturing and storage processes.



FROM THE PROCESS OF SYNTHESIZING ACTIVE INGREDIENTS (APIs)

This is the most common cause. The synthesis process may utilize solvents or raw materials that promote the reaction to create nitrosamines.

- Amine-containing solvents: dimethylamine, diethylamine, triethylamine
- Use nitrite salts: sodium nitrite, potassium nitrite
- For example: Dimethylamine + nitrite → NDMA. This is the cause of the nitrosamine crisis in sartan-type drugs in 2018.



FROM ENVIRONMENTAL POLLUTION IN PRODUCTION

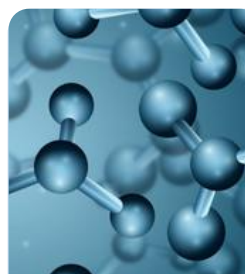
Many plants recycle solvents to reduce costs. If the solvent contains amine residues or nitrosamine residues and these are not properly controlled, nitrosamines can accumulate over multiple reuse cycles. Solvents containing amine or nitrosamine residues. Poor control in recovery and refining. The risk accumulates over multiple reuse cycles.



FROM REAGENTS OR RAW MATERIALS CONTAMINATED WITH NITRITE

Nitrite may be present in trace amounts in: pure water, inorganic reagents, excipients, and intermediate materials.

- Purified water
- Inorganic reagents
- Excipients
- Intermediate materials



FROM THE DEGRADATION OF PHARMACEUTICAL ACTIVE INGREDIENTS

Some active ingredients have structures containing secondary or tertiary amines. Under certain storage conditions, such as high temperature, high humidity, or the presence of nitrite, they can spontaneously form nitrosamines.



Examples have been reported with Ranitidine and Nizatidine. This is why many products containing Ranitidine have been recalled globally.

3 ACTIVE INGREDIENTS AND EXCIPIENTS WITH THE HIGH-RISK OF NITROSAMINE CONTAMINATION

a. Active ingredient (API)

Active ingredients containing secondary or tertiary amine groups are generally considered to have a higher risk of nitrosamine contamination during manufacturing or storage.



Examples of active ingredients of concern:

- Metformin
- Ranitidine
- Nizatidine
- Doxylamine
- Varenicline
- Sartans Group (Valsartan, Losartan, Irbesartan)

LIST OF ACTIVE INGREDIENTS WITH A RISK OF NITROSAMINE FORMATION

ACTIVE INGREDIENT	ACTIVE INGREDIENT	ACTIVE INGREDIENT	ACTIVE INGREDIENT	ACTIVE INGREDIENT	ACTIVE INGREDIENT
Abacavir	Clomipramine	Florbetapir F-18	Miglustat	Propoxyphene	Rizatriptan
Acarbose	Clozapine	Flutemetamol F-18	Mirabegron	Propranolol	Salmeterin
Acebutolol	Colistin	Folic Acid	Mitoxantrone	Propylhexedrine	Sarecycline
Almotriptan	Cyclobenzaprine	Formoterol	Moexipril	Protriptyline	In the Sietals
Amitriptyline	Degarelix	Fosdenopterin	Moxifloxacin	Pseudoephedrine	Spinosad
Amlodipine	Demeclocycline	Fostamatinib	Nadolol	Pyrimidine	Streptomycin
Amoxapine	Desloratadine	Frovatriptan	Neratinib	Quinupristin	Sumatriptan
Arformoterol	Desvenlafaxine	Furosemide	Nicardipine	Racepinephrine	Tafenoquine
Argatroban	Deucravacitinib	Gatifloxacin	Nifedipine	Ramipril	Tamoxifen
Articaine	Dexamethorphan	Hydrochlorothiazide	Nimodipine	Rasagiline	Tamsulosin
Atenolol	Dexchlorpheniramine	Hydroxychloroquine	Nintedanib	Relebactam	Telavancin
Avacopan	Dexmethorphan	Imipramine	Nisoldipine	Rifabutin	Telithromycin
Avanafil	Dichlorpheniramine	Isoproterenol	Nortriptyline	Rifampin	Terbutaline
Azithromycin	Difenhydramine	Isradipine	Olanzapine	Rilpivirine	Tetracaine
Bedaquiline	Dipivefrin	Ivacaftor	Oleridine	Risdiplam	Tetracycline
Belumosudil	Dobutamine	Levamisole	Obidaterol	Rivastigmine	Thonzylamine
Benazepril	Dorzolamide	Levobunolol	Ondansetron	Rolapitant	Ticagrelor
Bendroflumethiazide	Doxepin	Levoleucovorin	Oritavancin	Safinamide	Tigecycline
Benzonatate	Doxycycline	Levomefolic Acid	Ozaninod	Salmeterol	Timolol
Berotrastat	Duvelisib	Lisinopril	Ozenoxacin	Sapropterin	Tirofiban
Betaxolol	Elagolix	Maribavir	Padimate	Sertraline	Torsemid
Bicistate	Enalapril	Mecamylamine	Palbociclib	Sotalol	Tramadol
Bisoprolol	Ephedrine	Meclofenamic Acid	Perindopril	Sildenafil	Trandolapril
Brompheniramine	Ertapenem	Mefloquine	Pheniramine	Spinosad	Trientine
Bumetanide	Erythromycin	Meropenem	Maralixibat	Streptomycin	Trimethobenzamide
Bupropion	Escitalopram	Methadone	Phenylephrine	Sumatriptan	Trinipramine
Cabergoline	Escitalopram	Methamphetamine	Phenylephrine	Tafenoquine	Ulipristal Acetate
Cangrelor	Eszopiclone	Methylene Blue	Phenylephrine	Tamoxifen	Vancomycin
Carbinoxamine	Esmolol	Metolazone	Phenylephrine	Tamsulosin	Venlafaxine
Carteolol	Etravirine	Metoprolol	Pindolol	Telavancin	Vibegron
Carvedilol	Exemestane	Mifepristone	Plazomicin	Telithromycin	Vilanterol
Caspofungin	Felodipine		Plerixafor	Terbutaline	Viloxazine
Chlophedianol	Fenfluramine		Polythiazide	Tetracaine	Vortioxetine
Chloroquine	Fenoldopam		Pramipexole	Tetracycline	Zolmitriptan
Chlorpheniramine	Finerenone		Prilocaine	Thonzylamine	
Chlorpromazine	Flecainide		Primaquine	Ticagrelor	
Cinacalcet	Florbetaben F-18		Proline	Tigecycline	
Ciprofloxacin			Promethazine	Timolol	
Citalopram			Propafenone	Tirofiban	
Clarithromycin				Torsemid	
Clevidipine				Tramadol	

3 ACTIVE INGREDIENTS AND EXCIPIENTS WITH THE HIGH-RISK OF NITROSAMINE CONTAMINATION

b. Excipients

- Some excipients may contain traces of nitrite: the nitrite content is usually very low and varies between manufacturers.
- Excipients containing amines or amine groups: these excipients may participate in the reaction to form nitrosamines when a nitrite source is present.





EXCIPIENT GROUP	EXCIPIENTS	RISK MECHANISM	LEVEL
 FILLER	Microcrystalline Cellulose	May contain residual nitrite, with significant variations between suppliers	High
	Lactose	May contain residual nitrite	Medium
	Pregelatinized Starch	May contain residual nitrite	Medium
 DISINTEGRANT	Sodium starch glycolate	Some studies have noted relatively high nitrite levels	High
	Croscarmellose sodium	May contain residual nitrite	Medium
	Crospovidone	There are residual nitrites, which are also of pyridoxine origin	High
 BINDER	Povidone	May contain nitrite and amine impurities	High
	Copovidone	May contain nitrite and amine impurities	High
 POLYMER	Chitosan	Contains many free amino groups	High
	Polyethyleneimine	Contains primary, secondary, and tertiary amines	Very high
	Poly(allylamine hydrochloride)	Contains primary amines	High
	Polyvinylamine	Contains many free amino groups	High
 SURFACTANTS	Triethanolamine	Nitrosodimethylamine can be produced	Very high
	Diethanolamine	Typical Nitrosamine Properties	Very high
	Monoethanolamine	It may undergo nitration	High
	Oleylamine Ethoxylate	Contains amino groups	High
	Stearylamine Ethoxylate	Contains amino groups	High
	Laurylamine	Contains primary amines	High

4 REGULATIONS ON NITROSAMINE IMPURITY LIMITS

The regulations regarding the limits of some common nitrosamine impurities are presented in the following table, with 1 ng = 1/1,000,000 mg.



 NITROSAMINE IMPURITIES	 LIMIT (NANOGRAMS/ DAY)
NDMA (N-Nitrosodimethylamine)	96
NMBA (N-Nitroso-N-methyl-4-aminobutyric Acid)	96
NDBA (N-Nitrosodibutylamine)	96
NDEA (N-Nitrosodiethylamine)	26.5
NMPA (N-Nitrosomethylphenylamine)	26.5
NIBEA (N-Nitrosoisopropylethylamine)	26.5
NDIPA (N-Nitrosodiisopropylamine)	26.5



* Please refer to the regulations regarding nitrosamine impurity limits for more information

[CDER Nitrosamine Impurity Acceptable Intake Limits](#)



METHODS FOR TASTE MASKING OF BITTER DRUGS

IN PHARMACEUTICAL FORMULATION

TASTE-MASKING SOLUTIONS FOR
IMPROVED PATIENT COMPLIANCE
AND THERAPEUTIC OUTCOMES



“

TASTE MASKING IS MORE THAN
A SENSORY EXPERIENCE,
IT IS A **TECHNICAL SOLUTION**

TASTE MASKING TECHNIQUE



Prevents the API from coming into contact with taste receptors in the oral cavity while ensuring drug release upon reaching the stomach.

METHODS FOR TASTE MASKING OF BITTER DRUGS IN PHARMACEUTICAL FORMULATIONS

An effective solution to mask the bitter taste, stabilize the API, and optimize the patient experience



1 WHY IS IT NECESSARY TO MASK THE BITTER TASTE OF THE API?

In the pharmaceutical industry, optimizing the patient experience with medication is becoming increasingly important. Besides therapeutic efficacy, factors such as taste, form, and convenience of medication also play a crucial role in patient compliance to treatment.

A common problem is that many medicinal substances, especially those of natural origin or complex chemical compounds, often have an unpleasant bitter taste. This bitterness not only makes it difficult to swallow the medicine but can also cause nausea and vomiting, particularly in children and the elderly, thereby affecting the effectiveness of treatment.

THE INFLUENCE OF BITTERNESS ON DRUG USE.

COMPLIANCE TO TREATMENT



SUITABLE FOR CHILDREN



SUITABLE FOR THE ELDERLY



MODERN DOSAGE FORM



THE BITTER TASTE MAKES IT DIFFICULT TO TAKE THE MEDICINE

It reduces the ability to accept medication, especially in children and the elderly.



IMPACT ON TREATMENT EFFECTIVENESS

The bitter taste can cause nausea, leading to discontinuation of the medication or incorrect dosage.

ADVANTAGES OF MASKING THE BITTER TASTE OF APIS



Increase patient compliance to treatment.



Reduce patient reactions to medication such as vomiting and discomfort.



Improve usability for children and elderly people with taste sensitivities.



Increase the commercial competitiveness of pharmaceutical products.



Allow for the development of modern dosage forms and new APIs.



Contribute to improving the stability of certain active substances.

2 APIS OFTEN NEED TO MASK THE BITTER TASTE

API GROUP	ILLUSTRATION	FOR EXAMPLE	CHARACTERISTIC
1 ANTIBIOTIC		<ul style="list-style-type: none"> Erythromycin Azithromycin Clarithromycin 	Many antibiotics have a very strong bitter taste, which is often difficult to tolerate, especially in children.
2 ANTIVIRAL		<ul style="list-style-type: none"> Oseltamivir Lamivudine 	Some antiviral medications have a lingering bitter taste, making them difficult to take.
3 PAIN RELIEF, FEVER REDUCTION		<ul style="list-style-type: none"> Paracetamol Ibuprofen 	Paracetamol and ibuprofen have a mild to moderate bitter taste, which affects the user experience.
4 CARDIOVASCULAR		<ul style="list-style-type: none"> Diltiazem Propranolol 	Some cardiovascular medications have a bitter taste, making them difficult to swallow and hindering adherence to treatment, especially during long-term therapy.
5 ANTIHISTAMINES		<ul style="list-style-type: none"> Cetirizine Loratadine 	Newer generation antihistamines can still leave an unpleasant bitter taste.
6 TREATMENT OF STOMACH AND DUODENAL ULCERS		<ul style="list-style-type: none"> Ranitidine Famotidine 	Anti-ulcer medications, especially those in syrup/suspension form, often have a bitter taste.
7 ANTIAMOEBCIC		<ul style="list-style-type: none"> Metronidazole Sacnidazole 	Antiamoebic drugs have a very strong bitter taste, and often require effective masking.

FUNCTIONAL GROUPS ARE OFTEN ASSOCIATED WITH BITTERNESS

$-NH_2$ Amine	$-OH$ Hydroxyl	$\begin{matrix} O \\ \\ C \end{matrix}$ Ketone	$-COO-$ Ester	$-COOH$ Carboxyl	 Lactam	 Nitrogen-containing heterocycles
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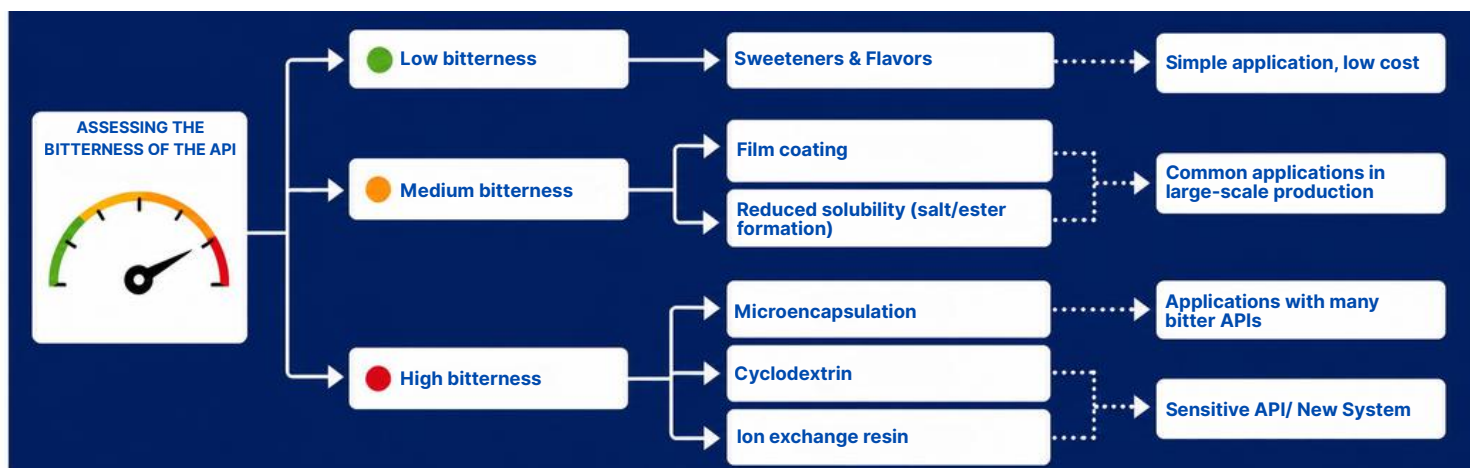
THE VARIOUS DOSAGE FORMS OFTEN REQUIRE MASKING OF THE BITTER TASTE

SOLID DOSAGE FORM				LIQUID DOSAGE FORM	
Chewable tablets	Lozenges	ODT tablets	Powder/granules for suspension	Oral syrup	Oral suspension

3 COMMON METHODS FOR MASKING BITTER TASTE

METHOD OF MASKING BITTER TASTE	ILLUSTRATION	BITTER TASTE MASKING MECHANISM	EXCIPIENTS USED
1 Use sweeteners and flavors		<ul style="list-style-type: none"> Reduces the perception of bitterness through sweet taste and pleasant flavors. 	SWEETENERS: <ul style="list-style-type: none"> Sucrose, fructose, sorbitol, mannitol, xylitol, maltose, sucralose, aspartame, acesulfame K, saccharin sodium, stevia, trehalose FLAVORS: <ul style="list-style-type: none"> Fruity scents, mint, orange, strawberry,...
2 Film coating		<ul style="list-style-type: none"> Forms a coating layer that prevents the API from coming into contact with saliva while dissolving in the stomach. 	<ul style="list-style-type: none"> Ethyl cellulose Methacrylate copolymer Cellulose acetate HPMC, PVA, PLGA, HPMC
3 Microencapsulation		<ul style="list-style-type: none"> Completely or partially encapsulates the API with a protective polymer layer. 	<ul style="list-style-type: none"> Ethyl cellulose, gelatin, alginate, chitosan, PVA, PLGA, HPMC
4 Complex formation with cyclodextrin		<ul style="list-style-type: none"> The API is entrapped within the cyclodextrin cavity, thereby reducing the amount of free drug available to interact with taste receptors. 	<ul style="list-style-type: none"> β-Cyclodextrin HP-β-cyclodextrin SBE-β-cyclodextrin α-cyclodextrin
5 Complex formation with ion exchange resin		<ul style="list-style-type: none"> The API forms an complex with the excipient, preventing drug release in saliva while enabling release in gastric fluid. 	<ul style="list-style-type: none"> Ion exchange resins
6 Reduce solubility in saliva by forming salts or ester derivatives		<ul style="list-style-type: none"> Reduces the amount of API dissolved in the oral cavity. 	<ul style="list-style-type: none"> No excipients are used, and the chemical form of the API is not altered.
7 Lipid coating using melt-based processing techniques		<ul style="list-style-type: none"> The hydrophobic lipid layer limits the dissolution of the API in saliva. 	<ul style="list-style-type: none"> Glyceryl dibehenate Glyceryl monostearate Carnauba wax, beeswax Stearic acid
8 Adsorption onto solid carriers		<ul style="list-style-type: none"> Reduces the amount of free API exposed to taste receptors. 	<ul style="list-style-type: none"> Colloidal silicon dioxide Bentonite, kaolin Magnesium silicate Calcium silicate
9 Control the solubility of the API		<ul style="list-style-type: none"> Maintains the API in an undissolved particulate form during its residence time in the oral cavity. 	<ul style="list-style-type: none"> Xanthan gum, CMC-Na HPMC, MCCMC Carbomer, sodium alginate
10 Creating nano-systems/nanopolymers		<ul style="list-style-type: none"> The API is entrapped within a nanosystem, thereby limiting direct contact with taste receptors. 	<ul style="list-style-type: none"> PLGA, chitosan, alginate PVA, poloxamer Solid lipid excipients

COMPARING AND CHOOSING METHODS FOR MASKING BITTER TASTE



OYSTER EXTRACT POWDER

MALE PHYSIOLOGICAL SUPPORT

FROM MARINE NUTRIENTS



NATURAL SOURCES OF ZINC

Maintaining testosterone levels supports male physiology and immunity.



ARGININE

Involved in the synthesis of Nitric Oxide, which supports blood circulation.



TAURINE

Supports energy metabolism, reduces fatigue, and increases endurance.



PEPTIDES FROM THE SEA

Supports antioxidant activity and protects cells.



EXTRACT FROM OYSTERS

PACIFIC OYSTER (*CRASSOSTREA GIGAS*)

4% TAURINE
35 - 55% PROTEIN

STABLE ZINC LEVELS

HEAVY METAL
CONTROL

Zn

SEA OYSTER POWDER EXTRACT

STRATEGIC MATERIALS

MALE PHYSIOLOGICAL SUPPORT & IMMUNE SYSTEM ENHANCEMENT



MALE PHYSIOLOGICAL SUPPORT



BOOST YOUR IMMUNE SYSTEM



IMPROVE PHYSICAL FITNESS

1 GENERAL INTRODUCTION TO OYSTER EXTRACT

Oyster extract is an extract from the Pacific oyster (*Crassostrea Gigas*), which is concentrated and standardized into powder form to optimize the content of bioactive compounds.

Unlike regular oyster powder, Oyster extract is produced by freeze-drying the oyster meat and removing the shells.



Increase the active ingredient content to 4% taurine and 35 – 55% protein



Ensure purity and consistency across production batches.



Stabilize zinc levels



Heavy metal control



Oyster extract is a strategic ingredient in the functional food industry, especially in product lines that support male physiology, maintain testosterone levels, and boost immunity.

2 ACTIVE INGREDIENTS IN OYSTER EXTRACT

NATURAL BIOAVAILABLE ZINC



- Maintain normal testosterone levels
- Enhancing male physiological function
- Support the immune system
- Protecting cells from oxidative stress

ARGININE AND ESSENTIAL AMINO ACIDS



- Involved in the synthesis of Nitric Oxide
- Supports blood circulation
- Improve physical fitness
- Increase protein metabolism

TAURINE & GLYCOGEN



- Supports energy metabolism
- Reduce fatigue
- Increase endurance and recovery

MARINE-DERIVED BIOPEPTIDES



- Antioxidant support
- Cell protection

3 ADVANTAGES OF OYSTER EXTRACT



High natural zinc content
Provides easily absorbed bioavailable zinc, supporting physiological and immune functions.



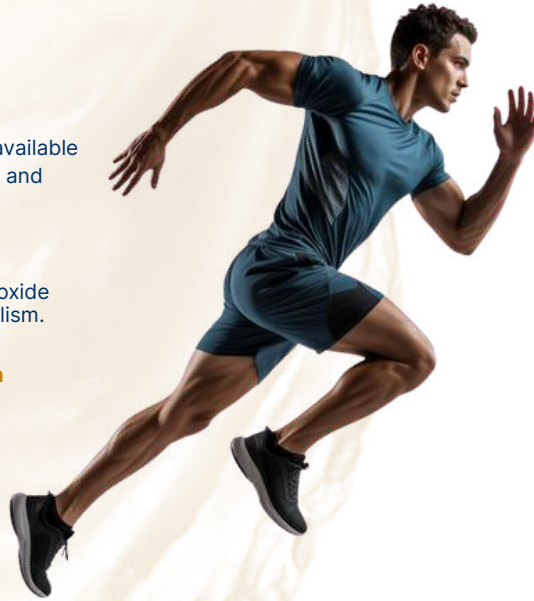
Rich in amino acids
Rich in arginine and essential amino acids involved in nitric oxide synthesis and protein metabolism.



Rich in taurine and glycogen
Supports energy metabolism and protects cells.



Marine-derived biopeptides
It has antioxidant potential and supports physiological function.



Standardization & flexible customization
The extraction ratio and API content can be adjusted according to the formula requirements.



Strict quality control
Meets international standards for heavy metals, microorganisms, and impurities.



Flexible application
Suitable for a wide range of pharmaceutical and dietary supplement formulations.



Zinc is a prominent active ingredient in Oyster Extract, playing a crucial role in immunity, male physiology, and testosterone metabolism.

4 APPLICATIONS OF OYSTER EXTRACT



Male physiology and reproductive health support

Zinc and arginine contribute to maintaining testosterone metabolism and normal reproductive function.



Boost immunity

Zinc, amino acids, and peptides support the function of immune cells, enhancing resistance.



Boost energy and endurance

Glycogen and taurine support energy metabolism, reduce fatigue, and improve physical performance.



Antioxidant support

Bioactive peptides and minerals help reduce oxidative stress at the cellular level.

SUITABLE FOR DOSAGE FORMS



Tablets



Hard capsules



Chewable tablets/lozenges



ODT tablets



Sachets



Powder



Oral suspension

FORMULATION COLLABORATOR

MATERIAL SOLUTIONS FOR PREMIUM PHARMACEUTICALS

Biorich offers sophisticated raw material solutions that facilitate optimal formulation, improve efficacy, and guarantee the quality of your pharmaceutical products.

CUSTOMERS REQUIREMENT

-  Material samples
-  COA / Specification
-  R&D support
-  Technical documentation
-  Appropriate excipient solution
-  Detailed quotation

CONTACT BIORICH

- ✓ Sending samples for testing
- ✓ Providing COA / technical documentation
- ✓ Formulation and excipient consulting
- ✓ Support formulation and process optimization

We are dedicated to collaborating with businesses to create high-quality pharmaceutical products



CLEAR ORIGIN

Complies with international standards



CONSISTENT QUALITY

Adhering to rigorous GMP requirements



TECHNICAL SUPPORT

Dedicated technical consultation



WORLDWIDE NETWORK

Connects with reputable global manufacturers

BIORICH

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



COLLABORATION & CONSULTING

Partnering for sustainable
development



CONTACT US

For samples and
technical documentation



+84 834 560 500



director@biorichgroup.com