WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL RESEARCH

Review Article

2025
Volume: 02
Issue: 04
Page: 59-84

# EXPLORING VARIOUS GASTRO-RESISTANT POLYMERS IN DRUG DELIVERY: A COMPREHENSIVE REVIEW

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**Received: 21 February 2025** **Revised: 11 March 2025** **Accepted: 01 April 2025**

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## ABSTRACT

Gastro-resistant polymers play a crucial role in the development of oral drug delivery systems, especially for the drugs that are sensitive to gastric acidity and also for the targeted release in the small intestine or other parts of the gastrointestinal (GI) tract. These are the polymers which are used to protect active pharmaceutical ingredients (APIs) from the harsh acidic environment of the stomach, preventing premature drug release and degradation. The primary mechanism of action involves pH-sensitive polymers that remain intact in the acidic stomach but dissolve or degrade in the alkaline environment of the small intestine. Common gastro-resistant polymers include acrylic derivatives such as Eudragit L100 and Eudragit S100, cellulose derivatives like cellulose acetate phthalate (CAP), and natural polymers such as shellac. These polymers are frequently used in enteric coatings for tablets, capsules, and granules, ensuring that drugs are released at the optimal site for absorption. The development of gastro-resistant formulations not only improves the stability of acid-labile drugs but also enhances therapeutic efficacy by ensuring sustained or delayed release. This review explores the various types of gastro-resistant polymers, their mechanisms of action, applications in pharmaceutical formulations and advantages of gastro-resistant polymer use in controlled and

targeted drug delivery are also discussed, highlighting their significance in modern pharmaceutics.

**KEYWORDS:** Gastro-resistant polymers, pH-sensitive Polymers, Enteric Coatings, Acid-labile Drugs, Controlled Release, Targeted Drug Delivery.

## INTRODUCTION

Gastro-resistant polymers, often referred to as enteric polymers, are specialized materials designed to protect pharmaceutical formulations from the acidic environment of the stomach while ensuring controlled release of the active pharmaceutical ingredient (API) in the intestinal tract. These polymers are integral to the development of modified-release dosage forms, such as enteric-coated tablets and capsules and also in the development of gastro retentive drug delivery systems (GRDDS), which aim to optimize therapeutic efficacy and minimize drug degradation in gastric conditions. By using gastric resistant polymers, pharmaceutical formulations can minimize gastrointestinal discomfort and improve therapeutic outcomes for patients.

### Background and Importance

The gastrointestinal (GI) tract presents a challenging environment for oral drug delivery systems due to its variable pH and enzymatic activity. The stomach's highly acidic pH, ranging from 1 to 3.5, can lead to the degradation of pH-sensitive APIs, especially those that areacid-labile. Additionally, certain APIs can irritate the gastric mucosa, necessitating protection until they reach the intestines, where absorption can occur. Gastro-resistant polymers play a pivotal role in addressing these challenges by providing a robust and functional barrier that dissolves only under alkaline pH conditions typically found in the small intestine.[1,2]

The primary mechanism of gastro-resistance relies on the pH-sensitive solubility of the polymer. These polymers remain intact in acidic conditions, preventing drug release in the stomach. However, upon exposure to higher pH levels in the duodenum or beyond, the polymers ionize and dissolve, enabling drug release. This selective dissolution profile makes gastro-resistant polymers ideal for delivering drugs like proton pump inhibitors (PPIs), which are highly unstable in gastric acid, or peptides and proteins, which are prone to enzymatic degradation.[3,4]

The choice of gastro-resistant polymer depends on several factors, including the physicochemical properties of the drug, the target site for drug release, and the desired therapeutic outcome. Commonly used polymers in enteric coatings include cellulose derivatives, such as hydroxypropyl methylcellulose phthalate (HPMCP), methacrylic acid copolymers, and polyvinyl acetate phthalate (PVAP). These polymers offer distinct advantages, such as mechanical strength, film-forming capabilities, and adaptable pH thresholds for dissolution.[1,5]

## SYNTHETIC POLYMERS[6,7,8]

Synthetic polymers are large molecules made from repeating structural units called monomers, which are chemically bonded together through a process known as polymerization. These polymers are predominantly derived from petrochemical sources, although they can also be synthesized from bio-based materials. These consists of long chains of monomers that can vary in length and structure, leading to diverse physical properties. Synthetic polymers are extensively used in pharmaceutical applications for their precise control over drug release, high stability, and customizable properties. Some of the synthetic gastro resistant polymers that are commonly used in pharmaceutical formulations to protect the API from gastric environment are Methacrylic acid copolymers (Eudragit®), Polyvinyl acetate phthalate (PVPA), Cellulose acetate Phthalate (CAP), Hydroxypropyl methylcellulose phthalate (HPMCP), Cellulose acetate trimellitate (CAT).

### Methacrylic acid copolymers (Eudragit®)[9,10,11,12]

Methacrylic acid copolymers, particularly known under the trade name Eudragit, are a group of synthetic polymers widely used in pharmaceutical formulations for enteric coating and controlled drug release. These copolymers are primarily composed of methacrylic acid and its esters, which endow them with specific properties suitable for various applications.

Eudragit polymers can be classified into different types based on their solubility and pH sensitivity.

**Eudragit L100:** It is an anionic copolymer of methacrylic acid and methyl methacrylate. Which is insoluble in acidic environments (pH < 5.5) but soluble in neutral to alkaline conditions, making it ideal for enteric coatings that protect drugs from gastric degradation. It is commonly used in modified-release formulations to ensure that the active pharmaceutical ingredient (API) is released in the intestine rather than the stomach.

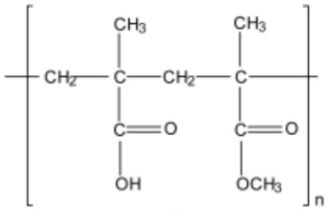


**Fig. 1: Eudragit L100.**

**Eudragit S100:** Similar to L100 but with a different ratio of carboxyl groups to ester groups, providing distinct solubility characteristics.

**Eudragit E100:** It is a cationic polymer that is soluble at lower pH levels, often used for immediate release formulations.

**Mechanism**

The primary function of Eudragit polymers, particularly L100, is to act as a barrier against gastric acids. When coated on tablets or capsules, they prevent the release of the drug in the acidic environment of the stomach, ensuring that the drug is only released once it reaches the more neutral pH of the intestines. This property is crucial for protecting acid-sensitive drugs and optimizing their bioavailability.

**Advantages**

- **Targeted Delivery**: Eudragit allows for precise control over where and when a drug is released within the gastrointestinal tract.
- **Stability**: The polymers provide a stable coating that can withstand various environmental conditions during storage and transit.
- **Versatility**: They can be used in various dosage forms, including tablets, capsules, and granules.

**Applications in Formulations**

Eudragit is extensively utilized in pharmaceutical formulations, particularly:

- **Enteric-Coated Tablets**: Protects drugs from degradation due to gastric acids.
- **Sustained-Release Formulations**: Controls the release rate of drugs over an extended period.
- **Taste Masking**: Used in formulations where unpleasant-tasting drugs need to be masked.

**Some examples of drugs that are coated with Eudragit polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Eluxadoline | Anwer MK, Al-Shdefat R *et al.*, (2017)[13] |
| **2.** | Omeprazole | Rezazadeh M, Safaran R *et al.*, (2021)[14] |
| **3.** | Lansoprazole | Fang Y, Wang G *et al.*, (2014)[15] |
| **4.** | Naproxen sodium | Patel AK, Jain V *et al.*, (2023)[16] |
| **5.** | Senna | Pawar AY, Tapkir AD *et al.*, (2022)[17] |
| **6.** | Esomeprazole | Shan R, Feng R *et al.*, (2023)[18] |

**Polyvinyl acetate phthalate (PVPA)[8,19,20]**

Polyvinyl acetate phthalate (PVAP) is a synthetic polymer widely used in the pharmaceutical industry, particularly for its role as an enteric coating agent. This polymer is synthesized through the esterification of partially hydrolysed polyvinyl acetate with phthalic anhydride, resulting in a compound that exhibits unique solubility characteristics. PVAP is characterized by its vinyl acetate backbone, which is modified by phthalate groups. This modification enhances its properties as a coating material. It is soluble in organic solvents such as ethanol and methanol but is insoluble in water. Its solubility profile allows it to function effectively in various pH environments, particularly in protecting drugs from gastric acids.

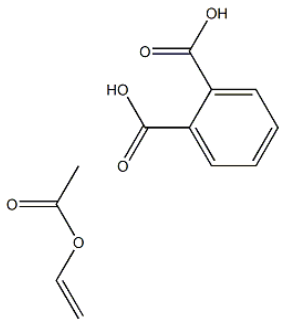



**Fig. 2: Polyvinyl acetate phthalate (PVPA)**

**Mechanism**

PVAP serves primarily as an enteric coating for tablets and capsules. It forms a protective barrier around the drug, preventing its release in the acidic environment of the stomach. Instead, the polymer dissolves at higher pH levels found in the intestines, allowing for the controlled release of the active pharmaceutical ingredient (API) at the desired site of absorption. This property is crucial for drugs that are sensitive to acid or require targeted delivery to enhance efficacy.

**Advantages**

- **Biocompatibility**: PVAP is generally regarded as safe for use in pharmaceutical applications.
- **Stability**: The polymer provides a stable coating that withstands various environmental conditions during storage and transport.
- **Versatility**: It can be employed in various dosage forms, including solid oral dosage forms and other pharmaceutical preparations.

**Applications in Formulations**

- **Enteric Coatings**: PVAP is extensively used to coat tablets and capsules to ensure that medications are released in the intestine rather than the stomach, thus improving bioavailability and reducing gastrointestinal irritation.
- **Core Sealing**: It acts as a sealing agent for tablet cores before sugar-coating processes, enhancing stability and protecting the drug from moisture and degradation.
- **Controlled Release Formulations**: PVAP can be utilized in formulations designed for sustained or controlled drug release, optimizing therapeutic outcomes.

**Some examples of drugs that are coated with PVAP polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Diclofenac Sodium | Zaid AN, Qaddomi A (2012)[21] |
| **2.** | Prednisolone | Merchant HA, Goyanes A *et al.*, (2014)[22] |

**Cellulose acetate phthalate (CAP)** [23,24]

Cellulose acetate phthalate (CAP) is a widely used synthetic polymer in the pharmaceutical industry, primarily recognized for its role as an enteric coating agent. This polymer is derived from cellulose acetate through the esterification process with phthalic anhydride, resulting in a compound that exhibits specific solubility characteristics beneficial for drug delivery applications. CAP is a cellulose derivative where some of the hydroxyl groups of cellulose are replaced by phthalate groups. The degree of substitution can vary, affecting its physical and chemical properties. The molecular weight of CAP typically ranges around 722.6 g/mol, with its structure comprising various functional groups that contribute to its solubility and stability in different pH environments. CAP is characterized by its pH-sensitive solubility. It remains stable and insoluble in the acidic environment of the stomach (pH < 5.5), which protects sensitive drugs from degradation. It dissolves readily in the mildly acidic to neutral

conditions found in the small intestine (pH ≥ 6.2), allowing for the controlled release of the active pharmaceutical ingredient (API) at the desired site of absorption.

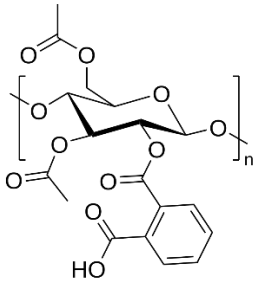


**Fig. 3: Cellulose acetate phthalate (CAP).**

**Mechanism**

- **Ionization of Carboxylic Groups**: In the low pH conditions of the stomach, the carboxylic acid groups within CAP remain un-ionized, contributing to its insolubility. As the pH increases in the intestinal tract, these groups become ionized, leading to solubilization and subsequent drug release.
- **Film Formation and Structural Integrity**: CAP is often used in enteric coatings due to its ability to form a stable film that can withstand gastric conditions. When exposed to acidic media, CAP maintains its structural integrity while other components (like gelatin) may dissolve or swell, revealing a CAP-based skeleton that remains intact until reaching a higher pH environment.

**Advantages**

- **Biocompatibility**: CAP is generally regarded as safe for pharmaceutical applications, making it suitable for use in various drug formulations.
- **Reduced Solvent Use**: Recent advancements have led to formulations that require less solvent during application compared to traditional methods, enhancing manufacturing efficiency.
- **Regulatory Approval**: CAP meets compendial specifications set by various pharmacopoeias, including the National Formulary (NF), Japanese Pharmacopeia, and European Pharmacopeia, ensuring its quality and safety for pharmaceutical use.

**Applications in Formulations**

- **Enteric Coating**: CAP is primarily utilized for coating tablets and capsules, ensuring that medications are released in the intestines rather than the stomach. This property is crucial

for drugs that are sensitive to gastric acid or require targeted delivery to enhance bioavailability.

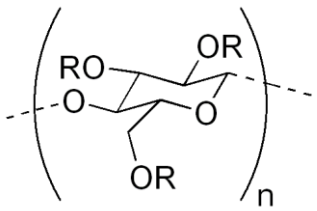
- **Matrix Material**: It can also function as a matrix material in solid dosage forms, contributing to sustained-release formulations.
- **Pharmaceutical Excipient**: Beyond its use in coatings, CAP has been explored for its antiviral properties, showing effectiveness against certain viruses, including HIV and herpesviruses, in laboratory studies.

**Some examples of drugs that are coated with CAP polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Sodium Valproate | Sanga DK, Chand T. (2013)[25] |
| **2.** | α-tocopherol acetate | Phothong N, Aht-Ong D *et al.*, (2024)[26] |
| **3.** | Omeprazole | Khatibi A, Zahedi P *et al*., (2021)[27] |
| **4.** | Aceclofenac | Nandi S, Banerjee A *et al*., (2021)[28] |
| **5.** | Methylprednisolone | Jagdale S, Chandekar A *et al.*, (2017)[29] |
| **6.** | Naproxen sodium | Gordon MS, Fratis A *et al.*, (1995)[30] |

**Hydroxypropyl methylcellulose phthalate (HPMCP)[31,32,33]**

Hydroxypropyl methylcellulose phthalate (HPMCP) is a synthetic polymer extensively utilized in the pharmaceutical industry, particularly as an enteric coating agent for tablets and granules. This polymer is a phthalic acid ester of hydroxypropyl methylcellulose and is recognized for its ability to protect drugs from degradation in the acidic environment of the stomach while allowing for their release in the more neutral pH of the intestines. HPMCP is characterized by a backbone of hydroxypropyl methylcellulose with phthalate groups attached. This structure contributes to its unique solubility properties. It typically appears as white to slightly off-white flakes or granules, is odorless, and has a barely detectable taste.




R = H or $CH_3$ or $CH_2CH(OH)CH_3$

**Fig. 4: Hydroxypropyl methylcellulose phthalate (HPMCP).**

**Mechanism**

- **pH-dependent solubility:** It is insoluble in acidic conditions (pH < 4.2), which allows it to protect sensitive drugs from gastric acid. The polymer becomes soluble at higher pH levels (pH ≥ 4.2), facilitating the release of the drug once it reaches the intestines.
- **Hydrophobic Phthalyl Groups**: The chemical structure of HPMCP includes hydrophobic phthalyl groups, which contribute to its gastro-resistance. These groups enhance the polymer's ability to remain stable and insoluble under acidic conditions, ensuring that the active ingredient is protected until it reaches the intestine where the pH is higher.

**Advantages**

- **Biocompatibility**: HPMCP is considered safe for use in pharmaceutical applications and has been included in various pharmacopoeias, including the U.S. National Formulary.
- **Stability**: The polymer exhibits good stability under recommended storage conditions and is resistant to microbial degradation.
- **Versatility**: Different grades of HPMCP (e.g., HP-55, HP-50) are available, allowing formulators to select specific types based on desired solubility characteristics and application requirements.

**Applications in Formulations**

- **Enteric Coating**: HPMCP is primarily used to coat tablets and granules, ensuring that medications are released in the intestines rather than the stomach. This is particularly beneficial for drugs that are sensitive to gastric acid or those that may cause gastrointestinal irritation.
- **Sustained Release Formulations**: It can also be employed in formulations designed for controlled drug release, where the release rate can be tailored based on the pH of the surrounding environment.
- **Taste Masking**: Due to its tasteless nature, HPMCP can be used to mask unpleasant tastes in oral dosage forms.

**Some examples of drugs that are coated with HPMCP polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Diclofenac sodium | Kim IH, Park JH *et al.*, (2003)[34] |
| **2.** | Delamanid | Nguyen HT, Van Duong T *et al.*, (2023)[35] |
| **3.** | Isoniazid | Ratih H, Pratiwi GK *et al.*, (2022)[36] |

**Cellulose acetate trimellitate (CATM)[37]**

Cellulose acetate trimellitate (CATM) is a derivative of cellulose, formed through the esterification of cellulose with acetic acid and trimellitic anhydride. This polymer exhibits unique properties that make it valuable in various applications, particularly in the pharmaceutical and materials science fields. CATM is characterized by the presence of both acetate and trimellitate groups attached to the cellulose backbone. This structure contributes to its distinctive solubility and mechanical properties.

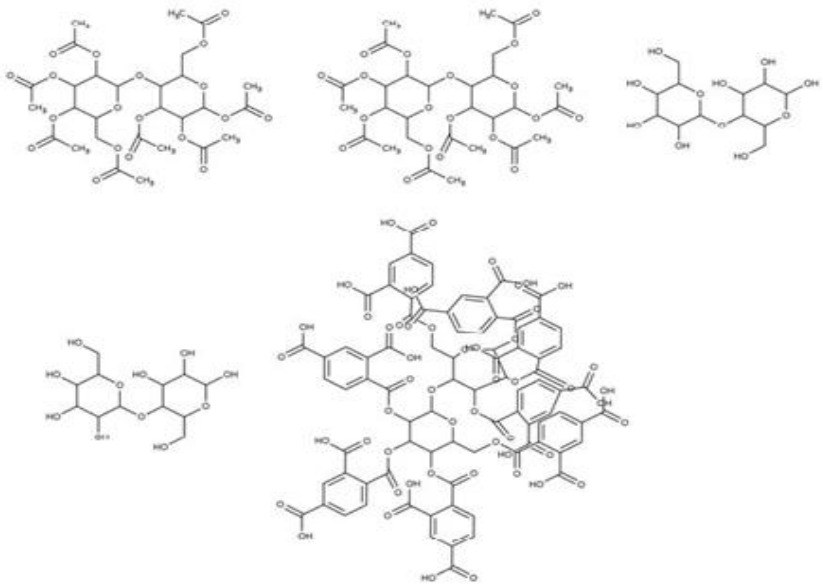


**Fig. 5: Cellulose acetate trimellitate (CATM).**

**Mechanism**

- **pH-sensitive solubility:** It remains stable and insoluble in acidic environments (pH < 5), which protects sensitive drugs from degradation in the stomach. CATM dissolves in neutral to alkaline conditions (pH ≥ 6), facilitating controlled drug release in the intestines.
- **Ionization of Functional Groups**: The presence of trimellitic acid groups in CATM contributes to its pH-sensitive behaviour. In acidic environments, these groups remain protonated and hydrophobic, preventing solubility. As the pH rises in the intestinal tract,

these groups ionize, leading to increased solubility and allowing for the controlled release of the drug.

- **Film Formation**: CATM can form a robust film when applied as a coating on tablets or capsules. This film acts as a barrier against gastric fluids, maintaining its integrity until it reaches the higher pH environment of the small intestine where it dissolves and releases the drug.

**Advantages**

- **Biocompatibility**: CATM is considered safe for pharmaceutical use and has been evaluated for its non-toxic properties.
- **Mechanical Strength**: The polymer exhibits high mechanical strength and chemical resistance, making it suitable for various industrial applications.
- **Versatility**: Its unique combination of acetate and trimellitate groups allows for a balance of properties, making it adaptable for different formulations.

**Applications in Formulations**

- **Pharmaceutical Formulations**: CATM is primarily used as an enteric coating for tablets and capsules, ensuring that drugs are released in the intestines rather than the stomach. This is particularly beneficial for drugs that are sensitive to gastric acids or those that may cause gastrointestinal irritation.
- **Controlled Release Systems**: It can be utilized in formulations designed for sustained or controlled drug release, optimizing therapeutic outcomes.
- **Biodegradable Materials**: Due to its cellulose content, CATM is being explored for use in biodegradable plastics and coatings, contributing to environmentally friendly material solutions.

**Some examples of drugs that are coated with CATM polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Indomethacin | Giunchedi P, Ltorre M *et al.*, (1995)[37] |
| **2.** | Ketoprofen | Giunchedi P, Ltorre M *et al.*, (1995)[37] |
| **3.** | Naproxen sodium | Gordon MS, Fratis A *et al.*, (1995)[30] |

**NATURAL POLYMERS[6,38,39]**

Natural polymers are large macromolecules produced by living organisms, composed of repeating structural units known as monomers. These polymers play crucial roles in biological processes and are found in various forms throughout nature. They are typically

biodegradable and can be categorized into several types based on their structure and function. Natural polymers are typically formed through condensation polymerization, where monomers bond together with the release of small molecules, often water. Their structures can be linear, branched, or cross-linked, depending on the type of monomers involved and the conditions of polymerization. Some of these natural polymers have gastro resistant property which are important in the pharmaceutical industry to protect API from degrading in gastric environment inside the stomach. Some of the natural polymers which have gastro resistant property are Chitosan, shellac, pectin, alginate, carrageenan, gellan gum.

**Chitosan**[40,41,42,43]

Chitosan is a natural polymer derived from chitin, which is found in the exoskeletons of crustaceans and certain fungi. It has gained significant attention in the pharmaceutical industry, particularly for its gastro-resistant properties. Chitosan is non-toxic and biodegradable, making it suitable for various biomedical applications. The presence of amino groups in chitosan gives it a positive charge at acidic pH levels, enhancing its interaction with negatively charged surfaces, such as the mucosal lining of the gastrointestinal tract. It exhibits strong mucoadhesive properties, allowing it to adhere to the gastric mucosa and prolong the retention time of drug formulations in the stomach.

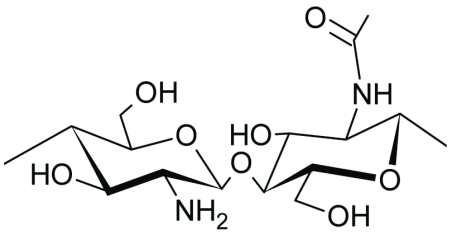



**Fig. 6: Chitosan.**

**Mechanism**

- **Swelling and Gel Formation**: Upon contact with gastric fluids, chitosan can swell and form a gel-like structure that protects encapsulated drugs from degradation in the acidic environment.
- **Controlled Release**: Chitosan-based formulations can be designed to release drugs gradually in response to changes in pH. While it remains stable in acidic conditions, it dissolves in neutral or alkaline environments (such as those found in the intestines), allowing for targeted drug delivery.

- **Enzymatic Degradation**: Chitosan is also susceptible to enzymatic degradation by intestinal enzymes, which can facilitate drug release once it reaches the intestine.

**Advantages**

- **Enhanced Bioavailability**: By improving drug retention time and protecting against gastric degradation, chitosan enhances the bioavailability of orally administered drugs.
- **Versatility**: Chitosan can be modified chemically to improve its properties or tailor its release characteristics for specific applications.
- **Safety Profile**: Its biocompatibility and low toxicity make chitosan a favourable choice for use in pharmaceutical formulations.

**Applications in Formulations**

- **Gastro-retentive Drug Delivery Systems (GRDDS)**: Chitosan is commonly used to develop GRDDS that enhance the bioavailability of drugs by prolonging their residence time in the stomach. This is particularly beneficial for drugs that require extended absorption times or are sensitive to gastric acid.
- **Microspheres and Pellets**: Chitosan microspheres can encapsulate drugs to protect them from degradation and improve their absorption. These microspheres can be formulated into gastro-resistant pellets for oral administration.
- **Antimicrobial Applications**: Beyond drug delivery, chitosan exhibits antimicrobial properties that can help prevent infections in the gastrointestinal tract.

**Some examples of drugs that are coated with Chitosan polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Omeprazole | Rezazadeh M, Safaran R *et al.*, (2021)[14] |
| **2.** | Capsaicin | Chen J, Huang GD *et al.*, (2013)[44] |
| **3.** | Methylprednisolone | Jagdale S, Chandekar A *et al.*, (2017)[29] |

**Shellac[45,46]**

Shellac is a natural polymer derived from the resin secreted by the lac insect, Kerria lacca, primarily found in Southeast Asia. It has gained significant attention in the pharmaceutical industry due to its gastro-resistant properties, making it an effective material for enteric coatings. shellac is composed of a mixture of esters of polyhydroxy carboxylic acids, including aleuritic acid, jalaric acid, and shellolic acid. These components contribute to its unique film-forming properties and resistance to gastric fluids. Shellac forms a hard, resistant film that is effective in protecting drugs from the acidic environment of the stomach. It

exhibits low solubility in gastric fluid (pH 1-2) but can dissolve in more neutral or alkaline conditions
(pH > 6).

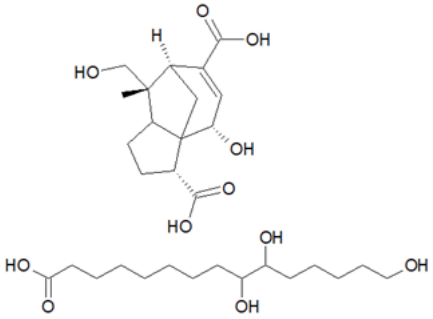



**Fig. 7: Shellac**

**Mechanism**

- **Acid Stability**: Shellac remains insoluble in the acidic conditions of the stomach, protecting sensitive drugs from degradation. This stability allows it to serve as an effective barrier until it reaches the higher pH environment of the intestines.
- **Controlled Release**: Once in the intestine, shellac dissolves, allowing for the controlled release of the active pharmaceutical ingredient (API). This targeted release is particularly beneficial for drugs that require absorption in the intestinal tract.

**Advantages**

- **Biocompatibility**: Shellac is considered non-toxic and physiologically harmless, making it suitable for use in both pharmaceuticals and food products. It is classified as Generally Recognized as Safe (GRAS) by the FDA.
- **Excellent Film-Forming Properties**: Shellac provides a strong, durable coating that enhances product stability while also offering good gloss and low permeability to gases and moisture.
- **Versatility**: The ability to modify shellac with plasticizers or surfactants can enhance its flexibility and adhesion properties, making it adaptable for various formulations.

**Applications in Formulations**

- **Enteric Coatings**: It is commonly employed as an enteric coating for tablets and capsules, ensuring that medications are released in the intestines rather than the stomach. This property is crucial for protecting acid-sensitive drugs and enhancing their bioavailability.

- **Sustained Release Formulations**: Shellac can be used in formulations designed for sustained or controlled drug release, optimizing therapeutic effects.
- **Microencapsulation**: The polymer is also used in microencapsulation processes to protect probiotics and other sensitive compounds from gastric degradation.

**Limitations**

- **Low Solubility in Intestinal Fluids**: While shellac provides excellent protection against gastric acids, its low solubility in intestinal fluids can hinder complete drug release. This characteristic may limit its effectiveness for certain applications where rapid dissolution is necessary.
- **Aging Effects**: Over time, shellac can undergo changes that reduce its gastric resistance and solubility, potentially affecting drug release profiles.

**Some examples of drugs that are coated with Shellac polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Ceftriaxone | Maghrabia AE, Boughdady MF *et al.*, (2019)[47] |
| **2.** | Ibuprofen | Heni Rachmawati, Diky Mudhakir *et al.*, (2023)[48] |
| **3.** | Naproxen | Nawal A Rajab, Zainab J Kadham *et al.*, (2017)[49] |

**Pectin**[50,51,52]

Pectin is a natural polysaccharide found in the cell walls of fruits and vegetables, primarily composed of α-D-galacturonic acid units. It is widely recognized for its ability to form gels and thicken solutions, making it a popular ingredient in the food industry. In recent years, pectin has also gained attention as a gastro-resistant natural polymer, particularly in pharmaceutical applications. Pectin consists mainly of galacturonic acid units linked by (1→4) glycosidic bonds. The degree of methylation (DM) and the presence of neutral sugars in its structure significantly influence its gelling properties and functional characteristics. Pectin is soluble in water and exhibits varying solubility depending on its degree of methylation. High-methylated pectin's gel in the presence of sugar and acid, while low-methylated pectin's require calcium ions for gel formation.

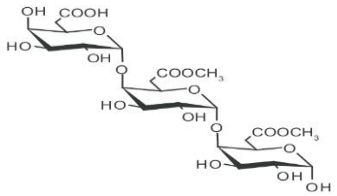



**Fig. 8: Pectin.**

**Mechanism**

Pectin exhibits several mechanisms that contribute to its gastro-resistant properties

- **Gelling Ability**: Pectin can form a gel-like matrix upon hydration, which helps trap drugs and protects them from degradation in the acidic environment of the stomach. This property enhances the retention time of drugs in the gastrointestinal tract.
- **Resistance to Digestive Enzymes:** Pectin is relatively resistant to enzymatic degradation by digestive enzymes, allowing it to maintain its structure during transit through the stomach and into the intestines.

**Advantages**

- **Biocompatibility**: Pectin is generally recognized as safe (GRAS) for use in food and pharmaceuticals, making it suitable for various applications without significant health risks.
- **Health Benefits**: As a soluble dietary fiber, pectin has been shown to have beneficial effects on gut health, including promoting beneficial gut microbiota, lowering cholesterol levels, and regulating blood sugar levels.
- **Versatility**: The ability to modify pectin through different extraction methods and chemical modifications allows for customization based on specific application needs.

**Applications in Formulations**

- **Enteric Coatings**: Pectin is commonly used as an enteric coating for tablets and capsules, ensuring that medications are released in the intestines rather than the stomach. This targeted delivery is particularly beneficial for drugs that are sensitive to gastric acid or require absorption in the intestines.
- **Controlled Release Systems**: Pectin can be incorporated into controlled release formulations that optimize therapeutic effects by regulating drug release rates based on pH changes in the gastrointestinal tract.
- **Mucoadhesive Formulations**: Due to its adhesive properties, pectin can be used in mucoadhesive drug delivery systems that enhance drug retention at the site of absorption.

**Some examples of drugs that are coated with Pectin polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Prednisolone | D. Raju, J. Padmavathy *et al.*, (2011)[53] |
| **2.** | Mesalamine | Singh A, Mandal UK *et al.*, (2021)[54] |
| **3.** | Doxorubicin hydrochloride | Zhu J, Zhong L *et al.*, (2019)[55] |

**Alginate**[56,57]

Alginate is a natural polysaccharide extracted from the cell walls of brown algae, primarily composed of two types of uronic acid monomers: mannuronic acid (M) and guluronic acid (G). It is widely used in the food and pharmaceutical industries due to its unique properties, including its **gastro-resistant characteristics**. Alginate is soluble in water, forming viscous solutions. Its solubility is influenced by pH; it remains soluble at neutral to alkaline pH but can precipitate at low pH levels (below pKa 3.38–3.65) due to the formation of insoluble alginic acid.

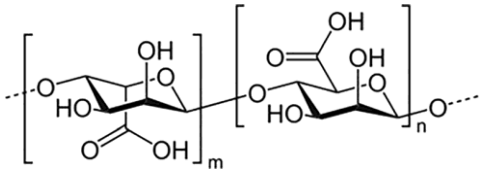



**Fig. 9: Alginate.**

**Mechanism**

- **Formation of Gel Matrix**: Upon contact with gastric fluids, alginate can form a gel-like matrix that protects encapsulated drugs from degradation in the acidic environment of the stomach. This gel formation is particularly enhanced in the presence of calcium ions, which cross-link the alginate chains.
- **Mucoadhesive Properties**: Alginate exhibits mucoadhesive characteristics that allow it to adhere to the mucosal lining of the gastrointestinal tract. This adhesion not only prolongs the retention time of drugs but also enhances their absorption.

**Advantages**

- **Biocompatibility**: Alginate is generally recognized as safe (GRAS) for use in food and pharmaceuticals, making it suitable for various applications without significant health risks.
- **Versatility**: The ability to modify alginate through different extraction methods allows formulators to customize its properties based on specific application needs.
- **Health Benefits**: As a soluble dietary fiber, alginate has been shown to have beneficial effects on gut health, including promoting satiety and regulating blood sugar levels.

**Applications in formulations**

- **Enteric Coatings**: Alginate is commonly used as an enteric coating for tablets and capsules. This ensures that medications are released in the intestines rather than the stomach, which is crucial for drugs that are sensitive to gastric acid or require targeted delivery.
- **Sustained Release Formulations**: Alginate can be incorporated into sustained-release formulations that optimize therapeutic effects by regulating drug release rates based on pH changes in the gastrointestinal tract.
- **Gastro-retentive Drug Delivery Systems (GRDDS)**: Due to its ability to form gels and adhere to mucosal surfaces, alginate is effectively used in GRDDS to enhance drug bioavailability by prolonging residence time in the stomach.

**Some examples of drugs that are coated with Alginate polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Mesalamine | Patole VC, Pandit AP. (2018)[58] |
| **2.** | Piroxicam | Jelvehgari M, Mobaraki V *et al.*, (2014)[59] |
| **3.** | Nifedipine | Mujtaba MA, Hassan KA *et al.*, (2018)[60] |
| **4.** | Diclofenac sodium | Bao TN, Trang PT *et al.*, (2023)[61] |

**Carrageenan**[62,63]

Carrageenan is a natural polysaccharide extracted from red seaweeds, particularly from the genera *Chondrus*, *Gigartina*, and *Eucheuma*. It is widely used in the food industry as a thickening, gelling, and stabilizing agent, and it has also gained attention in pharmaceutical applications due to its **gastro-resistant properties**. Carrageenan consists of linear chains of repeating disaccharide units made up of galactose and 3,6-anhydrogalactose. There are several types of carrageenan, including kappa, iota, and lambda, each differing in their gelling properties and interactions with ions. It is soluble in hot water and forms viscous solutions. Its solubility varies with the type; for instance, kappa-carrageenan forms gels in the presence of potassium ions, while iota-carrageenan requires calcium ions for gel formation.

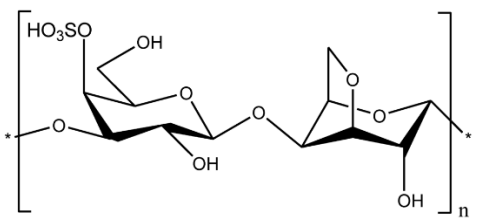



**Fig. 10: Carrageenan.**

### Mechanism

In the acidic environment of the stomach, carrageenan can form a gel-like matrix that protects encapsulated drugs from degradation. This gel formation helps prolong the retention time of drugs within the gastrointestinal tract. And it is also resistant to degradation by gastrointestinal enzymes, allowing it to maintain its structure during transit through the stomach and into the intestines. Studies suggest that while some degradation may occur under extreme conditions, significant breakdown does not typically happen in normal digestive processes.

### Advantages

- **Biocompatibility:** Carrageenan is generally recognized as safe (GRAS) for use in food and pharmaceuticals, making it suitable for various applications without significant health risks.
- **Versatility:** The different types of carrageenan (kappa, iota, lambda) allow formulators to select specific variants based on desired properties for various applications.
- **Health Benefits:** As a soluble fiber, carrageenan may contribute to digestive health by promoting satiety and regulating bowel movements.

### Applications in Formulations

- **Enteric Coatings:** Carrageenan is commonly used as an enteric coating for tablets and capsules. This ensures that medications are released in the intestines rather than the stomach, which is crucial for drugs that are sensitive to gastric acid or require absorption in the intestines.
- **Controlled Release Systems:** Its ability to form gels allows carrageenan to be incorporated into controlled release formulations that optimize therapeutic effects by regulating drug release rates based on pH changes.
- **Food Products:** In addition to its pharmaceutical uses, carrageenan is widely used in food products such as dairy alternatives, sauces, and desserts for its thickening and stabilizing properties.

**Some examples of drugs that are coated with Carrageenan polymer for gastric resistance**

| Sl no. | Drugs | Reference Authors |
|---|---|---|
| **1.** | Indomethacin | Vieira WT, da Silva MG *et al.*, (2023)[64] |
| **2.** | β-galactosidase | Silva RC, Trevisan MG *et al.*, (2020)[65] |
| **3.** | Mefenamic acid | Nicolini MV, Vieira WT *et al.*, (2023)[66] |

## CONCLUSION

Gastro-resistant polymers are essential components in the development of oral drug delivery systems, particularly for acid-sensitive pharmaceuticals. Their ability to protect active pharmaceutical ingredients (APIs) from the harsh gastric environment while facilitating targeted release in the intestines enhances both the stability and therapeutic efficacy of these drugs. This paper has explored various types of gastro-resistant polymers, including synthetic options like Eudragit and cellulose derivatives, highlighting their mechanisms of action, advantages, and applications in pharmaceutical formulations.

In conclusion, the advancements in gastro-resistant polymer technology have significantly improved the formulation of modified-release dosage forms. By ensuring that drugs are released at optimal sites for absorption, these polymers not only enhance bioavailability but also minimize gastrointestinal discomfort. Future research should focus on overcoming existing limitations such as manufacturing complexities and regulatory challenges to further optimize these polymers for controlled and targeted drug delivery. The ongoing development in this field promises to contribute substantially to modern pharmaceutics, ultimately improving patient outcomes through more effective drug therapies.

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