Available online on 15.07.2025 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

Emerging Applications of Marine-Derived Polymers in Targeted Drug Delivery: A Comprehensive Review of Sources, Structures, and Pharmaceutical Potentials

* Puja Gianani, Nalini Kurup, Nikhil Rajnani

Department of Pharmaceutics, Prin. K. M. Kundnani College of Pharmacy, Cuffe Parade, Mumbai- 400005, Maharashtra, India

Article Info:

Article History:

Received 22 April 2025
Reviewed 10 June 2025
Accepted 03 July 2025
Published 15 July 2025

Cite this article as:

Gianani P, Kurup N, Rajnani N, Emerging Applications of Marine-Derived Polymers in Targeted Drug Delivery: A Comprehensive Review of Sources, Structures, and Pharmaceutical Potentials, Journal of Drug Delivery and Therapeutics. 2025; 15(7):287-297
DOI: http://dx.doi.org/10.22270/jddt.v15i7.7270

*Address for Correspondence:

Puja Gianani, Department of Pharmaceutics, Prin. K. M. Kundnani College of Pharmacy, Cuffe Parade, Mumbai- 400005, Maharashtra, India

Abstract

Marine-derived polymers are increasingly recognized as versatile biomaterials for targeted drug delivery. This comprehensive review explores the sources, chemical structures, and pharmaceutical potential of key marine polymers, highlighting how their unique properties enable innovative drug delivery systems across multiple routes of administration. We classify major marine-derived polymers (e.g., alginate, chitosan, carrageenan, fucoidan, marine collagens) and explain their relevance based on biocompatibility, biodegradability, and functional diversity. We then examine their emerging applications in oral, buccal/sublingual, nasal, pulmonary, rectal, vaginal, ocular, and transdermal drug delivery, with two case studies per route illustrating recent preclinical or clinical advances. These case studies demonstrate how marine polymers enhance targeted delivery via mechanisms such as mucoadhesion, stimuli-responsive gelation, nanoparticle formation, and ligand-specific targeting. One illustrative graph and a summary table are included to visualize polymer classifications and key applications. The review also discusses recent innovations and patents, underscoring trends such as marine polymer-based nanocarriers for cancer therapy and microneedle patches for transdermal delivery. In conclusion, marine-derived polymers offer a rich platform for developing targeted, patient-friendly drug delivery systems. Their continued development, supported by growing clinical evidence and technological refinements, is poised to expand the pharmaceutical toolkit for precision medicine. Future prospects include scaled-up production, more in-depth safety profiling, and translational research to bring marine polymer-based delivery systems from bench to bedside.

Keywords: Marine-derived polymers; Targeted drug delivery; Polysaccharides; Chitosan; Alginate; Carrageenan; Mucoadhesive delivery; Nanoparticles

Introduction

The marine environment is a vast reservoir of biopolymers with distinctive structures and bioactivities that differ from terrestrial sources. Marine-derived polymers, particularly polysaccharides and glycoproteins from algae, crustaceans, and marine animals, have attracted significant interest in pharmaceutical research. These materials are generally biocompatible, biodegradable, and often exhibit inherent bioactivities (e.g. antimicrobial, anti-inflammatory) that can be advantageous in drug delivery systems (DDS). Compared to synthetic polymers, marine polymers can offer mucoadhesiveness, stimuli-responsive behavior, and low toxicity. Such properties make them ideal for formulating targeted and controlled-release therapeutics.

Targeted drug delivery aims to direct therapeutic agents to specific sites in the body, improving efficacy while minimizing off-target effects. Marine polymers contribute to this goal in multiple ways. For example, cationic chitosan (derived from crustacean shells) can adhere to negatively charged mucosal surfaces and transiently open tight junctions, enhancing drug absorption across epithelia[1]. Sulfated polysaccharides like fucoidan (from brown seaweed) or chondroitin sulfate (from fish/shark cartilage) can serve as targeting ligands by interacting with specific receptors or proteins in diseased tissue[2]. Meanwhile, algal-derived polymers such as alginate and carrageenan form hydrogels that protect payloads and enable site-specific release in response to pH or ionic changes. These functionalities illustrate the broad pharmaceutical potential of marine biomaterials.

This review provides a structured overview of marine-derived polymers in drug delivery, beginning with a classification of major polymers and their sources and features. We then discuss applications in various delivery routes – oral, mucosal (buccal/sublingual), nasal, pulmonary, rectal, vaginal, ocular, and transdermal – with two illustrative case studies for each route. Each case study highlights a recent clinical or preclinical example using a different marine polymer, underscoring the diversity of systems. Figure 1 offers a schematic summary of how marine polymers integrate into advanced drug delivery strategies, and Table 1 classifies the polymers with their key properties and uses. Finally, we address recent innovations (including noteworthy patents and products) and future prospects for translating these marine-based delivery systems into clinical practice.

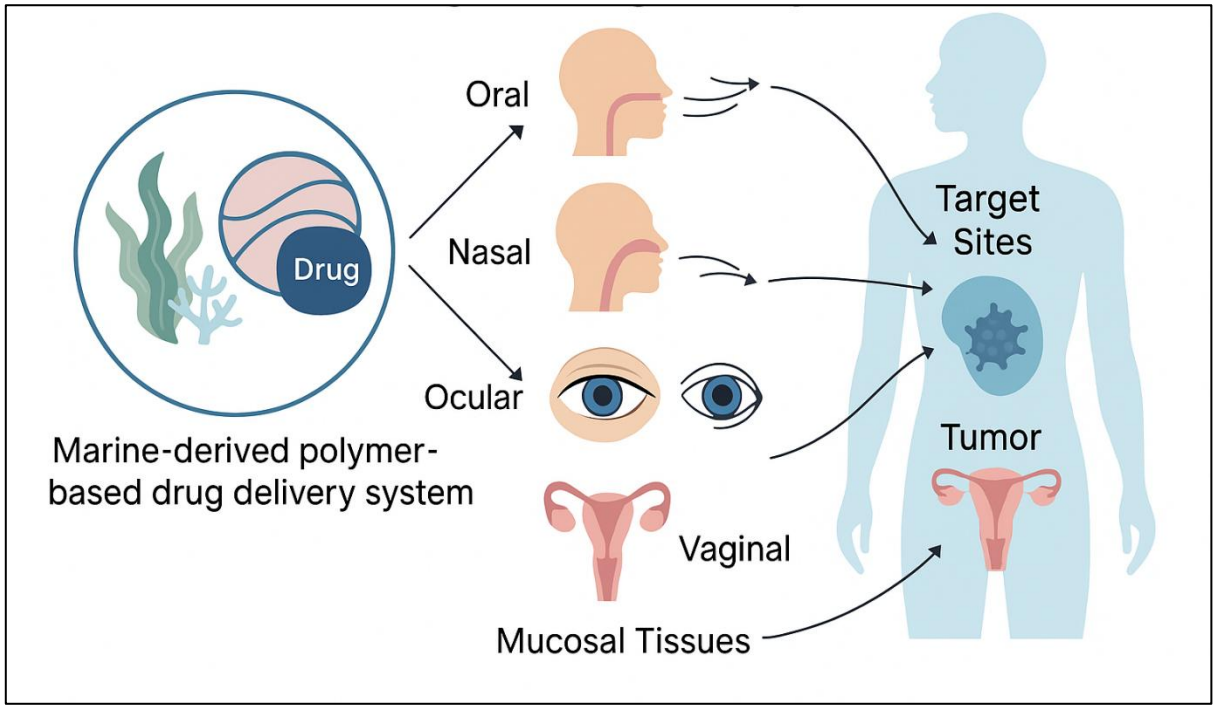

Figure 1: Schematic representation of marine-derived polysaccharides in advanced drug delivery systems. *Marine polymers such as alginate, chitosan, carrageenan, hyaluronan, and others can be processed into various drug carriers (nanoparticles, hydrogels, microneedles, etc.) enabling targeted, controlled, and stimuli-responsive delivery of therapeutic agents.* [1]

Classification of Marine-Derived Polymers

Marine polymers of pharmaceutical interest can be broadly grouped by their chemical nature and biological sources[1].The primary classes include marine polysaccharides (from algae, crustaceans, or marine animals) and marine-sourced proteins or glycoproteins. Below, we highlight representative polymers (selected for their pharmaceutical importance and structural diversity) within these classes:

- **Marine Polysaccharides:** This category encompasses *algal polysaccharides* such as alginate, carrageenan, agarose, fucoidan, and ulvan, as well as animal-derived polysaccharides like chitosan (from chitin in crustacean shells) and glycosaminoglycans (e.g. hyaluronic acid and chondroitin sulfate from fish or marine invertebrates). These polymers are typically high-molecular-weight carbohydrates with repeating monosaccharide units that may be sulfated or carboxylated. Their key properties include hydrophilicity and gel-forming ability (for alginate, carrageenan, agarose), mucoadhesion and positive charge (chitosan), and specific biological interactions (e.g., fucoidan's binding to cell-surface receptors). Most marine polysaccharides are biodegradable and non-toxic, and many exhibit bioactivities such as antioxidant, anticoagulant, or antiviral effects. These features make them attractive as drug excipients for improving solubility, controlling release, and targeting[1,2].
- **Marine Proteins and Derivatives:** Examples include **marine collagen** and its denatured form gelatin (often from fish skin or scales), and marine peptides or glycoproteins (such as marine mucins or polysaccharide-protein conjugates). Marine collagens are structural proteins that can form biodegradable scaffolds or nanoparticles, valued for their biocompatibility and mild antigenicity compared to mammalian collagens. Fish-derived gelatin has been used to form nanoparticles and films for drug delivery, offering a lower gelling temperature and different rheological properties than porcine or bovine gelatin. Additionally, marine exoskeleton-derived silica (e.g., from diatoms or sponges) and marine polyesters (e.g., polyhydroxyalkanoates produced by marine bacteria) are emerging as novel biomaterials, though they are less explored in drug delivery [2].

Table 1 provides an overview of selected marine-derived polymers, their natural sources, key structural features, and examples of pharmaceutical applications.

Table 1: Classification of Key Marine-Derived Polymers with Sources, Structures, and Applications

Polymer	Source	Structural Features	Key Properties	Drug Delivery Applications
Alginate	Brown algae (seaweed)	Anionic polysaccharide of guluronic and mannuronic acid units (linear block copolymer).	Forms hydrogels with divalent cations (Ca^{2+}); pH-responsive swelling; biocompatible.	Hydrogel beads and microspheres for oral controlled release; injectable gels for tissue engineering; wound dressings.
Chitosan	Crustacean shells (chitin)	Cationic polysaccharide of glucosamine (deacetylated chitin). Typically medium molecular weight.	Mucoadhesive; opens tight junctions; biodegradable; antimicrobial.	Nanoparticles for oral and nasal delivery (e.g., insulin, vaccines); buccal films; ophthalmic and transdermal microneedles (as binder).
Carrageenan	Red algae (e.g., *Kappaphycus*, *Gigartina*)	Sulfated galactan polysaccharide (varieties: κ, ι, λ differ in sulfation).	Forms thermoreversible gels; strong negative charge; mucoadhesive.	Matrix for oral tablets and capsules (sustained release); Mucoadhesive films for buccal drug delivery; antiviral nasal sprays (iota-carrageenan); vaginal microbicide gels.
Fucoidan	Brown algae (*Fucus*, *Undaria*)	Sulfated fucose-rich polysaccharide (branched).	High sulfate content imparts strong negative charge; binds growth factors and selectins; antioxidant.	Nanoparticles and microparticles for targeting inflammation and cancer (ligand for macrophage or tumor targeting); carriers for inhaled tuberculosis therapy (targeting alveolar macrophages).
Hyaluronic Acid (Hyaluronan)	Marine fish (rooster comb alternative) or microbial fermentation	Non-sulfated glycosaminoglycan of repeating disaccharides (glucuronic acid + N-acetylglucosamine).	Very hydrophilic; forms viscoelastic gels; excellent biocompatibility; binds CD44 receptors.	Viscous eye drops and inserts to prolong ocular drug residence (lubricant and absorption enhancer); nanoparticle surface coating for targeted delivery (e.g., to CD44-expressing cancer cells).
Chondroitin Sulfate	Cartilage of sharks, fish, etc.	Sulfated glycosaminoglycan (repeating disaccharide with sulfate esters).	Biocompatible, cartilage-mimetic; mildly anionic.	Often combined with chitosan or collagen in nanoparticulate systems for cartilage targeting or cancer (due to affinity for selectins); component of injectable hydrogels for sustained release.
Marine Collagen/Gelati n	Fish skin, scales, sea cucumber	Triple-helix protein (collagen); gelatin is denatured, amorphous form of collagen.	Biodegradable protein matrix; cell-friendly; lower melting point for fish gelatin.	Nanoparticles and hydrogels for protein or gene delivery; implantable sponges for tissue engineering (drug-eluting wound scaffolds); vaccine delivery depots.
Agarose / Agar	Red algae (*Gelidium*, *Gracilaria*)	Neutral galactose-based polysaccharide (agarose) often with agaropectin (charged) in agar.	Thermogelling (solidifies upon cooling); forms strong gels; non-toxic.	Culture media (classic use); in drug delivery, used in some hydrogel matrices for controlled release or as capsule shells; emerging use in implantable gel plugs for tissue-localized therapy.

† Note: Hyaluronic acid used in pharmaceuticals is often produced by fermentation; however, marine fish-derived HA is an alternative source used in some formulations.

This classification underscores the diverse chemistries and functionalities of marine-derived polymers. Such diversity allows tuning of drug delivery system properties by selecting appropriate polymers or combinations. For example, an oral nanoparticle can be engineered with an alginate core (to protect a drug through stomach acid) and a chitosan shell (to adhere to intestinal mucosa and enhance uptake). In the following sections, we delve into specific delivery routes and how these polymers are applied, with practical case studies illustrating their performance.

Table 2 provides an overview of various marketed products of marine-derived polymers.

Table 2: Marketed products of marine polymers

Product	Manufacturer	Use
Gaviscon	Reckitt	Antacid Formulation
NovaMatrix	FMC Biopolymer	Excipient in DDS
Kaltostat	ConvaTec	Wound dressing
Coseal	Baxter Healthcare	Surgical sealant for tissue adhesion
HemCon Bandage	HemCon Medical technologies	Bandage for wound care
Chitoclear gel & spray	ChitoTech Co	Wound healing
Soft Gel Capsules	Various pharmaceutical companies	Nutritional supplements, drugs
Fish Collagen Peptides	Wellnex, Rousselot, Nitta Gelatin	Dietary supplement (anti-aging)
Gelatin Sheets/Powder	Gelita, Lapi Gelatine, Nitta Gelatin	Food-grade gelling agent
Collagen-Based Wound Dressings	Smith & Nephew, Acelity	Wound healing

Oral Drug Delivery Systems

Oral delivery is the most convenient route for patients but presents challenges such as acidic gastric pH, digestive enzymes, and limited mucosal permeability for macromolecules. Marine-derived polymers have shown considerable promise in overcoming these barriers[3]. Chitosan, in particular, has been widely studied for oral nanoparticle systems due to its mucoadhesive and absorption-enhancing properties. Chitosan-based nanocarriers can transiently open tight junctions between intestinal epithelial cells, facilitating paracellular transport of drugs[1]. For instance, Prego and colleagues formulated chitosan–PEG nanocapsules for oral delivery of peptides, achieving low cytotoxicity and significantly enhanced intestinal absorption in vitro. Subsequent studies showed similar chitosan nanoparticle approaches improved oral delivery of insulin, by protecting the insulin from degradation and improving its uptake [1]. In one case study, insulin-loaded chitosan nanoparticles coated with alginate demonstrated improved bioavailability in animal models, attributed to mucoadhesion and pH-responsive protection of insulin through the stomach [1,4]

Another marine polymer, alginate, is frequently used in oral delivery for its ability to form gel beads or coatings that protect drugs from gastric acid and release them in the higher pH of the intestine. A noteworthy example is the development of pH-sensitive alginate-Chitosan beads for oral protein delivery. Bhattarai et al. prepared indomethacin-loaded beads from a conjugate of alginate and a temperature-sensitive polymer (PNIPAAm) along with chitosan; these beads exhibited dual stimuli-responsive release (slower release at low pH and lower temperature). This strategy could potentially protect acid-labile drugs in the stomach and then release them upon reaching intestinal conditions or body temperature. *Oral Insulin Nanoparticles.* In a recent study, insulin was encapsulated in a multilayer alginate–chitosan nanoparticle. The alginate core shielded insulin from gastric acid, while the chitosan outer layer adhered to the intestinal mucosa. In diabetic rat models, this formulation significantly reduced blood glucose levels, illustrating enhanced oral insulin absorption[1]. *pH/Thermosensitive Alginate Beads.* As mentioned, indomethacin-loaded alginate/PNIPAAm beads showed temperature- and pH-dependent release profiles. At body temperature and neutral pH, the beads softened and released the drug, whereas at acidic pH (stomach) and room temperature, their release was minimal. This dual-sensitivity system exemplifies an advanced oral DDS enabling on-demand drug release [1]

Overall, marine polymers like chitosan and alginate are enabling oral delivery of drugs that were previously injectable-only (e.g., peptides and vaccines) by improving stability in the GI tract and enhancing transmucosal transport [5]. Many oral formulations employing these polymers are in experimental or early clinical stages, indicating a promising pipeline for oral pills or capsules of biologics in the near future.

Buccal and Sublingual (Mucosal) Drug Delivery

Drug delivery via the buccal or sublingual mucosa (the lining of the cheek and the area under the tongue) bypasses first-pass metabolism and can provide rapid absorption into systemic circulation. The mucosal route also allows localized therapy in the oral cavity (for infections or lesions). Marine polymers with

mucoadhesive properties, such as carrageenan and chitosan, are particularly useful in this context. Carrageenan has been investigated as a film-forming polymer for buccal delivery, often in combination with chitosan to optimize film strength and adhesion[6]. Carrageenan's sulfate groups bind to mucins, while chitosan's cationic amino groups provide additional mucoadhesion, resulting in sustained contact with the oral mucosa [7].

Miconazole Buccal Film. Tejada and colleagues developed a mucoadhesive buccal film for anti-fungal delivery (miconazole) using a blend of λ-carrageenan and κ-carrageenan combined with chitosan. The inclusion of carrageenans markedly improved the film's mechanical properties and adhesion to pig buccal tissue compared to a chitosan-only film, with λ-carrageenan providing the greatest mucoadhesion[6]. This carrageenan-enhanced film showed prolonged retention in the mouth and effective local release of miconazole, highlighting how marine polysaccharides can improve therapies for oral thrush (candidiasis). *Multilayer Buccal Analgesic Films.* Volod'ko et al. fabricated a multi-layer buccal film using alternating layers of chitosan and κ-carrageenan, loaded with common analgesics (paracetamol, ibuprofen). The multilayer structure significantly increased the film's tensile strength and controlled the drug release better than single-layer films. In vitro tests showed that these films adhere well to bovine cheek mucosa and can provide a sustained release of pain relievers in the oral cavity [6]. Another study reported κ-carrageenan films plasticized with glycerol for ibuprofen delivery, noting that such films were promising for buccal NSAID administration.

Chitosan on its own has also been applied in buccal systems, often as part of a composite. Its mucoadhesive and permeability-enhancing effects can be leveraged for systemic delivery of peptides or vaccines via the buccal route. For example, chitosan-based buccal tablets for insulin have shown improved absorption in animal models (due to avoidance of GI degradation). In summary, marine polymers enable creation of flexible, strong, and adhesive films or tablets that adhere to the mucosal tissue, providing a platform for both local and systemic drug delivery without the need for swallowing a pill.

Nasal Drug Delivery

The nasal route offers a non-invasive entry to systemic circulation and even direct access to the central nervous system (via the olfactory region), but rapid mucociliary clearance in the nose can limit drug absorption. Marine-derived polymers can address this by providing mucoadhesion and by formulating drugs into particulate systems that protect and prolong nasal residence. Chitosan is one of the most effective polymers in nasal delivery due to its mucoadhesive nature and ability to transiently open tight junctions in the nasal epithelium. It has GRAS (Generally Recognized as Safe) status with the FDA, which facilitates its use in intranasal products [3]. Chitosan-based nasal formulations have been explored for vaccines and biologics that otherwise have low nasal uptake.

Intranasal COVID-19 Vaccine (Chitosan Nanoparticles). A recent preclinical study encapsulated a SARS-CoV-2 spike protein subunit vaccine into chitosan nanoparticles for intranasal administration [3]. The chitosan provided a depot effect in the nasal mucosa, and the formulation induced strong local immune responses. After nasal vaccination in mice, high levels of anti-SARS-CoV-2 IgA were detected in lung mucosa, along with robust tissue-resident T cell responses, which nearly completely blocked viral infection in challenge experiments by Yu et al. This demonstrates the capability of chitosan nasal carriers to enhance mucosal immunity, a key aspect for respiratory pathogens. Another example is a chitosan-hydroxybutyl derivative conjugated with an antihistamine (ketotifen) for allergic rhinitis; the chitosan-based nasal gel significantly improved drug uptake and symptom relief in animal models.

Iota-Carrageenan Antiviral Nasal Spray. Carrageenan, particularly the iota form, has gained attention as an antiviral agent in nasal sprays. Carrageenan can trap viruses in a polymer network, preventing them from infecting host cells. A notable clinical example is a Carrageenan-based nasal spray tested for common cold and COVID-19 prophylaxis. In randomized trials, an iota-carrageenan nasal spray significantly reduced viral load and symptoms in patients with early-stage common cold infections, compared to placebo[8–10]. Moreover, a recent trial in healthcare workers showed that regular use of iota-carrageenan spray was associated with lower incidence of COVID-19. The carrageenan acts as a broad-spectrum antiviral barrier in the nasal cavity. These sprays have been well-tolerated and are available in some markets as over-the-counter products for upper respiratory infection prevention.

In summary, marine polymers enable advanced nasal drug delivery strategies: chitosan-based nanoparticles for improved absorption and immune activation, and carrageenan gels or sprays for prophylaxis against respiratory viruses. Both approaches illustrate the value of mucoadhesive and bioactive marine polymers in extending the capabilities of intranasal therapy.

Pulmonary (Inhalation) Drug Delivery

Pulmonary delivery (inhalation into the lungs) is used for both local treatment of respiratory diseases (asthma, COPD, infections) and systemic delivery of peptides or small molecules. Inhalable carriers must be biocompatible and have aerodynamic diameters in the 1–5 μm range to effectively deposit in the lungs. Several marine-derived polymers have been formulated as inhalable microparticles or nanoparticles for targeted lung delivery. Chitosan again is prominent: it can be spray-dried into microparticles or nanocomplexes that improve drug dispersibility and lung retention. Importantly, chitosan's cationic nature helps it interact with the negatively charged pulmonary mucus, potentially improving drug penetration through sputum or mucosal layers[5]. Studies have reported that inhaled chitosan nanoparticles enhanced drug transport across the mucus barrier in a murine asthma model and increased deep lung deposition in a COPD model. Additionally, chitosan has inherent antimicrobial and

anti-inflammatory properties that can benefit pulmonary therapy.

Chitosan Nanoparticles for Asthma/COPD. Researchers developed inhalable chitosan nanoparticles carrying a corticosteroid and a bronchodilator for combination therapy in asthma. In rodent models, these chitosan NPs showed improved drug bioavailability in the lungs and prolonged retention time compared to solution formulations. The particles' mucoadhesive character led to more drug being absorbed across the bronchial epithelium. Similarly, for COPD, chitosan NPs loaded with an antibiotic achieved higher local drug concentrations in lung tissue and improved therapeutic outcomes in infected mice[11]. These findings underscore how chitosan can serve as a versatile platform for inhaled nanomedicines, providing controlled release and enhanced mucosal penetration.

Fucoidan Microparticles for Tuberculosis (TB). Fucoidan, a sulfated polysaccharide from brown seaweed, has a unique ability to target alveolar macrophages – the very cells that harbor Mycobacterium tuberculosis. Cunha et al. developed inhalable fucoidan microparticles co-loaded with two first-line TB drugs (isoniazid and rifabutin). The fucoidan's structure is recognized by receptors on macrophages, promoting uptake of the drug-loaded particles by these cells. The spray-dried microparticles had a mass median aerodynamic diameter of ~3.7 μm, suitable for deep lung deposition. In vitro, they showed high drug encapsulation (>95%) and no cytotoxicity to lung cells. Importantly, in a macrophage infection model, the fucoidan particles delivered drugs effectively into the host cells, achieving enhanced bacterial killing compared to non-targeted particles. This approach demonstrates the power of marine polymer targeting: the natural tropism of fucoidan for macrophages was harnessed to concentrate antibiotics at the site of infection. Such inhalable particulate systems could improve TB treatment by reducing systemic side effects and focusing therapy on infected cells[12].

These examples highlight a trend of using marine polymers not only to improve the formulation properties of inhaled drugs (stability, dispersibility) but also to actively target lung pathology (e.g., macrophage targeting in TB, or mucus penetration in asthma). As inhalation therapeutics grow beyond traditional small molecules to include biologics, the role of functional biomaterials like chitosan and fucoidan in pulmonary delivery is set to expand.

Rectal Drug Delivery

Rectal delivery can be advantageous for localized treatment of diseases such as ulcerative colitis or for systemic delivery when oral administration is not feasible (e.g., for patients with vomiting). The rectal route avoids much of the first-pass metabolism and can provide a fairly large absorption surface in the distal colon. However, drug formulation for rectal delivery must contend with limited fluid for dissolution and the tendency of dosage forms to be expelled. Mucoadhesive hydrogels and suppositories formulated with marine polymers can adhere to the rectal mucosa, prolonging drug residence and enhancing local therapy[4]. Chitosan is especially useful here: its mucoadhesive and biocompatible nature make it ideal for rectal gels or suppository coatings[5]. Additionally, chitosan can be chemically modified (e.g., with thiol or catechol groups) to further improve its adhesive strength in the mucosal environment.

Chitosan-Catechol Hydrogel for Ulcerative Colitis. Xu et al. developed a catechol-functionalized chitosan hydrogel intended for rectal administration of sulfasalazine, an anti-inflammatory prodrug used in ulcerative colitis. The catechol groups (inspired by mussel adhesive proteins) significantly enhanced the mucoadhesiveness of the chitosan gel, allowing it to stick to the colonic mucosa and resist quick elimination. In a comparative study, this chitosan-catechol hydrogel delivered sulfasalazine more effectively than oral administration, achieving higher local drug concentrations at the inflammation site and fewer systemic side effects[4]. The treated animals showed improved colitis symptoms and healing of the colonic tissue. This example illustrates how marine-derived polymer derivatives can be engineered for disease-specific needs – here, a bioadhesive hydrogel that stays in the rectum and slowly releases drug to the diseased colon tissue.

Carrageenan-Based Rectal Microbicide Gel. Carrageenan's antiviral properties have also been leveraged in rectal delivery, particularly for HIV prevention. A carrageenan-based rectal gel (often combined with an antiretroviral drug) can act as a microbicide to reduce transmission of HIV and other sexually transmitted viruses. For example, a formulation known as Carrageenan/MIV-150 (MIV-150 is a non-nucleoside reverse transcriptase inhibitor) was tested in macaque models of HIV. A single rectal application of a carrageenan gel containing MIV-150 provided significant protection against a rectal SHIV (simian-human immunodeficiency virus) challenge in monkeys[13]. The carrageenan not only serves as a gel matrix for the drug but also adds broad-spectrum antiviral action and mucoadhesion. In related studies, carrageenan gels with zinc acetate also showed synergistic protective effects, blocking >75% of viral challenges in mice[14]. These promising preclinical results have led to carrageenan-based microbicide gels being evaluated in early human trials for safety and acceptability. [14]

Overall, marine polymers in rectal delivery fulfill two main roles: (1) improving local therapy for rectal and colonic diseases by maintaining drug contact with the tissue (as seen with chitosan hydrogels for colitis), and (2) serving as carriers for preventative therapies (as seen with carrageenan antiviral gels). Rectal formulations with these polymers can be designed as enemas, suppositories, or gels depending on the indication. As with other routes, the mucoadhesive nature of many marine polymers is a recurring theme, crucial for ensuring that the drug remains at the site of action in the rectum.

Vaginal Drug Delivery

The vaginal route is used for local treatments (such as for infections, contraception, or menopausal symptoms) and can also achieve systemic absorption for certain drugs. The vaginal environment has a mucus barrier and is subject to fluid outflow, so retention of dosage forms is a challenge. Marine-derived polymers contribute significantly to modern vaginal drug delivery systems in the form of gels, inserts, films, and nanomedicine carriers. Chitosan and alginate are frequently studied for vaginal formulations due to their safety and mucoadhesive properties. Chitosan, for instance, is biodegradable and inherently antimicrobial, making it suitable for treating vaginal infections (e.g., candidiasis or bacterial vaginosis)[15]. It can form gels or nanoparticle-in-gel systems that adhere to vaginal tissue and gradually release drugs over many hours.

Chitosan Nanoparticle Hydrogel for Estradiol (Menopausal Therapy). Abou-Taleb et al. developed a hybrid gel composed of chitosan-coated solid lipid nanoparticles for vaginal delivery of estradiol, aimed at relieving menopausal symptoms. In this formulation, estradiol-loaded lipid nanoparticles (~500–800 nm in size) were stabilized and given mucoadhesive properties by a chitosan coating. The chitosan-coated nanoparticles were then incorporated into a thermosensitive gel. The result was a vaginal gel that could significantly increase estradiol permeation through the vaginal mucosa (over 2-fold higher compared to a simple estradiol gel) while also providing controlled release of the hormone. The chitosan's presence prolonged the gel residence time and enhanced tissue uptake of estradiol, yielding effective local estrogenization with minimal systemic exposure[15].Such a system addresses vaginal dryness and atrophy in postmenopausal women without the need for systemic HRT pills, thereby reducing systemic side effects.

Carrageenan-Based Vaginal Microbicide for STI Prevention. As with rectal delivery, carrageenan has been explored in vaginal gels to prevent sexually transmitted infections. One example is the product "Carraguard," a λ-carrageenan vaginal gel that was clinically tested for HIV prevention. While Carraguard's efficacy in a large trial was inconclusive, it demonstrated that carrageenan gels are safe and acceptable for regular vaginal use[14]. Building on this, researchers formulated a vaginal suppository combining κ-carrageenan with the antiviral drug tenofovir. In vitro release studies showed that the carrageenan-based suppository could release tenofovir steadily in simulated vaginal fluid, and the presence of carrageenan did not inhibit tenofovir's antiviral activity[14]. Additionally, a recent study by Perino et al. evaluated a carrageenan vaginal gel in HPV-positive women[16] and found it helped clear human papillomavirus infections more effectively than no treatment. The gel's components (including carrageenan and a probiotic extract) likely created a protective mucosal layer and modulated the local environment to assist the body in fighting the virus.

These case studies show how marine polymers facilitate vaginal drug delivery: chitosan enhances residence time and penetration for therapies like hormones or antimicrobials, and carrageenan provides a platform for safety and broad-spectrum antiviral action in microbicides. Vaginal films made of chitosan/alginate have also been studied for delivering drugs for vaginosis, showing prolonged drug release over several days[17]. The versatility of marine polymers allows vaginal products to be formulated as gels (easy application), films (discreet, dissolvable), or suppositories, each benefiting from the polymers' mucoadhesion and controlled-release capabilities.

Ocular Drug Delivery

Ocular drug delivery targets conditions of the eye (anterior or posterior segment) and often suffers from rapid clearance by tears and limited permeability of the cornea or conjunctiva. Eye drops, the most common ocular dosage form, typically have low bioavailability (<5% of drug penetrates the eye) because tears wash them away. To address this, viscosity-enhancing and mucoadhesive polymers are added to ophthalmic formulations. Marine-derived polymers, especially hyaluronic acid (hyaluronan) and chitosan, have become popular in ocular drug delivery owing to their favorable characteristics[18]. Hyaluronic acid is naturally present in the eye (vitreous humor) and is extremely biocompatible and hydrating. It exhibits pseudoplastic rheology – high viscosity at rest (helping it stay in the eye) and shear-thinning during blinking – which makes hyaluronan ideal for eye drops[18]. Chitosan, on the other hand, can interact with the negatively charged corneal surface and mucins, promoting drug retention and even penetration into deeper ocular tissues (e.g., across the cornea for drugs treating intraocular conditions).

Chitosan Nanoparticles for Glaucoma. Glaucoma treatment often requires delivering drugs (like timolol or latanoprost) to intraocular tissues. A chitosan-based nanomedicine approach has been examined to improve the delivery of these drugs. In one study, timolol maleate (a beta-blocker) was loaded into chitosan nanoparticles, which were then formulated as an ophthalmic suspension[19]. The chitosan nanoparticles adhered to the corneal surface and gradually released timolol, resulting in a more prolonged reduction of intraocular pressure (IOP) in rabbits compared to a standard eye drop. Chitosan's mucoadhesive property significantly increased the drug's contact time with the cornea. Furthermore, the study noted that chitosan nanoparticles were well-tolerated with minimal irritation. Another example involved chitosan–PEG grafted nanoparticles for tacrolimus delivery to the eye, which achieved higher corneal penetration while avoiding systemic absorption[20]. These systems demonstrate that chitosan can be a cornerstone for ocular nanocarriers, effectively targeting the drug to the eye and reducing dosing frequency (which can improve patient compliance in chronic diseases like glaucoma).

Hyaluronic Acid-Based Hydrogel for Dry Eye Therapy. Hyaluronic acid (HA) is already widely used in artificial tear eye drops for dry eye disease because it can retain moisture on the ocular surface and promote healing of the cornea. Building on that, recent innovations use HA

in more advanced delivery systems. One such system is an HA-based in situ forming hydrogel loaded with cyclosporine (an immunosuppressant used in severe dry eye and ocular inflammation). Upon instillation as drops, the HA solution, often lightly crosslinked or formulated with a thermo-gelling polymer, forms a gel on the eye that slowly releases cyclosporine. Casey-Power et al. reported that HA-based polyelectrolyte complexes could be used to carry drugs and then form a thin gel film on the eye, extending drug release for several hours (versus minutes for conventional drops)[18]. Additionally, HA can target CD44 receptors on corneal cells, potentially enhancing drug uptake (since HA naturally binds CD44). In another study, HA-coated liposomes loaded with dexamethasone achieved greater drug levels in the retina after topical instillation, suggesting that HA helped the liposomes penetrate ocular barriers [21]

In summary, marine-derived polymers contribute to ocular delivery by increasing precorneal residence time and facilitating drug transport into the eye. Their use has resulted in commercial or near-commercial products: for instance, there are contact lenses soaked in HA to slowly release comfort agents, and chitosan-N-acetylcysteine has been tested in eye drop form to improve antibiotic delivery to the cornea (due to its mucoadhesive and mucolytic effects). The gentle, biocompatible nature of these polymers is particularly important for the sensitive ocular tissues. Ongoing research is exploring nanoparticle-in-gel systems and microneedle-assisted delivery (e.g., using HA-based microneedles to deliver drugs to the ocular surface) – all indicating a robust future for marine polymers in ophthalmology.

Transdermal and Topical Delivery

Transdermal drug delivery (through the skin) provides a means to achieve systemic effects (as with transdermal patches for pain or hormone therapy) or to treat localized conditions (like wound healing or dermatological diseases) without injections. The outermost layer of skin, the stratum corneum, is a formidable barrier to most drugs, so advanced delivery techniques are needed. Microneedles, nanoparticles, and hydrogel dressings are among the strategies where marine-derived polymers play an enabling role. Chitosan and alginate have been investigated in these technologies: chitosan for its film-forming ability and skin compatibility, and alginate for its gel-forming, moist wound-healing properties.

Chitosan Microneedle Patch for Drug Delivery. Microneedle arrays are minimally invasive devices that painlessly create microscopic channels in the skin to enhance drug permeation. A recent trend is fabricating microneedles from biopolymers instead of silicon or metal. Chitosan-based microneedles have been developed as a dissolvable or swellable platform that can both insert into skin and then gradually release drug as the polymer matrix dissolves [5]. For example, a chitosan microneedle patch loaded with the anti-nausea drug levosulpiride was designed using thiolated chitosan (to improve mechanical strength). Upon application, the microneedles pierced the stratum corneum and subsequently dissolved, delivering levosulpiride into the skin in a sustained manner. The thiolated chitosan provided sufficient rigidity for skin insertion and then swelled to release the drug over 24 hours. In another study, microneedles made of chitosan were used to deliver insulin; the patch achieved a steady insulin release and effectively lowered blood glucose in diabetic rats for up to 6 hours [22]. These examples show that chitosan can double as a structural material for microneedles and a drug carrier, making the patch both biodegradable and capable of controlled drug delivery. Regulatory-wise, using a safe polymer like chitosan can simplify approval for microneedle systems[5].

Alginate-Based Wound Healing Hydrogel with Drug Nanoparticles. Marine polymers have a long history in wound dressings – for instance, alginate dressings are routinely used to manage exuding wounds due to their excellent absorption and gel formation. Researchers are now loading such dressings with active drugs or nanoparticles to create therapeutic wound patches. A compelling example is the integration of antibiotic-loaded nanotubes into an alginate hydrogel for infected wound healing [23,24]. In this system, Halloysite clay nanotubes carrying rifampicin (an antibiotic) and a photothermal agent were embedded in an alginate hydrogel matrix crosslinked with calcium. The alginate provided a moist environment and structural support, while the nanotubes released rifampicin in a sustained way and provided on-demand release upon near-infrared light irradiation (thanks to the photothermal agent). In infected wound models in rats, this composite hydrogel showed continuous antibacterial action for 7 days and significantly accelerated wound closure, fully regenerating tissue by 21 days. The marine polymer (alginate) was key to maintaining the depot of drug-loaded nanotubes at the wound site and conforming to the wound bed. This illustrates how marine polymers can be combined with nanotechnology for advanced transdermal therapy – here essentially creating a smart bandage for infected wounds.

Other innovations in transdermal delivery using marine polymers include film-forming sprays with chitosan for atopic dermatitis (forming a thin protective film that delivers anti-inflammatory drugs) and gelatin-based nanofiber mats that release drugs for burn treatment (fish gelatin nanofibers have shown the ability to incorporate and slowly release antibiotics while also promoting wound healing). Marine collagens are also being used in dermal fillers and scaffolds that deliver growth factors to skin for regenerative purposes. The inherent bioactivity of some marine polymers can be a bonus – e.g., chitosan is hemostatic (it can help stop bleeding) and has been used in wound dressings for that reason, aside from drug delivery.

In summary, marine-derived polymers find wide-ranging applications in transdermal and topical drug delivery, from components of microneedle systems to matrices for drug-loaded wound dressings. They improve these systems by providing biocompatible, flexible, and often bioactive platforms that can interface gently with skin tissue. As wearable and transdermal technologies (e.g., patches for vaccines or chronic disease drugs), marine

polymers are likely to be at the forefront of material choices given their excellent safety profile and multifunctionality.

Recent Innovations and Patents

Marine polymer-based drug delivery is a dynamic field, with numerous innovations emerging in the past few years. A notable trend is the combination of marine polymers with nanotechnology and stimuli-responsive systems to create smart DDS. For example, researchers have developed chitosan-based nanogels that respond to pH or enzymes to release drugs at tumor sites (active targeting in cancer therapy). Fucoidan and chondroitin sulfate have been used as targeting ligands on nanoparticles, exploiting their affinity for certain receptors overexpressed in tumors or inflamed tissues [2]. These advances enable *active targeting* – directing drugs to specific cells – which is a step beyond the passive targeting often achieved by conventional polymers.

On the translational side, several marine polymer formulations have reached clinical evaluation or commercialization. Carrageenan nasal sprays for viral infection prevention are one example already on the market in some regions (as discussed, effective against common cold viruses and under study for COVID-19 prophylaxis). Chitosan has been included in an intranasal vaccine formulation (for influenza) that reached Phase I trials, leveraging chitosan's adjuvant and delivery properties. In the realm of transdermal devices, chitosan microneedle patches for vaccine delivery have shown such promise that patent applications have been filed. For instance, a recent patent discloses a chitosan-based microneedle for delivery of a tuberculosis vaccine, highlighting claims of enhanced stability and immunogenicity[5]. Additionally, composite wound dressings that combine alginate and chitosan with growth factors are being patented for improved wound healing outcomes, indicating commercial interest in marine polymer tech for regenerative medicine.

Another burgeoning area is marine-inspired injectable hydrogels for localized drug delivery. Companies and research groups are patenting formulations like injectable chitosan-β glycerophosphate gels that solidify in situ for post-surgical drug release, or collagen/gelatin blends for cell therapy delivery[1]. The patents often emphasize the unique benefits of marine polymers: for example, one patent claims a "temperature-sensitive chitosan hydrogel for intra-tumoral chemotherapy delivery," capitalizing on chitosan's ability to be liquid at room temp and gel at body temp.

In terms of regulatory progress, GRAS designation for chitosan and the long history of safe use of alginate and agar in foods have smoothed the path for these materials in drug products. A significant innovation is the development of marine polymer derivatives with improved performance – such as thiolated chitosan (with enhanced mucoadhesion and a recent patent for its use in oral peptide delivery) and methylated alginates (patented for improved solubility and drug loading capacity). These derivatives often become part of the intellectual property when companies formulate them into novel DDS.

Marine biomaterials have also intersected with the field of biomedical devices. For example, a patent was granted for a "chitosan-based coating for implantable stents that delivers anti-inflammatory drugs" – combining a medical device with a marine polymer drug release layer. Similarly, contact lenses with a carrageenan-based drug depot have been prototyped to treat dry eye disease (with patents focusing on extended release over days).

Overall, the patent landscape indicates robust growth in marine polymer applications. In the last decade, dozens of patents have been filed on chitosan and alginate in drug delivery, covering everything from nanoparticle formulations to mucoadhesive films.

Recent innovations particularly focus on:

- **Nano-biotechnology**: e.g., seaweed polysaccharide-coated nanoparticles for cancer (with fucoidan or laminarin coatings for targeting and stealth).
- **Hybrid systems**: combining marine polymers with synthetic ones to yield superior properties (like poloxamer–chitosan nasal gels that are thermoresponsive).
- **Personalized medicine devices**: such as 3D-printed scaffolds of marine collagen loaded with patient-specific stem cells and drugs (patent applications in tissue engineering).

In essence, marine-derived polymers have transitioned from being academic curiosities to central components in cutting-edge drug delivery solutions. The flurry of patents and start-up companies in this area underscores confidence that these natural polymers can be key to solving drug delivery challenges. Industry interest also means future products containing these polymers are likely – we may soon see more marine polymer-based eye drops, transdermal patches, or oral nanopills entering the market.

Conclusion and Future Prospects

Marine-derived polymers have emerged as a rich resource for advancing targeted drug delivery. Through this review, we have seen that polymers like chitosan, alginate, carrageenan, fucoidan, and marine collagens offer a toolkit of desirable properties – mucoadhesion, biocompatibility, gel-forming ability, and inherent bioactivity – that can be strategically applied to overcome drug delivery barriers in virtually every administration route. From oral insulin nanoparticles to carrageenan antiviral gels and chitosan microneedle patches, marine polymers enable innovative therapies that improve drug stability, targeting, and patient convenience.

One clear advantage of marine polymers is their versatility. By modifying molecular weight, derivatization (e.g., thiolation, pegylation), or blending polymers, researchers can fine-tune drug release profiles and targeting capabilities. These materials are also often naturally abundant and renewable, aligning with trends toward sustainable and eco-friendly pharmaceuticals.

For instance, seafood industry waste (shrimp shells for chitosan, fish scales for collagen) can be upcycled into high-value medical products – a compelling circular economy story that may appeal to regulators and the public.

Looking ahead, there are several prospects and challenges for the field:

- **Clinical Translation**: While many marine polymer-based systems show promise in preclinical studies, more clinical trials are needed. Future work will likely focus on demonstrating safety and efficacy in humans for formulations like chitosan nasal vaccines, alginate-based oral peptide pills, and carrageenan microbicides. Regulatory approval will depend on consistent quality and clear benefits over existing therapies.
- **Optimization of Physicochemical Properties**: Continued research will refine polymer properties, for example by controlling polydispersity and purity of marine polysaccharides to ensure reproducible performance. Advanced characterization and standardization (perhaps through pharmacopeial standards for medical-grade chitosan or alginate) are important future steps.
- **Novel Polymer Sources**: There are many underexplored marine biopolymers (e.g., ulvan from green seaweed, glycoproteins from jellyfish, or sponge collagen) that may offer unique functionalities. Future studies may discover new polymers or novel derivatives with specialized targeting abilities (for instance, peptides from marine organisms that target specific receptors).
- **Drug Delivery Frontiers**: Marine polymers will likely play a role in emerging drug modalities. For example, gene therapy and mRNA delivery could benefit from chitosan-based nanoparticles as non-viral vectors (some early work shows chitosan can compact DNA and enable transfection). Cell and tissue engineering also intersect with drug delivery – injectable marine polymer hydrogels could deliver cells along with drugs or growth factors for regenerative medicine. The tunable microenvironment provided by such hydrogels can enhance cell survival and integration.
- **Challenges**: One challenge is the potential variability in polymer batches extracted from natural sources. Ensuring batch-to-batch consistency and removing impurities (like endotoxins, proteins, or heavy metals from seaweed extracts) will be crucial for clinical applications. Biotechnology approaches (microbial fermentation to produce chitosan or hyaluronan, for example) might be increasingly employed to obtain high-purity polymers. Additionally, some marine polysaccharides (like carrageenan) have faced scrutiny over safety in certain contexts (e.g., dietary use); careful toxicological evaluation specific to the route of administration is needed to dispel or confirm such concerns in drug delivery usage.

In conclusion, marine-derived polymers are no longer niche excipients but are becoming mainstay components of next-generation drug delivery systems. Their ability to address long-standing issues – poor bioavailability, systemic side effects, patient non-adherence – makes them instrumental in formulating therapies that are more effective and patient-friendly. As interdisciplinary collaboration grows (bringing together marine biology, polymer chemistry, pharmaceutical science, and clinical expertise), we can expect marine polymers to anchor many future innovations in targeted drug delivery. The ocean's bounty, when applied with ingenuity, is poised to make waves in medicine by enabling treatments that are safer, smarter, and more responsive to patients' needs.

Acknowledgements: The author would like to thank her guide Dr. Nalini Kurup and Mr. Nikhil Rajnani for their contribution and critical insights.

Author's Contribution: All authors have contributed equally.

Funding Source: Not applicable.

Conflicts of Interest: Not applicable.

Ethical Approval: Not applicable.

References

1. Cardoso MJ, Costa RR, Mano JF. Marine origin polysaccharides in drug delivery systems. Vol. 14, Marine Drugs. MDPI AG; 2016. https://doi.org/10.3390/md14020034 PMid:26861358 PMCid:PMC4771987

2. Galasso C, Ruocco N, Mutalipassi M, Barra L, Costa V, Giommi C, et al. Marine polysaccharides, proteins, lipids, and silica for drug delivery systems: A review. Int J Biol Macromol. 2023 Dec 31;253:127145. https://doi.org/10.1016/j.ijbiomac.2023.127145 PMid:37778590

3. Wang Y, Chen L, Wang Y, Wang X, Qian D, Yan J, et al. Marine biomaterials in biomedical nano/micro-systems. Vol. 21, Journal of Nanobiotechnology. BioMed Central Ltd; 2023. https://doi.org/10.1186/s12951-023-02112-w PMid:37926815 PMCid:PMC10626837

4. Xu J, Tam M, Samaei S, Lerouge S, Barralet J, Stevenson MM, et al. Mucoadhesive chitosan hydrogels as rectal drug delivery vessels to treat ulcerative colitis. Acta Biomater. 2017 Jan 15 ;48:247-57. https://doi.org/10.1016/j.actbio.2016.10.026 PMid:27769943

5. Gorantla S, Dabholkar N, Sharma S, Rapalli VK, Alexander A, Singhvi G. Chitosan-based microneedles as a potential platform for drug delivery through the skin: Trends and regulatory aspects. Int J Biol Macromol. 2021 Aug 1;184:438-53. https://doi.org/10.1016/j.ijbiomac.2021.06.059 PMid:34126145

6. Kristó K, Sangestani A, Hassan AAA, Rayya H, Pamlényi K, Kelemen A, et al. Study of the Effect of Temperature on the Production of Carrageenan-Based Buccal Films and Optimization of the Process Parameters. Pharmaceuticals. 2024 Dec 1;17(12). https://doi.org/10.3390/ph17121737 PMid:39770579 PMCid:PMC11678058

7. Tejada G, Lamas MC, Svetaz L, Salomón CJ, Alvarez VA, Leonardi D. Effect of drug incorporation technique and polymer combination on the performance of biopolymeric antifungal buccal films. Int J Pharm. 2018 Sep 5;548(1):431-42. https://doi.org/10.1016/j.ijpharm.2018.07.023 PMid:30008423

8. Ludwig M, Enzenhofer E, Schneider S, Rauch M, Bodenteich A, Neumann K, et al. Efficacy of a Carrageenan nasal spray in patients with common cold: A randomized controlled trial. Respir Res. 2013 Nov 13;14(1). https://doi.org/10.1186/1465-9921-14-124 PMid:24219370 PMCid:PMC3840586

9. Koenighofer M, Lion T, Bodenteich A, Prieschl-Grassauer E, Grassauer A, Unger H, et al. Carrageenan nasal spray in virus confirmed common cold: Individual patient data analysis of two randomized controlled trials. Multidiscip Respir Med. 2014;9(1). https://doi.org/10.1186/2049-6958-9-57 PMid:25411637 PMCid:PMC4236476

10. Bhatt A, Nainwal N, Purohit P. The Impact of Carrageenan on Pharmascience. Current Traditional Medicine [Internet]. 2024 Dec 1 https://doi.org/10.2174/0122150838266638231117180516

11. Gulati N, Dua K, Dureja H. Role of chitosan based nanomedicines in the treatment of chronic respiratory diseases. Int J Biol Macromol. 2021 Aug 31;185:20-30. https://doi.org/10.1016/j.ijbiomac.2021.06.035 PMid:34116092

12. Cunha L, Rodrigues S, da Costa AMR, Faleiro ML, Buttini F, Grenha A. Inhalable fucoidan microparticles combining two antitubercular drugs with potential application in pulmonary tuberculosis therapy. Polymers (Basel). 2018 Jun 8;10(6). https://doi.org/10.3390/polym10060636 PMid:30966670 PMCid:PMC6403622

13. Friedland BA, Hoesley CJ, Plagianos M, Hoskin E, Zhang S, Teleshova N, et al. First-in-Human Trial of MIV-150 and Zinc Acetate Coformulated in a Carrageenan Gel: Safety, Pharmacokinetics, Acceptability, Adherence, and Pharmacodynamics. 2016. https://doi.org/10.1097/QAI.0000000000001136 PMid:27437826 PMCid:PMC5172848

14. Pacheco-Quito EM, Ruiz-Caro R, Veiga MD. Carrageenan: Drug delivery systems and other biomedical applications. Vol. 18, Marine Drugs. MDPI; 2020. https://doi.org/10.3390/md18110583 PMid:33238488 PMCid:PMC7700686

15. Abou-Taleb HA, Fathalla Z, Naguib DM, Fatease A Al, Abdelkader H. Chitosan/Solid-Lipid Nanoparticles Hybrid Gels for Vaginal Delivery of Estradiol for Management of Vaginal Menopausal Symptoms. Pharmaceuticals. 2023 Sep 1;16(9). https://doi.org/10.3390/ph16091284 PMid:37765092 PMCid:PMC10536129

16. Laurie C, Tota JE, El-Zein M, Tellier PP, Coutlée F, Burchell AN, et al. Design and methods for the Carrageenan-gel Against Transmission of Cervical Human papillomavirus (CATCH) study: A randomized controlled trial. Contemp Clin Trials. 2021 Nov;110:106560. https://doi.org/10.1016/j.cct.2021.106560 PMid:34487919

17. Cirri M, Maestrelli F, Scuota S, Bazzucchi V, Mura P. Development and microbiological evaluation of chitosan and chitosan-alginate microspheres for vaginal administration of metronidazole. Int J Pharm. 2021 Apr;598:120375. https://doi.org/10.1016/j.ijpharm.2021.120375 PMid:33581271

18. Casey-Power S, Ryan R, Behl G, McLoughlin P, Byrne ME, Fitzhenry L. Hyaluronic Acid: Its Versatile Use in Ocular Drug Delivery with a Specific Focus on Hyaluronic Acid-Based Polyelectrolyte Complexes. Vol. 14, Pharmaceutics. MDPI; 2022. https://doi.org/10.3390/pharmaceutics14071479 PMid:35890371 PMCid:PMC9323903

19. Barwal I, Kumar R, Dada T, Yadav SC. Effect of Ultra-Small Chitosan Nanoparticles Doped with Brimonidine on the Ultra-Structure of the Trabecular Meshwork of Glaucoma Patients. Microscopy and Microanalysis. 2019 Dec 1;25(6):1352-66. https://doi.org/10.1017/S1431927619000448 PMid:31018876

20. Wu Q, Liu D, Zhang X, Wang D, DongYe M, Chen W, et al. Development and effects of tacrolimus-loaded nanoparticles on the inhibition of corneal allograft rejection. Drug Deliv. 2019 Jan 1;26(1):290-9. https://doi.org/10.1080/10717544.2019.1582728 PMid:30895841 PMCid:PMC6442111

21. Kari OK, Tavakoli S, Parkkila P, Baan S, Savolainen R, Ruoslahti T, et al. Light-activated liposomes coated with hyaluronic acid as a potential drug delivery system. Pharmaceutics. 2020 Aug 1;12(8):1-24. https://doi.org/10.3390/pharmaceutics12080763 PMid:32806740 PMCid:PMC7465487

22. Zhang P, Zhang Y, Liu CG. Polymeric nanoparticles based on carboxymethyl chitosan in combination with painless microneedle therapy systems for enhancing transdermal insulin delivery. RSC Adv. 2020 Jun 25;10(41):24319-29. https://doi.org/10.1039/D0RA04460A PMid:35516174 PMCid:PMC9055120

23. Carpa R, Remizovschi A, Culda CA, Butiuc-Keul AL. Inherent and Composite Hydrogels as Promising Materials to Limit Antimicrobial Resistance. Vol. 8, Gels. MDPI; 2022. https://doi.org/10.3390/gels8020070 PMid:35200452 PMCid:PMC8870943

24. Cristea AG, Lisă EL, Iacob S, Dragostin I, Ştefan CS, Fulga I, et al. Antimicrobial Smart Dressings for Combating Antibiotic Resistance in Wound Care. Vol. 18, Pharmaceuticals. Multidisciplinary Digital Publishing Institute (MDPI); 2025. https://doi.org/10.3390/ph18060825 PMid:40573221 PMCid:PMC12196261