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REVIEW article

Natural biodegradable materials for advanced pharmaceutical drug delivery systems: A comprehensive review

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Abstract: Natural biodegradable materials are gaining momentum as effective drug delivery systems owing to their eco-friendly nature, natural degradability, and good interaction with the body. These materials, derived from marine life, plants, and animals, include starch, cellulose, pectin, chitosan, alginate, gelatin, and collagen. They provide flexible platforms for the evolution of novel drug delivery systems. Recent technological advances with hydrogels, microspheres, phytosomes, lipid-based systems, and nanoparticles have greatly improved drug solubility, stability, bioavailability, and targeted distribution. In addition, recent formulation technologies such as coacervation, spray drying, freeze drying, nanoencapsulation, and supercritical fluid technology have been applied to improve the efficacy and performance of these systems. Natural polymers enable controlled and targeted drug delivery through mucoadhesion, ligand-receptor interaction, and stimuli-responsive targeting. That said, there are still issues to address, such as unpredictability, instability, and scalability. And looking ahead, there is hope for progress in nanotechnology, artificial intelligence, and personalised treatments. The development of new drug delivery systems using natural biodegradable materials, in general, is a logical and successful strategy.

Introduction

The development of drug delivery systems has significantly improved treatment outcomes by increasing the bioavailability, stability, and targeting efficacy of the drugs. These systems aim to reduce the side effects, to maintain the drug level in the body, and to release the medications in a controlled manner. Existing drug delivery strategies such as hydrogels, liposomes, microspheres, and nanoparticles allow for targeted treatment and long-lived therapeutic effects. Natural biodegradable materials have received attention because they interact well with biological systems and can degrade into non-toxic byproducts. These materials are good for short-term and long-term therapeutic applications, since they reduce the risk of long-term accumulation and toxicity [1]. Moreover, they can degrade naturally by diffusion, swelling, and enzymatic degradation, allowing a controlled release of the drug.

Natural polymers from plants such as cellulose, starch, and pectin, marine sources such as alginate and chitosan, and animal products such as gelatin and collagen provide a versatile and environmentally friendly approach to drug delivery. These polymers have special properties that can be tailored to specific requirements of drug delivery, such as mucoadhesion, biocompatibility, and the ability to form gels and films. These

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materials are particularly useful for natural bioactive compounds that suffer from low solubility, rapid metabolism, and poor absorption, thereby overcoming the limitations of traditional dosage forms. Novel formulations can preserve the stability of these compounds, increase their ability to cross biological barriers, and allow targeted delivery to specific cells or tissues [2].

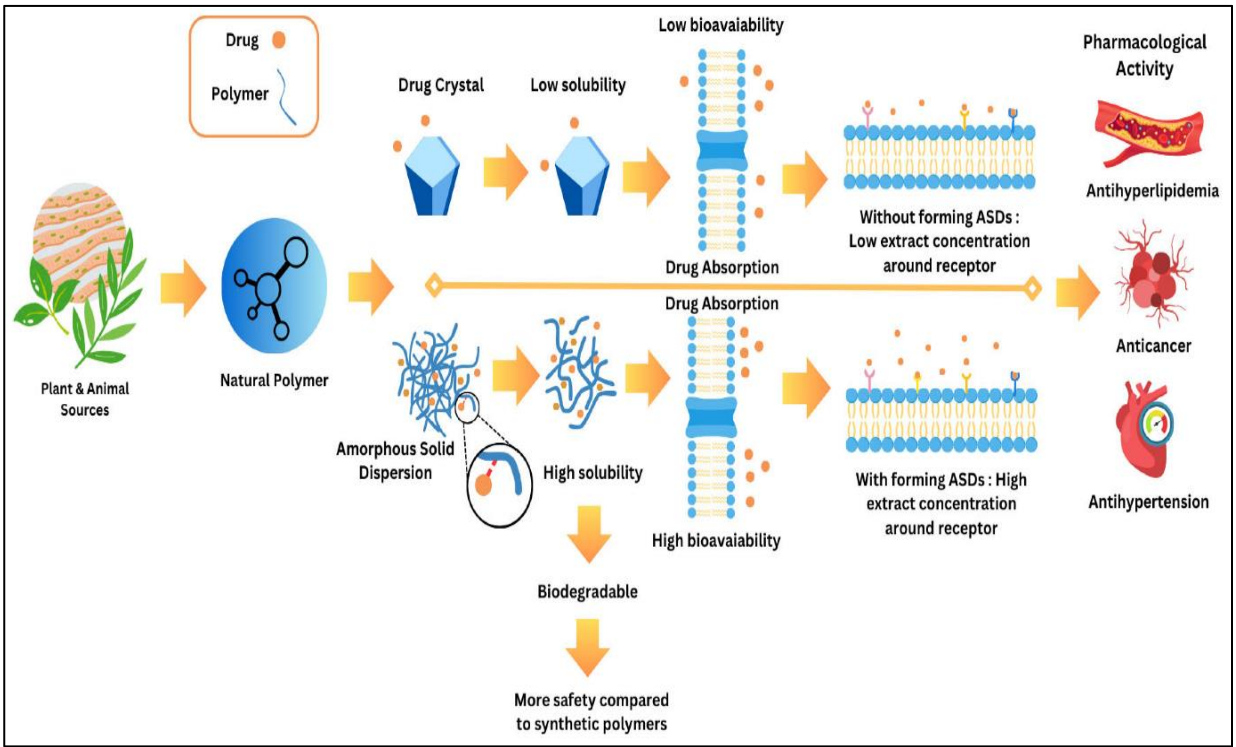

Figure 1: The advancement of advanced drug delivery systems

Natural biodegradable sources: Natural biodegradable sources refer to materials that are derived from biological sources and can decompose naturally into innocuous byproducts through physiological or environmental processes. These sources include polymers such as cellulose, starch, chitosan, alginate, gelatin, and collagen, which are mainly obtained from plants, animals, and marine creatures. Due to their natural biocompatibility, low toxicity, and eco-friendliness, they are often used in pharmaceutical and biological applications. Natural biodegradable materials are suitable carriers in drug delivery systems because they can encapsulate therapeutic compounds, protecting them from deterioration, and can also release them in a controlled and targeted fashion. Their renewable availability and ability to mimic biological habitats render them ideal for the development of advanced, sustainable, and patient-friendly formulations for drug delivery [3].

Plant-based polymers

Starch is a naturally occurring, renewable carbohydrate found in plants such as corn, potatoes, wheat, and rice, and is composed mainly of amylose and amylopectin. It is one of the most commonly used natural polymers in the field of pharmaceutical sciences because of its abundance, low cost, and easy availability. Starch is very biodegradable and biocompatible because it is readily broken down by enzymes to simple sugars like glucose, which can be easily metabolised by the body. These properties make it less likely to be toxic or build up, making it ideal for applications of delivery of medication. Starch is used for many different purposes in pharmaceutical formulations because of its diverse physicochemical properties. It is a binder that allows particle attachment during compression to make tablets cohesive. It acts as a disintegrant and helps tablets to dissolve and absorb drugs faster upon coming into contact with biological fluids. Moreover, starch serves as a matrix-forming component in controlled-release systems to regulate the rate of drug release by progressive polymer erosion, gel formation, and swelling.

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Cellulose and derivatives: Cellulose is the most abundant natural polymer in plant cell walls and is widely used in pharmaceutical applications due to its excellent durability, biocompatibility, and flexibility. Structurally, cellulose is a linear polysaccharide of β-(1→4)-linked glucose units that form a rigid, highly crystalline structure through strong hydrogen bonding. Its structural integrity gives it mechanical strength and resistance to degradation, making cellulose a reliable excipient in several drug delivery systems. Native cellulose is generally not soluble in water, and this limits its direct application. Often, chemical modification is used to improve the utility of native cellulose.

Examples of chemically modified cellulose derivatives that exhibit improved solubility, swelling behaviour, and processability are hydroxypropyl methylcellulose (HPMC), carboxymethyl cellulose (CMC), ethyl cellulose (EC), and microcrystalline cellulose (MCC). Due to their unique physicochemical properties, these compounds are well-suited for medicinal formulations. For example, HPMC is frequently used as a hydrophilic matrix former in sustained-release formulations where it hydrates to form a gel layer that controls the release of the drug. CMC is commonly used as a thickening, stabilising, and suspending agent in liquid formulations due to its high viscosity and water solubility. Cellulose derivatives are the key to controlled and sustained release of a drug in advanced drug delivery systems. They regulate the drug release rate by creating matrices, coatings, or barrier layers to alter the diffusion and erosion processes. Cellulose derivatives are used in film coating applications to provide protective coatings around tablets, providing stability, masking flavour, and allowing modified release profiles. They also improve the stability and uniformity of suspensions, emulsions, and gels by increasing viscosity.

Pectin is a naturally occurring polysaccharide obtained from plants, primarily from apple pomace and citrus fruits. It is well known for its outstanding gel-forming properties and biodegradability. It is mainly composed of galacturonic acid units, which may be partly esterified, influencing its solubility and gelling properties. Pectin is classified as high- and low-methoxyl pectin according to the degree of esterification, and they have different gelation mechanisms. This flexible excipient can be tailored for various pharmaceutical applications. Pectin is one of the most valued biopolymers in drug delivery systems as it is biocompatible and non-toxic and can form hydrogels, films, and matrix systems. It is one of the main advantages of its use in colon-targeted drug delivery. Pectin is relatively stable in the acidic environment of the stomach and the enzymatic environment of the small intestine. In the colon, pectin is degraded by pectinolytic enzymes produced by the colonic microbiota. This special property allows for colon-specific drug release and is highly beneficial for the treatment of various conditions such as colorectal cancer, Crohn's disease, and ulcerative colitis. Furthermore, pectin is often used in controlled-release formulations in which it controls the drug release by gel formation, swelling, and slow polymer degradation. It can be blended with other polymers or cross-linking agents such as calcium ions to enhance its mechanical strength and to alter its release profile. Modified pectin derivatives and pectin-based nanoparticles are also investigated to enhance the efficacy, stability, and targeting capacity of drug encapsulation [4].

Marine-based polymers

Chitosan is a deacetylated derivative of chitin, a naturally occurring, biodegradable polymer that provides structural support to the exoskeletons of crustaceans such as prawns and crabs. This compound's unusual physicochemical and biological properties are due to its chemical composition of β-(1→4)-linked glucosamine units, which contain reactive amino groups. Chitosan is a natural source, biocompatible with excellent low toxicity and biodegradability, which is broken down by enzymes into non-toxic oligosaccharides that the body can readily excrete. One of the most important properties of chitosan is its strong mucoadhesive ability to bind to mucosal surfaces, such as the gastrointestinal tract, nasal cavity, buccal cavity, and ocular mucosa. This adhesion enhances the bioavailability of drugs by increasing the contact time of the drug formulations at the absorption site. Moreover, chitosan has a special property to transiently open tight junctions between epithelial cells, and this property helps in enhancing drug permeation across biological membranes. Its properties make

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it particularly useful for delivering drugs that are poorly absorbed – peptides, proteins and nucleic acids. Chitosan is extensively used in making hydrogels, films, microspheres, and nanoparticles in advanced drug delivery systems. Chitosan-based nanoparticles are of special importance since they can encapsulate pharmaceuticals, protect from enzymatic degradation, and provide controlled and prolonged release. Due to its cationic nature, it is also a useful carrier in gene delivery systems, allowing electrostatic interaction with negatively charged molecules such as DNA and RNA. Chitosan can also be chemically modified to improve its targeting, stability, and solubility. Derivatives such as trimethyl chitosan and carboxymethyl chitosan have improved water solubility and functionality

Alginate is a naturally occurring anionic polysaccharide, which is composed of linear chains of β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues, and is mainly extracted from brown seaweed. The ratio and arrangement of these M and G blocks determine the physicochemical properties of XG, especially its gel strength and stability. Alginate has great value in pharmaceutical and biomedical applications due to its excellent biocompatibility, non-toxicity, biodegradability, and mild gelation conditions. This allows it to encapsulate a range of therapeutic compounds without loss of efficacy. One of the most remarkable characteristics of alginate is its ability to form ionotropic gels in the presence of divalent cations such as calcium ions. In this process, calcium ions cross-link the guluronic acid blocks to form a three-dimensional hydrogel network, which is often represented by the "egg-box" concept. Alginate has the gel-forming ability to encapsulate drugs, proteins, peptides, and even live cells effectively and protect them from degradation by the environment, and also allows for controlled release. Hydrogels, beads, and microspheres based on alginate are often used in drug delivery systems for controlled and sustained drug release. The release profile can be tuned by changing variables such as polymer concentration, cross-linking density, and particle size. Alginate is particularly used in the oral delivery of drugs because it can protect the drugs from the acidic environment of the stomach and release them in the more neutral pH of the intestine. Its mild gelling process can also be used to deliver delicate biomolecules such as proteins and vaccinations. Alginate is widely used in the treatment of wounds due to its ability to absorb water and to maintain a moist environment that favours tissue regeneration and accelerates the healing process. Alginate hydrogels also act as scaffolds in tissue engineering to promote cell growth, proliferation, and differentiation [5].

Animal-based polymers

Gelatin is mainly extracted from animal connective tissues such as skin, bones, and tendons, and can be hydrolysed to some extent to produce gelatin, an inherently occurring biodegradable protein. This unique combination of peptides and proteins rich in amino acids such as glycine, proline, and hydroxyproline gives rise to its unique physicochemical properties. Gelatin is widely used in pharmaceutical and biological applications because of its excellent biocompatibility, low immunogenicity, non-toxicity, and availability. It is very versatile in nature for formulation development as it dissolves in warm water and forms gels on cooling. One of the main properties of gelatin is its capacity to form gels, which allows the development of flexible and stable matrices suitable for drug encapsulation. It can form films, hydrogels, microspheres, and nanoparticles and can be used in a wide variety of drug delivery methods. Gelatin is widely used in capsule formulation to prepare soft and hard capsules. It provides a patient-friendly and effective dose form that masks bad taste and ensures accurate dosage. Gelatin is widely used in the preparation of nanoparticles and microspheres as a carrier for controlled and sustained drug release in improved drug delivery. This is very useful for delivering sensitive biomolecules such as proteins, peptides, and vaccines since gelatin forms a protective environment that maintains their biological activity. Moreover, gelatin is highly biodegradable due to the enzymatic degradation into harmless amino acids that can be easily taken up and/or metabolised by the body. Its surface characteristics may also be modified or cross-linked with agents such as glutaraldehyde to increase mechanical strength and control the rate of drug release. Moreover, the combination of gelatin with other polymers can improve its stability and usefulness in complex drug delivery systems.

Collagen is a significant structural protein that is widely distributed in connective tissues, including skin, tendons, bones, and cartilage, and is essential for preserving the body's strength and structural integrity. Its exceptional tensile strength and stability are attributed to its triple-helix structure, which is made up of three polypeptide chains that are rich in amino acids like glycine, proline, and hydroxyproline. Collagen's natural origin makes it extremely appropriate for a variety of pharmaceutical and biological uses due to its exceptional biocompatibility, biodegradability, and low immunogenicity. Collagen's capacity to promote cell adhesion, proliferation, and differentiation, closely resembling the extracellular matrix (ECM) seen in nature, is one of its most important characteristics. Because of this, it is the perfect material for tissue engineering, which uses it to create scaffolds that promote tissue regeneration and repair. Collagen scaffolds help mend injured tissues, including skin, bone, and cartilage, by creating an environment that is conducive to cell development. Collagen can form a variety of forms, including gels, films, sponges, and nanoparticles, making it an efficient carrier in drug delivery systems. These forms facilitate regulated and prolonged drug release as well as the encapsulation of medicinal substances. Collagen-based delivery systems are very helpful for focused and localised medication distribution, which lowers systemic adverse effects and enhances therapeutic results. Collagen can also preserve the biological action of delicate medications, such as growth hormones and proteins, by preventing their breakdown. Because it can be broken down by enzymes like collagenases into non-toxic peptides and amino acids that the body can naturally metabolise, collagen is also biodegradable. Cross-linking procedures improve its mechanical strength and stability while controlling the rate of degradation. Collagen can also be mixed with other synthetic or natural polymers to enhance its functional qualities and increase its use in cutting-edge medication delivery systems [6].

Properties of natural biodegradable materials

Biocompatibility is the ability of a material to cause an appropriate host response in a particular situation. This implies that the material can interact with the biological system without eliciting any adverse response such as inflammation, immunological response, or toxicity. Natural biodegradable materials easily integrate with tissues and cells, as they mimic parts of the human body. This feature is very important for medication delivery systems because it protects patients and increases the efficacy of the therapeutic agent without causing undesirable biological reactions.

Biodegradability is the ability of a substance to break down into simpler, harmless molecules, either by the activity of enzymes or by hydrolysis. Natural polymers degrade into metabolites that are readily cleared from the body, reducing the chances of accumulation and long-term toxicity. This feature is especially important for controlled drug delivery systems since it allows for long-term drug release and does not require the delivery device to be surgically removed after treatment.

Non-toxicity ensures that the substance and the byproducts of its breakdown will not have detrimental effects on the body. Natural biodegradable materials are generally accepted as safe because of their origin and compatibility with physiological systems. Therefore, they are ideal for frequent or prolonged usage in drug administration, as they reduce the possibility of cytotoxicity, organ damage, or other unfavourable side effects associated with synthetic materials.

Mucoadhesiveness: The potential of a substance to stick to mucosal surfaces, such as those in the buccal area, nasal cavity, or gastrointestinal system, is known as mucoadhesiveness. This characteristic increases the drug delivery system's residence duration at the absorption site, improving the medication's bioavailability. Strong mucoadhesive qualities seen in natural polymers like pectin and chitosan aid in focused and localised medication administration, lowering drug loss and boosting therapeutic effectiveness.

Ability to form gels, films, and matrices: The excellent physicochemical characteristics of natural biodegradable materials allow them to form gels, films, and matrix systems. When creating hydrogels, transdermal patches, and controlled-release tablets, among other drug delivery methods, certain structural shapes are essential. Drugs may be encapsulated thanks to the gel-forming ability, and films and matrices control the rate of drug release and offer structural stability. Because of their adaptability, they can be used for a variety of therapeutic purposes and methods of administration [7].

Advanced pharmaceutical drug delivery systems: Advanced pharmaceutical drug delivery systems are modern formulation techniques to deliver therapeutic agents in a precise, regulated, and targeted manner for the best possible therapeutic results. Unlike the traditional dose forms, these systems are focused on improving the medication stability, bioavailability, and site-specific activity with minimal adverse effects. To control the rate and site of drug release, they use state-of-the-art technologies such as hydrogels, liposomes, microspheres, nanoparticles, and stimuli-responsive devices. The need for advanced drug delivery systems arises from the need to increase the solubility of drugs, protect sensitive drugs from degradation, and allow continuous or targeted delivery to improve treatment efficacy, patient compliance, and overall healthcare [8].

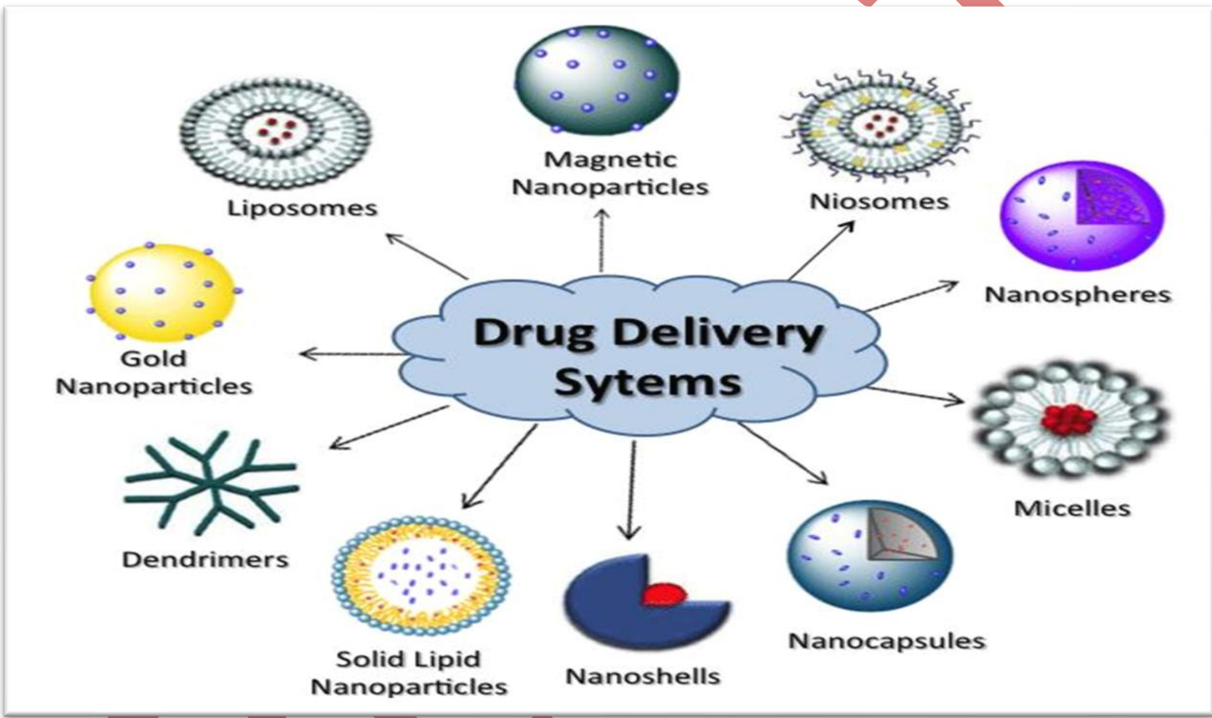

Figure 2: Advanced pharmaceutical drug delivery systems

Nanoparticle-based systems

Nanoparticles of natural polymers have been a very successful strategy for drug delivery systems in advanced pharmaceutics. In such systems, drugs are prepared in the form of nanosized carriers, which greatly improve the solubility of medication, especially for molecules that are weakly soluble in water. The protective matrix is made up of natural polymers such as chitosan, alginate, and gelatin, which protect the medicine from chemical and enzymatic destruction, thereby increasing the drug's stability and bioavailability. Moreover, these nanoparticles regulate the diffusion and degradation processes, enabling a controlled and sustained release of drugs, thereby maintaining a consistent therapeutic effect over time. They are small in size and can penetrate tissues and cells more easily. This makes them applicable for use in targeted drug delivery.

Hydrogels are three-dimensional networked hydrophilic polymers capable of absorbing and retaining high amounts of water without losing their structural integrity. Natural biodegradable polymers such as alginate, gelatin, and pectin are often used to prepare hydrogels due to their biocompatibility and gel-forming ability. These systems are frequently employed in controlled drug delivery, regulating the release of drugs and offering prolonged therapeutic effects. Hydrogels are also commonly used in tissue engineering as scaffolds for cell growth and repair, and in wound healing to maintain a moist environment that promotes tissue regeneration.

Lipid-based systems: Natural biodegradable lipids are used in lipid-based drug delivery systems to improve the stability and solubility of medicines. These systems, which provide distinct benefits in drug encapsulation and delivery, include liposomes, solid lipid nanoparticles, and nanostructured lipid carriers. They work especially well at preventing the breakdown of delicate substances and increasing the bioavailability of poorly soluble medications. Lipid-based carriers are useful in oral and parenteral drug delivery applications because they enable targeted and controlled medication release.

Microspheres and microcapsules: To encapsulate medications in a polymeric matrix or shell, microspheres and microcapsules are spherical particles made from natural polymers like chitosan, gelatin, and starch. These methods, which enable the medicine to be given gradually over a long period of time, are frequently utilised for sustained drug release. By guiding the medication to particular tissues or organs, they also make tailored administration possible, increasing therapeutic efficacy. Additionally, these systems can lower the frequency of doses and improve patient compliance by preserving steady medication levels in the body.

Phytosomes technology

To improve the absorption and bioavailability of natural bioactive substances, especially those produced from plants, phospholipids are complexed with them using phytosome technology. The medicinal potential of several phytoconstituents is hampered by their poor solubility and low permeability. These substances increase systemic availability, stability, and membrane permeability by generating phytosomes. This cutting-edge delivery method, which is frequently utilised in the creation of herbal and nutraceutical items, greatly boosts therapeutic efficacy [9, 10].

Advanced formulation technologies: Innovative methods and approaches utilised in pharmaceutical development to improve the efficacy, stability, and delivery of medicinal substances are referred to as advanced formulation technologies. By combining techniques like nanotechnology, lipid-based carriers, polymeric systems, and stimuli-responsive formulations, these technologies go beyond traditional methodologies to deliver precise and controlled drug release. They help enhance the targeting, bioavailability, and solubility of medications, particularly those with poor pharmacokinetic characteristics. Advanced formulation technologies are essential to the creation of more efficient, secure, and patient-friendly drug delivery systems because they enable site-specific distribution and minimise adverse effects [11].

Nanoencapsulation: A sophisticated formulation method called nanoencapsulation involves encasing medications in nanoscale carriers such as polymeric nanoparticles, liposomes, or nanospheres. By shielding medications from environmental deteriorators, including light, heat, and enzymatic activity, this method greatly improves their durability. Additionally, expanding their surface area and promoting greater absorption enhances bioavailability, especially for poorly soluble medications. Furthermore, regulated and prolonged medication release is made possible by nanoencapsulation, guaranteeing a steady therapeutic impact over time while reducing adverse effects [12].

Spray drying: In pharmaceutical formulation, spray drying is a common method for turning liquid medication solutions or suspensions into stable, dry powders. In this procedure, uniform and tiny particles are formed by quick drying with hot air. Because spray drying gives exact control over particle size and morphology, it is very useful for creating controlled-release formulations. Additionally, it makes medications more stable and manageable, which facilitates their storage, transportation, and incorporation into other dosage forms.

Freeze-drying (Lyophilisation) is another name for freeze-drying, a dehydration method used to preserve unstable and heat-sensitive bioactive substances. This method allows the frozen solvent to sublimate straight from solid to vapour by first freezing the product and then subjecting it to a vacuum. This technique aids in preserving the biological activity and structural integrity of medications, especially proteins, peptides, and natural extracts. Additionally, it greatly increases the stability and shelf life of medicinal formulations, enabling long-term preservation.

Coacervation: A polymer-rich coating is created around drug particles by the phase separation process of coacervation, which leads to the creation of microcapsules. A dense coacervate phase and a dilute equilibrium phase are the two separate liquid phases that result from the separation of a colloidal solution. This method is frequently used to microencapsulate medications, allowing for better drug stability, controlled release, and preservation of delicate chemicals. In coacervation procedures, natural polymers like gelatin and gum arabic are frequently utilised.

Supercritical fluid technology: Supercritical fluids, most frequently carbon dioxide, are used as a solvent or processing medium in supercritical fluid technology, an innovative and eco-friendly formulation technique. Highly pure, solvent-free medication particles with regulated size and shape may be produced with this method. It is especially helpful for improving the bioavailability and solubility of medications that are poorly soluble in water. Supercritical fluid technology also provides benefits, including better product quality, tighter control over formulation features, and less usage of hazardous organic solvents [13].

Evaluation of natural biodegradable materials

Determining the performance, safety, and applicability of natural biodegradable materials for therapeutic uses in advanced pharmaceutical drug delivery systems is a crucial first step. These materials, which come from marine, animal, and plant sources, have important benefits including eco-friendliness, biocompatibility, and biodegradability. Nevertheless, careful evaluation using a variety of physicochemical, biological, and pharmacological characteristics is necessary for their effective use.

***Physicochemical characterization**:* To comprehend the structural and functional characteristics of natural biodegradable materials, physicochemical examination is essential. Particle size, shape, surface morphology, porosity, swelling index, viscosity, and mechanical strength are among the parameters that are closely examined. Drug loading, release behaviour, and interaction with biological systems are all directly impacted by these features. The formulation is characterised using sophisticated analytical methods such as differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), dynamic light scattering (DLS), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). The drug delivery system's scalability and repeatability are guaranteed by consistency in these characteristics [14].

Drug loading capacity and encapsulation efficiency: Important measures of the carrier system's efficacy are drug loading capacity and encapsulation efficiency. Functional groups found in natural polymers, including chitosan, alginate, gelatin, and starch, enable effective encapsulation by fostering strong connections with drug molecules. A high encapsulation efficiency guarantees an appropriate therapeutic dosage and reduces medication waste. These factors are greatly influenced by the preparation technique, polymer concentration, and drug-polymer physicochemical compatibility.

In vitro drug release kinetics: The release profile and mechanism of drug liberation from the delivery device are assessed using in vitro drug release experiments. Diffusion, polymer swelling, erosion, and enzymatic degradation are some of the ways by which natural biodegradable materials provide regulated and continuous medication release. Release kinetics are frequently analysed using mathematical models such as the zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. For formulation design optimisation and in vivo performance prediction, these investigations are crucial.

Biocompatibility and cytotoxicity assessment: One of the most important criteria for natural biodegradable materials is biocompatibility. To make sure they don't cause toxicity, inflammation, or immunological responses, these materials' interactions with biological tissues are assessed. Cell lines are used in cytotoxicity studies to evaluate the material's effects on cell viability and proliferation. Common assays include haemolysis tests, MTT, and live/dead staining.

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***Biodegradation and bioresorption studies**:* Studies on biodegradation evaluate how materials break down in physiological settings. Natural polymers break down into readily excretable, non-toxic metabolites by hydrolytic or enzymatic processes. To preserve therapeutic efficacy, the degradation rate must be in line with the drug release profile. Materials with controlled degradation are perfect for long-term use because they avoid buildup in the body and premature drug release.

***Stability studies**:* To ascertain the formulation's shelf life and storage conditions, stability assessment is crucial. Environmental elements, including temperature, humidity, light, and microbial contamination, may have an impact on natural biodegradable materials. Stability tests are carried out in real-time and under expedited settings to track changes in drug content, release profile, and physical appearance [15].

Targeting efficiency and drug bioavailability: Enhancing targeting efficiency is one of the main benefits of improved medication delivery systems. Through surface modification, ligand attachment, or stimuli-responsive behaviour, natural biodegradable carriers can be designed for site-specific delivery. This reduces systemic exposure and adverse effects while increasing medication accumulation at the intended spot. Studies on bioavailability assess the degree and pace of medication absorption, which is frequently greatly increased by better solubility, resistance to degradation, and extended residence time.

In vivo pharmacokinetic and pharmacodynamic evaluation

Comprehensive insights into the behaviour of the drug delivery system within a living creature are provided by in vivo investigations. To comprehend drug disposition, pharmacokinetic characteristics, including absorption, distribution, metabolism, and excretion (ADME), are assessed. Pharmacodynamic studies evaluate the formulation's effectiveness and therapeutic impact.

Immunogenicity and safety profiling

Natural materials are typically harmless; however, depending on their source and purity, some may cause immunological reactions. To assess possible allergic or immunological responses, immunogenicity testing is carried out. Acute and chronic toxicity tests are part of the safety profile, which guarantees that the substance and its breakdown products are safe to use for extended periods of time.

Targeted drug delivery

A major development in pharmaceutics is targeted drug delivery, which uses natural biodegradable systems to deliver therapeutic compounds precisely to the site of action while reducing systemic exposure and adverse consequences. Because of their biocompatibility, biodegradability, and capacity to interact with biological tissues, natural polymers (chitosan, alginate, gelatin, and pectin) are essential in the design of these systems.

Mucoadhesion

The capacity of a drug delivery system to stick to mucosal surfaces, such as those in the buccal area, nasal cavity, gastrointestinal tract, and ocular tissues, is known as mucoadhesion. Chitosan, pectin, and alginate are examples of naturally occurring biodegradable polymers having functional groups that interact strongly with mucin. This adhesion increases medication uptake and bioavailability by extending the drug's residence time at the absorption site. It is also particularly effective for localised and long-term medication administration because it reduces drug loss via physiological clearance [16-18].

Ligand-receptor interactions

Drug carriers are functionalised with ligands, such as antibodies, peptides, or sugars, that may bind specifically to receptors on target cells in a highly precise targeting mechanism known as ligand-receptor interaction. These ligands can be readily incorporated into natural biodegradable materials. The mechanism is internalised inside the cell after binding, guaranteeing accurate medication delivery. This approach is very useful for treating cancer and other illnesses that call for specific cellular uptake.

Site-specific release

Drugs are delivered at a specific site in the body by site-specific release, which reacts to physiological factors like temperature, pH, or enzymes. Because of microbial enzyme activity, natural polymers like alginate and pectin can withstand breakdown in the upper gastrointestinal tract and release medications in the colon. This improves treatment results and minimises systemic adverse effects by guaranteeing that the medication is delivered precisely where it is required.

pH-responsive targeting

Drug delivery systems are made to release medications in reaction to variations in the body's pH levels using a sophisticated method called pH-responsive targeting. The pH conditions of many bodily parts, including the stomach, intestine, and tumour tissues, are different. It is possible to modify natural biodegradable polymers such that they release medications at one pH while remaining stable at another. To improve targeted delivery and therapeutic accuracy, for instance, drug carriers can stay intact in the acidic stomach but release their contents in the more neutral or slightly alkaline intestine or in the acidic milieu of tumours.

Enzyme-responsive targeting

Drug release is triggered via enzyme-responsive targeting, which makes use of the presence of particular enzymes in particular tissues or medical situations. Because they may be broken down by bodily enzymes, natural biodegradable materials are especially well-suited for this method. For example, colonic bacteria break down polymers like pectin, allowing for colon-specific medication delivery. In a similar vein, certain enzymes that are overexpressed in sick tissues can cause the carrier system to break down, guaranteeing that the medication is only delivered at the intended location. This tactic reduces off-target effects and improves specificity [19].

Applications of natural biodegradable materials in advanced drug delivery systems

Due to their safety, adaptability, and capacity to improve therapeutic efficacy, natural biodegradable materials have found extensive use in modern pharmaceutics. Their distinct physicochemical and biological characteristics make them appropriate for a range of delivery methods and medical situations.

Cancer therapy: Natural polymer-based nanoparticles, such as those derived from chitosan, alginate, and gelatin, are essential for cancer treatment because they allow anticancer medications to be delivered precisely. Through passive and active targeting methods, these systems minimise exposure to healthy tissues while improving drug accumulation at tumour locations. Chemotherapy-related adverse effects and systemic toxicity are greatly decreased by this focused strategy. Furthermore, these carriers can deliver prolonged and regulated medication release, which enhances therapeutic efficacy and patient outcomes.

Oral drug delivery: Oral drug delivery methods frequently employ natural polymers to increase the bioavailability of unstable or poorly soluble medications. Drugs can be better absorbed in the gut and shielded from deterioration in the hostile stomach environment by substances like starch, pectin, and chitosan. These polymers can also be employed to create colon-targeted and controlled-release systems, which guarantee the best possible medication release at particular gastrointestinal tract locations [20].

Transdermal delivery: Natural biodegradable polymers are utilised in transdermal drug delivery to enhance drug penetration through the skin and provide prolonged release. Films and patches that stick to the skin and control medication diffusion can be created using polymers like chitosan and cellulose derivatives. This approach enhances patient compliance, avoids first-pass metabolism, and offers a non-invasive way to continuously provide medication.

***Gene delivery**:* Natural polymers are being investigated extensively as non-viral gene delivery vectors, especially chitosan. Because of their cationic nature, they can interact with negatively charged DNA or RNA

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to form complexes that shield genetic material from degradation and promote cellular uptake. These systems have potential for gene therapy and the treatment of genetic disorders because they provide a safer substitute for viral vectors with lower immunogenicity and toxicity [21].

Ocular drug delivery: To increase medication retention in the eye, natural polymers are utilised in ocular formulations, such as gels, inserts, and nanoparticles. Conventional eye drops are not effective because of the quick turnover and outflow of tears. Chitosan and alginate are mucoadhesive polymers that extend the duration of drug residence, improving absorption and therapeutic impact while lowering dosage frequency [22].

Nasal drug delivery: Natural biodegradable polymer-based nasal medication delivery devices provide a quick and non-invasive method of delivering drugs locally and systemically. For the delivery of proteins, peptides, and vaccinations, these methods are very helpful. Mucoadhesive polymers are appropriate for targeted brain administration via the nose-to-brain route because they promote absorption through the nasal mucosa and increase drug retention in the nasal cavity [23].

Tissue engineering and regenerative medicine: Collagen, gelatin, and alginate are examples of naturally occurring biodegradable materials that are widely utilised in tissue engineering as scaffolds to promote cell growth, proliferation, and differentiation. These substances encourage tissue regeneration by imitating the extracellular matrix seen in nature. Additionally, they can be used with medications or growth hormones to speed up the healing and restoration of injured tissues [24].

Advantages of natural biodegradable materials in advanced drug delivery systems

Safe and biodegradable: Since natural biodegradable materials come from biological origins and the body can readily break them down into non-toxic byproducts, they are naturally harmless. The natural metabolization or excretion of their breakdown products, such as carbohydrates, amino acids, or simple chemical molecules, lowers the possibility of buildup and long-term toxicity. For short-term and long-term therapeutic purposes, this makes them ideal.

Environmentally friendly: These materials are sustainable and environmentally benign since they come from renewable resources, including plants, animals, and marine life. Natural biodegradable materials break down organically without polluting the environment, in contrast to manufactured polymers. Their application lessens the environmental impact of pharmaceutical production and waste management while promoting green chemistry concepts.

Improved patient compliance: By permitting regulated and prolonged medication release, which lowers the frequency of dosing, natural biodegradable solutions promote patient compliance. Convenient and non-invasive treatment alternatives are also provided by their compatibility with a variety of delivery methods, including oral, transdermal, and injectable. This improves patient comfort and therapeutic compliance.

Controlled and targeted drug delivery: These materials' capacity to deliver regulated and site-specific medication release is one of their main benefits. To guarantee that the medication is given at the intended site and pace, they might be designed to react to physiological factors like pH, enzymes, or temperature. While reducing adverse effects, this focused administration increases treatment effectiveness.

Excellent biocompatibility: Natural biodegradable materials can interact with tissues without triggering negative immune reactions since they closely mimic biological elements of the human body. They are perfect for delicate applications like tissue engineering and implanted drug delivery systems because of their great biocompatibility, which lowers the possibility of inflammation, irritation, or rejection.

Versatility and functional diversity: These materials may be utilised in a variety of forms, including hydrogels, films, microspheres, scaffolds, and nanoparticles, due to their diverse physicochemical characteristics. Their adaptability makes it possible to create specialised drug delivery systems that are suited to certain treatment requirements and administration methods.

Enhanced drug stability: Natural polymers can shield medications against environmental deterioration brought on by elements like light, heat, and enzymes, especially delicate bioactive substances like proteins, peptides, and herbal extracts. The stability and shelf life of medicinal formulations are improved by this protective action.

Cost-effectiveness and availability: Compared to synthetic polymers, natural biodegradable materials are typically more readily available and reasonably priced. They are economically feasible for large-scale manufacturing, especially in developing nations, because of their widespread availability from renewable sources.

***Ease of modification**:* To enhance their solubility, mechanical strength, and drug release behaviour, these materials can be chemically or physically altered. Researchers can create sophisticated, highly effective medication delivery systems with improved efficacy because of this flexibility [25].

Complications of natural biodegradable materials in advanced drug delivery systems

Natural biodegradable materials have many benefits, but they also have several drawbacks and difficulties that may restrict their effectiveness, reliability, and widespread use in cutting-edge pharmaceutical drug delivery systems. To solve these problems, careful thought and optimisation are needed.

***Variability in natural sources**:* Natural materials come from a variety of biological sources, including plants, animals, and marine life. These sources might change based on season, climate, location, and extraction techniques. Drug delivery systems' repeatability and dependability may be impacted by this variability, which can result in variations in composition, molecular weight, and physicochemical characteristics.

***Stability issues**:* Natural biodegradable polymers are frequently susceptible to environmental factors such as light, humidity, temperature, and microbial contamination. Over time, they may deteriorate or alter structurally, which would shorten their shelf life and diminish their medicinal effectiveness. To preserve their integrity, certain storage conditions and stabilisation methods are frequently needed.

Limited mechanical strength: Many natural materials have comparatively lower mechanical strength and structural stability than synthetic polymers. Their capacity to retain integrity throughout processing, storage, or application may be impacted by this restriction, especially in compositions like films, scaffolds, and implants. To increase their strength, they frequently need to be blended or cross-linked with other polymers.

Scale-up difficulties: For natural biodegradable systems, the shift from laboratory-scale preparation to industrial-scale manufacturing might be difficult. Large-scale production may be hampered by raw material variability, intricate extraction procedures, and sensitivity to processing conditions. Scaling up while maintaining consistency, quality, and cost-effectiveness is still quite difficult.

Batch-to-batch inconsistency: Batch-to-batch variation in polymer characteristics can be substantial due to natural variability and variations in extraction and purification procedures. Standardisation is challenging because of this variation, which can impact drug loading, release profiles, and overall formulation effectiveness.

Risk of microbial contamination: Natural polymers are more susceptible to microbial growth because of their organic character and nutrient content. Contamination can jeopardise product safety and stability if sterilisation and preservation are not properly performed. This needs stringent quality control methods in manufacturing and storage.

Limited solubility and processability: Certain natural polymers have restricted processability or low solubility in common solvents, which may limit their use in specific drug delivery systems. To improve their usage, chemical alteration or the application of specialised procedures can be necessary.

Potential Immunogenicity: Certain natural materials, particularly those produced from animal origins, may cause allergic or immunological reactions in some people while being usually biocompatible. Immunogenicity may be increased by impurities or leftover proteins, necessitating careful testing and purification [26, 27].

Future perspectives of natural biodegradable materials in advanced drug delivery systems

Development of smart biodegradable systems: The goal of future research is to create intelligent biodegradable systems that can react to certain physiological stimuli like pH, temperature, enzymes, or magnetic fields. These systems can minimise negative effects and improve therapeutic accuracy by releasing medications in a regulated and on-demand way. Innovative platforms for these kinds of applications include smart hydrogels and responsive nanoparticles.

Integration with nanotechnology and artificial intelligence (AI): It is anticipated that the combination of nanotechnology with natural biodegradable materials would improve therapeutic targeting, stability, and bioavailability. Furthermore, the development of sophisticated drug delivery systems can be accelerated by using AI in formulation design and optimisation. AI can enhance overall pharmaceutical development efficiency, optimise formulation parameters, and forecast drug-polymer interactions [28].

Personalized drug delivery systems: Natural biodegradable materials are being investigated for customised medication delivery systems that are suited to each patient's needs as precision medicine advances. These systems may be created based on physiological, genetic, and disease-specific variables, guaranteeing the best possible dosage and better therapeutic results while lowering side effects.

Sustainable pharmaceutical development: The increasing need for ecologically friendly pharmaceutical procedures is supported by natural biodegradable materials. Future advancements will concentrate on adopting green synthesis techniques, reducing waste production, and using renewable resources. This strategy supports international initiatives to lessen the impact on the environment and advance environmentally friendly medical treatments.

Advanced targeting strategies: More advanced targeting mechanisms, such as multifunctional carriers that can combine ligand-based targeting with stimuli-responsive release, will be included in future drug delivery systems. Drug delivery accuracy will be enhanced by these devices, especially in complicated conditions like cancer and neurological disorders.

Combination therapy and multi-drug delivery systems: It is anticipated that natural biodegradable carriers will be important in combination treatment, which involves the sequential or simultaneous administration of many medications. This method is very helpful in lowering medication resistance, increasing therapeutic efficacy, and treating chronic and complex disorders.

Development of hybrid and composite materials: To develop hybrid systems with improved mechanical strength, stability, and utility, future research will concentrate on fusing natural biodegradable polymers with synthetic materials or other natural polymers. These composite materials can perform better and overcome the drawbacks of separate parts.

Expansion in gene and protein delivery: It is anticipated that natural biodegradable materials will become more significant in the delivery of proteins, DNA, and vaccinations. Biotechnology developments will make it possible to create safer and more effective non-viral delivery methods, increasing their use in immunotherapy and gene therapy [29, 30].

Methods and materials: An evidence-based study was created by compiling research articles from a variety of offline and online peer-reviewed journals and databases, including PubMed, MedlinePlus, Sodhganga, Google Scholar, and others.

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Conclusion: Natural biodegradable materials play an important role in the improvement of pharmaceutical drug delivery systems by providing safe, long-lasting, and efficient alternatives to manufactured polymers. Their distinct features, including biocompatibility, biodegradability, and adaptability, enable the creation of novel delivery platforms like nanoparticles, hydrogels, and tailored systems that increase medication effectiveness and patient compliance. These materials have shown promising results in a variety of applications, including cancer therapy, wound healing, oral and transdermal distribution, gene transfer, and tissue engineering. However, issues such as unpredictability in natural sources, stability problems, and difficulty in large-scale manufacturing must be handled with caution through technical developments and standardisation. It is anticipated that future advancements in smart delivery systems, integration with cutting-edge technology, and sustainable pharmaceutical practices will improve their efficacy and expand their clinical uses. To sum up, natural biodegradable materials have enormous potential to transform contemporary medication delivery methods and support safer, more efficient, and ecologically friendly medical solutions.

References

1. Sharma S, Sudhakara P, Singh J, Ilyas RA, Asyraf MRM, Razman MR. Critical review of biodegradable and bioactive polymer composites for bone tissue engineering and drug delivery applications. Polymers. 2021; 13(16): 2623. doi: 10.3390/polym13162623
2. Idrees H, Zaidi SZJ, Sabir A, Khan RU, Zhang X, Hassan S-u. A review of biodegradable natural polymer-based nanoparticles for drug delivery applications. Nanomaterials. 2020; 10(10): 1970. doi: 10.3390/nano10101970
3. Geszke-Moritz M, Moritz M. Biodegradable polymeric nanoparticle-based drug delivery systems: comprehensive overview, perspectives and challenges. Polymers. 2024; 16(17): 2536. doi: 10.3390/polym 16172536
4. Sharma A, Babu Sharma R, Verma A, Thakur R. Insight on nanoparticles, green synthesis and applications in drug delivery systems: A comprehensive review. International Journal of Life Science and Pharma Research. 2022; 12(5): P68-P84. doi: 10.22376/ijpbs/lpr.2022.12.5.P68-84
5. Gandhi KJ, Deshmane SV, Biyani KR. Polymers in pharmaceutical drug delivery systems: A review. International Journal of Pharmaceutical Sciences Review and Research. 2012; 14(2): 57-66. doi: Nil.
6. Singh M, Das MK. A comprehensive review on the role of natural polymers in gastro-retentive drug delivery systems (GRDDS). Drug Delivery Letters. 2025; 15(2): 83-94. doi: 10.2174/0122103031301526241010021238
7. Gatenholm P, Kubát J, Mathiasson A. Biodegradable natural composites. I. Processing and properties. Journal of Applied Polymer Science. 1992; 45(9): 1667-1677. doi: 10.1002/APP.1992.070450918
8. Sheraz M, Sun XF, Siddiqui A, Hu S, Song Z. Research advances in natural polymers for environmental remediation. Polymers (Basel). 2025; 17(5): 559. doi: 10.3390/polym17050559
9. Yap KM, Sekar M, Fuloria S, Wu YS, Gan SH, Mat Rani NNI, et al. Drug delivery of natural products through nanocarriers for effective breast cancer therapy: A comprehensive review of the literature. International Journal of Nanomedicine. 2021; 16: 7891-7941. doi: 10.2147/IJN.S328135
10. Anju V, Saumya K, Anjali K, Kumar SP. Revolutionizing herbal medicine delivery through phytosome technology. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2026; 6(2): 17-26. doi: 10.5281/ zenodo.19930875
11. Samir A, Ashour FH, Hakim AAA, Bassyouni M. Recent advances in biodegradable polymers for sustainable applications. Npj Materials Degradation. 2022; 6(68): 1-27. doi: 10.1038/s41529-022-00277-7
12. Bhat R, Bhat SS. Targeted nano-constructs for the treatment of autoimmune diseases: A comprehensive review of advances, mechanisms, and clinical potential. Mediterranean Journal of Medicine and Medical Sciences. 2025; 1(2): 8-16. doi: 10.5281/zenodo.16117843
13. Panchal SS, Vasava DV. Biodegradable polymeric materials: Synthetic approach. ACS Publications, 2020; 5(9): 4370-4379. doi: 10.1021/ACSOMEGA.9B04422
14. Sundarababu J, Anandan S, Griskevicus P. Evaluation of mechanical properties of biodegradable coconut shell/rice husk powder polymer composites for lightweight applications. Materials Today: Proceedings. 2021; 39(P4): 1241-1247. doi: 10.1016/j.matpr.2020.04.095
15. Hazrati KZ, Sapuan SM, Zuhri MYM, Jumaidin R. Extraction and characterization of potential biodegradable materials based on *Dioscorea hispida* Tubers. Polymers (Basel). 2021; 13(4): 584. doi: 10.3390/polym1 3040584
16. Syed SN, Bobade NN, Wankhade VP, Atram SC, Pande SD, Dhore NS, et al. Mucoadhesive buccal films: A patient-centric approach to rapid and efficient drug delivery. Mediterranean Journal of Medical Research. 2026; 3(1): 114-126. doi: 10.5281/zenodo.19126240

17. Dhore NS, Bobade NN, Pande SD, Wankhade VP, Atram SC, Faiza S, et al. Mucoadhesive vaginal tablet: A novel approach for vaginal drug delivery. Mediterranean Journal of Medicine and Medical Sciences. 2026; 2(2): 13-23. doi: 10.5281/zenodo.19543738
18. Mussa FH. Development and evaluation of muco-adhesive buccal films containing metronidazole for the treatment of periodontal diseases. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2025; 5(4): 47-57. doi: 10.5281/zenodo.17554356
19. Santana RF, Bonomo RCF. Thermal analysis for evaluation of biodegradable films: A review. Journal of Thermal Analysis and Calorimetry 2024; 149(14): 7155-7168. doi: 10.1007/S10973-024-13339-6
20. Sayed Patwary MA, Surid SM, Gafur MA. Properties and applications of biodegradable polymers. Journal of Research Updates in Polymer Science. 2020; 9: 32-41. doi: 10.6000/1929-5995.2020.09.03
21. Coelho JF, Ferreira PC, Alves P, Cordeiro R, Fonseca AC, Góis JR, Gil MH. Drug delivery systems: Advanced technologies potentially applicable in personalized treatments. EPMA Journal. 2010; 1(1): 164-209. doi: 10.1007/S13167-010-0001-X
22. Mussa F, Almani F, Treki MS. Mechanism of ibuprofen release from chitosan granules. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2022; 2 (3): 31-38. doi: 10.5281/zenodo.7115168
23. Harun-Or-Rashid M, Aktar MN, Hossain MS, Sarkar N, Islam MR, Arafat ME, et al. Recent advances in micro- and nano-drug delivery systems based on natural and synthetic biomaterials. Polymers (Basel). 2023; 15(23): 4563. doi: 10.3390/polym15234563
24. Guo W, Tao J, Yang C, Song C, Geng W, Li Q, et al. Introduction of environmentally degradable parameters to evaluate the biodegradability of biodegradable polymers. PLOS one. 2012; 7(5): e38341. doi: 10.1371/journal.pone.0038341
25. Demetzos C, Pippa N. Advanced drug delivery nanosystems (aDDnSs): A mini-review. Drug Delivery. 2014; 21(4): 250-257. doi: 10.3109/10717544.2013.844745
26. Sasikumar R, Prabagaran S, Venkatesh R, Kumaravel S. A review of biomaterial degradation assessment approaches employed in the biomedical field. Nature. 2024; 14(18): 22647-22655. doi: 10.1007/S13399-023-04465-6
27. Liechty WB, Kryscio DR, Slaughter BV, Peppas NA. Polymers for drug delivery systems. Annual Review of Chemical and Biomolecular Engineering. 2010; 1: 149-173. doi: 10.1146/annurev-chembioeng-073009-100847
28. Nizamuddin SFS, Ikramuddin M, Dhore NS. Artificial Intelligence in pharmaceutical sciences: Transforming drug discovery, formulation, and manufacturing. Mediterranean Journal of Medical Research. 2025; 2(4): 269-275. doi: 10.5281/zenodo.17945149
29. Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, et al. Advances in drug delivery systems, challenges, and future directions. Heliyon. 2023; 9(6): e17488. doi: 10.1016/j.heliyon.2023.e17488
30. Vroman I, Tighzert L. Biodegradable polymers. Materials (Basel). 2009; 2(2): 307-344. doi: 10.3390/ma2020307

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