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Advancements in Pharmaceutical Dosage Forms: From Traditional Tablets to 3D-Printed Drug **Delivery Systems**

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Abstract: The development of pharmaceutical dosage forms designed according to modern drug delivery technology plays a crucial role in ensuring the precision and safety of drug delivery. This review summarize all aspects of diverse dosage forms, including some, their design, clinical application, and manufacturing process. It covers both classic and novel formulations (Ex- solids, liquids, semi-solids, or even novel systems such as nanoparticles and 3D-printed tablets). The review also discusses issues such as drug stability, patient compliance and regulatory compliance, along with trends in DMF submissions, personalized medicine, AI-informed formulations, and sustainable practices, while accounting for future developments. This paper highlights the crucial contribution of dosage forms toward better therapeutic outcomes and the future of healthcare by integrating advancements from multiple relevant disciplines..

Keywords: solid, liquid, gases, route of administration, dosage form

I. INTRODUCTION

Pharmaceutical dosage forms play a vital role in converting active pharmaceutical ingredients (apis) into safe, efficacious, and patient-friendly drug products. They are designed to maximize drug delivery, providing therapeutic efficacy while minimizing undesirable effects. Factors determining the selection for dosage forms include type of disease, route of administration, properties of the drug, as well as patient requirements. In this paper, we will explore the design and manufacturing of various pharmaceutical dosage forms, providing critical insights into current technologies under development and potential future directions.

Definition:-A dosage form is a manner in which drug molecules are delivered into sites of action within the body so as to achieve perfect desired effects and minimum adverse effect. Excipients combined with Active Pharmaceutical Ingredients (API) make up the dosage forms.

DOSAGE FORM = API + EXCIPIENTS

Active Pharmaceutical Ingredients for chemical substances that are used for diagnosis, treatment, disease prevention -More about development & regulatory approval in future articles. They include inactive substance that help the drug or other active substances.

Such as- preservatives, colouring agents, flavoring agents.

Types of Dosage Forms

1) Solid Dosage Forms:-The most commonly employed dosage forms are solid dosage forms, i.e. Tablets and capsules, owing to their, ease of administration, stability, and suitability for accurate dosing.

Granules and Powders: These are often reconstituted for oral use, such as oral rehydration salts.

Tablets: These include immediate-release (Ex- aspirin for pain relief), sustained-release (Ex- metformin for diabetes), and orally disintegrating tablets (Ex- pediatric allergy medications).

Capsules: Hard gelatin capsules (Ex- amoxicillin) and soft gelatin (Ex-vitamin D supplements) are widely used for their versatility.

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Advantages:-

- Solid dosage forms offer more accurate dosing Solid dosage forms offer more accurate dosing, effortlessly
 administration and stability.
- Their easy common covering storage and transport has resulted in wide spread use.
- In addition, the controlled release formulation allows prolonged therapeutic effect.

Disadvantages:-

- Tablets are hard to swallow in children and unconscious patients.
- Oily drugs which have unpleasant odour or bitter taste may be sensitive to oxygen and therefore, may need to be coated or encapsulated. Advancement
- Drugs with unpleasantodour or bitter testing can be sensitive to oxygen, hence they require coating or encapsulation.

Advancement:-

Solid dosage forms include the development of 3D printed medicines, customized medicine

Formulations and controlled release intelligent polymers. They have been designed to address existing deficiencies and enhance therapeutic efficacy.

Other key recent developments include: 3D printing technology, Co-crystal engineering, nanosizing technology.



Liquid Dosage Forms:-Liquid formulations, including solutions, suspensions, and emulsions, are ideal for patients with swallowing difficulties.

Liquid dosage forms are classified:-

Monophasic - liquid solutions including more than one component in single phase.

Biphasic-liquid solutions comprising one or more components in two different phases.

True solutions - homogeneous mixtures prepared by dissolving solutes in solvents. Other forms of liquid dosage Syrup,

Linctus, Elixirs, Gargles, Mouthwash, Lotions, Liniment, Nasal drops, Ear drop.

Solutions: Homogeneous mixtures like cough syrups(Ex- Nasal saline sprayfor nasal congestion).

Suspensions: Dispersed particles in liquid, such as antacids(Ex- Maalox for heartburn and indigestion).

Emulsions: Oil-water mixtures used for nutrient supplements(Ex- Eucerin for Moisturizing lotion for dry skin).

Advantages:-

- Rapid absorption
- flexible dosing

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- ease of swallowing
- Enhanced taste convenience transportation and preservation.

Disadvantages:-

- · Liquid dosage has stability issues and risks contamination
- Difficulties in measurement
- Bulky packaging
- Possibility for leakage

Advancement:-

Monophasic Liquid Formulations:

Improvements have enhanced solubility and stability to make better absorption possible and shelf life longer. Recent solubilization methods provide for poor water-solubility drug dissolution. Improved preservatives ensure safety and minimize break-down. Dosage is less difficult ingeriatric and pediatricpatients. There is more consistency and reliability because of formulation innovation.

Biphasic Liquid Formulations (Suspensions and Emulsions):

Enhanced stabilization techniques have improved the uniformity and stability of suspensions and emulsions. Formulations of controlled release enable longer duration of drug action, with less frequent dosing. Nanotechnology is being brought in for better bioavailability and targeted delivery of drugs. Stabilizers ensure that there is no phase separation and also enhance shelf life. New emulsions provide improved nutrient uptake and improved drug delivery.

True Solutions (Homogeneous Mixtures):

Quick absorption and quick onset of effect are salient features of true solutions. Personalized designs provide the route of administration for precise dosages, particularly in patients with dysphagia. New stabilizers and novel excipients provide higher stability and a longer shelf life. Modern solubilization has boosted drug bioavailability. Increased delivery systems, i.e., nasal sprays, provide quicker relief from acute ailments.

Suspensions

New stabilizers and technology prevent particle sedimentation by uniform dispersion of particles in suspensions. New controlled-release dosage forms now create extended therapeutic effect. Suspensions are less bitter and more acceptable to swallow, and are better tolerated by patients, especially pediatric patients. Increased stability and longer shelf life are achieved from new suspension methods. New technologies improve patient compliance by minimizing dosing intervals.

Emulsions (Oil-Water Mixtures):

Stabilization technologies have stabilized and made emulsions uniform. Nanoemulsions increase bioavailability and drug absorption. The potential of formulation customization delivers tailored therapies to the individual patient need. Emulsions are now more compatible for therapeutic as well as cosmetic applications. Advances in formulation technology provide texture improvement, and emulsions are best suited for skin care and nutritional supplements.

Semi-Solid Dosage Forms:-Semi-solid forms, such as creams, ointments, and gels, are used for localized treatment.

Creams: Water-based formulations for hydration (Ex- hydrocortisone for eczema).

Ointments: Oil-based formulations for barrier protection (Ex-petroleum jelly).

Gels: Alcohol-based formulations for antifungal treatments (Aloe Vera Gel for soothing skin burns, sunburns, and minor cuts).

Advantages:-

- Drug contact time is longer at absorption site hence long release of drug in comparison with normal semisolids.
- Drug usage is more so dosing frequency becomes less and amount of required dose is less.
- Bioavailability of drug increases in comparison to conventional semisolids.
 - Better patient compliance

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Disadvantages:-

- Semi solid drug forms such as creams and ointments, may have limitations in providing exact dosage control.
- Measuring and dispensing precise quantities may be difficult compared to solid or liquid dosage forms, with potential for drug delivery fluctuations.
- Those containing active ingredients or excipients, may be skin irritants or skin sensitizers. This may limit their application in certain patient populations and require careful formulation ingredient selection.
- Semisolid drug products are temperature and environmental sensitive.

Advancement:-Semi solid dosage forms have brought about considerable innovation in drug delivery, enhancing therapeutic effectiveness and patient compliance. Progress in this category is directed primarily towards avoiding the constraints that come with traditional formulations like ointments and creams. The principal advances are: nanotechnology integration, microstructure design, transdermal drug delivery systems, hydrogels and mucoadhesive drug delivery systems.

Gaseous dosage forms :-Gaseous dosage forms are drug products where the active constituent is in the gaseous state, generally meant for administration by inhalation, such as-

Inhalable Gases: They are gases that exert therapeutic action when inhaled. Examples include:

Anesthetic Gases: Nitrous oxide, halothane, and sevoflurane for anesthesia.

Therapeutic Gases: Oxygen to be used in ventilatory support and nitric oxide to treat pulmonary hypertension.

Aerosols: Nebulized mist formulations that release drugs as gases through inhalers. Examples include:

Metered-Dose Inhalers (MDIs): In asthma or COPD, for bronchodilators like albuterol.

Dry Powder Inhalers (DPIs): For bronchodilators or corticosteroids.

Gaseous Solutions: Some drugs are dissolved in gases. Volatile anesthetics, for example, are dissolved in a carrier gas like nitrous oxide.

These forms are used in anesthesia, respiratory therapy, pain management, and emergency practice. The problem with gaseous forms is control of dosage, stability, and compliance by the patient.



Metered dose inhaler37

Dry powder inhalers³⁸

Nebulizer machine39

Advantages:-

- Rapid Onset of Action: Gaseous drugs, especially anesthetics or drug in respiratory therapy, are quickly absorbed by the lungs and have rapid therapeutic action.
- Non-invasive: They are delivered by inhalation, which minimizes the need for intramuscular injection or oral intake, with chances to improve patients' compliance.

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- Controlled Dosage: Controlled dosage is obtained through the utilization of devices like metered-dose inhalers, specifically for inhaled medication, i.e., bronchodilators and corticosteroids.
- Targeted Delivery: Preparations administered by inhalation may be deposited in the lungs to exert localized effects in treating pulmonary disease.
- Ease of Administration in Critical Care: Gases like oxygen and nitric oxide play a critical role in emergency and critical care, with the potential to start therapy for life-threatening disease within minutes.

Disadvantages:-

- Difficulty in Dosing: It is easier to measure the precise dose of a solid or liquid drug than a gas, leading to opportunities for under or overdose.
- Stability Issue: Gaseous drugs will lose their stability and require specific storage conditions (e.g., pressurized cylinders) in order to prevent degradation.
- Patient Adherence: Patients can not be able to use inhalers or other devices that deliver gas in the right way, thus leading to an incorrect dose.
- Short Shelf Life: Aerosolized drugs and gases have a short shelf life if they need specific storage conditions.
- Cost: Gaseous drug delivery systems and formulations, like nebulizers and inhalers, are expensive.

Development in Gaseous Dosage Forms:-

- Smart Inhalers: Advanced technologies in inhaler devices, including smart inhalers, include monitoring of patient usage and correct administration of drug.
- Improved Aerosol Technology: Advanced aerosol propellants and drug delivery systems have introduced better and efficient delivery of gases like bronchodilators and corticosteroids.
- Nanotechnology: Particles and other nanotechnologies are employed to augment delivery and stability of gas drugs, especially in the treatment of the lung disease.
- Personalized Medicine: Increased understanding of genetic and environmental influences is enabling more personalized inhalation therapy with improved patient outcomes.
- Hybrid Systems: Merging gas with liquid or solid dosage forms, or with new delivery devices, can improve effectiveness and precision of gaseous dosage forms

Advanced Dosage Forms:-Innovative systems like nanoparticles, implants, and 3D-printed tablets are revolutionizing drug delivery.

- Drug Delivery through Nanoparticles:-Particle-based drug delivery systems use particles with sizes ranging from 1 to 100 nm to deliver drugs with high accuracy. Nanoparticles can enhance the bioavailability of poorly soluble drugs and target the delivery of such drugs to tissues or cells with minimal side effects. They are applied in cancer therapy, where the drug is targeted to the tumor. Liposomes, dendrimers, and nano emulsions are some of the examples. The use of nanoparticles enables drug release, increased stability of drugs, and improved therapeutic action.
- Transdermal Drug Delivery Systems (TDDS):-Transdermal drug delivery systems are drug-delivery patches delivering drugs into the blood stream from the skin. The method skips the gastrointestinal system and first-pass metabolism, offering sustained and controlled medication delivery. Examples include patches of nicotine for smoking cessation, HRT, and fentanyl patches for managing pain. The advantages are prolonged, continuous dosing, ease of use, and non-invasive administration with improved patient compliance and decrease side effects.
- Osmotic Pump Systems:-Osmotic pump products utilize osmotic pressure to provide drugs in a sustained and controlled manner over a period of time. The products release the drug at a constant rate, removing drug concentration oscillations related to immediate-release products. Products are such that Glucotrol-XL is an example of glipizide. Osmotic pumps ensure constant levels of the drug, removing side effects and maximum therapeutic effects, particularly for drugs that need constant delivery, e.g., diabetic drugs.

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- Biodegradable Implants:-Biodegradable implants are long-term devices that release medication slowly over a period of time and are biologically degradable in the body. They are applied for long-term drug delivery, reducing frequent drug administration. They consist of Zoladex for cancer of the prostate and intrauterine devices (IUDs) for pregnancy prevention. They provide sustained and controlled drug delivery, ensuring patient compliance as well as relief from long-term diseases or disorders that require long-term treatment.
- Targeted Drug Delivery Systems:-Targeted drug delivery refers to the use of targeted carriers (e.g., monoclonal antibodies or liposomes) to release drugs at the target site, e.g., cancer cells, with least harm to normal tissues. This reduces side effects and enhances the therapeutic effect of drugs. Antibody-drug conjugates (ADCs) and liposomal preparations like Doxil (liposomal doxorubicin) are good examples. The chief advantage is that it allows drug delivery at the site of the disease with maximal effectiveness and minimal systemic toxicity.
- Inhalable Drug Delivery Systems:-Inhalation drug delivery systems deliver the drugs to the lungs directly with quick absorption and action. These have extensive applications in respiratory illnesses like asthma, COPD, and other diseases of the lung. Metered-dose inhalers (MDIs), dry powder inhalers (DPIs), and nebulizers are some examples. The advantage is quick delivery to the desired site (lungs), ideal for drugs like bronchodilators and corticosteroids, which have quick action and fewer systemic side effects.
- Gene and RNA Therapeutics:-Gene and RNA therapies involve the introduction of genetic material, DNA or mRNA, to treat disease by fixing genetic flaws or controlling gene expression. They include gene therapy for genetic illness and mRNA vaccines like the Pfizer-BioNTech COVID-19 vaccine. The potential of these treatments is vast, as they could treat genetic illnesses and provide tailored treatment. The technology is still immature, with problems in effective delivery and stability.
- Liposome and Nanostructured Lipid Carriers (NLCs):-NLCs and liposomes are lipid drug carriers that can encapsulate drugs, enhance stability and bioavailability, and regulate release rates. Drugs like Doxil (liposomal doxorubicin) are used in oncology. Targeted delivery, enhanced solubility for water-insoluble drugs, and reduced side effects are provided by these systems. Liposomes can protect the drug from degradation and enhance its therapeutic activity by targeting it to specific cells or tissues.
- Microencapsulation:-Microencapsulation refers to the temporary entrapment of medication in fine particles or capsules for the control of their release, prevention of degradation, or hiding their taste. Microencapsulation is used in controlled-release capsules and tablets where medicine is delivered over a period of time. Examples include some painkillers and antibiotics. The main advantage is that the release of a drug can be prolonged, compliance with treatment is increased, and sensitive drugs can be protected from the environment.
- 3D-Printed Drug Delivery Systems:-Three-dimensional printing technology is used to create patient-specific drug delivery devices with a controlled geometry, release, and dosage. Personalization of drugs based on individual patient needs is possible with this technology. Implants and tablets made by 3D printing, for example, can be designed to deliver different drugs at different time points. The technology has the potential to improve compliance of patients with their medication regimen, allowing individualized treatment, and even reducing the time consumed in drug development.
- Oral Thin Films:-Oral thin films are solid dosage drugs that rapidly disintegrate in the oral cavity and permit drugs to be released via oral mucosa. They are used by drugs that need prompt absorption, such as nausea, pain, or vitamins. Ondansetron (anti-nausea) and CBD are such films. Rapid onset of action, ease of use, no need for water or swallowing, and compatibility for pediatric and geriatric patients or swallowing-disabled patients are some benefits.
- Microneedle Patches:-Microneedle patches consist of small needles piercing painlessly through the skin to deliver drugs directly into the bloodstream. The systems are used in vaccines, insulin, and other therapy. Microneedles form an injection-free drug delivery system, as opposed to injections, which are less painful to give and easier to use. Examples are insulin microneedles and vaccine microneedles. Advantage is painless drug delivery, ease of use, and potential for home use.

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Bringin revolutionary advancements in drug delivery through the potential to tailor tablets to individual doses and patient requirements. The technology allows for targeted dosing, concurrent encapsulation of multiple drugs into one tablet, and formulation of controlled or extended-release tablets. Creation of new shapes or layers of tablets improves drug absorption and dissolution. 3D printing also cuts drug development expense and time through quicker prototyping and on-demand, lower-expense production, especially for personalized medicine.

Nanoparticles:

Advantages:-

- Improved Drug Delivery: Nanoparticles can be targeted to areas of the body, increasing drug activity and lowering side effects.
- Improved Absorption: Polymeric nanoparticles, for example, can help increase absorption of drugs, thus making them effective even at reduced doses.
- Targeted Delivery: Liposomes (e.g., Doxil) allow direct delivery of drugs to cancer cells, potentially bypassing damage to normal tissues.

Disadvantages:-

- Difficult Manufacturing: Manufacturing of nanoparticles can be complicated and expensive.
- Potential Toxicity: The long-term effect of nanoparticles on the human body is being studied, and there could be unintended harm, specifically organ accumulation.
- Regulatory Challenges: Nanoparticles have stringent regulatory approval due to their complexity, thus inducing a delay in approval.

Implants:

Advantages:-

- Long-Lasting Effects: Implants like Nexplanon provide consistent, long-term release of medication without having to visit daily.
- Lower Risk of Non-Compliance: Since implants are often beneath the skin, patients aren't required to remember to swallow a pill on a daily basis.
- Localized Action: Some implants are able to administer medication at a local location, eliminating systemwide side effects.

Disadvantages:-

- Surgical Procedure: Insertion and removal of implants requires a surgical procedure, possibly painful or dangerous for some individuals.
- Side Effects: Side effects can happen locally at the site of the implant (e.g., infection, irritation).
- Limited Flexibility: Release of the drug, after insertion of the implant, is more likely to be continuous, and hence potentially unadjustable in case a patient needs a different dosage.

3D-Printed Tablets:

Advantages:

- Customization: Customized tablets can be designed for a patient's specific dosage needs through 3D printing, increasing therapeutic efficacy.
- Flexible Dosage Forms: 3D printing enables tablets with controlled-release mechanisms or a combination of multiple drugs within one tablet.
- Rapid Production: 3D printing is able to achieve rapid, small-scale drug production, which can be useful for small or experimental drug productions.

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Disadvantages:-

- Technology Cost: The material and equipment used for 3D printing are expensive, which may make the production process pricey.
- Limited Access: This technology is still not ubiquitous or accessible in large-scale pharmaceutical production.
- Regulatory Issues: 3D printing within the pharmaceutical sector is raising regulatory concerns regarding quality control and drug consistency during production.

Advancement:-

Nanoparticles:

- Targeted Drug Delivery: One of the biggest breakthroughs is the ability to target disease locations, for example, tumors in cancer therapy, specifically with minimal effect on normal cells, reducing side effects and increasing therapeutic effects.
- Enhanced Bioavailability: Nanoparticles have significantly improved the bioavailability of drugs, especially those with poor solubility, for increased absorption and efficacy even at lower doses.
- Controlled Release: Advanced nanoparticle design has enabled controlled or sustained release of drugs, reducing the rate of administration and increasing patient compliance.
- Smart Nanoparticles: Advances have been made in "smart" nanoparticles that release drugs when they recognize particular stimuli (e.g., phor temperature change), providing even more targeted drug delivery.

Implants:

- Long-Acting Drug Delivery: Implants have evolved to achieve weeks, months, or years of controlled and sustained release of drugs, rendering infrequent dosing unnecessary and improving patient compliance.
- Biocompatible Materials: Advances in biocompatible and biodegradable materials employed by implants reduce the risk of complications and infection, rendering the implants safer and more effective for patients.
- Minimally Invasive Techniques: Technological advancements in the techniques of inserting implants (e.g., less incisions or needle technology) have minimized recovery and rendered procedures safer, painless, and more time-effective.
- Specific Applications: Implant technologies like Nexplanon have made better chronic disease management possible, e.g., extended birth control or hormone replacement therapy.

3D-Printed Tablets:

- Personalized Medicine: 3D printing allows customized tablets to be manufactured based on an individual patient's specific needs, including precise dosage, combination of drugs, and controlled release. This could enhance the efficacy of treatment and minimize side effects.
- Rapid Prototyping and Production: The use of 3D printing technology has allowed for the rapid manufacturing of drug formulations, hastening the development cycle and enabling personalized medicines for one.
- Complex Dosage Forms: 3D printing allows the creation of multi-layered or multi-drug tablets, which cannot be easily developed using conventional tablet manufacturing techniques. This may enhance combination therapy and patient compliance.

Routes of Administration

• Oral Route:-The oral route is the most common, utilizing , capsules, syrups and tablets. Challenges include first-pass metabolism and gastrointestinal irritation.

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- Parenteral Route:-Parenteral administration, including intramuscular (IM), intravenous (IV) and subcutaneous (SC) injections, bypasses the digestive system for rapid action.Examples include antibiotics for sepsis and insulin for diabetes.
- Topical/Transdermal Route:-Topical creams and transdermal patches deliver drugs locally or systemically. Examples include psoriasis treatments and nicotine patches for smoking cessation.
- Inhalation Route:-Inhalable forms like metered-dose inhalers (Ex- albuterol for asthma) provide direct lung delivery for rapid relief.
- Other Routes:- ophthalmic/nasal routes (Ex- glaucoma eye drops) offer alternative delivery methods and Buccal/sublingual (Ex- nitroglycerin for angina).

Manufacturing Processes

1) Solid Dosage Forms

- Tablet Presses: Single-punch for small-scale production and rotary presses for high-speed manufacturing.
- Coating Machines: Apply film coatings for taste-masking or controlled release.
- Capsule Filling Machines: Automated systems ensure precision.

2) Liquid Dosage Forms

- Autoclaves: Sterilize injectables at high pressure and temperature.
- Homogenizers: Create uniform emulsions.

3) Semi-solid Dosage Forms

- Formulation and Mixing
- Emulsification and API Incorporation
- Homogenization and Cooling

4) Advanced Manufacturing

- 3D Bioprinters: Fabricate personalized tablets layer-by-layer.
- High-Pressure Homogenizers: Produce nanoparticles.

Challenges and Solutions

Drug Stability	Use of improved preservatives, innovative solubilization methods, and innovative stabilizers
Patient Compliance	Easy-to-swallow newer formulations, reduced frequency dosing, and patient-tailored dosage form.
Accurate Dosing	Solid dosage forms, extended-release drugs, and 3D-printed tablets for precise dosing
Flavor Masking	Encapsulation or coating of drugs with bad odor or bitter flavor
Targeted Drug Delivery	Nanoparticles, liposomes, and targeted drug delivery systems to deliver drugs to targeted areas with fewer side effects

Regulatory Considerations

Pharmaceutical dosage forms must comply with stringent regulatory standards to ensure safety, efficacy, and quality. Major guidelines include:

- FDA/EMA Regulations: ICH Q8 for manufacturing.
- Quality Control: Tests for content uniformity, dissolution and sterility.
- Global Harmonization: WHO's Good Manufacturing Practices (GMP).

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Future Directions

Sustainability
Biodegradable Polymers: Replace plastic in packaging.
Green Chemistry: Solvent-free manufacturing processes
Personalized Medicine

Pharmacogenomics: Tailoring formulations to individual metabolism rates
Printing: Customized doses based on genetic profiles.
Smart Drug Delivery
Stimuli-Responsive Systems: Temperature/ph-sensitive nanoparticles.
Implants with Sensors: Devices that release insulin based on glucose levels.

II. CONCLUSION

Pharmaceutical dosage forms are leading the field of drug delivery innovation, encouraged by technological advances and patient-focused care. Though issues such as drug stability and regulatory compliance continue to challenge the industry, upcoming trends like nanotechnology, AI-based formulations, and green practices hold the potential for revolutionary solutions. Interdisciplinary collaboration between pharmacology, engineering, and data science will be essential to shaping the future of drug delivery.

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