Advanced Pharmaceutical Technologies and Drug Development

Mrs. MONISHA J
Dr. S. UMADEVI
Dr. VIJAYAKUMAR MURUGESAN
Dr. A. VENKATESH

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Mrs. MONISHA J

Assistant Professor, Department of Pharmaceutics
School of Pharmaceutical Sciences
Vels Institute of Science, Technology & Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.

Dr. S. UMADEVI

Professor, Department of Pharmaceutics
School of Pharmaceutical Sciences
Vels Institute of Science, Technology & Advanced Studies (VISTAS), Chennai, Tamil Nadu, India.

Dr. VIJAYAKUMAR MURUGESAN

Department of Pharmaceutics, School of Pharmacy
JSS Academy of Higher Education and Research
Mauritius.

Dr. A. VENKATESH

Professor & Head
Department of Conservative Dentistry & Endodontics
Sree Balaji Dental College & Hospital
Chennai, Tamil Nadu, India.

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PREFACE

The rapid evolution of pharmaceutical sciences has ushered in a new era of innovation, where advanced drug delivery systems, molecular therapeutics, and intelligent technologies converge to redefine modern healthcare. *Advanced Pharmaceutical Technologies and Drug Development* is a comprehensive volume that captures these transformative developments, emphasizing both foundational principles and emerging trends that are shaping the future of therapeutics.

A central theme of this book is the advancement of novel drug delivery systems designed to enhance therapeutic efficacy, safety, and patient compliance. From liposomes, niosomes, and phytosomes to dendrimers and biodegradable polymers, the chapters explore a wide spectrum of nanocarriers and excipient technologies that enable targeted and controlled drug release. These systems not only improve bioavailability but also address critical challenges associated with conventional dosage forms, paving the way for more precise and efficient treatment strategies.

The integration of cutting-edge technologies into pharmaceutical research is another defining aspect of this volume. The application of artificial intelligence in microbiome profiling for diseases such as inflammatory bowel disease highlights the growing importance of data-driven and personalized medicine. Similarly, advancements in mRNA vaccine development extend beyond pandemic applications, showcasing their potential in treating a variety of infectious and non-infectious diseases.

This book also delves into the scientific and technological foundations of drug formulation, including preformulation studies and the development of sustained and prolonged-release systems. These aspects are crucial in ensuring drug stability, efficacy, and optimal therapeutic performance. The inclusion of research on eco-friendly excipients and biodegradable polymers reflects the increasing emphasis on sustainability in pharmaceutical development, aligning innovation with environmental responsibility.

Clinical perspectives are also incorporated to provide a holistic understanding of disease management. Discussions on conditions such as oral ulcers and nutritional deficiencies offer insights into the practical applications of pharmaceutical formulations in improving patient outcomes. Furthermore, the exploration of commercial aspects and translational potential bridges the gap between laboratory research and industrial implementation, highlighting the real-world impact of pharmaceutical innovations.

The chapters collectively emphasize a multidisciplinary approach, integrating pharmaceutics, biotechnology, nanotechnology, and computational sciences. This convergence is essential for addressing complex healthcare challenges and developing next-generation therapeutics that are both effective and accessible.

This volume is intended for researchers, academicians, industry professionals, and students in pharmaceutical and allied sciences. By presenting a balanced blend of theory, innovation, and application, the book aims to inspire continued research and foster advancements in drug delivery and therapeutic development. It is hoped that this work will serve as a valuable resource and a catalyst

for future innovations in the ever-evolving field of pharmaceutical sciences.

We extend our sincere thanks to our publisher, Scientific Research Reports, Chennai, India, for their dedicated efforts in preparing this book and for ensuring the inclusion of enriched and high-quality technical content.

Wishes and Regards,

Mrs. MONISHA J
Assistant Professor
Department of Pharmaceutics
Vels Institute of Science, Technology & Advanced Studies (VISTAS),
Chennai, Tamil Nadu, India.

Dr. S. UMADEVI
Professor
Department of Pharmaceutics
School of Pharmaceutical Sciences
Vels Institute of Science, Technology & Advanced Studies (VISTAS),
Chennai, Tamil Nadu, India.

Dr. VIJAYAKUMAR MURUGESAN
Department of Pharmaceutics
School of Pharmacy
JSS Academy of Higher Education and Research, Mauritius.

Dr. A. VENKATESH
Professor & Head
Department of Conservative Dentistry & Endodontics
Sree Balaji Dental College & Hospital
Chennai, Tamil Nadu, India.

CONTENTS


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Chapter 1

AI-Driven Microbiome Profiling for Precision Management of Inflammatory Bowel Disease

S.Thagasin[a], J.Monisha[b*]

[a]*School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, SPS, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Inflammatory bowel disease, or IBD, comprises crohn's disease and ulcerative colitis, chronic inflammatory disorders mediated by alterations in the human microbiome. Recent studies indicate that imbalance in the microbiome significantly contributes to disease severity and treatment response in IBD patients. In the current era of next-generation sequencing and other omics-based approaches, artificial intelligence, or AI, has been successfully applied to analyze the human microbiome data to identify specific microbial patterns to aid in the diagnosis of IBD, disease classification, and prediction of treatment outcomes. In addition, non-invasive biomarker discovery through stool samples of affected individuals can be achieved, thus enabling a more precise approach to disease management in IBD patients. Though there are certain limitations in applying AI in microbiome analysis, including data variation and validation, this approach appears to be a promising area of research to improve diagnosis, disease relapse, and treatment of IBD, thus enabling a

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more precise approach to disease management in affected individuals.

Keywords: Inflammatory Bowel Disease, Artificial Intelligence, Gut Microbiome, Microbiome Profiling, Precision Medicine.

1. Introduction

Inflammatory bowel disease (IBD) is a common, long-lasting inflammatory disease of the gastrointestinal tract. It represents two major conditions: Crohn's disease (CD) and ulcerative colitis (UC). The prevalence of IBD worldwide has increased markedly over the last several decades, and this represents a substantial healthcare burden. An important aspect of IBD is thought to be the interplay of multiple and complex factors. These factors include genetic predisposition, environmental factors, and immune response (both local and systemic), as well as changes or abnormalities in the gut microbiome [1]. The human gut microbiome is critical for maintaining homeostasis of the intestines, providing metabolic function; and regulating the immune system. Many studies now indicate that there is an imbalance in the content and diversity of gut microbial ecosystems (dysbiosis) in individuals with IBD. Many studies show that individuals with IBD have reduced microbial diversity and have altered the abundance of both beneficial and pathogenic microorganisms, which leads to chronic inflammation in the intestines [2]. Metagenomics and other omics-based technologies that employ high-throughput sequencing (HTS) have enabled the detailed characterization of gut microbiota. However, this type of technology produces vast amounts of complex data that require the use of sophisticated and advanced computational tools to interpret. Algorithms that involve artificial intelligence (AI) and machine

learning (ML) represent potentially useful tools in the analysis of microbiome data and to identify micro-biotic signatures associated with disease [3]. Through the use of Artificial Intelligence (AI), researchers are developing new methods to diagnose and classify disease in inflammatory bowel disease (IBD) through the development of novel AI-driven methods to create microbiome profiles. Through combining both microbiome characteristics with strict clinical and molecular evaluation data, multiple microbe populations can be evaluated as potential targets for creating personalized medical therapies. By developing these microbial profiles, as well as the potential responses of patients to current treatments, precision medicine approaches can be developed to improve the patient's overall experience with IBD [4].

2. Pathogenesis of inflammatory bowel disease

The gastrointestinal tract has chronic inflammation, which leads to the development of a condition known as inflammatory bowel disease (IBD). IBD contains both Crohn's disease and ulcerative colitis. The cause of IBD is complicated because there are many factors that can contribute to it. These factors include genetic risk to developing the illness, external influences, the immune system, problems with protection from infection within the intestines, and differences in the intestinal bacteria (5). Having an inherited genetic predisposition to developing IBD is critical to the development of the disease. Many genome-wide association studies have been performed that have identified many potential "susceptibility" genes that may affect how our bodies respond to the bacteria we are exposed to on a daily basis, i.e., how our bodies will protect themselves from bacterial infection (6). Antibiotics, diet, smoking, stress, and whether or not you have been exposed to an infection are all examples of external

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environmental influences that may influence both the composition and the function of the gut bacteria. For individuals who have an inherited genetic predisposition to develop IBD, these external environmental factors have the potential to disrupt the normal balance present in the intestines and activate inflammation (7).

3. Role of gut microbiome in inflammatory bowel disease

The gut microbiome plays a vital role in regulating the health of the intestine and the balance of immunity. The intestinal tract of humans is home to a diverse array of microorganisms that aid in digestion and metabolism as well as provide a barrier to the entry of pathogens. Healthy individuals have a healthy interaction with their microbes, which aids in holding the immune system and epithelial barrier of the intestines in balance (8).Dysregulated gut microbial composition can be found in inflammatory bowel disease (IBD) patients. Microbial dysbiosis refers to an imbalance of factors that leads to decreased diversity of the multiple microbial communities and increased relative abundance of both good and bad bacteria. For instance, studies show that levels of Faecalibacterium prausnitzii are often low in IBD patients, while potentially pathogenic bacteria are significantly increased. These changes to the gut microbiome may lead to increased intestinal inflammation and contribute to the overall progression of the disease (9). The gut microbiome is also a significant regulator of immune responses occurring within the intestine. Commensal microorganisms interact with epithelial cells and immune cells, leading to immune tolerance and maintenance of a balanced immune response. When this balance is broken, abnormal immune activation may occur, which may lead to the production of pro-inflammatory cytokines and to chronic inflammation of the intestinal mucosa. Additionally, beneficial gut microbiota are able to

produce multiple compounds that promote a healthy immune response. (10)

4. Microbiome analysis technique

Sequencing technologies have made great strides in understanding the gut microbiome of patients with inflammatory bowel disease. Some common methods used to analyze the gut microbiome include 16S rRNA gene sequencing, whole-genome shotgun metagenomics, metatranscriptomics, metabolomics, and metaproteomics. Of these, 16S rRNA gene sequencing is used most often to identify the composition of the bacterial community, whereas shotgun metagenomics is used to gain detailed information about microbial genes and their functional pathways. Metatranscriptomics allows us to study how microorganisms express their genes, and metabolomics allows us to identify the metabolic products of microorganisms that play a role in interactions between hosts and their gut microbiomes. These different methods of analysis generate large datasets that provide researchers with a better understanding of what changes occur in the gut microbiome when dysbiosis persists, how immune function is altered, and how metabolism is affected as patients with IBD progress through their disease. By integrating the data generated from all of these different types of analyses, we have been able to develop a more comprehensive understanding of the diversity of microorganisms present in the gut microbiome and how they are functionally altered in IBD. Additionally, this research has helped lay a foundation for developing precision diagnostics and therapies for IBD. (11)

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5. Ai-driven microbiome profiling for precision management

Using artificial intelligence to examine the microbiome offers many new insights into disease states and treatment. AI can identify unique and previously unknown microbes associated with inflammatory bowel disease (IBD) and reveal potential targets for treatments. Utilizing machine learning will provide valuable data from multiple sources, allowing for more comprehensive analyses of microbial dysfunction related to IBD, such as changes in disease state, inflammatory markers, and response to therapy. Models based on AI can provide predictive information for early identification of IBD, as well as help guide a clinician's decision-making process regarding treatments that target specific microbes (i.e., probiotics, prebiotics, diet modification, or fecal microbiome transplantation). Digital models built on AI data will provide clinicians with real-time assessment of IBD severity over time; thus, AI data models will continue to help inform clinicians during the IBD treatment process by demonstrating how to tailor treatment options based on specific microbial signatures. These approaches will accelerate the move towards personalized medicine by establishing therapeutic plans according to individualized IBD-specific microbiome characteristics, ultimately improving the quality of care for IBD patients (12).

6. Challenges and Limitations

The ability of artificial intelligence (AI) to provide high-precision management of inflammatory bowel disease (IBD) could be enhanced by obtaining and analyzing the microbial profile of patients, but there are numerous limitations preventing this from happening. One major limitation is that each person has a gut microbiome with varied composition due to the influence of dietary habits, age, inherited

genes, lifestyle, and the use of medications amongst other factors, therefore making it difficult to consistently identify microbial biomarkers linked to IBD. This inherent variability in gut microbiome composition impairs the reproducibility of microbiome studies across diverse populations and locations. Moreover, there is currently no standard methodology used when conducting studies on the microbiome, which further limits our ability to use AI to help us manage IBD. Some inconsistencies that exist between the various microbiome studies are caused by variations in the sample collection process and variations in the method used to extract DNA from biological samples, as well as the sequencing platforms utilized and the data analysis pipelines used. The inconsistencies result in a difficulty when comparing and validating microbiome data among different research groups. The collection of the microbiome data represents a very complex and high-dimensional dataset; therefore, developing robust artificial intelligence/machine learning models from microbiome data is very challenging. This is due to the thousands of different microbial taxa and functional genes that microbiome data contain, therefore requiring advanced computing techniques and a considerable quantity of data to conduct analyses accurately. Unfortunately, most microbiome studies are completed with small sample sizes, making AI and ML predictive models based on these data less robust and generalizable to the population at large (13).

7. Future direction

To continue research in the area of AI-based microbiome profiling, researchers should aim to integrate microbiome data with other biological datasets, including but not limited to genomics, transcriptomics, and metabolomics in a multi-omics approach to

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elucidate how these multi-faceted mechanisms are involved with Inflammatory Bowel Disease and lead to the identification of reliable microbial biomarkers to assist with early diagnosis and treatment index. Another important area for future research will be to develop large-scale microbiome datasets, including samples collected from diverse populations in multiple geographic regions and patient groups, such that the overall size of the dataset will increase the reliability and predictive performance of the artificial intelligence (AI) and machine learning (ML) models being applied to study the microbiome. Additionally, the application of enhanced machine learning and bioinformatics tools will increase researchers' ability to analyze complex microbiome data and allow them to make superior predictions regarding disease progression, relapse risk, and treatment response for patients with IBD. The ability to analyze the microbiome data using AI may also support the development of personalized treatment options through microbiome-directed therapies such as probiotics, prebiotics, and fecal microbiota transplantation .In summary, as we continue to experience advancements in sequencing technologies, computational techniques, and cross-disciplinary teamwork, the utilization of AI-based microbiome profiling in the precision treatment of inflammatory bowel disease will only continue to improve in years to come (14).

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Chapter 2

Biodegradable Polymers and Eco-Friendly Excipients in Pharmaceutical Drug Delivery Systems

Indrajit V S[a], Monisha J[b*]

[a] *B Pharm IInd year, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b*]*Assistant Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author:* monisha.sps@vistas.ac.in

Abstract

Biodegradable polymers play a vital role in modern pharmaceutical and medical device development due to their ability to safely degrade within the body, eliminating the need for surgical removal. Polymers such as PLA, PGA, and PLGA are widely used in absorbable sutures, orthopedic devices, and advanced drug delivery systems, including implants, microspheres, nanoparticles, and in situ gels. Their degradation occurs through bulk or surface erosion, enabling controlled and sustained drug release. This chapter outlines the classification, chemistry, synthesis, and mechanisms of polymer degradation, along with formulation techniques such as single and double emulsification methods. It also discusses scale-up strategies, quality control measures, regulatory considerations, and economic perspectives.

Keywords: PLA, PGA, PLGA, microspheres, nanoparticles.

1. Introduction

Biodegradable polymers have gained significant attention in the pharmaceutical and medical device industries due to their ability to safely degrade within the body. The first FDA-approved biodegradable product was Dexon, an absorbable surgical suture introduced in 1970 by Davis and Geck. This innovation led to the development of biodegradable orthopedic devices such as pins, screws, and cranio-maxillofacial plates. During the 1990s, biodegradable polymers were widely adopted in pharmaceutical research for advanced drug delivery systems, especially long-acting depot injections. A notable example is Lupron, manufactured by Takeda Pharmaceutical Company, which is used in the treatment of prostate cancer. Despite major scientific and commercial progress, expertise in biodegradable polymer technology remains concentrated among a limited number of companies due to the complexity of polymer chemistry and formulation processes. Understanding polymer degradation in biological systems has enabled the development of sustained and targeted drug delivery systems, including implants, microspheres, nanoparticles, microcapsules, and in situ gels. Owing to their flexibility, strength, and biocompatibility, biodegradable polymers are widely used in medical devices and tissue engineering, with promising future applications in sustainable pharmaceutical technologies.

2. Biodegradability

Biodegradability is one of the most important features of environmentally friendly excipients, as it allows them to naturally break down through biological processes (5). These materials typically degrade via enzymatic action by microorganisms, producing harmless end products such as modified starch and cellulose derivatives and

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showing excellent biodegradation capacity, often decomposing within weeks to months under environmental conditions (6).

3. Renewability

Excipients obtained from renewable resources support sustainable production systems and decrease reliance on petrochemical-based materials (7). Plant-based agriculture sources offer materials that can be renewed annually, while marine resources provide continuous natural regeneration. Life cycle and carbon footprint assessments indicate that renewable excipients can lower greenhouse gas emissions by approximately 40-60% compared to synthetic materials (8).

3.1 Toxicology profile

Evaluation of environmental safety includes assessing both short-term and long-term effects on aquatic organisms, land ecosystems, and the potential for bioaccumulation (9). Contemporary eco-friendly excipients exhibit low environmental toxicity, with LC50 values generally above 100 mg/L in aquatic species, suggesting minimal ecological risk. Additionally, their bioaccumulation potential remains within accepted regulatory limits, ensuring safety across different levels of the food chain.

3.2 Classification

Biodegradable polymers are broadly classified into natural and synthetic types. Natural biodegradable polymers are mainly proteins and polysaccharides that undergo enzymatic degradation in the body. Examples include alginate, chitosan, agarose, collagen, and starch derivatives. These polymers are widely used due to their biocompatibility and eco-friendly nature. Synthetic biodegradable polymers contain hydrolysable linkages such as ester, amide,

peptide, urethane, urea, or anhydride groups within their backbone, enabling degradation through hydrolysis in the human body. Major synthetic polymers include polyesters like polylactic acid (PLA), polyglycolic acid (PGA), poly(lactide-co-glycolide) (PLGA), and poly(ε-caprolactone) (PCL), as well as polyanhydrides, polyethylene glycol derivatives, polyvinyl alcohol, polyamides, and polyhydroxyalkanoates. PLGA, a copolymer of PLA and PGA, is considered an excellent biomaterial for drug delivery. PLA exists in stereoisomeric forms—PDLA and PLLA—due to the presence of an asymmetric carbon, influencing its physical and degradation properties.

3.3 Chemistry and synthesis

PLGA is a synthetic, biodegradable polyester widely used in biomedical applications. It is produced from monomers such as lactic acid, glycolic acid, dioxanone, trimethyl carbonate, and ε-caprolactone. When a polymer is formed from only one type of monomer, it is known as a homopolymer, such as polylactic acid (PLA) or polyglycolic acid (PGA). In contrast, polymers made from two or more different monomers are called copolymers; PLGA, for example, is formed by combining lactic acid and glycolic acid. Lactic acid, the basic unit of PLA, is commonly obtained through bacterial fermentation of carbohydrate-rich materials like corn or sugarcane, often using Lactobacillus species. PLA can then be synthesized through polycondensation or ring-opening polymerization. The final properties of these polymers—such as strength, degradation rate, solubility, and thermal behavior—depend on the monomer ratio, arrangement, and end-group chemistry. After synthesis, purification steps are carried out. out to remove residual monomers, ensuring better stability, safety, and overall product quality.

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4. Applications

Eco-friendly excipients are increasingly used in pharmaceutical formulations due to their functional performance and environmental advantages. In conventional dosage forms such as tablets, natural polymers like starch and cellulose derivatives are widely used as binders and disintegrants. These materials provide adequate mechanical strength, ensure proper tablet disintegration, and support uniform drug release. Natural gums and modified pectins are also commonly applied in sustained-release formulations, where they regulate drug diffusion over extended periods. In many cases, these natural materials perform similarly to synthetic polymers while offering improved environmental compatibility. Life-cycle assessments further demonstrate their cost-effectiveness and market advantages. Finally, regulatory compliance is essential for the approval of sustainable pharmaceutical excipients. Proper documentation of safety, quality, and environmental impact is required. Standardized validation procedures and evolving regulatory frameworks have made it easier for pharmaceutical companies to adopt eco-friendly excipients in modern drug formulations.

5. Conclusion

Biodegradable polymers have become highly important materials in pharmaceutical and medical device applications. Their ability to degrade safely within the body removes the need for surgical removal and supports the development of advanced therapeutic systems. Polymers such as PLA, PGA, and PLGA are widely used because of their versatility and biocompatibility. These materials are applied in various medical products, including absorbable sutures, orthopedic implants, and advanced drug delivery systems such as microspheres,

nanoparticles, implants, and in situ gels. Preparation techniques such as single emulsification and double emulsification have further expanded the application of biodegradable polymers by allowing formulation adjustments based on drug properties and clinical requirements. In addition, increasing attention is being given to environmentally friendly pharmaceutical excipients. Biodegradable polymers contribute to sustainability because they are often renewable, less toxic, and environmentally safer. Their use can also improve manufacturing efficiency and reduce environmental impact. Overall, biodegradable polymer technologies show great potential for the future. Continued research, improved production methods, and wider regulatory acceptance are expected to further expand their role in modern healthcare.

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Chapter 3

Dendrimers: A New Class of Nanopolymers

Vinisha.S[a], Sudhakar.A[a], Monisha. J[b]*

[a]*School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Dendrimers are nanosized, radially symmetrical molecules that possess a well-defined, uniform, and monodisperse structure. They generally consist of a central core, an inner branching layer, and an outer functional surface. Traditional macromolecular architectures often produce polydisperse molecules with different molecular weights, whereas dendrimers provide a more controlled structure. Various types of dendrimers have been developed, exhibiting biological properties such as polyvalency, self-assembly, electrostatic interactions, chemical stability, low cytotoxicity, and good solubility. Due to these unique properties, dendrimers have gained significant attention in the medical field. This review highlights the different applications of dendrimers in medicine and drug delivery.

Keywords: Dendrimers, polydisperse, solubility, medicine, drug delivery.

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1. Introduction

Dendrimers are nanosized, highly branched macromolecules that possess a well-defined and uniform structure. They consist of a central core, repetitive branching units forming the interior layers, and multiple functional groups on the outer surface. Because of their controlled architecture and monodisperse nature, dendrimers exhibit unique physicochemical and biological properties.

The concept of dendrimers was first introduced by Fritz Vogtle in 1978. Later, Donald Tomalia and his co-workers developed these molecules further in the early 1980s. Around the same time, George R. Newkome independently synthesized similar structures called “arborols,” meaning tree-like molecules.

Dendrimers are characterized by their symmetrical branching pattern, high number of surface functional groups, and compact molecular structure. These molecules show important properties such as polyvalency, self-assembly, electrostatic interactions, good solubility, and relatively low cytotoxicity. Because of these unique features, dendrimers have attracted significant attention in many scientific fields, especially in drug delivery, diagnostic imaging, and anticancer therapy.

As the dendrimer generation increases, their size and molecular weight also increase, resulting in a more globule structure. Due to their tunable size, surface functionality, and ability to interact with biological systems, dendrimers are considered promising nanoscale carriers for various biomedical and pharmaceutical applications.

1.1 Types of dendrimers

It includes structures with phenylacetylene subunits where third-generation branches may occupy the same space and fourth-

generation layers can overlap with second-generation layers. Another type is parquette-type dendrons, which are chiral and non-racemic molecules that exhibit intramolecular folding mainly driven by hydrogen bonding interactions.

2. Structure and Chemistry

Dendrimers are highly branched molecules that start with a central atom or group called the core. From this core, branches known as dendrons grow outward through repeated chemical reactions. Their structure is still discussed by researchers, especially whether dendrimers remain fully extended with dense outer surfaces or fold inward forming a compact interior. Unlike many linear polymers, dendrimers can be synthesized with high structural control, producing nearly uniform, globular macromolecules with many surface functional groups. Examples include repeat units such as 1,3-diphenylacetylene, developed by Moore. Dendrimers are a new class of polymeric materials and represent a rapidly developing area in modern chemistry. Dendrimer chemistry has its own specific terms and abbreviations used to describe structural features and reactions occurring on the dendrimer surface. Dendrigrafts are a type of dendritic polymer similar to dendrimers and can be synthesized with a well-defined, nearly monodisperse molecular structure. Due to their unique branched architecture, dendrimers provide excellent opportunities for host–guest interactions and multivalent binding. One of their earliest proposed uses was as container molecules, where small compounds can be trapped within internal cavities. Studies have also shown that dendrimers can exhibit unimolecular micelle-like behavior, similar to hyperbranched polymers.

2.1 Synthesis

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Dendrimers represent a link between molecular chemistry and polymer chemistry. They are synthesized through a controlled step-by-step process similar to molecular chemistry, while their repetitive monomer units relate them to polymer chemistry. Unlike traditional macromolecules such as linear, cross-linked, and branched polymers that often produce polydisperse products, dendrimers can be synthesized as monodisperse and well-defined structures similar to biological macromolecules. Dendrimers are mainly prepared by two methods: divergent synthesis and convergent synthesis. In these methods, dendrimers grow outward from a multifunctional core. The core reacts with monomers containing one active and two protected groups to form the first-generation dendrimer, and further reactions with additional monomers produce higher generations.

3. Properties

3.1 Pharmacokinetic Properties

Pharmacokinetic properties are important for the successful biomedical use of dendrimers. They influence applications such as drug delivery, imaging, photodynamic therapy, and neutron capture therapy. Dendrimers can be modified at their surface groups to form conjugates such as antibody–dendrimer and peptide–dendrimer complexes. They can also form dendritic boxes that encapsulate guest molecules, increasing their usefulness in medical applications.

3.2 Covalent Conjugation Strategies

Covalent conjugation is a method used to attach small drug molecules to polymeric carriers in order to improve their pharmacological properties. In many cases, dendrimers act as prodrugs, where the drug is linked to the dendrimer structure and released after entering the target cell. This controlled release helps

improve drug activity and therapeutic effectiveness.

3.3 Polyvalency

Polyvalency is an important property of dendrimers that allows multiple functional groups to be attached to their surface. This feature enables strong and multiple interactions with biological receptors. Such multivalent interactions are especially useful in designing antiviral drugs and other therapeutic agents.

3.4 Self-Assembling Dendrimers

Self-assembly is the spontaneous and organized association of molecules through specific intermolecular forces. Dendrimers have attracted attention in this field because they contain three structural components: a central core, branched units, and surface end groups. These features allow different strategies for dendrimer self-assembly. One approach involves designing dendrons with core units capable of recognizing each other, leading to the spontaneous formation of dendrimer structures. Self-assembling dendrimers based on pseudorotaxane interactions have also been reported.

3.5 Electrostatic Interactions

Electrostatic interactions occur due to the presence of many identical functional groups on the surface of dendrimers. When these surface groups carry charges, the dendrimer behaves like a polyelectrolyte and can attract oppositely charged molecules through electrostatic forces. Examples include the aggregation of methylene blue on the dendrimer surface and the binding of charged species such as copper complexes and nitroxide cation radicals used in EPR studies.

4. Application of Dendrimers

Dendrimers have many important applications in medicine and

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pharmaceutical sciences due to their unique structure and high functionality.

4.1 Biomedical Applications

Dendrimers are widely used in the biomedical field because their structure is similar to biological molecules such as proteins and enzymes. Drugs and other molecules can be attached to the surface of dendrimers or encapsulated inside their internal cavities. They are also studied as potential blood substitutes.

4.2 Anticancer Drug Delivery

Dendrimers are promising carriers for anticancer drugs. They improve drug properties such as solubility, stability, and circulation time in the body. Drug–dendrimer conjugates can accumulate selectively in tumor tissues through the enhanced permeability and retention (EPR) effect, reducing toxicity to normal cells.

4.3 Drug Delivery Systems

Dendrimers can act as molecular containers that carry drug molecules inside their internal spaces. Their host–guest properties allow drugs to bind with dendrimers and be delivered effectively to target sites in the body.

4.4 Transdermal Drug Delivery

Dendrimers help improve the penetration of drugs through the skin. They are particularly useful for hydrophobic drugs with poor water solubility and help maintain therapeutic drug levels for a longer period.

4.5 Gene Delivery

Dendrimers are used as carriers for delivering DNA or genetic material into cells. They protect DNA from degradation and help in

efficient gene transfer, making them useful in gene therapy research.

4.6 Magnetic Resonance Imaging (MRI) Contrast Agents

Dendrimer-based metal complexes are used as contrast agents in MRI because their structure allows multiple imaging molecules to be attached, improving imaging quality.

4.7 Dendritic Sensors

Dendrimers can function as chemical sensors due to the large number of functional groups on their surface. These groups can interact with metal ions or other molecules, producing detectable signals such as fluorescence.

4.8 Enhancement of Drug Solubility

PAMAM dendrimers are widely used to improve the solubility of poorly soluble drugs. Their hydrophilic surface and internal cavities give them a unimolecular micelle-like structure. Because of this property, dendrimer-based nanocarriers can increase drug solubility and improve oral bioavailability, especially for drugs with low water solubility or those affected by efflux transporters.

4.9 Photodynamic Therapy (PDT)

Photodynamic therapy involves the activation of a photosensitizing drug using visible or near-infrared light. This activation produces reactive singlet oxygen that can destroy tumor cells through necrosis or apoptosis. Dendrimers are used as carriers for PDT agents to improve tumor targeting, drug retention, and pharmacokinetic properties.

4.10 Miscellaneous Applications

Dendrimers also have several other applications in biological and

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chemical fields. They are used in cellular drug delivery, water purification by removing toxic metal ions and inorganic contaminants, and in cosmetic products. In addition, dendrimers are applied in highly sensitive analytical devices, MRI contrast agents, prion research, burn treatment, and EPR imaging.

5. Conclusion

Dendrimers are unique macromolecules with well-defined structures, numerous surface functional groups, and compact architecture. These properties make them promising candidates for many applications, especially in medicine and drug delivery systems. Since their discovery, research on dendrimers has grown rapidly, focusing on their synthesis, properties, and potential uses. Although significant progress has been made, the multistep synthesis process of dendrimers is still complex and requires considerable effort. Further research may improve their synthesis methods and expand their practical applications in various scientific fields.

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Chapter 4

Development and Technology of mRNa Vaccines and Therapeutics beyond COVID-19

Vishnupriya.S[a], Nithyasri.K[a*], J.Monisha[b*]

[a]*School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

This study is based on the application of mRNA vaccines for the treatment of various infectious diseases and different cancer types. An mRNA vaccine is a new type of vaccine that introduces cells into the human body that produce harmless protein to trigger the immune system to develop immunity-producing antibodies against antigens. These vaccines were developed after the global outbreak of COVID-19. This significantly helped the scientists to invent vaccines in a short period of time compared to the traditional vaccines. The main role is to reduce the death rate by controlling the spread of disease. In the case of cancer, mRNA vaccines help the immune system to recognize and destroy the cancer cells by producing the tumor-specific antigens. In order to create targeted mRNA technology, including its applications in vaccines, immunotherapies, protein replacement therapy, and genome editing as well as its distribution to particular cell types and organs.

Currently researchers are in their role to treat lung cancer, breast

cancer, and so on by providing personalized treatments. Since the mRNA vaccines do not contain live pathogens, they are safer to use and offer a promising future for cancer treatment.

Keywords: *mRNA vaccines, immunogenicity, antibodies, COVID-19, cancer immunotherapy.*

1. Introduction

The covid-19 pandemic was noted as a significant development of mRNA vaccines Moderna and Pfizer-BioNTech, which are major public health threats. The challenges in the distribution of COVID-19-based vaccines have most supplies in high-income countries, whereas low- and middle-income countries have the least access to them. The manufacturing capacity for future mRNA vaccines and therapeutics (e.g., human immunodeficiency virus, TB, dengue) and using local production of new lipids, enzymes, and other reagents. The mRNA technology also provides a novel approach to treat both communicable and non-communicable diseases as well as immune-related and non-immune diseases. Diseases like cancers, diabetes, and cardiovascular and respiratory conditions are experiencing an epidemiological transition. This mainly focuses on a comprehensive mRNA-based vaccine and its therapeutic use in clinical development in which it is part of the WHO-MPP mRNA technology transfer program.

1.1 History and Development of mRNA Vaccination

mRNA, which is known as a messenger of RNA, acts as a messenger by carrying the genetic information from DNA to ribosomes, where the proteins are synthesized. It was first discovered by Sydney Brenner, François Jacob, and Matthew Meselson in 1961.

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This mRNA made a tremendous change in our current lifestyle. Besides the disadvantages like instability of mRNA molecules, rapid degradation by the enzyme, and difficulty in delivery, it is one of the most promising innovations in modern biotechnology.

In 1990, it was proved by the scientist that the prepared synthetic RNA could be injected into the mouse muscle cells to produce proteins. Hence, mRNA could be used to instruct cells to make specific proteins inside the body.

During 2005, scientists Katalin Karikó and Drew Weissman discovered that changing the nucleoside in the messenger RNA reduces the immune reactions by preventing the immune system from recognizing the mRNA as a foreign invader. Our immune system uses PRRs, which are known as pattern recognition receptors, like TLR3, TLR7, and TLR8 (Toll-like receptors). These receptors play an important role in detecting the foreign RNA, e.g., viruses. They recognize unmethylated single-stranded or double-stranded RNA. After modifying it with N1-methyl pseudouridine or pseudouridine, the modified bases look similar to those that are present in mammalian RNA. Therefore, it allows them to bypass the detection by these pattern recognition receptors. This innovation made mRNA safer and more effective for medical use.

1.2 Later Technologies

Scientists developed LNP, which is known as Lipid Nanoparticle Technology. They are critical, versatile drug delivery systems.

mRNA vaccines: The covid-19 mRNA vaccines were only possible due to LNP technology. They improve therapeutic efficacy.

2. mRNA DEVELOPMENT BEYOND COVID-19

mRNA vaccine technology utilizing lipid nanoparticles for delivery is expanding rapidly beyond Covid-19. Allowing for rapid development of vaccines and therapeutics for both communicable and non-communicable diseases.

2.1 Cancer immunotherapy

Previous research focused on using mRNA to trigger the immune response against tumors. Current research is based on the personalized vaccines that target specific neoantigens in a patient's tumor. Instead of directly killing the tumor cells, these vaccines stimulate the immune system to recognize and destroy the cancer cells.

2.2 Mechanism involves

An mRNA cancer vaccine contains messenger RNA encoding tumor-associated antigens and is administered into the body. After administration, the mRNA enters the body cells and instructs them to produce the tumor antigen. This activates T-cells (T-lymphocytes), which are white blood cells of the immune system that mature in the thymus and protect the body from pathogens and cancer.

Activation: They are activated in the second lymphoid organs, like lymph nodes, where they encounter specific antigens presented by other immune cells, like dendritic cells. Activated T-cells recognize and destroy the cells by expressing the same antigen.

Merits of mRNA vaccines in cancer immunotherapy include the following:

- They are capable of personalized cancer treatment based on the

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patients.

- Highly specific targeting of tumor antigens
- These vaccines are noninfectious because no live viruses were used and are therefore safe to use.
- Well known for their ability to produce a strong immune response.
- They can be rapidly designed and manufactured
- Demerits of mRNA vaccines in cancer immunotherapy include the following:
- They are expensive for personalized vaccines
- They are still under clinical research for many cancers.

Companies like Moderna and BioNtech are currently working on personalized mRNA cancer vaccines by conducting clinical trials

3. Applications Beyond COVID-19

- It has been proven that it is effective in treating cancer and infectious disease.
- The therapeutic as well as the preventive roles of mRNA technology have been used in the treatment of infectious diseases.
- mRNA vaccines have several applications for various human infectious diseases caused by pathogens such as arboviruses (dengue and chikungunya), HIV, and rabies.

3.1 Advantages of Mrna Vaccines

- The main advantage of mRNA vaccines is the speed at which the vaccines can be designed and manufactured in response

to pathogens.

- mRNA vaccines are developed in the lab by synthesizing an infectious disease virus's genetic material by testing and manufacturing the newly discovered infectious disease.
- In Phase III trials the Pfizer-BioNTech (BNT162b2) and Moderna (mRNA1273) vaccines were more than 90% Effective in preventing symptomatic COVID-19
- According to efficacy, mRNA vaccines have cellular immune responses, and they are very strong against infectious diseases, cancer, and autoimmune disorders.
- Another benefit of mRNA technology is personalized cancer vaccines. Tumors have mutagens or neoantigens that can be targeted with mRNA vaccines, and the immune system destroys the cancer cells without affecting the normal cells.

3.2 Limitations of Mrna Vaccines

- The ultra-cold storage has only been distributed in limited regions because of its high cost.
- Innovative methods such as lyophilized (freeze-dried) formulations or thermostable LNPS are active to defeat this barrier.
- The unstable mRNA should be stored in extremely cold conditions to prevent its degradation. The Pfizer-BioNTech COVID-19 vaccine was to be stored at -70°C (-94°F), while the modern vaccine was to be stored at -20°C (-4°F).
- In low-income countries, the cold chain storage was not available, leading to a lack of vaccines.

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- In clinical trials, the mRNA has mild to moderate side effects such as infection
- site pain, fatigue, and headache and a serious reaction like anaphylaxis in rare conditions.
- mRNA vaccines are costly. So if they are not distributed in low-income countries, it will lead to a lack of distribution of vaccines.

3.3 Other Major Applications of mRNA Vaccines Includes

3.3.1 Cardiovascular Technology

mRNA is emerging as a therapeutic approach for cardiovascular disease by delivering genetic instructions to cells to promote tissue repair and reduce fibrosis. The current research aims to treat myocardial infarction, which is a heart attack, and heart failure and ischemia. The process includes lipid nanoparticles delivering mRNA directly to cardiomyocytes to treat conditions like heart failure.

3.3.2 Genetic Disorder

- mRNA therapy treats the genetic disorder by delivering the synthetically modified mRNA through LNP cells.
- mRNA acts as a blueprint and instruction to create necessary proteins and address the disease caused by protein deficiencies.
- It focuses on the rare metabolic disorders, e.g., methylmalonic acidemia and Fabry disease.

3.3.3 Methylmalonic acidemia

It is a rare inherited metabolic disorder characterized by the body's inability to properly break down certain proteins and fats, causing

toxic methyl malonic acid to accumulate in the blood and tissues.

4. Fabry Disease

It is a rare, x-linked genetic lysosomal storage disorder caused by a deficiency of the alpha-galactosidase enzyme.

4.1 Infectious disease

mRNA vaccines are being developed to protect against several infectious diseases like influenza, malaria, and meningitis.

4.2 Autoimmune diseases

- mRNA plays an important role in autoimmune disease.
- Patients with autoimmune inflammatory rheumatic diseases are at high risk for infections and can use mRNA vaccines, which have high efficacy.

5. Structure and Components of mRNA Vaccines

- The structure of the mRNA vaccine mainly focuses on delivering the genetic information safely into the cells so that they will be able to produce the specific antigens in the immune system to stimulate an immune response.
- mRNA being a nucleic acid (polymer of nucleotides). It consists of a ribose sugar, a phosphate group, and a nitrogenous base like adenine, uracil, guanine, and cytosine.
- mRNA (Messenger RNA): It is the major and an important active component of the vaccine, which is responsible for protein synthesis inside the human body.
- It contains genetic instructions for producing a viral antigen protein. Eg: spike protein, which is responsible for covid-19.
- It consist of a 5' cap, 5' UTR, coding region, 3' UTR, and 3'

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poly(A). Tail.

5'cap

7-methyl guanosine is added to the 5' end and protects it from degradation by exonuclease and assists in ribosome binding.

5'UTR

Which is a 5' untranslated region. It is a region between the 5' cap and the start codon that regulates translation and stability.

Translation : It is the process of carrying the genetic information from DNA to ribosomes for protein synthesis.

Coding region: The coding regions are composed of codons, which will be coding for the specific amino acid. It starts with a start codon (AUG) and ends with a stop codon (UAA, UAG, or UGA).

3'UTR (untranslated region): This region is located after the stop codon. They act as binding sites for proteins and microRNAs that dictate when, where, and how much protein is produced from a transcription.

Poly(A) Tail: A string of 50-250 adenine nucleotides added to the 3' end that protects the molecule from degradation and increases the translation process efficiently.

6. Conclusion

Based on the above study, it is proved that mRNA plays a significant role in the current medical technology. They provide a safe, efficient, and rapid method for preventing various diseases. From the outbreak of Covid-19 and still now, it has been useful in various ways for the treatment of infectious disease, genetic disorder, and autoimmune disorder.

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Chapter 5

Liposomes: A Novel Drug Delivery System

Parvath S[a], Santhosh S[a], J.Monisha[b*]

[a]*School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, SPS, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Liposomes are microscopic vesicular structures composed mainly of phospholipids and cholesterol that form bilayer membranes similar to those found in biological cells. These vesicles are widely used as carriers for drug delivery in pharmaceutical research because of their ability to encapsulate both hydrophilic and lipophilic drugs. Liposomes protect the incorporated drug molecules from degradation and enhance their stability in biological environments. They also improve the therapeutic efficiency of drugs by delivering them to specific tissues or organs while minimizing harmful side effects. Due to their biocompatibility, biodegradability, and versatility, liposomes are considered an important component of modern drug delivery systems. They can be administered through different routes, including oral, topical, intravenous, nasal, ocular, and transdermal routes. Liposomal formulations are widely used in the treatment of cancer, infections, and other diseases. In addition, liposomes are used in vaccine development, gene delivery, and cosmetic formulations. The development of liposomal drug delivery systems has significantly improved the effectiveness and safety of many

pharmaceutical products.

Keywords: *Liposomes, Drug Delivery, Phospholipids, Cholesterol, Vesicles, Targeted Therapy.*

1. Introduction

Liposomes are small spherical vesicles consisting of lipid bilayers that closely resemble biological cell membranes. These vesicles are primarily composed of phospholipids and cholesterol, which arrange themselves into bilayer structures when placed in an aqueous environment. Liposomes are capable of encapsulating therapeutic agents and delivering them to specific sites within the body.

The concept of liposomes was first introduced in the 1960s during studies on biological membranes. Since then, liposomes have gained great importance in pharmaceutical research as efficient drug carriers. Their ability to protect drugs from enzymatic degradation and deliver them directly to target tissues makes them valuable in modern drug delivery systems.

1.1 Components of drug delivery system

Liposomes are formed by several lipid components that contribute to the structure and stability of the vesicles.

1.1.1 Phospholipids

Phospholipids are the main structural components of liposomes. They are amphiphilic molecules containing a hydrophilic head and hydrophobic fatty acid chains. When placed in water, these molecules arrange themselves into bilayer structures, forming closed vesicles. Common phospholipids used in liposome preparation include:

- Phosphatidylcholine

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- Phosphatidylethanolamine
- Dipalmitoyl phosphatidylcholine
- Distearoyl phosphatidylethanolamine
- Dioleoyl phosphatidylethanolamine

These phospholipids provide the basic membrane structure for liposomes.

1.1.2 Cholesterol

Cholesterol is an important component in liposomal formulations. It stabilizes the lipid bilayer and reduces the permeability of the membrane. By increasing membrane rigidity, cholesterol helps prevent leakage of the encapsulated drug.

1.1.3 Sphingolipids

Sphingolipids contain a sphingosine backbone and contribute to membrane stability and surface charge. Examples include sphingomyelin and glycosphingolipids.

1.1.4 Additional Substances

Other substances may be added to improve liposome performance, such as surfactants, charged lipids, and stabilizing agents. These components help enhance drug loading, stability, and delivery efficiency

2. Mechanism of Drug Delivery

Liposomes deliver drugs through different mechanisms, including adsorption to the cell surface, fusion with cell membranes, endocytosis by cells, and direct release of the encapsulated drug at the target site. These mechanisms help improve drug Targeting and controlled drug release

2.1 Classification

Liposomes are classified based on their size, number of bilayers, and composition.

Based on Structure

Multilamellar Vesicles (MLV)

These liposomes consist of several lipid bilayers arranged concentrically like an onion. Their size typically ranges from 500 nm to 10,000 nm.

Small Unilamellar Vesicles (SUV)

These vesicles have a single lipid bilayer and are usually smaller than 100 nm in diameter.

Large Unilamellar Vesicles (LUV)

These liposomes also have a single bilayer but are larger in size compared to SUVs.

Giant Vesicles

These are extremely large liposomes that may reach sizes up to several micrometers.

Based on Function

Liposomes may also be classified according to their function and composition:

- Conventional liposomes
- Cationic liposomes
- Stealth liposomes
- Targeted liposomes

Each type has specific applications in drug delivery and therapeutic treatments.

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3. Methodology

Liposomes are prepared using various techniques such as thin-film hydration, reverse-phase evaporation, and sonication methods. These methods help in forming vesicles capable of encapsulating both hydrophilic and lipophilic drugs.

4. Conclusion

Liposomes are highly effective carriers for drug delivery in modern pharmaceutical science. Their bilayer membrane structure allows them to encapsulate a wide range of drugs and protect them from degradation. Liposomes improve drug stability, enhance therapeutic effectiveness, and reduce unwanted side effects. They are widely used in cancer therapy, gene delivery, vaccines, and cosmetic formulations. Although certain challenges such as cost and stability remain, ongoing research continues to improve liposomal technology. With further advancements, liposomes are expected to play an even greater role in the development of safe and effective drug delivery systems.

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Chapter 6

Advances in Novel Drug Delivery Systems: Mechanisms, Applications and Commercial Aspects

S.Jayakumari[a], Sharon Peniel.S[b], Vaishnavi.K[b], J.Monisha[c*]

[a]*Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Pallavaram, Chennai.*

[b] *School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[c] *Assistant Professor, Department of Pharmaceutics, SPS, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

The novel drug delivery system is an advanced technology or formulation approach designed to transport pharmaceutical compounds into the body more safely and effectively than conventional methods (like tablets or injections). Key goals include controlling the rate of release, improving drug targeting to specific tissues, and enhancing bioavailability. The performance of an existing medicinal molecule in terms of patient compliance, safety, and efficacy can be greatly enhanced by evolving it from a traditional form to a unique delivery mechanism. An old medication molecule can be given new life as a novel drug delivery system. The limitations of the conventional drug delivery methods are addressed by the innovative drug delivery system, which is a novel method of drug administration. A significant improvement in the ability to release a drug at a specified

spot and rate is possible with a novel drug delivery system that is properly developed. Pharmaceutical companies are working to create novel drug delivery systems in order to give medications to patients effectively and with fewer side effects. NDDS include carrier-based systems such as liposomes, nanoparticles, microspheres, niosomes, solid lipid nanoparticles, and polymeric systems, as well as non-carrier-based approaches. The integration of nanotechnology and controlled-release strategies has significantly enhanced therapeutic efficacy while reducing toxicity and side effects. This review highlights the principles, advantages, disadvantages, approaches, and applications of novel drug delivery systems, emphasizing their role in modern pharmaceutical research and future therapeutic development.

Keywords: *Pharmaceutical companies, Pharmacokinetics, Nanoparticles, Bioavailability, Phytopharmaceutical.*

1. Introduction

A herbal formulation is a dosage form that contains one or more raw or processed herbs in specified quantities to offer particular health, nutritional, or cosmetic benefits. Plant parts, whole plants, or broken or chopped plants are subjected to processes including distillation, extraction, expression, fractionation, purification, concentration, or fermentation to create herbal medicines. These consist of separated or tinctured botanical resources, processed exudates, expressed juices, and necessary oils. The efficacy of a medication can be significantly impacted by the way it is administered. Certain medications have an ideal concentration range where the greatest therapeutic benefit can be obtained; dosages above or below this range may be hazardous or have no effect at all. Conversely, the

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sluggish advancement in the effectiveness of treating severe diseases has indicated an increasing demand for a multidisciplinary strategy in delivering medicines to targets within tissues. This led to the development of novel concepts for managing the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and effectiveness of pharmaceuticals. These innovative tactics, which go by the name "drug delivery systems" (DDS), are founded on multidisciplinary methods that bring together molecular biology, pharmaceutics, polymer science, and bioconjugate chemistry. The process of delivering a medication to a patient in a way that raises the drug's concentrations in the body and boosts its therapeutic efficacy is known as novel drug delivery. Prolonged, localized, targeted, and protected therapeutic interactions with sick tissues are the goals of targeted drug delivery. Compared to the targeted drug release system, which releases the medication in the dose form, traditional drug delivery involves the drug being absorbed across a biological membrane. The benefits of a targeted release system involve reducing a patient's dosage, improving the medication's therapeutic impact gradually, eliminating adverse effects, and minimizing variations in the drug's level in circulation. NDDS is the advanced technique and new dosage form, which is far better than the conventional dosage form. Researchers have recognized for more than 20 years the potential advantages of nanotechnology in offering significant advancements in medication delivery and targeting. Patients stand to gain greatly through improved delivery methods that reduce toxicity and increase efficacy, and this also creates new opportunities for pharmaceutical and medication delivery businesses.

2. Classification

Carrier-Based/Particulate Systems (Nanotechnology)

These use sub-micron particles to encapsulate drugs for targeted or sustained release.

Liposomes & Niosomes: Phospholipid or surfactant vesicles for delivering hydrophobic/hydrophilic drugs.

Nanoparticles & Nanocapsules: Polymeric or solid lipid nanoparticles that enhance bioavailability.

Dendrimers: Branched polymers for targeted drug delivery.

Carbon Nanotubes: Used for high-capacity drug loading and, in some cases, imaging.

Controlled/Sustained Release Systems

Osmotic Pumps: Use osmotic pressure to release drugs at a constant rate.

Diffusion-Controlled Systems: Include reservoir and matrix systems that use polymers to regulate release.

Implantable Devices: Provide long-term, localized drug action, such as subcutaneous implants.

Targeted Delivery Systems

Active Targeting: Uses ligands to target specific cells or receptors.

Passive Targeting: Relies on the Enhanced Permeability and Retention (EPR) effect in tumors.

Antibody-Drug Conjugates (ADCs): Delivers toxic agents specifically to cancer cells.

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Route-Specific Systems

Transdermal Drug Delivery Systems (TDDS): Patches that deliver drugs through the skin, avoiding first-pass metabolism.

Gastroretentive Systems: Designed to remain in the stomach for extended periods.

Naso-pulmonary Systems: Targeted to the nose or lungs for systemic or local action.

3. Mechanism and approaches

Mechanism

Diffusion-Controlled System: Drug release is governed by the diffusion of the active agent through a rate-controlling membrane or matrix (e.g., reservoir or matrix systems). Dissolution-Controlled System: The drug is coated or embedded in a material with a slow dissolution rate, limiting the drug's availability for absorption. Osmotic Pump System (Osmotically Controlled): Utilizes osmotic pressure to drive the drug through a laser-drilled orifice at a constant rate.

Erosion-Controlled System: The carrier matrix erodes over time due to enzymatic or hydrolysis reactions, releasing the drug. Targeted/Carrier-Mediated Mechanism: Uses nanocarriers to deliver drugs specifically to tissues or cells, such as through ligand-mediated targeting (targeting receptors on specific cells) or passive accumulation in tumor tissues.

4. Approaches in Novel Drug Delivery Systems

These strategies are categorized by their technology or route of administration:

Nanotechnology-Based Systems: Includes liposomes, nanoparticles,

solid lipid nanoparticles, dendrimers, and niosomes, which improve drug solubility, stability, and cellular uptake. Targeted Drug **Delivery Systems**

First-order: Passive targeting to specific organs or capillary beds.

Second-order: Targeting specific cell types (e.g., cancer cells).

Third-order: Targeting specific intracellular organelles.

Controlled and Sustained Release Systems: Systems designed to provide a steady-state plasma concentration over an extended period, reducing the need for frequent dosing. Site-Specific Systems: E.g., Floating Drug Delivery Systems (FDDS) for gastric retention or transdermal patches for systemic delivery via the skin.

Pharmaceutical application and evaluation

Targeted Drug Delivery: Uses carriers like liposomes, nanoparticles, and micelles to deliver drugs specifically to affected tissues (e.g., tumor sites), minimizing systemic toxicity.

Controlled and Sustained Release: Modulates the release of medication over time to maintain optimal drug levels, improving bioavailability.

Enhanced Solubility: Improves the bioavailability of poorly water-soluble drugs.

Specific Examples

Liposomes: Used for targeted delivery to minimize side effects.

Solid Lipid Nanoparticles (SLN): Used to enhance bioavailability and increase tissue concentration for drugs, such as in the treatment of diseases.

Hydrogels: Utilize three-dimensional networks for prolonged drug

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release.

Multiarticulate systems are employed to reduce risks like dose dumping.

Mouth-Dissolving Films: Improve patient compliance.

5. Evaluation Techniques for NDDS

Physicochemical Characterization: Drug Entrapment Efficiency: Measures the amount of drug successfully loaded into the carrier.

Particle Size and Zeta Potential: Evaluates the stability and distribution of particles.

Morphology: Uses Scanning Electron Microscopy (SEM) for surface analysis.

In Vitro Release Studies: Studies the drug release profile under controlled conditions.

Stability Studies: Assesses the shelf-life and stability of the formulation.

6. Regulatory and commercial aspects

Regulatory Aspects

Safety and Efficacy Assessment: Comprehensive, often more challenging, assessments are required to evaluate the safety of novel materials (biocompatibility, long-term toxicity).

Quality-by-Design (QbD): Regulators emphasize QbD principles (ICH Q8 and Q9) to ensure that the manufacturing process is robust and reproducible and that the product maintains consistent quality.

Characterization: Detailed physicochemical characterization (particle size, charge, surface functionalization) is mandatory.

Safety Considerations: Key concerns include immunogenicity,

biodegradation, and accumulation in non-target organs (e.g., liver/spleen).

Commercial Aspects

Manufacturing and Scalability: A critical challenge is scaling up production from lab-scale to industrial levels while maintaining particle uniformity and sterility.

High Development Costs: The complexity of NDDS, including specialized excipients and sophisticated manufacturing, often leads to high R&D and production costs.

Market Drivers: Increased patient compliance (reduced dosage frequency), better targeting (especially in cancer therapy), and the ability to deliver challenging biologics (e.g., mRNA, siRNA) are key commercial drivers.

Intellectual Property (IP): Patenting specific formulations, drug-carrier combinations, or manufacturing techniques is essential to protect investment.

7. Conclusion

Novel Drug Delivery Systems (NDDS) represent a transformative advancement in pharmaceutical science, designed to overcome the limitations of conventional dosage forms such as low solubility, poor bioavailability, and lack of site specificity. By utilizing advanced nanotechnology, biotechnology, and material sciences, these systems improve therapeutic outcomes and patient compliance. International Journal of Pharmaceutical Sciences. International Journal of Pharmaceutical Science Core Benefits: NDDS, including liposomes, nanoparticles, micelles, and hydrogels, provide controlled, sustained, and targeted release of therapeutic agents, enhancing solubility and

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drug stability while minimizing toxic side effects. Technological Advancements: The integration of smart, stimuli-responsive (pH, temperature, magnetic), and AI-assisted systems enables more precise, site-specific, and personalized treatments, particularly for chronic diseases and cancer. Key Challenges: Despite their potential, NDDS face hurdles regarding high manufacturing costs, complex formulation processes, scalability, regulatory approvals, and long-term toxicity concerns. Future Outlook: The future of NDDS lies in improving the biocompatibility, biodegradability, and targeting accuracy of carriers. Continued interdisciplinary research is crucial to transitioning from laboratory findings to commercial, patient-accessible therapies.

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Chapter 7

Oral Noisome and Proniosomes: Mechanistic Insights, Formulation Strategies, and Therapeutic Applications in Enhancing Bioavailability and Targeted Drug Delivery

Theyshnee. S[a], Monisha. J[b*]

[a] *Department of Pharmaceutics, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, SPS, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Oral drug delivery is still the easiest and most popular way to take medicine, but it comes with a lot of problems. Some drugs just don't dissolve well in water, or they can't pass through the gut easily. Others break down because of enzymes or get wiped out by first-pass metabolism, so the body barely absorbs them, and they don't work as well as they should. That's where vesicular systems like liposomes and their dry forms, proniosomes, come in. These carriers, made from non-ionic surfactants and cholesterol, protect drugs from breaking down in the digestive tract and let the medicine release slowly over time. How you put these together really matters. Things like the type of surfactant, how much cholesterol you use, the size of the vesicles, and their surface charge—all these affect how much of the drug gets into your system and how quickly. Modifying the surface, say by adding PEG or coating with chitosan, helps the drug stick to mucosal surfaces, improves how well it passes through, and makes it tougher

against enzymes. Drugs get absorbed better thanks to things like increased endocytosis, tweaks to tight junctions, and transport through the lymphatic system. This review digs into how these vesicular systems are designed, how they help drugs get absorbed, what you need to look for when testing them, and what it takes to actually use them in real-world treatments.

Keywords: Niosomes, proniosomes, oral bioavailability, vesicular drug delivery, lymphatic transport.

1. Introduction

Oral delivery is the most common route but faces challenges like poor solubility, enzymatic breakdown, and first-pass metabolism. Vesicular carriers such as niosomes and proniosomes help overcome these issues by protecting drugs, controlling release, and enhancing gut absorption. Niosomes are vesicles made from non-ionic surfactants and cholesterol, capable of carrying both hydrophilic and lipophilic drugs. Proniosomes are dry powders that easily convert to niosomes upon hydration, offering better handling and stability. Both systems are cost-effective, safe, and improve oral bioavailability. These carriers are especially useful for drugs treating neurological disorders, cancer, and infections. For example, chlorpromazine and trifluoperazine delivered via vesicular gels or nanocarriers avoid first-pass metabolism, stay longer in circulation, and show enhanced therapeutic effects. Factors like surfactant type, particle size, and surface charge affect absorption and guide formulation design. Overall, niosomes and proniosomes are transforming oral drug delivery, making treatments more effective and patient-friendly.

2. Methods and Mechanisms

Niosomes and proniosomes enhance oral drug delivery by protecting

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drugs from gut enzymes and improving absorption through the intestinal wall. Vesicle size, surfactant type, and charge influence uptake via endocytosis, tight junction modulation, or lymphatic transport. Proniosomes are stable powders or gels that convert to niosomes on hydration, making them easier to store and handle. Niosomes are typically prepared by thin-film hydration, while proniosomes use slurry, spray-coating, or freeze-drying. Optimization tools like factorial design help control vesicle size, drug entrapment, and release rate. Characterization includes DLS for size and PDI, zeta potential for stability, TEM for morphology, and in vitro/ex vivo methods (Franz diffusion, dialysis, or tissue studies) for drug release and absorption. These vesicles improve oral bioavailability by enhancing solubility, protecting drugs from enzymes, facilitating cellular uptake, opening tight junctions, enabling lymphatic transport, and inhibiting P-glycoprotein efflux. Pharmacokinetic studies consistently show higher AUC, Cmax, and Tmax. Safety: Non-ionic surfactants are generally safe, but long-term toxicity, especially with chronic use, requires more study. Regulatory Challenges: Lack of standardized tests, variable manufacturing methods, and incomplete toxicology data slow clinical translation. In mental health treatments, such as chlorpromazine and trifluoperazine delivery, these systems bypass first-pass metabolism and maintain steady drug levels, highlighting their potential for chronic therapies.

3. Formulation strategies

Choosing the right components is key: surfactant type and HLB influence bilayer packing, phase transition, and drug entrapment, while cholesterol controls membrane rigidity and release. Edge activators (e.g., Tween-80) improve flexibility in transferosomes, and

polymers like chitosan, HPMC, or Carbopol enhance mucoadhesion or gel formation. Common preparation methods include thin-film hydration for niosomes/transferosomes and slurry, coacervation, spray-coating, or spray-drying for proniosomal powders, with freeze-drying plus cryoprotectants improving stability. Optimization uses Design of Experiments (DOE) to fine-tune particle size, drug entrapment, and release, with process factors (solvent, temperature, agitation, and drying) affecting vesicle properties. Surface modifications like polymer coating, PEGylation, or ligands (peptides, folate) enhance mucoadhesion, mucus penetration, and targeted delivery. Vesicles can be incorporated into in-situ gels, nanogels, capsules, or tablets. Characterization involves DLS (size/PDI), zeta potential (stability), TEM/SEM (morphology), ultracentrifugation/gel filtration (entrapment), and in vitro/ex vivo methods (Franz cells, simulated fluids) for release and permeation studies.

4. Therapeutical Application

Psychiatry & CNS: Intranasal niosomal gels deliver drugs like chlorpromazine directly to the brain, bypassing first-pass metabolism. Transdermal or oral nanogels maintain steady levels for drugs like trifluoperazine.

Oncology: Vesicles enhance tumor targeting, improve drug accumulation in cancer tissue, and reduce systemic side effects. Surface ligands enable precise delivery of poorly soluble drugs.

Infectious Diseases: Encapsulation protects antibiotics and antiparasitic drugs from degradation, improves absorption, and makes proniosomal powders ideal for stable oral formulations.

Vaccines & Immunomodulators: Niosomes/proniosomes deliver antigens to immune cells (e.g., Peyer's patches), boosting local and

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systemic immune responses.

Ocular, Nasal, & Topical: Incorporation into gels (Carbopol, HPMC) prolongs drug retention and provides sustained release.

Metabolic & Systemic Drugs: Improve absorption of poorly soluble drugs, bypass first-pass metabolism, and extend drug action.

Practical Notes: Intranasal/transdermal gels suit CNS drugs; oral proniosomes fit unstable or poorly soluble drugs. Promising results exist, but larger clinical trials are needed.

5. Comparative Evaluation

Niosomes and proniosomes improve poorly absorbed drugs by enhancing solubility, protecting them from enzymatic breakdown, and enabling lymphatic uptake, with surfactant type, cholesterol content, particle size, and surface charge influencing pharmacokinetics (AUC, Cmax, and Tmax). Proniosomes, as stable dry powders, outperform liquid niosomal suspensions and can be made via spray-coating or spray-drying, while liquid niosomes require freeze-drying with cryoprotectants. Proniosomes suit oral solids, converting to niosomes in the GI tract, whereas niosomes and transferosomal nanogels are ideal for mucosal or transdermal delivery due to their flexibility and mucoadhesion. Non-ionic surfactants are generally biocompatible, but safety depends on particle characteristics and residual solvents, with long-term CNS studies still needed. Proniosomes scale efficiently using industrial methods, and tools like QbD and DoE help control particle size, encapsulation, and release. In practice, proniosomes are best for stable oral solids, niosomes for hydrophilic and lipophilic drugs, and transferosomal systems for skin or nasal delivery.

6. Challenges

Safety and Long-Term Biocompatibility The long-term behavior of surfactant-based vesicles is not well understood. Possible concerns include toxicity with repeated use, effects on the gut lining and microbiome, and immune reactions. Most studies only evaluate short-term safety. Stability and Product Integrity Liquid niosomal suspensions may undergo fusion, leakage, or chemical degradation during storage. Proniosomes improve stability, but maintaining vesicle structure and drug content after drying and rehydration remains challenging. Manufacturing and scale-up laboratory methods such as thin-film hydration are difficult to scale for industrial production. Techniques like spray-drying, spray-coating, and quality by design (QbD) approaches are required for consistent large-scale manufacturing. Analytical and Standardization Issues There is no standardized method to measure vesicle size, integrity, drug encapsulation, leakage, or in-body behavior, making it difficult to compare studies and obtain regulatory approval. Clinical and Regulatory Challenges Most current evidence comes from animal studies or small pharmacokinetic trials. Larger clinical studies and clearer regulatory guidelines are needed for broader clinical use.

7. Future Directions

Standardized Characterization Consistent testing methods such as DLS, cryo-TEM, encapsulation efficiency tests, gut stability assays, and in vitro–in vivo correlation models are needed to ensure reliable results and support regulatory approval. Next-Generation Systems Hybrid proniosomes combining lipids, biodegradable polymers, targeting ligands, and stimuli-responsive triggers (pH or enzymes) are being developed for site-specific drug delivery and reduced side

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effects. QbD and Green Manufacturing: Applying Quality by Design (QbD) and using scalable techniques like spray-drying and continuous coating, along with greener solvents, can improve efficiency and sustainability in manufacturing. Targeted Clinical Trials Well-designed clinical trials are required to compare vesicular systems with standard therapies, especially for CNS drug delivery, focusing on efficacy, safety, and patient outcomes. Regulatory Collaboration Early collaboration between researchers, clinicians, and regulatory agencies can establish clear standards and accelerate clinical adoption of these drug delivery systems.

8. Conclusion

Niosomes and proniosomes are promising drug-delivery systems for oral and mucosal administration. By selecting appropriate surfactants and cholesterol and applying tools such as Design of Experiments (DOE) and Quality by Design (QbD), formulations like proniosomal powders, in-situ gels, and nanogels can protect drugs, control release, and improve bioavailability. They are especially useful for poorly soluble drugs, drugs affected by first-pass metabolism, and those requiring intranasal or transdermal brain delivery. However, challenges remain, including stability issues, difficulties in large-scale production, lack of standardized analytical methods, and limited long-term safety data. Future progress depends on QbD-based scale-up, improved standardization, and well-designed clinical trials to translate these systems into clinical practice.

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Chapter 8

Oral ulcers: In clinical aspects

Ranganayaki M[a], Santhosh S[a], J.Monisha[b*]

[a]*School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, SPS, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Oral ulcers are generally painful lesions that are related to various conditions developing within the oral cavity. They can be classified as acute or chronic according to their presentation and progression. Acute oral ulcers are associated with conditions such as trauma, recurrent aphthous stomatitis, Behcet's disease, bacterial and viral infections, allergic reactions, or adverse drug reactions. Chronic oral ulcers are associated with conditions such as oral lichen planus, pemphigus vulgaris, mucosal pemphigoid, lupus erythematosus, mycosis, and some bacterial and parasitic diseases. The correct differential diagnosis is necessary to establish the appropriate treatment, taking into account all the possible causes of ulcers in the oral cavity. In this second part of this two-part review, chronic oral ulcers are reviewed

Keywords: *Chronic oral ulcers, acute oral ulcers, bacterial, parasitic diseases.*

1. Introduction

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Secondary lesions with a loss of tissue are called ulcers. They are extremely prevalent lesions of the oral mucosa that impact both the epithelium and the underlying connective tissue. A loss of tissue affecting both the epithelium and underlying connective tissue characterizes ulcers, which have a variety of causes. They tend to be unpleasant and are quite prevalent in the oral mucosa.

Knowing the relative frequency or prevalence of these lesions at a specific time and location is crucial for making a diagnosis. Axe Ell discovered in 1976 that the most prevalent oral mucosal lesions in Sweden were ulcers (aphthae) linked to recurrent aphthous stomatitis, followed by those linked to prosthesis-induced stomatitis, recurrent herpes labialis, and geographic tongue.

2. Acute oral ulcers

Recurrent aphthous disease

Recurrent aphthous stomatitis (RAS) is an inflammatory condition whose exact cause remains unknown, marked by the occurrence of painful mouth ulcers (aphthae) that recur. It is prevalent in approximately 20% of the overall population, making it the most frequently encountered type of oral ulceration. There are several factors considered to contribute to the onset of RAS, such as genetic traits from families, immune system reactions, hormonal fluctuations, allergic responses to specific foods, medications, deficiencies in blood, lack of zinc, psychological stress, tobacco use, local injuries, infectious organisms, and various systemic health issues. Aphthae appear to be less frequent among individuals who smoke, indicating that tobacco may have a protective effect.

There are three distinct clinical types: minor aphthae, major aphthae, and herpetiform aphthae.

The most frequent type, minor aphthae, accounts for about 80% of cases. These lesions typically manifest as 1-5 clearly defined superficial ulcers that are either round or oval in shape and measure less than 10 mm in diameter, covered with a whitish or grayish membrane, and bordered by a red halo. They generally occur on non-keratinized mucosal areas and are uncommon on keratinized gingiva, the roof of the mouth, or the surface of the tongue. These lesions can appear over various periods and usually resolve within 10 to 14 days without leaving scars.

Major aphthae (10%), also referred to as periadenitis mucosa necrotica recurrens or Sutton's disease, share similarities with minor aphthae but are larger in size (exceeding 10 mm) and cause significant pain. They can present as single ulcers or clusters of multiple lesions. While they can develop in any region, they tend to favor the lips.

3. Behcet's disease

BD causes inflammation in blood vessels, with recurring mouth and genital sores, skin rashes, and eye, muscle, heart, stomach, and nerve issues. 12, 25 It often starts in a person's 30s or 40s. Genetics, environment, infections, the immune system, and blood factors may play a part. Mouth sores, big, small, or herpetiform, show up in the mouth, on the gums, on the lips, on the soft palate, and in the throat. These sores usually appear in everyone.

3.1 Necrotizing sialometaplasia

Necrotizing sialometaplasia is a rare condition causing large ulcerative lesions with very hard borders that are mainly located on the hard and/or soft palate. It is a non-cancerous and self-resolving necrotizing inflammatory disease of the minor salivary glands but

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may be mistaken for a malignant tumor. The main reason is thought to be ischemia secondary to injury or to damage from a chemical or biological agent.

Necrotizing sialometaplasia is a rare condition causing large ulcerative lesions with very hard borders that are mainly located on the hard and/or soft palate.

4. Principles of topical treatment for oral mucosal conditions

A thorough medical history and oral examination of the patient, along with additional diagnostic techniques, are crucial for obtaining a precise diagnosis of oral ulcers. The diagnosis, the severity of the oral condition, and whether or not there are accompanying extraoral lesions are the primary factors that guide the choice of topical treatment.

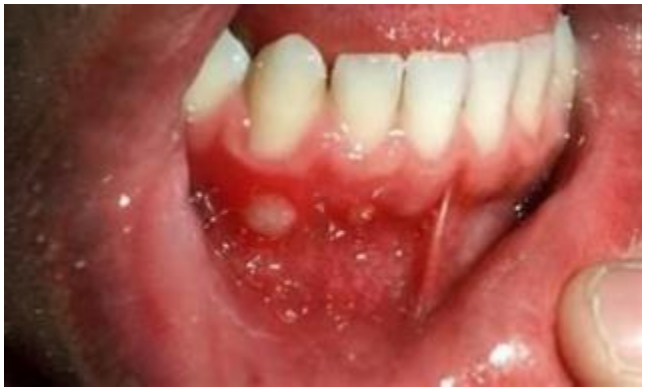

Figure 1: Oral mucosal conditions

Patients should steer clear of precipitating factors if they exist (for instance, in cases of traumatic ulcers). Infectious conditions (whether viral, bacterial, or fungal) must be treated with suitable topical and/or systemic medications (antivirals, antibiotics, or antifungals). For oral ulcers with undetermined causes or those associated with autoimmune d isorders, topical corticosteroids (TC) play a central role

in their management.

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Chapter 9

Phytosomes in Novel Drug Delivery System

Vasanth. A[a], Abishek. T[a], J.Monisha[b*]

[a]*School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b]*Assistant Professor, Department of Pharmaceutics, SPS, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Herbal products have shown a wide range of therapeutic benefits in the management of many health conditions. However, the clinical effectiveness of several phytoconstituents is often limited because of poor solubility, low absorption, instability, and reduced bioavailability. These limitations restrict the efficient delivery of plant-derived compounds in the body. To overcome such challenges, novel drug delivery systems have been developed, among which phytosomes have emerged as a promising approach. Phytosomes are complexes formed between plant active constituents and phospholipids, commonly phosphatidylcholine, which improve the lipid compatibility and membrane permeability of herbal compounds. This interaction facilitates better absorption through biological membranes and enhances overall bioavailability. Phytosomal systems also provide improved stability and protect phytochemicals from degradation, resulting in enhanced therapeutic performance when compared with conventional herbal extracts. Studies reported in scientific databases such as PubMed, Scopus, Web of Science, and Google Scholar highlight the growing importance of phytosomes as

an effective nanocarrier system. In comparison with other delivery systems like liposomes, phytosomes demonstrate improved pharmacokinetic properties and distribution efficiency. They can be administered through various routes, including oral, topical, and intranasal delivery. Because of these advantages, phytosomes are being widely explored for applications in inflammatory disorders, metabolic diseases, neurological conditions, liver disorders, and cancer therapy.

Keywords : *Phytosomal drug delivery, Herbal bioactive compounds, Phospholipiphytoconstituent complex, Enhanced bioavailability, Nanocarrier systems.*

1. Introduction

Herbal medicines have been used for centuries for the prevention and treatment of many diseases. According to the World Health Organization, plant-derived medicines continue to play an important role in healthcare systems worldwide. Herbal products contain a variety of biologically active compounds such as flavonoids, terpenoids, alkaloids, and polyphenols that exhibit therapeutic properties. These phytochemicals are known for their antioxidant, anti-inflammatory, antimicrobial, and anticancer activities.

Despite their therapeutic potential, many herbal constituents show limited clinical effectiveness due to poor solubility, low permeability, and instability in biological environments. These issues often lead to poor absorption and reduced bioavailability when administered in conventional dosage forms. To overcome these challenges, researchers have focused on the development of novel drug delivery systems (NDDS) that can enhance the pharmacokinetic performance of plant-derived compounds.

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2. Limitations of Herbal Drugs

Although herbal medicines possess a wide range of therapeutic benefits, their effectiveness is often limited by several pharmacokinetic challenges. The most common problem associated with plant-derived compounds is their poor aqueous solubility. Many phytochemicals are hydrophobic in nature, which restricts their dissolution in biological fluids and limits their absorption in the gastrointestinal tract.

Another major limitation is low bioavailability. Several active constituents of medicinal plants undergo rapid metabolism and elimination in the body, resulting in reduced therapeutic concentrations in systemic circulation. For instance, compounds such as curcumin and quercetin exhibit significant pharmacological activities but demonstrate poor oral absorption and rapid degradation.

Instability of phytoconstituents under physiological conditions is also a critical issue. Some herbal compounds are susceptible to degradation in the presence of gastric acid, digestive enzymes, or environmental factors such as light and oxygen. Furthermore, the complex chemical composition of plant extracts may lead to variability in drug absorption and pharmacological response.

3. Concept and Structure of Phytosomes

Phytosomes are advanced lipid-based drug delivery systems designed to improve the bioavailability of plant-derived active compounds. The term “phytosome” is derived from the combination of the words “phyto,” meaning plant, and “some,” referring to cell-like structures. In this system, bioactive phytoconstituents form molecular complexes with phospholipids, typically phosphatidylcholine.

The structure of phytosomes involves the interaction of polar functional groups present in phytochemicals with the polar head of phospholipids through hydrogen bonding and other intermolecular interactions. This complex forms a lipid-compatible structure that can easily integrate with biological membranes. As a result, phytosomal complexes demonstrate improved membrane permeability and enhanced absorption compared to conventional plant extracts.

4. Preparation Methods

Several techniques have been developed for the preparation of phytosomal complexes. These methods generally involve the interaction of plant extracts or isolated phytoconstituents with phospholipids in suitable solvents.

One commonly used technique is the solvent evaporation method. In this process, the phytoconstituent and phospholipid are dissolved in an appropriate organic solvent and heated under controlled conditions to promote complex formation. The solvent is then removed using rotary evaporation, resulting in the formation of phytosomal complexes.

Another widely used method is lyophilization. In this approach, the phytochemical and phospholipid are dissolved separately in solvents and then mixed together. The resulting mixture is frozen and subjected to freeze-drying to obtain the phytosome complex.

5. Applications

Phytosomes have gained significant attention in pharmaceutical research due to their wide range of therapeutic applications. These delivery systems have been explored for the treatment of various

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diseases affecting different organ systems.

In liver disorders, phytosomal formulations such as silybin phytosomes have shown hepatoprotective activity by improving the bioavailability of active compounds. Phytosomal curcumin has demonstrated anti-inflammatory and antioxidant properties and has been studied for the management of cancer, metabolic disorders, and osteoarthritis.

6. Conclusion

Phytosomes represent an innovative and effective approach for improving the delivery of plant-derived bioactive compounds. By forming complexes with phospholipids, phytosomes enhance the solubility, stability, and bioavailability of phytoconstituents. This advanced delivery system helps overcome many limitations associated with conventional herbal formulations. The growing interest in phytosomal technology has led to the development of numerous pharmaceutical and nutraceutical products with improved therapeutic efficacy. With continued research and technological advancements, phytosomes are expected to play an important role in the future development of herbal drug delivery systems.

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Chapter 10

Preformulation Studies in Formulation of New Dosage Forms

Jithendhra R[a], Monisha J[b*]

[a]*B.Pharm IInd year, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

[b*]*Assistant Professor, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology & Advanced Studies, Chennai*

** Corresponding Author: monisha.sps@vistas.ac.in*

Abstract

Preformulation studies are a crucial step in pharmaceutical development, focusing on evaluating the physical, chemical, and biopharmaceutical properties of a drug to design safe, stable, and effective dosage forms. Emerging with advances in physical pharmacy, these studies transformed drug formulation from an empirical practice to a scientific process. Key parameters assessed include crystal structure, polymorphism, solubility, partition coefficient, particle size, density, hydrolysis, oxidation, racemization, and polymerization. The Biopharmaceutics Classification System (BCS) classifies drugs based on solubility and permeability, guiding bioequivalence and regulatory decisions. Preformulation data support excipient selection, manufacturing methods, packaging, and stability assessment. Overall, these studies form the foundation for developing bioavailable, stable, and therapeutically effective pharmaceutical products while ensuring quality, safety, and efficient large-scale

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production.

Keywords: *Preformulation, biopharmaceutics, physicochemical, stability, manufacturing, packaging.*

1. Introduction

Preformulation studies were developed as an essential step in modern pharmaceutical research to ensure safe, stable, and effective dosage forms. It is defined as testing of physical and chemical properties of a drug substance alone and in combination with excipients that are used in the formulation. The history of preformulation is linked to the evolution of pharmaceutics and drug development science. The development of physical pharmacy during the 1950s – 1960s marked the beginning of scientific preformulation studies. During this time, emphasis was placed on physicochemical characterization. This period established the foundation of preformulation as a scientific discipline. Preformulation studies became a formal and mandatory step in drug development from the 1970s. Thus, pre-formulation is a multidisciplinary study that includes medicinal chemistry, pharmacology, toxicology, formulation research, analytical research, biopharmaceutics, and pharmacokinetics.

1.1 Objective

The main objective of preformulation studies is to generate useful information for developing a stable, bioavailable, and therapeutically effective formulation that can be manufactured on a large scale. The physicochemical parameters of the drug are established by this study. The stability, bioavailability, and therapeutic efficacy you can see can be affected by the physicochemical properties of the drug. So proper consideration should be given to these properties before designing the dosage form (2).

1.2 Areas of preformulation research

The main areas of preformulation research are the physicochemical parameters of the drug. These are listed as:

1.2.1 Crystal character

In crystalline solids molecules are tightly packed in an orderly and repetitive pattern throughout the entire structure. The melting point of a crystal is the temperature at which the orderly lattice breaks down after absorbing enough energy to overcome the attractive forces between the particles. The unit cell is the smallest repeating structural unit of a crystal. In a pure crystal, all unit cells are identical in size and contain the same number of uniformly arranged atoms, ions, or molecules.

The size and shape of crystals of the same substance may vary depending on the conditions under which they form. The flat surfaces of a crystal are called faces, and the angle between two faces is known as the interfacial angle. For a given design substance, this angle remains a constant principle known as the law of constancy of interfacial angles (3).

2. Polymorphism

A polymorph is a solid crystalline form of a compound that arises because the molecules are in themselves in more than one way in the solid state. Please note the term "polymorphism" comes from Greek, where "poly" means "many" and "morph" means "form" or "ability of a solid substance to exist in two or more different pressure forms with different molecular arrangements or lattice structures."

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2.1 Types of polymorphism

Enantiotropy

When two polymorphic forms have similar vapor pressures, one form can reversibly transform into the other at a specific temperature called the transition temperature. One form remains stable above this temperature while the other is stable below it. Such forms are known as enantiotropes. Example: Sulfur

Monotropy

In this type, one polymorphic form is stable and the other is metastable at all temperatures below the melting point. The transformation is irreversible, and no transition temperature exists because their vapor pressure differs. Example: Phosphorus.

Dynamic allotropy

At certain temperatures some substances exist in multiple molecular forms that remain in equilibrium. This form differs in molecule composition but behaves similarly to enantiotropic systems. Example: In sulfur several molecular species such as S6, S7 and S8 may exist (4).

Partition coefficient

When one solute is introduced into a system containing two invisible liquids, it distributes itself between the two layers in a fixed proportion. This phenomenon is known as the Nernst distribution law. For distribution to occur, the solute must be soluble in both liquids. The ratio of its concentrations in the two phases at equilibrium is called the partition coefficient (K) (1).

Hydrolysis

Hydrolysis is one of the most common pathways of drug degradation.

It usually occurs because of exposure to water during isolation or formulation or due to the presence of functional groups that are prone to hydrolysis. This reaction commonly proceeds via acid- or base-catalyzed mechanisms, so it may also occur at neutral pH where water can function as a base. Functional groups containing carbonyl moieties such as esters, lactones, amides, lactams, carbamates, and imides are particularly susceptible to hydrolysis (4).

One way to minimize hydrolysis in vivo is true steric protection. Introducing a bulky group near the reactive functional group can block the approach of nuclei or enzymes first, thereby decreasing the chance of hydrolysis.

3. Oxidation

Oxidation is a major cause of instability in pharmaceutical products. In some reactions, oxygen is directly added, while in others hydrogen is removed. When a molecule of oxygen participates, the reaction is known as auto-oxidation. This process can occur at room temperature, but usually at a slower rate (5).

Both hydronium and hydroxyl ions can catalyze oxidative degradation. Each antibiotic and vitamin preparation has an optimal pH range for maximum stability. Stability can be enhanced by adding appropriate antioxidants, maintaining optimal pH, and using chelating agents to bind trace metals.

4. Reduction

Production is another common pathway in drug metabolism. Liver microspores facilitate various reduction reactions, often requiring NADPH as a cofactor (6). Cytochrome P-450 enzymes catalyze their reduction of azo and nitro groups. For example, chloral hydrate is

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reduced by alcohol dehydrogenase to its active metabolite, trichloroethanol. Similarly, prednisolone and cortisone are reduced to form the active metabolite hydrocortisone. Azo dyes used as coloring. agents in pharmaceutical products or foods may also be reduced to amines in the liver and by intestinal microflora.

5. BCS classification

The purpose of the Biopharmaceutics Classification System [BCS] is to illuminate the in vivo behavior of a drug formulation based on in vitro data related to its solubility and permeability.

5.1 Importance of BCS classification

It helps determine the need for clinical bioequivalence studies, thereby improving the efficacy of drug development and regulatory evaluation. It enables classification of drug products by considering their dissolution characteristics along with solubility and permeability properties (7). It serves as a regulatory framework that allows certain bioequivalence studies to be waived when reliable in vitro dissolution data are available.

5.2 Application of Pre-formulation studies in the development of dosage forms and their impact on stability

Preformulation evaluation is the initial and essential step in the systematic development of a dosage form for a new drug molecule. It applies biopharmaceutical principles to choose appropriate excipients, determine the correct composition, establish suitable processing methods, and select proper packaging materials. The main objective is to create an optimal, economical, safe, stable, therapeutically effective, and patient-friendly product. By generating critical data required for large-scale manufacturing, pre-formulation studies form the foundation for developing reliable formulations and

help shorten the overall drug development timeline. Preformulation testing is carried out after a new chemical entity has been successfully synthesized or isolated and shown to possess therapeutic activity. At this stage, essential information such as chemical structure, molecular weight, possible salt forms, pharmacological category, anticipated dose, available quantity of a drug substance, projected development timeline, and intended dosage form is gathered. Once the compound clears toxicity studies, formal preformulation investigations begin (8).

During pre-formulation studies, the stability of the proposed dosage form is also assessed. Based on the stability results for more appropriate expiry dates under recommended storage conditions are established to ensure maximum stability under quality of the final product.

6. Conclusion

Pre-formulation plays a crucial role in drug development, influencing not only the selection of the drug candidate but also the choice of formulation ingredients and manufacturing processes for the active pharmaceutical ingredient [API] under the finished product somewhere under the appropriate container closure system. It also supports the development of analytical methods, determination of API retest periods, selection of a synthetic pathway, and planning of toxicological strategies to stop.

With increasing globalization and rapid technological progress, significant pressure is being placed on industries and institutions to modernize their practices and stop the conventional role of pre-formulation studies scientists, which largely relied on manual methods, is no longer sufficient to remain competitive in the global

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market.

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Chapter 11

Development and Evaluation of a Prolonged-Release Amla Formulation for Long-Term Prevention of Scurvy

Madhumitha. V[a]*, Keerthana. J[b]*, Monisha. J[c]*

[a] *Vels Institute of Science and Technology and Advanced Studies, Pallavaram,Chennai-600117.*

[b] *Vels Institute of Science and Technology and Advanced Studies, Pallavaram, Chennai-600117*

[c] *Assistant Professor, Department of Pharmaceutics, SPS-Vels Institute of Science and Technology and Advanced Studies, Chennai.*

** Corresponding Author: madhudpharma18@gmail.com*

ABSTRACT:

Scurvy is the nutritional condition marked by symptoms like bleeding gums, exhaustion, poor wound healing and anemia, is caused by long-term vitamin C deficiency. Amla (Emblica officinalis) as potent antioxidant qualities and is a well known natural source of ascorbic acid (vitamin C). However, in order to maintain therapeutic levels ascorbic acid (vitamin C) must be administered frequently due to its short biological half-life and poor stability. In order to provide prolonged vitamin C delivery for the long-term prevention of scurvy, the current study intends to develop and assess a sustained-release formulation of amla extract. In this study, a sustained-release hydrogel containing amla extract was created using sodium alginate and carbopol 934 as polymers. In order to improve gel strength and control the drug release profile, calcium chloride was used as a cross-linking agent. The stability, in vitro drug release, drug content,

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swelling behavior and gel strength of the prepared formulation were assessed. The outcomes show controlled and prolonged release of vitamin C over a long period of time, demonstrating effective sustained-release characteristics. According to stability studies, the formulation held up well under certain storage circumstances. Therefore, a promising natural and patient-friendly method for sustaining therapeutic ascorbic acid (vitamin C) levels and preventing scurvy over and extended period of time is offered by the developed sustained-release amla formulation.

Keywords:

Emblica officinalis, Ascorbic acid (vitamin C), Wound healing, Sustained release formulation, Antioxidant activity.

Introduction:

Ascorbic acid, another name for vitamin C is water-soluble vitamin that is essential for many physiological functions. Collagen production, wound healing and connective tissue maintenance all depend on it. Furthermore, vitamin C functions as a potent antioxidant to shield cells from oxidative damage brought on by free radicals. The lack of the enzyme L-gulonolactone oxidase prevents humans from synthesizing vitamin C. As a result, it must come from food source like fruits and vegetables. Fatigue, bleeding gums joint pain and delayed wound healing are some of the symptoms of scurvy, a disease caused by a vitamin C deficiency. Even though most modern diets contain enough vitamin C, some people may still be deficient because of bad eating habits, malnourishment or illness that interfere with the absorption of nutrients. Long-term vitamin C deficiency causes scurvy. In the past, sailors who traveled long distances without access to fresh produce were more likely to contract the

illness. After a few weeks or months of insufficient vitamin C intake, symptoms usually start to show. After being administered, conventional formulations frequently release the active ingredient quickly. This may necessitate frequent dosing and lead to short-lived therapeutic levels. In order to maintain constant drug levels in the body, sustained release formulations are made to release the active ingredient gradually over time.

Materials:

- Amla fruits
- Sodium alginate
- Carbopol 934
- Calcium chloride
- Ethanol
- Distilled water
- Phosphate buffer (pH 6.8)

Methods:

Preparation of amla extract:

To get rid of dirt and contaminants, fresh were thoroughly cleaned with water. The pulp was chopped into tiny pieces after the seeds were extracted. For a few days, the material was shade-dried until it was completely dehydrated. After being dried, the material was ground into a powder using a grinder and then put through an appropriate sieve to achieve a consistent particle size. Ethanol and water were used as the solvent system for Soxhlet extraction of the powdered material. The extraction procedure was carried out until the solvent in the siphon tube was almost colorless, signifying that

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all of the phytoconstituents had been extracted. A water bath used to remove the solvent, resulting in a concentrated extract that was subsequently kept in an airtight container for later use.

Preparation of sodium alginate solution:

The necessary amount of sodium alginate was dissolved in distilled water while being constantly stirred to create a homogenous solution. The polymer solution that contained sodium alginate and Carbopol was mixed with the prepared amla extract. To create a uniform dispersion, the mixture was constantly stirred.

Preparation of cross linking solution:

Calcium chloride was dissolved in distilled water to create a calcium chloride solution. The sodium alginate is cross-linked by this solution.

Preparation of Insitu gel:

Gradually add the amla extract solution to the sodium alginate solution while stirring continuously. Then, add the Carbopol dispersion to the mixture and stir gently while adding 0.1g sodium benzoate and 5ml glycerin. Finally, add distilled water to bring the final volume up to 100ml. Stir gently to create a homogenous, freely-flowing in-situ gel solution.

Evaluation:

Swelling behavior:

To assess the polymeric gel ability to absorb water, swelling tests were carried out. The gel were taken out after a predetermined amount of time and weighed once more. The following formula was used to determine the swelling index:

Swelling Index (%) = (Wt – W0) / W0 × 100

Where, W0 = initial weight and Wt = weight after swelling

Gel strength:

To assess the gel mechanical stability, gel strength was calculated. Stronger cross-linking within the polymer matrix is indicated by higher gel strength.

Drug content:

To find out how much amla extract was in the formulation, drug content analysis was done. UV-visible spectrophotometry was used to analyze the gel after they had been dissolved in an appropriate solvent.

In vitro drug release study:

Phosphate buffer was used as the dissolution the medium in a dissolution apparatus used for the in-vitro release investigation. To ascertain the amount of drug released, samples were taken out at prearranged intervals and subjected to spectrophotometric analysis.

Stability studies:

To assess how storage conditions affected the formulation, stability studies were conducted. Samples were kept in accelerated humidity and temperature conditions.

Results and discussion:

To evaluate stability, physical appearance, drug content and release profile were assessed on a regular basis. The produced polymeric gel had a consistent shape and good physical qualities. The swelling study revealed a slow fluid absorption, indicating that the polymer matrix could regulate drug diffusion and water uptake. The

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uniform distribution of the active ingredients within the gel was verified by drug content analysis.

Applications and future prospects:

Herbal medication delivery may benefit from sustained release formulations made with natural polymers. By offering controlled release and safeguarding sensitive compounds, these systems may increase the therapeutic efficacy of plant extracts

Future studies may focus on:

- Assessment of the formulation in vivo
- Polymer ratio optimization
- Commercial nutraceutical product development

Conclusion:

Using sodium alginate and Carbopol 934, the current study successfully created a sustained release formulation containing amla extract. Stable polymeric gel that could regulate the release of vitamin C were created using the ionic gelation method with calcium chloride. The evaluation's findings showed good stability, consistent drug content, sustained release profile and acceptable swelling behavior. Improved use of natural herbal resources and long-term prevention of vitamin C deficiency may be possible with this formulation approach.

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Mrs. Monisha J, M.Pharm (Ph.D.), is a pharmacy faculty with over six years of experience. She completed her B.Pharm and M.Pharm at SRM University, Kattankulathur, and is currently pursuing her Ph.D. in Pharmacy at the same institution. Her research focuses on Novel Drug Delivery Systems, innovative pharmaceutical formulations, and Clinical Pharmacy Research, aiming to bridge theory and practice. She is a lifetime member of the Association of Pharmacy Professionals (APP), Association of Pharmaceutical Teachers of India (APTI), and the Pharmacy Council of India (PCI). She has 10 publications (including 5 Scopus-indexed), 8 book chapters, 15 presentations, 7 awards, and 2 patents, and has worked at Netmeds Marketplace and Tagore College of Pharmacy.

Dr.S.Umadevi, M.Pharm, Ph.D., serves as a Professor in the Department of Pharmaceutics, School of Pharmaceutical Sciences. She brings extensive experience as a dedicated teacher and an active researcher in the field of Pharmaceutical Sciences. She effectively combines classroom instruction with hands-on research practice, contributing significantly to academic and scientific advancement. Dr. Umadevi actively conducts high-quality pharmaceutical research and has successfully published numerous research articles, patents, and scholarly works. She has guided several undergraduate, postgraduate, and doctoral research projects, mentoring students toward academic excellence and innovation. She demonstrates strong expertise in patent drafting, research manuscript preparation, book publication, and the development of competitive research proposals. Her commitment to teaching and research continues to strengthen pharmaceutical education and innovation.

Dr. Vijayakumar Murugesan He is an experienced professional in technology transfer, holding a Master's degree in Pharmacy from BITS Pilani. With over 19 years of expertise, he has significantly contributed to Research & Development and technology transfer, particularly in the area of cancer drug formulations. His core competencies include process optimization, scale-up, and ensuring regulatory compliance, facilitating a seamless transition from development to commercialization. Currently pursuing a Ph.D. in Regulatory Affairs, specializing in cosmetics, he is deepening his understanding of global regulatory standards. He is also actively engaged in pioneering research focused on advancing cancer drug formulations, with a strong emphasis on enhancing efficacy, safety, and patient outcomes.

Dr. A. Venkatesh, M.D.S., is a distinguished academician and clinician specializing in Conservative Dentistry and Endodontics. He serves as Professor and Head of the Department at Sree Balaji Dental College and Hospital and is the Director of Jayvee Dental Centre, Chennai. He completed his B.D.S. from Annamalai University (2002) and M.D.S. from Dr. MGR Medical University. He is an Executive Committee member of the Indian Association of Conservative Dentistry and Endodontics, serving a second consecutive term, and Treasurer of CEAT and ECCLIRES. He has coordinated international conferences, published extensively in indexed journals, serves as a reviewer, delivers global keynote lectures, organizes academic events, and contributes to society through dental camps and oral health awareness programs.

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