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COMPREHENSIVE REVIEW OF NOVEL DRUG DELIVERY SYSTEMS: CURRENT STATUS AND FUTURE DIRECTIONS

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ABSTRACT
It is now necessary to target the cells involved in the onset and progression of diseases specifically due to developments in molecular pharmacology and our growing understanding of the mechanisms underlying the majority of diseases. This is particularly true for the majority of terminal illnesses that call for therapeutic drugs with a host of negative side effects, necessitating precise tissue targeting to reduce internal exposure. Current drug delivery systems (DDS) are designed using cutting-edge technology to minimize off-target accumulation in the body and maximize therapeutic efficacy by accelerating systemic drug delivery to the precise target region. They so have a crucial role to perform when treating and managing illness. Advanced drug delivery systems (DDS) are more advantageous than traditional drug administration systems because of their improved efficacy, automation, performance, and precision. They are composed of multifunctional nanomaterials or tiny devices with long circulating half-life that are biocompatible, biodegradable, and have high viscoelasticity. As a result, this review offers a thorough understanding of the development of drug delivery systems' technological history. It provides an update on the newest drug delivery systems, their therapeutic uses, the challenges in using them, and the directions that will hopefully lead to better performance and utilization in the future.

Keywords: Novel Drug Delivery System, Targeted Drug Delivery System, Recent Drug Delivery Systems, Applications, Classification, Challenges

1. INTRODUCTION

Drug delivery systems are technological systems that formulate and store drug molecules into suitable forms like tablets or solutions for administration. They has not the reach of drugs to the specific targeted site in the body, thereby maximizing therapeutic efficacy and minimizing off-target accumulation in the body [1,2].

1.1 Classification and Routes of Drug Administration

Drugs have various routes through which they can be introduced into the body, they include but are not limited to the oral route of administration [3,4], buccal and sublingual routes of administration [5], nasal and ophthalmic, transdermal and subcutaneous [6,7], anal and transvaginal and intravesical. The components of the drug account for its physiochemical properties and are responsible for the changes it influences in the body system when taken. Over the past few decades, DDS have been applied effectively in the treatment of diseases and improvement of health due to increased systemic circulation and control of the pharmacological effect of the drug. The advancement of

pharmacology and pharmacokinetics showed the importance of drug release in determining therapeutic effectiveness, giving rise to the concept of controlled release [8].

1.2 Controlled Release and Its Advantages in Therapy

The controlled-release formulation of a drug was first approved in the 1950s, and it has since attracted considerable attention due to its significant advantages over conventional drugs. It releases drugs at a predetermined rate and for a specific period of time. In addition, controlled drug delivery systems are not affected by physiological conditions and can thus last for days to years. It also provides spatial control over drug release, with constant or variable release rates [9]. it improves drug solubility, target site accumulation, efficacy, pharmacological activity, pharmacokinetic properties, patient acceptance, and compliance, and reduces drug toxicity [10].

1.3 Targeted and Stimuli-Responsive Approaches in Modern Drug Delivery

Recently, several drug delivery systems (NDDS) have been developed using advanced systems for more convenient, controlled, and targeted delivery. Each drug delivery system has its own peculiarities that determine its release rate and mechanism. This is largely due to the differences in the physical, chemical, and morphological characteristics which will ultimately affect their affinities for various drug substances [11]. Studies on these have identified diffusion, chemical reaction, solvent reaction, and stimuli control as major release mechanisms [12,13]. since most cancer cells can proliferate the porous blood vessels and lymphatic system, the drug can easily permeate through this opening to reach the target tissues. This is referred to as Enhanced Permeability and Retention (EPR) [14]. EPR is a passive diffusion mechanism well researched and applied in the delivery of many chemotherapeutic agents. Although EPR is a controversial concept, this effect has been observed by many researchers in various types of human tumors and is the basis for the use of nanomedicine in cancer treatment [15]. Active targeting overcomes the lack of specificity and selectivity found in passive targeting. It involves attaching to the carriers, certain ligands, and molecules that can actively bind to the surface of target tissues [16,17]. Selectivity of ligands to target cells, immunogenicity, and chances of lysosomal degradation after macrophage endocytosis still pose solid challenges to the full development of actively targeting Drugs [18,19].

2. NOVEL DRUG DELIVERY SYSTEMS

2.1 Definition and Concept of NDDS

A new strategy involving innovative formulations, innovative approaches, and safe delivery of pharmaceutical chemical substances to the body as required to produce their intended pharmacological effects is known as a Novel Drug Delivery System, or NDDS. When NDDS is a sort of traditional drug delivery method, the plasma drug level oscillates innovative drug delivery strategy to reduce side effects and boost therapeutic effect innovative drug delivery strategy to reduce side effects and boost therapeutic effect Many medications, including vaccines, peptides, proteins, antibodies, and gene based pharmaceuticals, should generally be administered via a traditional drug delivery route due to the possibility of enzymatic degradation, low bioavailability, and reduced intestinal mucosal penetration. It is possible to distinguish between two main strategies for targeting the targeted areas for medication release: Active targeting and passive targeting. To accomplish the desired therapeutic effect and reduce adverse or toxic effects, NDDS medications are made to target the location of the site. Generally, the pharmaceutical drug delivery system consists of: Localized drug delivery devices provide drug action through rate-limiting drug release in the vicinity of the target. which controls the molecular diffusion of drug molecules in systemic circulation. a suitable dosage form (pharmaceutical formulations) that carries the drug into the body the release mechanism of a drug from the dosage form to the organ/cells of targeting after administration an optimum medical device/pharmaceutical technique used for manufacturing the dosage form [20].

2.2 Advantages of Novel Drug Delivery System

- Decreased rate of increase in blood drug concentration.
- Blood level that is constant and sustained within the therapeutic window.
- Minimizing exposure to toxic.
- ability to achieve a particular drug release.
- Make tissue macrophages become more widely spread.

2.3 Disadvantages of Novel Drug Delivery System

- Dose dumping.
- Reduced potential for accurate dose adjustment.
- Need for additional patient education.

3. RECENT DRUG DELIVERY SYSTEMS AND APPLICATIONS

Significant progress has been made in recent years toward the successful development of drug delivery systems based on organic, inorganic, and hybrid nanoparticles as drug carriers for active targeting, particularly in chemotherapy. Recent drug delivery systems (DDS) are formulated with improved properties such as smaller particle size, increased permeability, increased solubility, efficacy, specific site targeting, stability, toxicity, and sustained delivery. They can significantly improve therapeutic agent performance over conventional dosage forms [21].

In the development of an optimal drug delivery system, recent drug delivery systems are recognized to be the newest developments and innovative understanding of the pharmacokinetic and pharmacodynamic behavior of pharmaceuticals. Because these DDS are transporters, they can keep medication concentrations in the therapeutic range for a long time while also delivering material to the site of action. The adoption of the delivery mechanism is directly tied to the commercial and therapeutic success of the innovation. This would entail involving patients early in the development process, recognizing any problems, and ensuring they receive the most out of the device. Improving delivery systems that reduce toxicity while increasing efficacy [22].

The different types of drug delivery systems are depicted in Fig. 1.

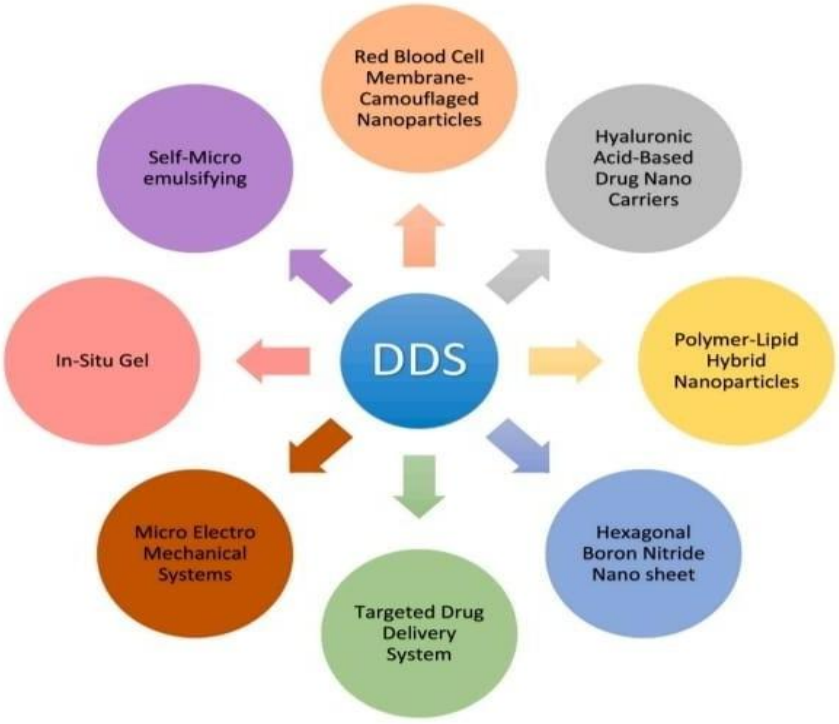

Fig. 1. Several types of recent drug delivery systems for different therapeutic purposes.

3.1 Red blood cell membrane-camouflaged nanoparticles drug delivery system

Researchers have recognized the potential benefits of nanotechnology in vastly improving medicine delivery methods throughout time. Red blood cell membrane-camouflaged nanoparticles are a new class of drug delivery systems. The nature and biological significance of red blood cells (RBCs) allow for their use as an efficient system as a nanoparticle camouflaging material [23]. Because red blood cells (RBCs) are the most abundant circulating cells in the body, their biocompatibility (non-immunogenic), biodegradability, and extended circulating half-life, making them an ideal vehicle for drug delivery [24]. Engineered RBCs have been investigated and found to be an excellent carrier for a variety of bioactive chemicals, including enzymes, medications, proteins, and macromolecules [25].

Because of their abundance, red blood cell membranes serve as a "camouflage," allowing nanoparticles to combine the benefits of native red blood cell membranes with those of the nanomaterial. Several strategies have been developed to load therapeutic agents onto RBCs without comprising the structure and the physiological function of RBCs. The coated nanoparticles will mimic RBCs and interact with the environment to establish long systemic circulation when injected. Sonication is the most common method for creating RBC camouflaged nanoparticles. Other methods of RBC fusion with nanoparticles include in-situ polymerization, microfluidic electroporation, and extrusion. The hypotonic treatment will help to remove unwanted cells and plasma [26].

3.2 Hyaluronic acid-based drug nanocarriers drug delivery systems

The usage of hyaluronic acid is one of the drug delivery techniques. Hyaluronic acid is a novel polymer that can be used to make medication delivery systems [27]. It has a linear macromolecular mucopolysaccharide made up of proportionately connected glucuronic acid and N-acetylglucosamine saccharide units [28].

It exhibits biocompatibility, biodegradability, and high viscoelasticity, and it can be coupled with a specific cell surface receptor [29]. Because Hyaluronic acid is a natural component of eye tissue and plays an important function in wound healing, it makes sense to use it as a carrier for ocular drug delivery as long as the integrated the plasma and other unwanted cells. The resulting pure red blood cells are subjected to hypotonic hemolysis and are used to coat selected nanoparticles which are intravenously injected into the blood to maintain long systemic circulation. The RBCM-NPs permeate the tumor tissue via the EPR effect and finally enter into the tumor cells by endocytosis for therapeutic effect. pharmaceuticals are released consistently. They aid in the thickening, sustained release, and transdermal absorption of drugs, as well as improving drug targeting. Drug distribution to cancer cells was significantly improved using active targeted HA- based drug nanocarriers. Benefits of utilizing HA-based nanocarriers for cancers with elevated expression of the CD44 receptor include improved drug delivery, increased therapeutic efficacy, higher cytotoxicity, and considerable reduction of tumor development, as well as a high potential for targeted chemotherapy [30].

3.3 Polymer-Lipid Hybrid Nanoparticles Drug Delivery System

Nanocarriers are becoming more and more popular as drug delivery systems due to their enhanced storage stability, better ability to target disease cells, longer drug release, and better encapsulation capacity. Polymeric and liposome nanoparticles are the most extensively used of the widely acknowledged nanoparticles currently being employed for medication delivery. The polymeric nanoparticle, a polymer-based nanoparticle, was able to overcome this limitation by demonstrating high encapsulation/drug loading ability as well as stability. Liposomes, lipid- based nanoparticles, showed excellent biocompatibility but still experienced drug leakage and instability upon storage [31]. (Figure 2)

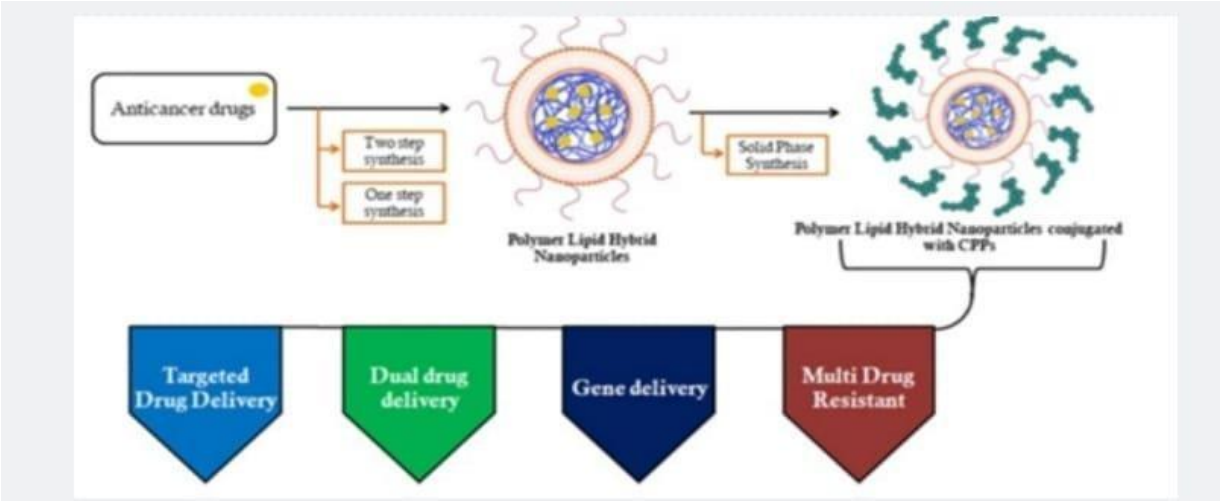

Figure 2: Polymer-lipid hybrid nanoparticles in anticancer activity.

But it also had a lesser biocompatibility, which was one of its shortcomings. The term "Polymer-lipid hybrid nanoparticles" refers to the hybrid system that researchers have created to combine the special qualities of the two classes of nanoparticles in order to overcome these drawbacks and produce an effective nanomaterial [31].

This technology is currently being used for several therapeutic objectives in addition to diagnostic applications due to its effectiveness. is composed of three separate parts, which are as follows: A polymeric core capable of efficiently encapsulating both hydrophilic and hydrophobic medication [31].

A lipid-polyethylene glycol (PEG) that is found in the outer part and covered by a lipid layer to provide increased steric stability, prevent immune recognition, and increase time for circulation, as well as a lipid shell that provides biocompatibility and high stability, all contribute to this high sustained release which is shown in Figure 3 [32].

3.4 Self-micro emulsifying drug-delivery system

Recently, lipid-based drug preparations have received a lot of interest, with a specific focus on self-micro emulsifying drug-delivery systems (SMEDDS) [33]. Inadequate bioavailability is one of the most difficult aspects of developing oral dosage forms of drugs [34].

Accordingly, minimal hydrophilicity is an essential factor for bioavailability in this context, because drugs cannot be absorbed via the gastrointestinal tract (GIT) except it exists in solution forms [35]. Aqueous solubility is a problem for many chemical compounds having notable and favorable pharmacological effects [36]. Furthermore, almost 30% of widely marketed medicinal entities and nearly 50% of innovative drug compounds accessible for product manufacture are hydrophobic in nature, meaning they have low water solubility [37].

The utilization of a lipid-based carrier system to boost the bioavailability of less water-soluble medications has grown in popularity in recent years [38]. The main rationale behind this formulation is to sustain the hydrophobic components in solution all through the digestive system [39,40]. Lipid-based carriers come in a variety of forms, including suspensions, dry emulsions, microemulsions, and self-emulsifying drug delivery systems (SEDDS) [41,42]. SEDDS' ability to incorporate hydrophobic drugs was previously reported. SEDDS has also been revised as self-micro emulsifying drug-delivery systems (SMEDDS) and self-nanoemulsifying drug- delivery systems (SNEDDS). Emulsions, on the other hand, are created by dispersing a liquid phase containing macroscopic particles in a different liquid phase composed of surfactant [43,44].

The production of Nanoemulsions with droplet sizes smaller than 100 nm, on the other hand, requires either mechanical or chemical energy [45]. Consequently, Nanoemulsions globules are shown to be stable across a variety of situations, including varied dilutions and temperatures, while microemulsions are mostly impacted by factors including dilutions and temperature [46].

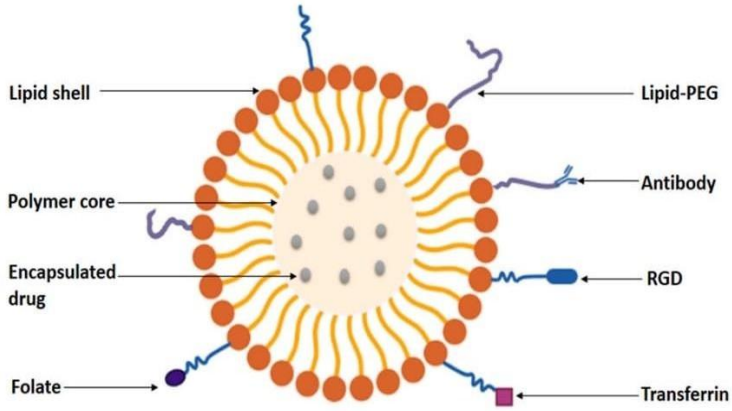

Fig. 3. The formation of a Polymeric-Lipid Hybrid Nanoparticle. The Hybrid contains three distinct components which include: A polymeric core that encapsulates both hydrophilic and hydrophobic drugs effectively. A lipid shell that provides biocompatibility and high stability and a lipid polyethylene glycol (PEG) that is found in the outer part and covered by a lipid layer to provide increased steric stability, prevent immune recognition and increase time for circulation.

3.5 Micro electromechanical systems (MEMS) for drug delivery

MEMS technology is widely used in areas like inkjet printing, motion detection, accelerometers, actuators, and medication delivery. By using microfabrication processes, the devices made possible by this technology can create mechanical, electromechanical, and micro- or nano-sized implants. The most often utilized materials and design techniques for these MEMS-based devices are numerous. combine inventive combinations of different micromachining processes, including lithography (a patterning process), etching (a subtractive process), deposition (an addictive process), ink jetting, ion implantation, oxidation, and micro molding. With the use of MEMS technology, miniaturized systems made of silicon, glass, metals, and nitrides can be created, in addition to polymers, micropumps, sensors, microvalves, reservoirs, actuators, and high-performance CPUs [47]. Together, these several parts work in concert to provide MEMS devices their widely acknowledged multifunctionality and precision in comparison to other traditional drug delivery methods. Actuators, for example, are primarily responsible for the drug release process by applying pressure to the drug reservoir, hence facilitating drug release. Each of these aspects' functions strategically. With a single reservoir architecture, one medicine can be contained in a comparatively big port. Due to its refillable nature, it can hold a comparatively greater volume of medication and is ideal for extended use [48].

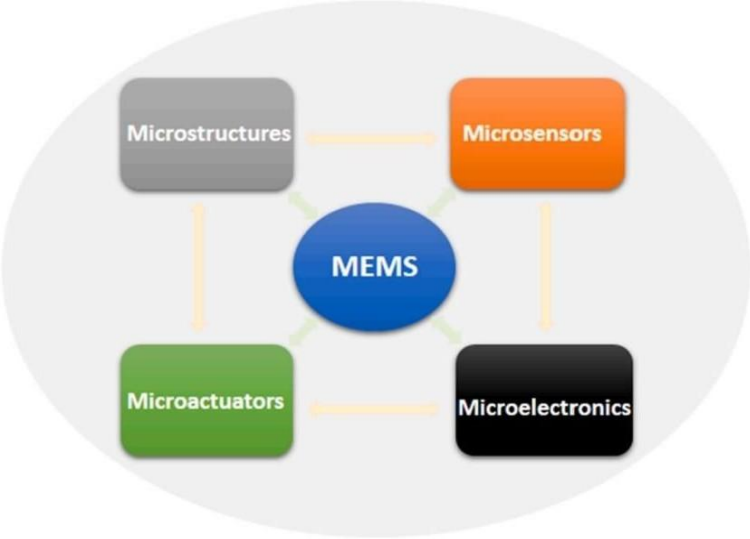

Figure 4: Schematic representation of MEMS components.

Improved therapeutic efficacy, prolonged half-life, sustained drug release, and reduced immunogenicity and cytotoxicity were all demonstrated by the cell-based therapy. Its migratory and chemotaxis potential were unaffected by the combination of nanoparticles and exploit cells. Because of this, the combined medication delivery approach is thought to be a viable strategy for medical therapy and pharmacological research [49,50].

4. TARGETED DRUG DELIVERY SYSTEM

This approach is an advanced technique employed recently due to its efficiency and reduced side effects. It is a system that delivers drugs in a targeted sequence which in turn leads to an increase in the drug concentration as it is being delivered to its target site [51]. The dosage of the drug is reduced to minimize side effects but its efficacy and strength remain untouched. This approach employs other drug carriers such as soluble polymers, biodegradable microsphere polymers, neutrophils, liposomes, micelles, and artificial cells amongst others [51].

This technique is gaining wide acceptance as it proves useful, especially in the fight against cancer. A study conducted by Murugan showed effectiveness in the use of this drug delivery system. Topotecan (TPT) and quercetin (QT) were delivered using polyacrylic acid chitosan surface-modified mesoporous silica nanoparticle (MSN) to target negative breast cancer cells (TNBC) (MDA-MB-231) and multidrug-resistant breast cancer cells (MCF-7) [52]. The surface of the nanoparticles was grafted with RGD-peptides which is an amino acid made up of Arg-Gly- Asp sequences. This was done to effectively target αvβ3 integrin. The RGD peptide led to an effective release of encapsulated drugs as well as cellular uptakes by the cancer cells. Both cell lines showed cell death, molecular and structural changes of cellular nucleus, endoplasmic reticulum, and mitochondria. A synergistic antiproliferative effect was also observed [52].

They reported 84.94% release in the tumor with a pH of 3.5 within 48 h. Their study showed higher antitumor activities across the cell lines that were investigated. Lin et al. used this approach to target HeLa cells. Mitomycin C (MMC) and 10-hydroxycamptothecin (HCPT) were co-delivered using a folate-functionalized soybean phosphatidylcholine micellar Nano formulation to determine their therapeutic effect on the HeLa Cells [53].

The study reported enhanced cellular uptake both in vitro and in vivo and an enhanced decrease in tumor burden compared to free drugs. These findings and much more suggest that a targeted drug delivery system is an area researchers' ought to also pay more attention to [53].

Table 2: The summary of recent drug delivery systems, their uses and merits, and demerits.

Drug Delivery System	Merits	Demerits	Therapeutic Uses
Targeted Drug Delivery	Compliance, controlled release	Costly, immunogenicity, non-specific targeting	Cancer, tumors
Self-Micro emulsifying System	Good for poorly soluble drugs, stable	Possible drug interactions, oxidation	Pulmonary infections
RBC Membrane-Camouflaged Nanoparticles	Immune evasion, long circulation, biocompatibility	Regulation, protein identification issues	Antitumor, anticancer research
Polymer-Lipid Hybrid Nanoparticles	Stability, biocompatibility, cell efficacy	Poor drug loading/entrapment	Targeted anticancer therapy
Combination Drug Approach	Higher loading, efficacy, low toxicity	Poor compliance, toxicity, inflexible doses	Chemotherapy, hypothermia therapy
Hyaluronic Acid-Based Nano Carriers	Biocompatible, biodegradable, immunologically safe	May promote cell proliferation	Cancer chemotherapy

4.1 Nanoparticulate Drug Delivery Systems

Typically, nanoparticulate drug delivery systems consist of two primary components: the therapeutic substance being delivered and the nanoparticle itself. To prevent devaluation and denaturing, the medication is either covalently bonded to the surface or, alternatively, is encapsulated and contained by the nanoparticle. Thakor & Gambhir [54].

The ideal particle size is around 100 nm tiny, which allows for immediate lymphatic system

clearance, blood brain barrier penetration, and sufficient drug delivery because of a large surface area. In order to extend blood circulation, water-soluble polymers like polyethylene glycol (PEG) or polysorbate 80 have been used in polymer coating more recently. Typically, nanoparticulate drug delivery systems consist of two primary components: the therapeutic substance being delivered and the nanoparticle itself. To prevent devaluation and denaturing, the medication is either covalently bonded to the surface or, alternatively, is encapsulated and contained by the nanoparticle [54].

4.2 Fast Dissolving Drug Delivery Systems

In subject-specific literature, FDTs are also referred to as porous tablets, quick melting/disintegrating tablets, or dispersible tablets. After being moistened by the salvia, the dissolution or disintegration occurs within a minute without the need for additional liquid or mastication throughout the administration procedure. The invention of fast dissolving oral films (FDOFs) was prompted by a number of environmental factors, including costly packaging, poor formulas that result in disagreeable flavors, friability, and challenging handling during manufacturing and shipping [55].

Oral solid dose forms that are most commonly used include tablets and capsules. These are still problematic even though they have many advantages over other delivery routes, such as self-medication, painlessness, and exact dose. The main issue with syrups and other liquid orals is appropriate dosing, even if tablets and capsules might be difficult for elderly, young, and dysphagic patients to swallow and fear suffocation. A unique oral medicine delivery technique is also required in exceptional instances such kinesis, allergic shocks, or just not having access to water [55].

During the 1970s, rapid dissolving medication delivery devices were primarily created to address swallowing issues. Approximately twenty-five years later, the FDA authorized Zaydis ODT, the first fast-dissolving tablet (FDT) containing the antihistamine loratadine in terms of object qualities like shape and thickness, oral strips are made up of a collection of flat, beautiful films that resemble postage stamps. A single dose up to 30 mg is possible. An optimal film should possess the following properties: good physicochemical capabilities along with flexibility, elasticity, and softness. Fast dissolving films have been the subject of numerous further studies that assess them as innovative drug carriers for various medications, highlighting their significance as novel drug delivery methods [56].

5. CHALLENGES ASSOCIATED WITH CURRENT DRUG DELIVERY SYSTEMS

Despite advances in drug delivery, especially for plant-based and nanomedicine approaches, various challenges remain.

A major obstacle is the limited and inconsistent literature on drug delivery systems and nanomedicine. The lack of uniform, detailed publications hinder the progression of research and the transformation of nanomedicines from the lab to clinical settings. Another key issue is the unknown safety and limited data regarding nanoparticles: while their benefits are well- recognized, information about their safety, interactions with non-target proteins, and effects on non-target organs is scarce. Some delivery systems use large particles, leading to poor absorption, low solubility, in vivo instability, reduced bioavailability, target-delivery difficulties, and adverse side effects. Smaller particles help but introduce new challenges [57].

Target-specific delivery-while reducing toxicity and improving treatment efficacy is unreliable if the drug cannot consistently reach the intended site in sufficient concentrations. For example, systemically administered siRNA is degraded by enzymes, and its negative charge impedes absorption. Nanoparticles like micelles and liposomes are limited by reactions in the body (e.g., phagocytic absorption, hepatic filtration), lowering their efficiency, and may cause toxicity [57].

Biocompatibility and immune acceptability are ongoing problems, especially since biological and synthetic materials interact differently with the body. Natural biological barriers, such as the blood-brain barrier (BBB), often prevent drug carriers from entering the brain, hindering treatment of cerebral diseases. Some carriers like monoclonal antibody-bound liposomes can provoke immune responses or be eliminated before effective action. Lastly, natural detoxifying organs like the liver

and kidney treat nanoparticles as waste, sometimes causing their accumulation and further limiting delivery effectiveness [58].

6. CONCLUSION

In conclusion, NDDS represent a paradigm shift in drug delivery, holding the potential to revolutionize treatment regimens across a wide spectrum of diseases. The field of novel drug delivery systems (NDDS) is undeniably transforming the landscape of medicine. Their ability to optimize drug action, minimize side effects, and personalize therapy for individual patients offers a brighter future for healthcare and improved quality of life for millions. As the field continues to evolve, we can anticipate even more groundbreaking innovations, ushering in a new era of personalized and precise medicine. From cutting-edge nanocarriers delivering drugs directly to diseased cells to personalized 3D-printed dosage forms, the possibilities offered by NDDS are truly remarkable. Recent advancements in gene therapy vectors, stimuli-responsive systems, and organ-on-a-chip technology further push the boundaries of innovation, promising even more targeted and effective treatments in the near future [59].

REFERENCES

1. Jain KK. An overview of drug delivery systems. Drug delivery systems. 2019 Aug 22:1-54.
2. Tiwari G, Tiwari R, Sriwastawa B, Bhati L, Pandey S, Pandey P, Bannerjee SK. Drug delivery systems: An updated review. International journal of pharmaceutical investigation. 2012 Jan;2(1):2.
3. Garbayo E, Pascual-Gil S, Rodríguez-Nogales C, Saludas L, Estella-Hermoso de Mendoza A, Blanco-Prieto MJ. Nanomedicine and drug delivery systems in cancer and regenerative medicine. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology. 2020 Sep;12(5):e1637.
4. Saraf, S. "Applications of novel drug delivery system for herbal formulations." Fitoterapia 81.7 (2010): 680-689.
5. Sarangi, Manoj Kumar, and Sasmita Padhi. "Novel herbal drug delivery system: An overview." Archives of Medicine and Health Sciences 6.1 (2018): 171-179.
6. Zhang J, Yang F, Wu H, Ong HL, Arnold P, Zhang M, Jiang Y, Bahar D, Yuan Z, Yang X, Fu YQ. Wearable transdermal drug delivery system controlled by wirelessly powered acoustic waves. Journal of Controlled Release. 2025 May 10;381:113619.
7. Bahraminejad S, Almoazen H. Sublingual and Buccal Delivery: A Historical and Scientific Prescriptive. Pharmaceutics. 2025 Aug 20;17(8):1073.
8. Prausnitz MR, Langer R. Transdermal drug delivery. Nature biotechnology. 2008 Nov;26(11):1261-8.
9. Dodou K. Exploring the unconventional routes—rectal and vaginal dosage formulations. Pharmaceutical Journal. 2012 Aug 29;289(7721):238.
10. Park H, Otte A, Park K. Evolution of drug delivery systems: From 1950 to 2020 and beyond. Journal of Controlled Release. 2022 Feb 1;342:53-65.
11. Markman M. Intraperitoneal antineoplastic drug delivery: rationale and results. The lancet oncology. 2003 May 1;4(5):277-83.
12. Al-Qaysi ZK, Beadham IG, Schwikkard SL, Bear JC, Al-Kinani AA, Alany RG. Sustained release ocular drug delivery systems for glaucoma therapy. Expert Opinion on Drug Delivery. 2023 Jul 3;20(7):905-19.
13. Alavi SE, Alavi SZ, Nisa MU, Koohi M, Raza A, Ebrahimi Shahmabadi H. Revolutionizing wound healing: exploring scarless solutions through drug delivery innovations. Molecular Pharmaceutics. 2024 Jan 30;21(3):1056-76.
14. Jin JF, Zhu LL, Chen M, Xu HM, Wang HF, Feng XQ, Zhu XP, Zhou Q. The optimal choice of medication administration route regarding intravenous, intramuscular, and subcutaneous injection. Patient preference and adherence. 2015 Jul 2:923-42.
15. Wu J, Chen G, Jia Y, Ji C, Wang Y, Zhou Y, Leblanc RM, Peng Z. Carbon dot composites for

bioapplications: A review. Journal of Materials Chemistry B. 2022;10(6):843-69.
16. Chu E, DeVita Jr VT, DeVita Jr VT. Physicians' Cancer Chemotherapy Drug Manual 2024. Jones & Bartlett Learning; 2023 Dec 14.
17. Domingo C, Saurina J. An overview of the analytical characterization of nanostructured drug delivery systems: towards green and sustainable pharmaceuticals: a review. Analytica Chimica Acta. 2012 Sep 26;744:8-22.
18. Yun YH, Lee BK, Park K. Controlled Drug Delivery: Historical perspective for the next generation. Journal of Controlled Release. 2015 Dec 10;219:2-7.
19. Kamaly N, Yameen B, Wu J, Farokhzad OC. Degradable controlled-release polymers and polymeric nanoparticles: mechanisms of controlling drug release. Chemical reviews. 2016 Feb 24;116(4):2602-63.
20. Bhagwat RR, Vaidhya IS. Novel Drug Delivery Systems: An Overview. Int J Pharm Sci Res. 2013;4(3):970-982
21. Dadwal A, Sonker A, Randhawa JK, Puri AK. Nanoparticle-Based Drug Delivery in Cancer Therapy and Its Role in Overcoming Multidrug Resistance. Front Pharmacol. 2020;11:762
22. Ma X, Zhao Y, Liang XJ. Advances in nanomaterial-based targeted drug delivery systems for cancer therapy. Front Bioeng Biotechnol. 2023;11:1177151
23. Malhotra S, Dumoga S, Singh N. Red blood cells membrane-derived nanoparticles: Applications and key challenges in their clinical translation. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2022 May;14(3):e1776
24. Xia Q, Zhang Y, Zhou F. Red blood cell membrane-camouflaged nanoparticles: Novel biomimetic platform for drug delivery. J Control Release. 2019 Jul 26;302:158-173
25. Vincy A, Kumar P, Kumar G. Recent Progress in Red Blood Cells-Derived Particles as Novel Bioinspired Drug Delivery Systems: Challenges and Strategies for Clinical Translation. Front Chem. 2022 Apr 26;10:90525
26. Wang X, Huang Y, Chen Q. Red blood cell derived nanocarrier drug delivery system: A new paradigm for targeted drug delivery. Inflammopharmacology. 2024 Jan;32(1):375-389
27. Chen WYJ, Abatangelo G. Functions of hyaluronan in wound repair. Wound Repair Regen. 1999;7(2):79-89
28. Zhao C, et al. Application of hyaluronic acid-based nanocarriers as a novel drug delivery system: a comprehensive review. Front Pharmacol. 2021;12:1105.
29. Mattheolabakis G, et al. Hyaluronic acid targeting of CD44 for cancer therapy: from receptor biology to nanomedicine. J Drug Target. 2015;23(7-8):605-618
30. Zhou M, et al. Targeted delivery of hyaluronic acid-coated solid lipid nanoparticles for rheumatoid arthritis therapy. Drug Deliv. 2018;25(1):716-722
31. Sivadasan D, Rahat I, Palakkott A, et al. Polymeric Lipid Hybrid Nanoparticles (PLNs) as Emerging Multimodal Nano-Carriers for Biomedical Applications. Pharmaceutics. 2021;13(8):1092
32. Rahat I, Mahato S, Bharadwaj S, et al. Polymer lipid hybrid nanoparticles: Emerging platforms for phytochemical delivery. Beilstein J Nanotechnol. 2024;15:118.
33. Pouton CW. Formulation of self-emulsifying drug delivery systems. Adv Drug Deliv Rev. 1997;25(1):47-58
34. Lipinski CA. Drug-like properties and the causes of poor solubility and poor permeability. J Pharmacol Toxicol Methods. 2000;44(1):235-249
35. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: Importance and enhancement techniques. ISRN Pharm. 2012;2012:195727
36. Gupta P, Vyas SP. Lipid based drug delivery systems: an update. Int J Pharm Sci Res. 2012;3(9):2828-2840
37. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res. 1995;12(3):413-420
38. Constantinides PP. Lipid microemulsions for improving drug dissolution and oral absorption:

physical and biopharmaceutical aspects. Pharm Res. 1995;12(11):1561-1572
39. Shah NH, Carvajal MT, Patel CI, Infeld MH, Malick AW. Self-emulsifying drug delivery systems (SEDDS) with polyglycolyzed glycerides for improving in vitro dissolution and oral absorption of lipophilic drugs. Int J Pharm. 1994;106(1):15-23
40. Pouton CW. Self-emulsifying drug delivery systems: formulation and performance. Adv Drug Deliv Rev. 2000;45(1):25-50
41. Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 2000;45(1):89-121
42. Tadros T, Izquierdo P, Esquena J, Solans C. Formation and stability of nano-emulsions. Adv Colloid Interface Sci. 2004;108-109:303-318
43. Kumar R, Indira S, Chella N, Ruchika TK. Nanoemulsion and microemulsion: A pharmaceutical review. World J Pharm Pharm Sci. 2016;5(4):527-546
44. Shah SA, Sayed N, Zafar H, Niaz S, Ahmad S. Surfactants used in microemulsions: A review. Giardia. 2021;7(2):319-33
45. Anton N, Vandamme TF. Nano-emulsions and micro-emulsions: Clarifications of the critical differences. Pharm Res. 2011;28(5):978-985
46. Wang L, Gao Y, Yang S, et al. Microemulsion and nanoemulsion as novel drug delivery systems: A review. J Drug Target. 2020;28(2):174-181
47. Elman NM, Ho Duc HL, Cima MJ. An Implantable MEMS Drug Delivery Device for Rapid Delivery in Ambulatory Emergency Care. Massachusetts Institute of Technology; 2015,425-451.
48. Islam S, Hossain MA, Uddin MJ, et al. Recent Advances in Micro-Electro-Mechanical Devices for Biomedical Applications. Micromachines. 2020;11(7):681
49. Gopi S, Abjel A, Sukheshkumar. MICRO ELECTRO MECHANICAL DRUG DELIVERY SYSTEM. Int J Novel Res Devel. 2023;8(10):468-480
50. Bashir R. MEMS: Enabled Drug Delivery Systems and Their Applications. J Control Release. 2015;219:205-214
51. Liu C, Wang Q, Yao Z, Deng H, Wang Q. Sequential Drug Delivery in Targeted Cancer Therapy: Strategies and Mechanisms. J Control Release. 2022 Mar 4;349:387-406
52. Li J, Cao Y, Zhang X, An M, Liu Y. Sequential Drug Release Strategies in Cancer Therapy. Biosci Health Manag. 2023 Oct;1(1):25-39
53. Pang Z, Cui Z, Yu Y, Yin W, Wang Y. Nanomedicine in cancer therapy: Current strategies and future perspectives. Signal Transduct Target Ther. 2023;8(1):29
54. Thakor AS, Gambhir SS. Nanooncology: The Future of Cancer Diagnosis and Therapy. CA Cancer J Clin. 2013 May-Jun;63(3):151-169
55. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. Int J Pharm Investig. 2013;3(2):67-76
56. Zaffar S, Verma AK, Raushan R, et al. Comparative Analysis of Fast Dissolving Tablet Vs. Oral Dissolving Film. Int J Recent Res Rev. 2024;17(1):1-15
57. Jahangirian H, Lemraski EG, Webster TJ, Rafiee-Moghaddam R, Abdollahi Y. A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. International journal of nanomedicine. 2017 Apr 12:2957-78.
58. Gupta TK, Budarapu PR, Chappidi SR, YB SS, Paggi M, Bordas SP. Advances in carbon based nanomaterials for bio-medical applications. Current Medicinal Chemistry. 2019 Nov 1;26(38):6851-77.
59. Vikas K, Arvind S, Ashish S, Gourav J, Vipasha D. Recent advances in ndds (novel drug delivery system) for delivery of anti-hypertensive drugs. Int. J. Drug Dev. Res. 2011 Jan;3(1):252-9.