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Advancing healthcare: Exploring recent innovations in drug delivery systems

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Abstract
It has been demonstrated that drug delivery systems can enhance therapeutic efficacy, decrease toxicity, increase patient compliance, and even enable whole new medical treatments. Drug delivery systems are technological processes that shape and preserve drug molecules into forms that are appropriate for administration, such as tablets or liquids. They expedite drug delivery to the precise targeted region in the body, maximising therapeutic effectiveness and reducing buildup of off-target substances in the body. Modern drug delivery systems (DDS) are designed with the aid of cutting-edge technology to accelerate systemic drug delivery to the intended target location, hence increasing therapeutic efficacy and reducing accumulation off-target in the body. As a result, they are crucial to the management and treatment of disease. These (DDS) are multifunctional, biocompatible, biodegradable, and have high viscoelasticity with an extended circulation half-life. They are made of nanomaterials or miniature electronics. This review covers the advanced information regarding Drug Delivery Systems and critical analysis of its importance to enhance drug efficacy.

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1. Introduction

The way a medicine is administered can significantly affect how effective it is. Some medications have an ideal concentration range where the greatest benefit is obtained; dosages outside or inside of this range can be harmful or have no therapeutic benefit at all. The very modest improvement in the effectiveness of treating serious diseases, on the other hand, has indicated an increasing need for a multidisciplinary approach to the delivery of medicines to targets in tissues. This led to the development of novel strategies for managing the pharmacodynamics, pharmacokinetics, non-specific toxicity, immunogenicity, bio recognition, and efficacy of medications. These novel approaches-often referred to as drug delivery systems (DDS)-are founded on interdisciplinary methodologies that unite polymer science, pharmaceutics, bio conjugate chemistry, and molecular biology. Drug delivery systems are technological processes that shape and preserve drug molecules into forms that are appropriate for administration, such as tablets or liquids. They expedite drug delivery to the precise targeted region in the body, maximising therapeutic effectiveness and reducing buildup of off-target substances in the body [1-2]. Due to improved systemic circulation and control over the drug's pharmacological action, DDS have been used successfully over the past few decades in the treatment of diseases and enhancement of health. The concept of controlled release emerged as a result of the development of pharmacology and pharmacokinetics, which demonstrated the significance of drug release in determining therapeutic success [3]. For more convenient, regulated, and targeted medication delivery, a number of drug delivery systems (NDDS) have recently been developed using innovative technologies. Every drug delivery system has unique characteristics that affect how quickly and how it works. This is mostly caused by the variations in their morphological, chemical, and physical properties, which will ultimately influence their affinities for different pharmacological compounds [4].

Aberrant gene expressions and new targets are constantly being discovered as we learn more about the biology of disease. However, because of their poor targeting effectiveness, therapies against these targets frequently fail in later phases of research [5].

We require a greater comprehension of how drug delivery materials interact with the extracellular matrix and the wide variety of cell types in the target tissue and along the route in order to overcome biological barriers and accomplish targeted distribution at both the tissue and cellular levels.

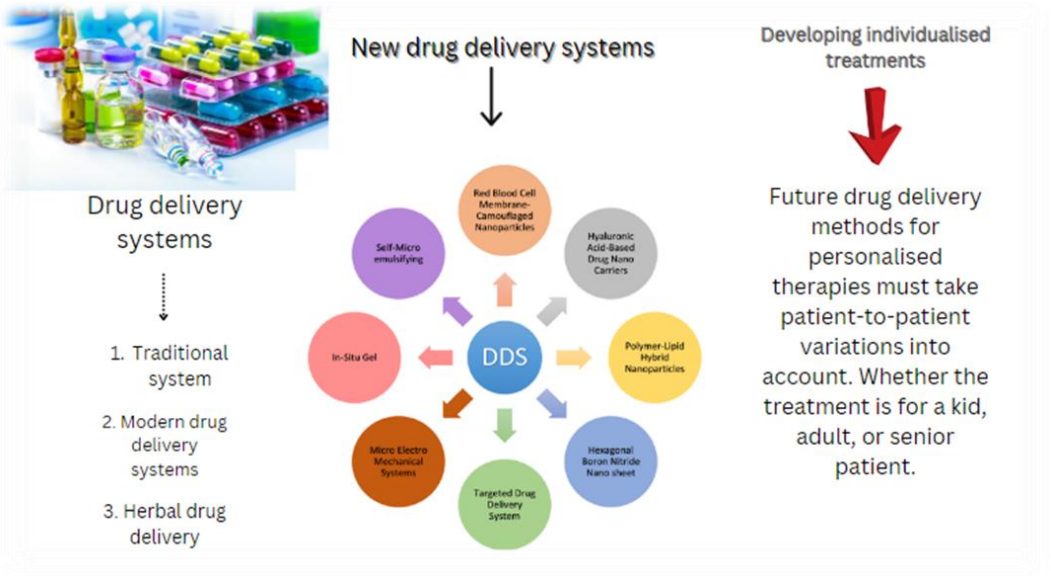

Fig 1: Graphical Abstract

2. Traditional drug delivery system

People in ancient times relied on medicinal plants. Despite being helpful, they lacked uniformity, homogeneity, and precision in drug distribution [6]. All medications were produced and kept in pill or capsule form before the use of controlled drug administration. It dissolves when it comes into touch with digestive juices, permeating the gut wall, and is then taken up by blood capillaries and absorbed into the bloodstream.

The drug's actual rate of release was influenced by this coating technique. However, it was adopted in the 10th century in the form of tablets with gold, silver, and pearl coatings. Advanced coating technology was also introduced in the 20th century with the use of keratin, shellac, sugar, enteric coating, and pearl coating; however, keratin and shellac were ineffectual due to storage instability and high pH for proper breakdown in the small intestine [7]. When Jatzkewitz created the first polymer-drug conjugate in 1955, he reported the development of the first nanoparticle therapy. The earliest nanotechnology, known as liposomes (lipid vesicles), was found in the 1960s [8-9]. The first protein-based microspheres were created in 1972 by Scheffel and a collaborator.

Peter Paul Speiser's research team created drug-loaded nanoparticles and microcapsules in 1976 using "micelle" and "emulsion" polymerization processes [10]. In order to address the issues with earlier forms of drug delivery and increase performance and sustainability, numerous new drug delivery methods must be created throughout this time. However, the difficulties involved in directing a medicine to a particular site and ensuring continuous release over a predetermined length of time make it frequently exceedingly difficult to build a viable carrier system.

3. New drug delivery system approaches

To reduce medication loss and degradation, to avoid negative side effects, to improve drug bioavailability, and to enhance the percentage of the drug accumulated in the necessary zone, a variety of drug delivery and drug targeting systems are currently being developed. The effective development of drug delivery systems based on organic, inorganic, and hybrid nanoparticles as drug carriers for active targeting, particularly in chemotherapy, has advanced significantly in recent years. Recently developed drug delivery systems (DDS) have improved qualities such smaller particle size, greater permeability, increased solubility, effectiveness, specific site targeting, stability, toxicity, and sustained delivery. Compared to traditional dosage forms, they can greatly increase the performance of medicinal agents [11-12]. Recent drug delivery systems are acknowledged to be the most recent advancements and creative comprehension of the pharmacokinetic and pharmacodynamic behaviour of pharmaceuticals in the building of an ideal drug administration system. Improving delivery systems that increase effectiveness while decreasing toxicity. Figure 1 shows the various kinds of drug delivery methods.

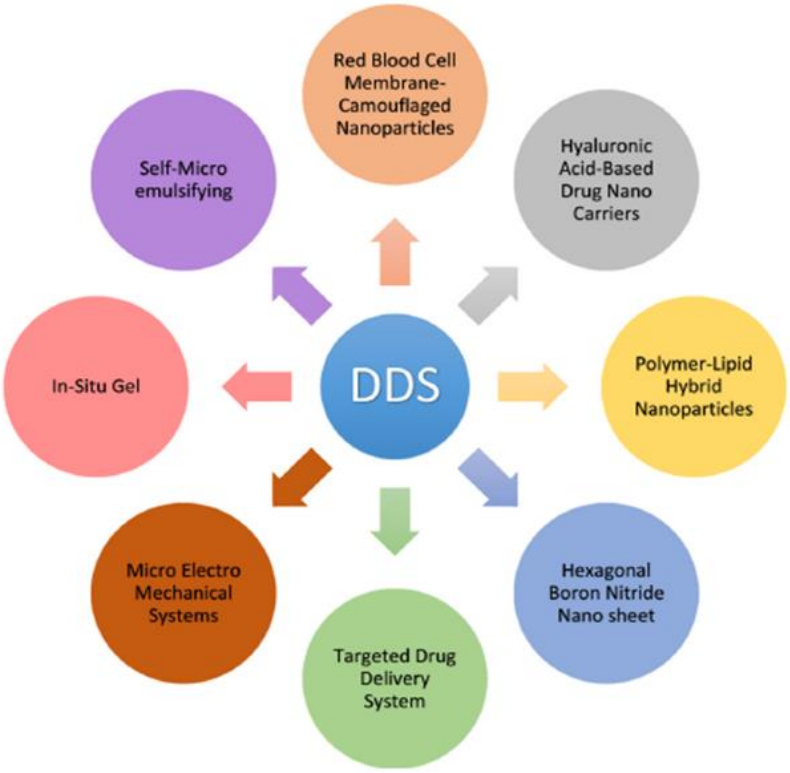

Fig 2: Some new recent drug delivery systems, source: Heliyon

For more than 20 years, scientists have seen the potential of nanotechnology to significantly enhance drug delivery and therapeutic targeting. Patients expect to gain greatly from improved delivery methods that reduce toxicity and increase efficacy, and new markets are made available to pharmaceutical and drug delivery businesses. Other methods of drug delivery concentrate on finding acceptable and alternative routes for the delivery of protein drugs other than through the gastrointestinal tract, where degradation may take place, or on bridging specific physical barriers, such as the blood-brain barrier, in order to better target the drug and improve its effectiveness.

3.1. Red blood cell membrane-camouflaged nanoparticles drug delivery system

Due to their low immunogenicity and capacity to maintain a lengthy systemic circulation (a lifespan of 120 days), the use of RBCM-NPs as drug delivery vehicles is very promising and offers a number of advantages. RBC vesicles are also naturally biocompatible and biodegradable because to the abundance of cell membranes, and they can quickly achieve high load capacities, leading to greater accumulation at the target region. Surprisingly, erythrocyte membrane-coated nano-formulations have been widely used in anticancer research to significantly improve, treat, and prevent cardiovascular disorders, encephalopathy, and other diseases [13-15].

3.2. Hexagonal Boron Nitride nanosheet drug delivery system

It has been demonstrated that hexagonal boron nitride is helpful in the development of drug delivery methods. According to Jedrzejczak-Silicka and colleagues' research, when exposed to H-BN enriched with gold particles, MCF-7 cell line cultures proliferated less than the typical L929 cell lines. H-BN was chemically exfoliated using a modified Hummers' process, subjected to a sonication procedure, and then functionalized with gold particles for the investigations and analysed using Neutral Red (NR) uptake assay [16]. Another study demonstrated the efficacy of H-BN as a therapeutic agent in photodynamic treatment (PDT), in situ monitoring, and miR-21 imaging when it was coupled with DNA oligonucleotide and copper (II) phthalocyanine (CuPc). Today, boron compound is acknowledged as an effective chemotherapeutic agent [17].

3.3. Polymer-lipid hybrid nanoparticles drug delivery system

Because of their greater stability in storage, improved ability to target disease cells, sustained drug release, and higher encapsulation ability, nanocarriers are becoming increasingly popular as drug delivery methods. Liposomes and polymeric nanoparticles are the most popular nanoparticles for drug delivery that are currently in use. Although lipid-based liposomes demonstrated great biocompatibility, they experienced drug leakage and instability after being stored, whereas polymeric ability and stability were not affected by this. By having a high encapsulation/drug loading, a polymer-based nanoparticle was able to overcome this restriction [18].

3.4. Self-micro emulsifying drug-delivery system

Lipid-based carriers come in a variety of forms, including suspensions, dry emulsions, microemulsions, and self-emulsifying drug-delivery systems (SEDDS) [19]. SEDDS' ability to incorporate hydrophobic drugs was previously reported. SEDDS has also been revised as self-microemulsifying 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 [20].

3.5. In-situ gel drug delivery system

One of the most cutting-edge methods for drug delivery is the use of in-situ gels. The in-situ gel drug delivery system aids in the prolonged and controlled release of drugs, as well as increased patient compliance and comfort, thanks to its special ability to change from Sol to Gel [21]. A range of organic and synthetic polymers are used to create in situ gel drug delivery systems. In-situ gel biomaterials are known to form through four different processes: (1) temperature and pH changes; (2) changes in the physical properties of the biomaterials, such as solvent exchange and swelling; (3) biochemical modification, such as enzymatic and chemical reactions; and (4) photo-polymerization [21-22].

3.6. Micro electro mechanical systems (MEMS) for drug delivery

MEMS technology has vast applications in fields such as actuators, drug delivery, motion sensing, accelerometers, and inkjet printing [23]. In order to create micro/nano-sized electromechanical and mechanical devices or implants, this technology uses microfabrication processes. It's interesting to note that by providing for extensive control over the topography, microarchitecture, and size of the final devices, the adoption of these approaches improves the effectiveness of these devices [24-25]. Due to the integration of their miniaturised sizes with multifunctional components, drug delivery systems made with MEMS technologies provide a number of advantages over traditional distribution techniques, including improved performance, automation, precision, and efficacy. It also contributes to the devices' less uncomfortable and invasive features [26].

3.7. Hyaluronic acid-based drug nanocarriers drug delivery systems

It has a linear macromolecular mucopolysaccharide composed of glucuronic acid and N-acetylglucosamine saccharide units that are proportionally linked. It has great viscoelasticity, is biocompatible, biodegradable, and can be linked with a particular cell surface receptor. It makes sense to employ hyaluronic acid as a vehicle for ocular medication delivery as long as the integrated pharmaceuticals are delivered regularly because it is a natural component of eye tissue and serves a crucial role in wound healing. They support medication targeting improvement, transdermal absorption, prolonged release, and thickening [27-28]. The use of HA-based nanocarriers for tumours with high levels of CD44 receptor expression has several advantages, including enhanced drug delivery, better therapeutic efficacy, higher cytotoxicity, significantly reduced tumour growth, and a high potential for targeted treatment [29].

3.8. Combined drug delivery approach

Drug resistance has frequently been a problem in medical care. Because of its wider target specificity and compatibility in boosting therapeutic effectiveness and improving clinical outcomes, combination therapy is more practical nowadays. In order to combat multidrug resistance, the combined medication delivery strategy has been widely used in cancer research and therapy. According to reports, using a combined drug delivery strategy lowers therapeutic dosage and side effects while maintaining effectiveness and a decline in drug resistance [30]. According to a review paper written by Pang et al., nanoparticles loaded in cells were more efficient than the nanoparticle drug delivery system in a specific combination drug delivery technique that focused on utilising cells in conjunction with nanoparticles. Improved therapeutic efficacy, longer half-lives, prolonged drug release, and less immunogenicity and cytotoxicity were all characteristics of the cell-based therapy [31].

3.9. Targeted drug delivery system

The drug's dosage is decreased to decrease side effects, but its effectiveness and strength are unaffected. Other drug carriers used in this method include soluble polymers, biodegradable microsphere polymers, neutrophils, liposomes, micelles, and synthetic organisms [32]. This technique is gaining wide acceptance as it proves useful, especially in the fight against cancer.

Murugun's investigation demonstrated the efficiency of this drug delivery method. Mesoporous silica nanoparticles (MSN) with polyacrylic acid chitosan surface modifications were used to deliver topotecan (TPT) and quercetin (QT) to target negative breast cancer cells (TNBC) (MDA-MB-231) and multidrug-resistant breast cancer cells (MCF-7). RGD-peptides, an amino acid composed of Arg-Gly-Asp sequences, were grafted onto the surface of the nanoparticles. This was carried out to successfully target v3 integrin. The RGD peptide caused the cancer cells to absorb the medications that were enclosed and released them effectively. Both cell lines displayed cell death as well as molecular and structural alterations to the mitochondria, endoplasmic reticulum, and cellular nucleus. Additionally, a synergistic antiproliferative impact was seen [33].

4. Herbal drug delivery

The relatively acidic pH of the stomach makes it likely that many components in herbal extracts will be destroyed. The liver may metabolise other substances before they enter the circulation. As a result, the necessary dosage of the medication might not get into the blood. There won't be a therapeutic impact if the medicine doesn't get to the blood at the'minimum effective level,' as it is also known. The body can more quickly and easily metabolise natural compounds. As a result, they have fewer, if any, side effects and offer greater bloodstream absorption, leading to more complete and efficient therapies.

Innovative herbal formulations such as liposomes, phytosomes, nanoemulsions, microspheres, transferosomes, and ethosomes have been developed using bioactive and plant extracts [34]. Phytosomes are unique molecules made up of phospholipid and lipophilic complexes of elements having plant origin, such as Silybum Marianum, Ginkgo Biloba, ginseng, and others. Additionally, they are known as phytolipids delivery systems. They have enhanced bioavailability, high lipophilicity, and therapeutic benefits. More research needed to develop effective herbal that would provide evidence of efficacy.

5. Developing individualized treatments

Future drug delivery methods for personalised therapies must take patient-to-patient variations into account. Whether the treatment is for a kid, adult, or senior patient, whether it requires a sustained-release or pulsative-release formulation, the patient's lifestyle, and how to handle the variations in biological barriers among various patients are some of the crucial aspects. Recent advances in machine learning and proteograph were used to analyse the contribution of manufactured nanoparticles to the protein corona

composition for deep and large-scale plasma proteomics, which assisted in the identification of protein variations among patients [35]. In order to create a customised strategy for drug delivery, future drug delivery systems must be thoroughly examined to better understand how physical and chemical features affect the crossing of biological barriers in a particular disease subtype as well as a specific patient group. For example, Due to changes in the degree of physical activity between patients with early or late-stage osteoarthritis, the mechanical loading in knee joints can affect an intraarticular drug delivery system [36].

6. Concluding remarks

Drug delivery and nanomedicine have recently attracted a lot of attention in research, testing, and several clinical trials, and they have become a very fascinating subject of study in contemporary science [37]. The future of medicine delivery looks bright and exciting. Drug delivery methods are still developing as the present therapeutic landscape transitions from small molecules to biologics. We anticipate the development of novel technologies that will improve the stability and encapsulation of biologics, allow for their prolonged release, and effectively transport them over intricate physiological barriers. Future technologies will also have an impact on healthcare internationally by improving the accuracy and efficacy of therapies as well as their accessibility and cost. Even though they are curative, the majority of innovative treatments are now only accessible to those who can afford them. It will be very important for the public, especially for those who do not have easy access to medical resources, to cut the cost of new pharmaceutical therapies rather than waiting for cheaper generic alternatives. To improve the effectiveness of these contemporary medication delivery methods and address the difficulties associated with their use, a lot more clinical studies and research are still required and to fill the knowledge gap

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