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REVIEW ON NOVALITIES AND DIFFICULTIES IN CONTEMPORARY DRUG SUPPLY

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Abstract : The contemporary drug supply system has undergone significant transformation due to advances in pharmaceutical manufacturing, digital technologies, globalization, and regulatory frameworks. These innovations have improved the efficiency, safety, and accessibility of medicines through automated inventory management, e-pharmacies, cold chain logistics, barcode tracking, and real-time supply monitoring. However, the system continues to face several challenges, including supply chain disruptions, shortages of essential medicines, counterfeit drugs, rising costs, regulatory complexities, and unequal access to healthcare, particularly in low- and middle-income countries. Global events such as pandemics, geopolitical conflicts, and natural disasters have further exposed vulnerabilities in pharmaceutical supply chains. Addressing these challenges requires stronger regulatory oversight, international collaboration, adoption of advanced technologies, resilient supply chain strategies, and equitable distribution policies. This article reviews the major novelties and difficulties in the contemporary drug supply system and highlights strategies for improving its efficiency, resilience, and sustainability. Novel drug delivery technologies have gained the importance to achieve modified delivery of herbal drugs their by increasing the therapeutic value as well as reducing toxicity. The main goal for developing such delivery systems is to minimize drug degradation and loss, to prevent harmful side effects and to increase bioavailability. Targeting is the ability to direct the drug loaded system to the site of interest. Among drug carrier one can name soluble polymers, microparticles made of insoluble (or) biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes and micelles.

Keywords - Technology and digital innovations, Supply chain management and logistics, Security, Compliance, Quality, Contemporary strategies, Global trends.

I.INTRODUCTION :

The field of drug delivery systems (DDS) has experienced remarkable growth, revolutionizing the way therapeutics are administered. Drug delivery systems encompass technologies that facilitate the targeted delivery of drugs to specific tissues or organs, improving efficacy while minimizing side effects. These advancements have been essential in the treatment of various diseases, including cancer, cardiovascular disorders and neurological conditions. This article delves into the innovations, challenges and future directions in drug delivery systems, highlighting their significance in modern medicine. Nanotechnology

has opened new avenues for drug delivery, enabling the development of nanoparticles, liposomes and dendrimers. These nanocarriers can encapsulate drugs, protecting them from degradation and enhancing their bioavailability. Additionally, nanocarriers can be engineered to target specific cells or tissues, reducing systemic toxicity. For example, liposomal doxorubicin, a nanotechnology-based formulation, has shown improved outcomes in cancer therapy by delivering the drug directly to tumour cells. Polymeric systems, including hydrogels, micelles and biodegradable polymers, offer controlled and sustained drug release. These systems are particularly useful in chronic conditions where long-term medication is required. For instance, biodegradable polymer-based implants are used to deliver drugs over extended periods, reducing the need for frequent dosing. This approach has been successful in treating conditions like diabetes and cardiovascular diseases. Targeted drug delivery systems are designed to deliver drugs to specific sites within the body, minimizing off-target effects. This is achieved through various mechanisms, such as ligand-receptor binding, magnetic targeting, or Ph sensitive release. Monoclonal antibodies, for example, can be used to target cancer cells, sparing healthy tissues and reducing side effects. This precision medicine approach has transformed the treatment landscape for diseases like cancer and autoimmune disorders. Trans dermal delivery systems provide a non-invasive method of drug administration through the skin. These systems use patches, gels, or creams to deliver drugs over an extended period. Transdermal patches have been successfully used for hormone replacement therapy, pain management and smoking cessation. The development of microneedles has further enhanced transdermal delivery, allowing for the painless administration of vaccines and biologics. Maintaining drug stability within delivery systems is a significant challenge. Many drugs, especially biologics, are sensitive to environmental conditions such as temperature and Ph. Ensuring the stability of these drugs during storage and administration is essential to maintaining their efficacy. While targeted drug delivery systems have shown promise, achieving precise targeting remains challenging. Factors such as the complexity of the human body, the heterogeneity of disease sites and the potential for off target effects complicate the development of highly specific delivery systems [1,2].

1.1 Globalization and Geopolitical Uncertainty:

- Increasing global interconnectedness exposes supply chains to geopolitical uncertainties, trade disputes, and disruptions.
- diversification of suppliers and manufacturing locations, real-time risk monitoring, and strategic partnerships to navigate geopolitical challenges.

1.2Digitalization and Technology Integration:

- Rapid technological advancements and the rise of Industry 4.0 require supply chains to adapt to new tools and processes.
- Implementation of technologies like IoT, blockchain, AI, and machine learning for real time visibility, predictive analytics, and automation to enhance efficiency.

1.3 E-commerce Growth:

- The exponential growth of online retail demands more agile and flexible supply chains to meet customer expectations for quick and reliable deliveries.
- Integration of e-commerce platforms with supply chain systems, use of advanced analytics to forecast demand, and investments in last-mile delivery solutions.

1.4 Sustainability and Environmental Concerns:

- Increasing awareness of environmental issues necessitates sustainable practices throughout the supply chain.
- Adoption of eco-friendly packaging, energy-efficient transportation, and the establishment of sustainable sourcing practices to align with corporate social responsibility goals.

1.5 Supply Chain Resilience:

- The COVID-19 pandemic highlighted vulnerabilities in supply chains, emphasizing the need for greater resilience.
- Development of robust contingency plans, diversified sourcing strategies, and the use of predictive analytics to anticipate and mitigate potential disruptions.

1.6 Talent Shortages and Skill Gaps:

- Rapid changes in technology and processes require a skilled workforce, and there is a shortage of talent in the supply chain sector.
- Investment in employee training, collaboration with educational institutions, and the adoption of talent management strategies to attract and retain skilled professionals.

1.7 Regulatory Compliance:

- Evolving regulations and trade policies pose challenges in maintaining compliance across international borders.
- Continuous monitoring of regulatory changes, investment in compliance management systems, and proactive engagement with regulatory authorities.

1.8 Cybersecurity Threats:

- Increased reliance on digital systems makes supply chains vulnerable to cyber threats and data breaches.
- Implementation of robust cybersecurity measures, regular audits, and employee training to mitigate the risk of cyberattacks.

1.9 Temperature control and cold chain logistics:

- Maintaining product integrity for temperature sensitive drugs requires robust cold chain systems

Patient centric supply chain:

- Focus on timely delivery affordability and accessibility to improve patient outcomes and satisfaction [3,4].

II.General overview:

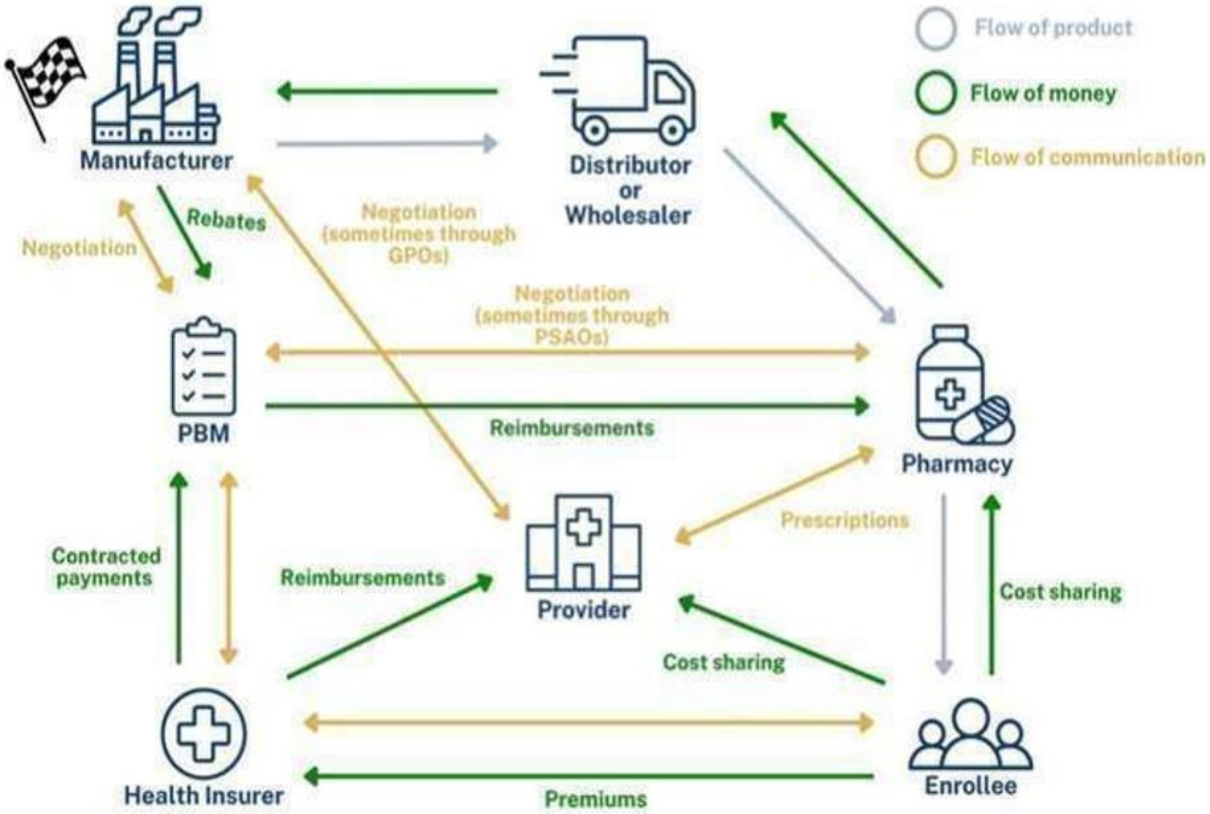

Figure.1. Drug supply chain system

2.1 Methods of the Contemporary Drug Supply System:

The contemporary drug supply system uses a combination of traditional and modern methods to ensure medicines are available, safe, and delivered efficiently.

1.Storage

Medicines are stored under recommended temperature, humidity, and security conditions. Cold-chain systems are used for vaccines and other temperature-sensitive drugs.

2.Distribution

Medicines are transported from manufacturers to warehouses, hospitals, pharmacies, and healthcare centres using efficient logistics systems.

3.Digital Supply Chain Management

Electronic inventory systems, barcode scanning, RFID, and GPS tracking improve accuracy, traceability, and real-time monitoring.

4.Quality Assurance

Regular inspection, quality testing, and compliance with Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP) ensure medicine quality and safety.

5.Pharmacovigilance

Monitoring adverse drug reactions and product safety after medicines reach patients.

6.Waste Management

Expired, damaged, or recalled medicines are collected and disposed of safely according to environmental and regulatory guidelines [6,7].

Figure. 2. Challenges contemporary drug supply

III.Nanotechnology in Drug Delivery System:

An extensive examination of the prior developments of drug delivery systems (DDS) based on nanoparticles will be covered in this study, along with novel research findings on the therapeutic improvement of antiretroviral therapy. Practitioners will be able to provide medications to target particular body parts thanks to the use of nanoparticle DDS. The application of nanoparticles as a DDS is having a discernible therapeutic impact in the treatment of cancers. DDS will also be used in medical imaging to illuminate brain function, cancers, or other body cellular activities. There is great promise for using nanoparticle DDS to enhance human health. Its unique features, such as its nanoscale structure, improved permeability and retention capacity, higher surface-area-to-volume ratio, ability to be functionalized on the surface etc., make it a successful drug delivery method for the administration of antiviral treatments. The more important variables that impact target-specific drug delivery, optimal cellular uptake, degree of opsonization by host immune cells, drug retention time, transcytosis, biological half-life extension, in vivo stability, and cytotoxicity are nevertheless the size, shape, charge, and surface topology of the nanoparticles. The review will shed light on the significant obstacle of clinical safety and efficacy as well as the elaborate role of drug delivery based on nanotechnology [9].

Applications:

1. Crossing Biological Barriers

a) Some nanoparticles can cross barriers such as the blood–brain barrier.
b) Useful in treating neurological disorders like Alzheimer's disease and Parkinson's disease.

2. Gene and Vaccine Delivery

a) Delivers DNA, RNA, and proteins into target cells.
b) Widely used in modern vaccine development and gene therapy.

3. Treatment of Infectious Diseases

a) Improves delivery of antibiotics and antiviral drugs.
b) Helps reduce drug resistance by enhancing drug concentration at infection sites.

4. Diagnostic Imaging (Theragnostic)

a) Nanoparticles act as imaging agents for early disease detection.
b) Can combine diagnosis and treatment in a single platform.

5. Oral and Transdermal Drug Delivery

a) Improves drug absorption through the gastrointestinal tract or skin.
b) Enables non-invasive drug administration.

6. Treatment of Chronic Diseases

a) Used for diabetes, cardiovascular diseases, arthritis, and respiratory disorders.
b) Provides long-lasting therapeutic effects with fewer side effects [10].

IV.Intelligent Drug Delivery Systems:

Intelligent drug delivery systems have emerged as one of the most dynamic research frontiers in the field of pharmaceutical formulations, integrating advances from nanotechnology, biomaterials, biomedical engineering, and artificial intelligence. Compared with conventional drug delivery strategies, intelligent systems enable precise spatial and temporal control of drug distribution and release within the body. However, current delivery platforms still face challenges such as insufficient targeting efficiency, limited responsiveness to complex physiological environments, and barriers to clinical translation. Addressing these challenges is essential for improving therapeutic efficacy, minimizing adverse effects, and enhancing patient compliance [11,12].

Special issue information:

This special issue “Intelligent Drug Delivery Systems” focuses on cutting-edge research and technological innovation in advanced drug delivery. It aims to highlight innovative strategies that enable targeted deliver and bio responsive release, thereby promoting the translation of intelligent delivery platforms from laboratory research to clinical applications. Closely relevant topics beyond this scope mentioned above are also expected.

- Micro- and nano-scale drug delivery systems.
- Targeted and site-specific drug delivery strategies.
- Bio responsive and stimuli-responsive drug release system.
- Cell–drug conjugates and cell-mediated delivery platforms.
- Drug–device combination products.
- Artificial intelligence–assisted design and control of drug delivery systems. (13)

V.Biomimetics in drug delivery systems

The application of biomimetics to prove the substantial issues in medicine and pharmaceutics is a promising method for the treatment of incurable diseases like cancer. In the recent studies, scientists made an effort to understand the biological systems and process, precisely. The comprehension of macromolecular structure and their sophisticated process at the cellular and subcellular level (like the structure of proteins and their biological functions) helps scientist to inspire and mimic these natural procedures for biomedical applications. The concept of bio mimesis in cellular processes includes the comprehensive understanding of cell growth and division, metabolic regulation, cellular interactions, and hormone signalling pathways [18].

Today, the researches on drug delivery systems are concentrated on targeted drug delivery which could transfer drugs into the cytoplasm of targeted cells without harmful toxic effects for healthy tissues or organs. Prior that, by the emergence of nanotechnology, the possibility of the encapsulation of drugs into nanocarriers was provided. Also, the problems with insoluble drugs, biodegradable therapeutic agents, and the drugs with high toxicity for biological systems were resolved considerably. Also, the small size of these nanoparticles enabled them for intercellular diffusion However, the targeted release of drugs within specific cells was not applicable thoroughly by these nanoparticles.

Therefore, biomimetics in advanced drug delivery systems created inherent abilities in biomimetic drug carriers, only by the surface modification with some amino acids, saccharides and lipids. For this purpose, the specific attention to the basic core materials, size, and the shape of drug carriers are so critical to have the capability of mimicking natural cells for cellular internalization. Additionally, a localized drug delivery within target cells may be obtained by biomimetic surface functionalization of these nanocarriers with specific biological ligands or moieties similar to the combination and functionality of external cell membrane Also, there are two main types of biomimetic drug carriers on the basic fundamental material: existing biological entities like inactivated viral vectors, bacteria vectors, and synthetic drug carriers which are biomimetic engineered nanoparticles with properties similar to biological materials[19].

For each section, the applied biomimetic methods for improvement in drug efficiency as well as drug release profile within target cells are studied. In the following, one can see these separated parts and their applications as drug carriers, which are included as biomimetic hydrogels, biomimetic micelles, biomimetic liposomes, biomimetic dendrimers, biomimetic polymeric carriers and biomimetic nanostructures. Although there are some reviews for the introduction of these drug carriers, the biomimetic papers have not been reviewed thoroughly [20].

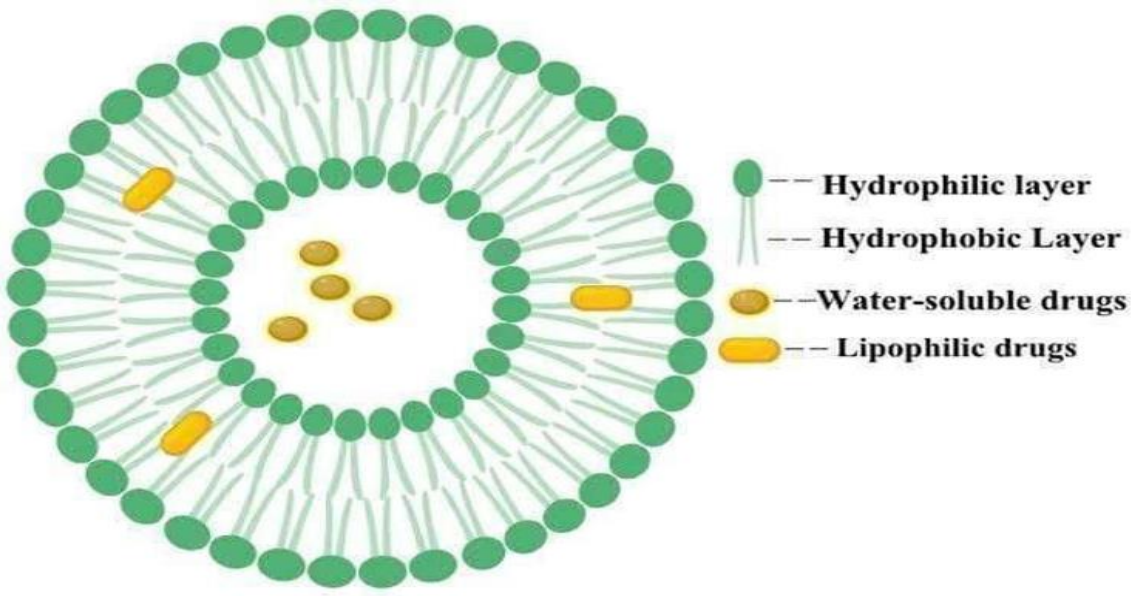

Figure.3. Biomimetics in drug structure

V. Extracorporeal Device

Intensive supportive therapy is all that is required for most patients suffering from dose related, drug toxicity, and drug removal by extracorporeal methods generally is indicated only for those patients whose condition deteriorates despite institution of these more conservative measures. However, a decision to intervene with extracorporeal therapy may be prompted by other clinical and pharmacologic considerations that are listed. For example, most in toxications with phenobarbital can be managed by a combination of supportive care and minimization of renal tubular reabsorption of this drug by forced diuresis and urine alkalinization. However, extracorporeal therapy is indicated if the serum phenobarbital level exceeds 100 µ g/ml [14].

General clinical considerations

- Clinical deterioration despite intensive supportive therapy.
- Severe intoxication indicated by depression of midbrain function or measured plasma or serum level.
- Condition complicated by pneumonia, sepsis, or other coexisting illness.
- Extracorporeal intervention can increase drug elimination significantly.
- Drug clearance is slow due to pharmacologic properties of intoxicant or patient's impaired renal or hepatic function.
- Intoxicant has a toxic metabolite or has toxic effects that are delayed.

VI. Targeted Drug Delivery:

Over the past few decades, extensive research has focused on targeted with the drug delivery system purpose of improving current Targeted drug delivery comprises the use of nano medicinal systems that are designed to preferentially and efficiently deliver a drug payload to the site of disease (i.e., the tumour microenvironment), with the aim of increasing the use of targeted drug delivery systems also avoids the use of solubilize (e.gTween-80 in Taxotere), thereby effectively preventing excipient-associated toxicity .

In studies, multiple nano medicinal systems have been used, and these encompass drug containing based on liposomes, polymers and proteins. While someformulations merely provide solubilization (e.g., Abraxane and Cellax), other nano carrier systems share the property of prolonged circulation kinetics (due to reduced clearance from the circulation) and increased tumour accumulation. The latter is predominantly mediated by the increased permeability of the_tumour vasculature _most passive targeting systems are dependent on this so-called ‘enhanced permeability and retention’ (EPR) effect. Recently, distinct nano medicinal strategies were pursued to investigate their utility for targeted delivery of taxanes in prostate cancer models. For these approaches, a clear distinction should be made between nontargeting and tumour targeting_nano medicines [16].

Advantages

- Protection from toxicity.
- Improving tissue macrophages distribution.
- Sustained delivery.
- Constant drug levels maintenance.
- Reducing the number of emergency visits.

Disadvantages

- The immune reactions can be occurred against intravenous administered carrier systems.
- Requires highly sophisticated technology for the formulation of NDDS drugs.
- Requires skilled man power for manufacturing, storage and administration.
- Difficult to maintain stability of dosage forms.
- Drug loading can be slow.

Applications

a) Nano-drug delivery systems that deliver large but highly localized quantities of drugs to specific areas to be released in controlled ways.
b) Controllable release profiles, especially for sensitive drugs.
c) Materials for nanoparticles that are biocompatible and biodegradable.
d) Architectures / structures, such as biomimetic polymers, nanotubes.

Conclusion

Drug delivery systems have significantly improved the way drugs are administered, offering new hope for the treatment of various diseases. While challenges remain, ongoing research and technological advancements are paving the way for more precise, efficient and patient-friendly delivery systems. As we look to the future, the continued evolution of drug delivery systems will play a precarious role in shaping the landscape of modern medicine. Supply chain management in 2023 is marked by a complex interplay of global factors, technological advancements, and changing consumer expectations. Successfully navigating these contemporary issues requires a proactive and adaptive approach, where businesses leverage technology, foster collaboration, and prioritize sustainability to build resilient and efficient supply chains. As the landscape continues to evolve, staying informed and agile remains crucial for supply chain professionals aiming to drive success in their organizations.

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