# Overview on Controlled Drug Delivery System (CDDS)

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**Abstract: Controlled Drug Delivery Systems (CDDS) have revolutionized pharmaceuticals by enabling precise control over drug release within the body. Beginning in the mid-20th century with basic sustained-release formulations, CDDS has progressed significantly, encompassing various types like reservoir, matrix, and targeted systems. These systems employ diverse approaches such as diffusion-controlled, stimuli-responsive, and implantable devices to regulate drug delivery. Polymers play a pivotal role in CDDS, influencing release kinetics. Both natural (e.g., chitosan) and synthetic polymers (e.g., PLGA) are utilized, determining release rates based on their biodegradability and compatibility with drugs. Design and performance of CDDS depend on multiple factors including drug characteristics, choice of polymers, device design, and environmental conditions. The advantages of CDDS include improved therapeutic outcomes, reduced side effects, and enhanced patient compliance. However, challenges like complex manufacturing processes and potential issues like dose variability exist. The future of CDDS holds promise in personalized medicine, nanotechnology-driven smart drug delivery, and bioengineered systems, paving the way for highly tailored therapies and further advancements in healthcare.**

**Keywords: controlled release, dissolution, diffusion, polymers, oral, parenteral, matrix, encapsulation, reservoir, ionisation, dissociation.**

## INTRODUCTION

With so many high-tech products available on the market, controlled release drug delivery systems have drawn a lot of attention in the last 20 years [1]. Traditional drug delivery systems (DDS) have almost no control on the successful target concentration and very little control over the drug distribution. This dose method will provide unexpected, constantly-varying plasma concentrations [2]. In order to facilitate rapid and complete systemic absorption of the treatment, many common oral medications, including capsules and tablets, are made to release the active ingredient as soon as the oral route is administered [3]. Many hydrophilic polymers have been studied recently and are being utilized in the creation of intricate controlled release systems [1].

1. Drugs and Drug Delivery Systems

Drug delivery systems are designed to make the administration of medications more efficient. The medication is the most crucial component of any formulation. The purpose of the remaining components in a formulation, referred to as excipients, is to increase the drug's effectiveness [4]. In recent years, there has been a lot of attention paid to the development of DDS that involves, for example, the use of several carrier membranes to handle prolonged delivery duration with minimum changes in delivery speed [5]. DDS, which can precisely target medications at a particular body location or monitor discharge, has a significant influence on the health system [6]. Over the last 40 years, oral controlled release (CR) formulations have been developed because of their many therapeutic benefits [7].

## HISTORICAL PERSPECTIVE OF CDDS (CONTROLLED DRUG DELIVERY SYSTEM):

The Journal of Controlled Release (JCR) released its inaugural issue in 1984. The two founding editors of JCR, Jorge Heller and Jan Feijen, made it very evident in their inaugural editorial that the journal's purpose was to be the premier platform for drug delivery experts to share ideas through excellent papers [8].

1. Origin of CDD:

While pumping rabbit blood within a Silastic® (silicone rubber) arterio-venous shunt in the mid-1960s, Harvard's Judah Folkman, MD, discovered that the rabbits would go to sleep if he exposed the tubing to anesthetic gasses on the outside [9]. He suggested that if silicone didn't fluctuate in size or composition, small, sealed pieces of such tubing carrying a medicine may be implanted and turn into a constant rate drug delivery system [10]. In addition, he demonstrated—which is evident now—that the rate dropped as tube thickness grew. This was the first indication, however, of a zero order controlled drug delivery implant in vivo. In the meanwhile, exceptional synthetic drug scientist and entrepreneur Alejandro ("Alex")

Zaffaroni, located in Palo Alto, California, had been considering the idea of controlled delivery devices and zero order delivery while working across the nation. After learning about Folkman's work, he traveled to Boston to speak with him about it. Inspired by Folkman's research as well as his own ideas, Zaffaroni established a business in the late 1960s that was centered around the notion of controlled drug delivery (also known as CDD). Taking the first two initials of his first and surname names, he dubbed it Alza. He extended invitations to Folkman and Takeuchi ("Tak") Higuchi, a drug delivery expert at the University of Kansas, to join his Scientific Advisory Board or to assume senior administrative roles with Alza. Both made the decision to join Alza's SAB. He persuaded Alan Michaels, the inventor and president of Amicon Corp. and a former MIT chemical engineering professor, to become president of Pharmetrics, a new business he established in 1970 to create and develop the unique zero order DDS for Alza [10].

2. The zero-order "controlled" drug delivery mechanism "MACRO era":

Alza's initial designs for CDD devices were macroscopic in size. One was an intrauterine device (IUD) known as Progestesert that delivered the contraceptive steroid progesterone at a steady rate in the uterine cavity; the other was an ocular insert called Ocusert® that released the anti-glaucoma medication pilocarpine in the eye at a constant pace. In a constant rate, reservoir DDS device, each employed poly(ethylene-co-vinyl acetate) or polyEVA as the rate-controlling membrane (RCM), resulting in a zero order, flat PK. Later, the Population Council created the Norplant, a subcutaneous contraceptive implant made of six silicone rubber tubes (crosslinked polydimethylsiloxane, or PDMS) that were loaded with the contraceptive steroid levonorgestrel. This was a clear development of the proposal made by Folkman and Long in their 1964 paper [10].

3. The "MICRO era" featured phase-separated depot delivery systems, biodegradable microparticles, and sustained release:

In the 1960s and 1970s, biodegradable polymers of poly(hydroxy acids) were created for sutures; drug delivery researchers embraced this technology in the 1970s, and it entered clinical use in the 1980s. As a result, "sustained release" macro/microscopic biodegradable depot systems, which initially entered clinical use in the mid-to late 1980s, replaced the macroscopic, zero order PK devices that dominated the field of controlled DD in the 1970s and 1980s. Poly(glycolic acid) (PGA) was created and patented in the 1960s by Ed Schmitt and "Roco" Polestina of Davis & Geck, Cyanamid Co. to be used as a biodegradable suture [11]. George Boswell and Richard Scribner, two Du Pont researchers, combined peptide medications with PLA in the late 1960s to create microparticles and pellet depot DDS. It's noteworthy to notice that they filed the patent application in 1969, even though they patented this technique in 1976 [12]. Southern created a [D-Trp-6 LHRH]/PLGA microparticle for DebioPharm in the early 1980s to treat prostate cancer. In 1986, this product—known as Decapeptyl® LP—was introduced to European clinics. It is still available on the market today and was the first injectable, degradable microparticle depot DDS to get clinical approval [13].

| 1950 | 1980 | 2010 |
|---|---|---|
| 1st Generation | 2nd Generation | 3rd Generation |
| Basics of Controlled Release | Smart Delivery System | Modulated Delivery System |
| Oral<br>• Once-a-day or twice a day | Zero-order<br>• zero-order vs First-order | Poorly soluble drug<br>• Non-toxic excipients |
| Transdermal<br>Once-a-day, once-a-week | Peptide & protein<br>Durable depot with biodegradable polymers<br>Delivery to pulmonary sites | Peptide & protein<br>• Delivery for >6 months<br>• Control of release kinetics<br>• Non-invasive delivery |
| Drug release mechanisms<br>Dissolution<br>Diffusion<br>Osmosis<br>Ion-exchange | Smart polymers & hydrogels<br>Responsive to the condition<br>Auto-release | Smart polymers & hydrogels<br>• Signal specificity &sensitivity<br>• Rapid response kinetics |
| | Nanoparticles<br>• Tumor-specific delivery | Targeted drug delivery<br>• Non-toxic to non-targetcells<br>• Overcoming the barrier of blood-brain |
| Successful control of physicochemical properties of delivery | Cannot overcome the biological barriers | Should surmount both biological and physiochemical barriers |

Fig. 1: Background from 1950 on drug delivery technologies and technology needed for the future [14].

TYPES OF CONTROLLED DRUG DELIVERY SYSTEMS:

Controlled drug delivery systems are broadly classified as follows:

1. Oral controlled release systems
2. Parenteral delivery systems
3. Dental systems
4. Ocular systems
5. Transdermal systems
6. Vaginal & uterine systems
7. Injections & implants. [15]

1) Oral controlled release system:

Oral delivery is necessary for protein and peptide medical products, which are appropriate for administering therapeutic agents that are specifically absorbed into the gut. Gelatin capsules were coated with sodium alginate, linked to appropriate calcium chloride concentrations, and subjected to in vitro tests for intestinal and stomach resistance. Human volunteers were asked to test gelatin capsules coated with 20 percent w/v of the polymer that produced the most promising in vitro findings for its in vivo gastrointestinal tract action. According to radiographic examinations, the alginate-coated gelatin capsules have remained unstable for up to three hours in the stomach, but the uncoated gelatin capsules crumbled into the stomach after fifteen minutes of ingestion [16].

2) Parenteral conteolled release system:

Parenteral Kushwaha found that the amount of drug placed into the matrix, the solution, and the medium discharge all affect how long the drug takes to release and discharge. This was achieved by combining the polymer polyvinyl alcohol with the natural macromolecule gum Arabica. This system's adjustable plasticizer, homopolymer, and cross-linker compositions allow for fine-tuning the release kinetics of the system. Progesterone delivery under control has been achieved with chitosan 45–300 μ microspheres [17].

3) Dental controlled release system:

Somayaji et al. employed the ethylcellulose strip to decrease sub-gingival bacteria in periodontal pocketing for metronidazole and tetracycline. Based on the length of time the medication was applied, the patients were split into five groups and superficial scaling was administered. The following have been marked at sites: metronidazole, tetracycline, and placebo. In order to acquire samples of critical microbiology for gram staining and culture techniques, the sites were cleaned, insulated, and prepared [18]. Several controlled distribution methods, such as solvent-activated hydrogels and osmotic pumps, biodegradable chemically controlled and biodegradable compounds, macromolecule-controlled matrices and storage tanks, and biodegradable compounds were being developed in the 1960s to monitor the release of the macromolecule. With continued advancements, "smart" materials have been developed that release drugs to excite the surroundings. Pharmaceutical nanotechnology led to the development of liposomes, dendrimers, polymer nanospheres, and polymer micelles. Microelectronics is one of the CR technologies that enables remote and pulsative therapeutic release [19].

VARIOUS APPROACHES IN THE DESIGN OF CONTROLLED DRUG DELIVERY SYSTEM:

These are those methods or process by which we have to design the Controlled relesse formulations they are:-

1) Diffusion controlled release

Diffusion can happen via polymer chains or through holes in the polymer matrix. A drug's release rate in a diffusion system is determined by how quickly it diffuses past an inert membrane barrier. This barrier is often made with an insoluble polymer [15]. The water circulation and consequent release of the dissolved substance in these systems are controlled by the water-insoluble polymer. When the components of the CR system pass through a medication, diffusion takes place. Diffusion can happen through chains of polymers or through holes in the polymer matrix. The two groups are narrowly divided:

a) Reservoir Devices.

b) Matrix Devices.

The fundamental mechanics of drug release are drastically different from these two processes: a. Reservoir Devices:

This approach involves encasing a core medication in a water-insoluble polymer. The medication separates into the membrane and switches out the tablet or particles that surround the liquid. The active agent is released into the environment via the ratelimiting membrane. In these systems, the pace of medication delivery is comparatively steady.

b. Matrix Devices:

The medication or active ingredient will be dispersed throughout a polymer matrix in the homogenous system, also known as a matrix system. Diffusion occurs when the medication leaves the polymer matrix and enters the external environment. This kind of device often lowers its rate if the release goes forward since the active agent has a longer trip distance and requires more time to release. [20–21].

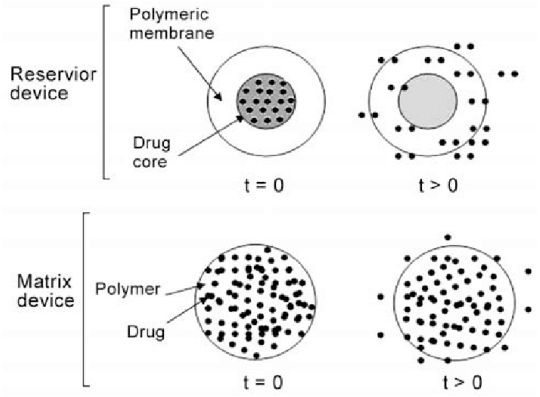


Fig. 2: Schematic representation of diffusion-controlled reservoir and matrix-controlled reservoir [22]

According to Fick's first law of diffusion (Equation (1)), the concentration gradient (dc/dx) determines the molar flux (J) owing to diffusion. According to Fick's second law (Equation (2)), the second derivative of concentration with space and the rate of change in the solution's concentration at a given location in space are proportionate. It addresses how the concentration gradient varies over time and at any distance. Fickian diffusion is defined as drug release that complies with Fick's law; non-Fickian or anomalous diffusion is defined as drug release that does not comply with the law [23].

Fick's first law:

$$J \propto dc/dx \text{ or } J = D. dc/dx \quad (1)$$

Fick's second law:

$$dc/dt = D. d^2c/dx2 \quad (2)$$

dc = change in concentration of drug (g/cm3 ),
dx = change in distance (cm),
D = diffusion constant (cm2/s),
J = flux (cm−2 s −1),
dt = change in time (s).

Membrane-controlled and monolithic or matrix systems are two categories for diffusion-controlled systems. In membrane-controlled systems, a thin polymeric membrane covers the medication, which is kept within the core as a reservoir. There are two possible membrane states: porous and non-porous. medications are released by membrane diffusion, and the rate of release is determined by the membrane's thickness, porosity, and the physicochemical properties of the medications (diffusion coefficient, molecular size and diffusivity, protein binding, and dose). Compaction and press coating of tablets are common techniques for creating membrane-controlled reservoir systems [23].

2) Dissolution controlled release

Slow-soluble polymers or microencapsulation control how quickly the medication dissolves in these materials. After the covering dissolves, the medication may be dissolved. The thickness and makeup of the coat can be changed to control the rate at which the medication releases. Certain formulations include a portion of the total dose that is released immediately after ingestion to create a pulse dosage. For pellet dosage forms, diffusion-controlled pharmaceuticals can be made as tablets or encapsulated. Two categories of products can be distinguished by their dissolution:

a) Encapsulation Dissolution controls.
b) Matrix Dissolution control.

a. Encapsulation Dissolution control:

With this gadget technique, the medications are covered with granules or individual particles of a slow-dissolving material. Tablets can be made by immediately packing (or storing in capsules) the coated particles. The pace at which the medication dissolves (and hence the availability for absorption) is regulated via microencapsulation. Until the covering dissolves, the material is susceptible to dissolution. The thickness and makeup of the coat can be changed to control the rate at which the medication releases. These things shouldn't be chewed on since the covering may become weak. Embedded pellets have the advantage of being less sensitive to stomach emptying before absorption occurs. Generally speaking, pellets enter the small intestine (where the majority of absorption occurs) more uniformly than non-disintegrating tablets do.

b. Matrix Dissolution control:

Using a slow-dissolving carrier, the medication is compressed using a different technique in this apparatus. This regulates the rate of drug release through the matrix's porosity, the presence of hydrophobic additives, the moistening system, and the particle surface [24, 25].

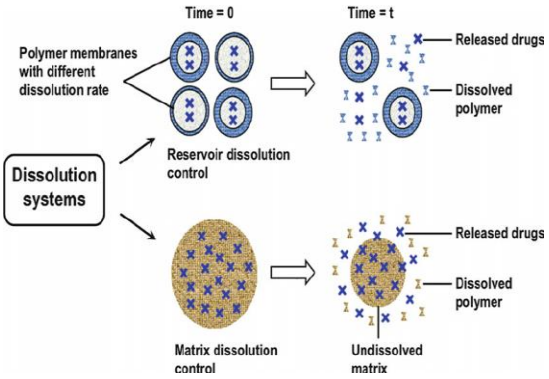


Fig. 3: Schematic of Dissolution controlled release systems reservoir (encapsulation) method and matrix method. [26]

3) Ion exchange resins:

Water-insoluble substances called resins have cationic or anionic groups arranged in repeating patterns along their resin chain. The process of creating the drug-charged resin involves either repeatedly subjecting the resin to the drug in a chromatographic column or allowing the resin to remain in contact with the drug solution for prolonged periods of time. After that, the drug-resin is dried to produce particles or beads and cleaned to get rid of any contaminating ions. The drug molecules are exchanged and diffuse out of the resin into the bulk solution when a large concentration of a suitably charged ion comes into contact with the ion-exchange group [15].

POLYMERS USED FOR CONTROLLED RELEASE DELIVERY SYSTEMS:

Research on pharmaceuticals has always centered on creating or discovering powerful medications with novel forms of biological activity. More focus is being placed on the mode of delivery of these medications, which is still a crucial area of study. Drugs have been incorporated into solid polymers as one method. The most promising are controlled release polymeric systems because they minimize unwanted side effects, enhance medication safety and efficacy, and improve patient compliance by reducing the frequency of administration. There is a wide variety of polymers and formulation factors that may be used to regulate the rate of medication release from controlled-release devices. The drug's physical and chemical characteristics, the intended location of administration, and the desired release rate and duration are taken into consideration while choosing among these factors.

Characteristics of Ideal polymer system

An ideal polymer system should possess the following characteristics:

1. It should be inert and compatible with the environment.
2. It should be non-toxic.
3. It should be easily administered.
4. It should be easy and inexpensive to fabricate.
5. It should have good mechanical strength.

Criteria followed in polymer selection:

A polymer that is selected as a possible drug carrier has to have the following characteristics:

1. The polymer needs to have a limited distribution, a finite molecular weight, and be easily synthesized.
2. It need to offer locations for drug attachment or release so that drug-polymer connections may potentially be included.
3. The polymer must not be harmful, allergic, or provocative in any other way in order to be compatible with the biological environment.
4. It must be biodegradable or leave the organism once its purpose has been fulfilled [27].

FACTORS INFLUENCING THE DESIGN AND PERFORMANCE OF CONTROLLED RELEASE PRODUCTS:

1. dosage size:

0.5–1 grams is the highest limit for taking medications orally, usually as a single dosage.

2. Ionization and Dissociation constant:

According to the pH partition theory, unmodified drug species would be absorbed by different body tissues first, hence it is very important to take into account the relationship between the drug's environment and its dissociation constant. In conventional dose forms, the medication entirely dissolves in the stomach and absorbs in the small intestine; however, in the controlled system, the medication may remain in solid form in the gut, indicating that the drug's solubility may change as it is released. Because medication dissolution will limit the release duration of the dose form in the GI tract (GIT), those compounds with lower solubility need to be intrinsically regulated. 0.1 mg/ml is shown to be the minimum limit of solubility for a drug to be formulated for CR.

3. Partition coefficient:

Higher partition coefficient chemicals are often lipid-soluble and have higher bioavailability, whereas lower partition coefficient compounds penetrate the membrane less and have lower bioavailability.

4. Stability of the drug:

pharmaceuticals that exhibit instability in the stomach area are given in a regulated manner, allowing for a delayed release into the intestine. This can also be detrimental to pharmaceuticals that undergo

gastrointestinal degradation. Therefore, medications that are typically unstable in the gastrointestinal system should not be used for CR.

5. Molecular weight:

High molecular weight compounds are not ideal candidates for use in CR. The drug's ability to permeate the membrane is known as diffusivity, and it is based on the dimensions and composition of the membrane's cavities.

6. Biological Half-life:

Compounds having a half-life of less than eight hours make excellent candidates for CR. Drugs with a half-life of less than two hours, however, require higher dosages for CR. In CR, compounds having half-lives longer than eight hours are not used. Thus, if the location, extent, etc. of the metabolic reaction is understood, medicines with extremely short or long half-lives are not suited for CR form can be produced [28–31].

7. Drug properties:

A drug's physicochemical features, such as its solubility, stability, charge, partitioning characteristics, and protein binding property, are crucial to the functioning and design of controlled release systems.

8. Drug delivery route:

Depending on the technical advancement of a suitable controlled release mechanism or device, the area of the body in which pharmaceuticals will be given or delivered may be restricted. The physiological restrictions imposed by the route, such as first pass metabolism, gastrointestinal motility, blood flow, and the liver and spleen's retention of minute foreign particles, may also have an impact on the performance of the controlled release systems.

9. Target sites:

It is preferable to increase the percentage of the dosage that reaches the target organ or tissue in order to reduce undesirable side effects. By employing carriers or municipal administration, this can be accomplished in part.

10. Acute or chronic therapy:

When building controlled release systems, it's crucial to take into account whether the goal is to cure a condition or regulate it. It also helps to determine how long medication therapy should last. Furthermore, compared to traditional dose forms, rate-controlled drug delivery devices typically have different long-term toxicity.

11. The illness:

The pathological alterations that occur during a disease can have a big impact on how a good medication delivery system is designed.

12. The patient: A controlled release product's design may be influenced by the patient's characteristics, such as age, weight, gauntness, or ability to walk or remain bedridden. For instance, due to variances in individual G.I. motility, single unit-controlled release products are more vulnerable to intra- and inter-subject variation [32].

BIOLOGICAL FACTORS INFLUENCING THE DESIGN AND PERFORMANCE OF CONTROLLED RELEASE PRODUCTS:

A thorough understanding of the drug's disposition should serve as the foundation for the creation of a controlled release product. This would need a thorough analysis of a drug's ADME properties after several dosages. It is assumed throughout the discussion that the drug's biological action is matched by its concentration in bodily tissue or blood [33].

1. Absorption:

The medicine needs to be consistently released from the controlled release mechanism and then uniformly absorbed in order to maintain a steady blood or tissue level. Drug breakdown through solvolysis or metabolism, drug binding to proteins, physical loss, or maybe site- or dosage-dependent absorption can all contribute to the proportion of drug absorbed from a single non-controlled dose or medication being relatively low at times. It is well known that the absorptive character of the various segments of the G.I. tract varies, which in turn can influence the amount and rate of absorption of certain drugs. If the drug were to be absorbed erratically, as might happen in a route of administration with variable absorptive surface, such as the G.I.tract, the design of a controlled release product would be more difficult or prohibitive compared to the oral route. These medications include the amino glycosides Gentamycin, the quaternary ammonium compounds, and the oral anticoagulant dicoumarol [34–37].

2. Distribution:

Since drug distribution into tissues not only reduces the concentration of circulating drug but can also be rate limiting in its equilibration with blood and extracellular fluids, it can play a significant role in the total drug elimination kinetics.

3. Drug metabolism:

Drug metabolism can either inactivate an active substance or change an inert substance into an active metabolite. Drugs can undergo metabolic modification

in a range of tissues, some of which have higher enzyme concentrations than others. For instance, the liver is the organ primarily in charge of metabolism; as a result, the most metabolic conversion happens after a medication has entered the bloodstream.

4. Length of action:

Clearly, a drug's biological half-life and, consequently, its length of action, are important factors to take into account when deciding whether to provide a medication under controlled release. A drug's distribution, metabolism, and removal all have an impact on its biological half-life [38].

5. Total clearance (Cl):

The CL is the estimated volume of unmetabolized drug distribution that is removed per unit of time by any drug removal pathway. The dosage D, absolute bioavailability, and AUC may all be used to get the value of CL.

$$Cl = D.F / AUC$$

The Cl is the key to estimate the dose rate R° for controlled release dosage forms and is related to the mean steady state concentration [39].

ADVANTAGES AND DISADVANTAGES OF CONTROLLED RELEASE PREPARATIONS [40-43]:

Advantages:

1. A decrease in how frequently drugs are administered.
2. A rise in patient adherence.
3. Less variation in blood medication levels.
4. A decrease in the overall amount of drugs used in comparison to traditional therapy.
5. Less drug buildup when receiving long-term care.
6. A decrease in the local and systemic toxicity of drugs.
7. Stabilization of health status (due to more consistent drug dosages).
8. Some medications have improved absorption due to spatial control.
9. Cost-effective for both patients and medical professionals.

Limitations:

1. Delay in onset of drug action.
2. The potential for dosage dumping in the event of an inadequate formulation plan.
3. Enhanced capacity for initial metabolic pass.
4. A stronger reliance on the dose form's GI residence duration.
5. The potential for occasionally less precise dosage adjustments.
6. Compared to normal dosages, the cost per unit dose is greater.
7. Not all medications can be prepared in an ER dose form.

The future of "controlled" drug delivery

The future of controlled DDS has both great promise and several obstacles. Our capacity to create serum-stable, quickly absorbed nano-scale DDS that target particular places and pathways inside cells, elude the endosome, and are efficiently taken up by certain cells will grow along with our understanding of biology, particularly cell biology and DNA. The field of controlled DDS will become increasingly more biological and less materials-oriented in nature as a result of the greater capacity to regulate the efficiency and specificity of the delivery process as well as the enhanced ability to create strong biomolecular medications with minimal adverse effects. Furthermore, as our knowledge of which DNA sequences encode for which diseases grows, we will be able to forecast accurate therapy regimens for each individual's optimal treatment of those diseases based on the sequences found in that same individual's DNA. With our "controlled" delivery methods, "personalized medicine" will put pressure on drug delivery scientists to be more exact and precise in terms of biology. As the field of controlled drug delivery transitions from the MACRO-MICRO-NANO POLYMERIC DDS eras to the BIO-DDS age of bio-controlled delivery systems for biomolecular pharmaceuticals, it will ultimately be even more exciting—or is it truly a new beginning [44].

Human life expectancy has increased as a result of notable advancements in medication creation as well as improved and earlier diagnoses for preventative medicine. This calls for the creation of more medications to treat a variety of illnesses, including diabetes mellitus, coronary artery disease, chronic pain, chronic lower respiratory disorders, Parkinson's disease, and Alzheimer's disease. The first and most crucial step is to find medications to treat these illnesses. Medication candidates with short half-lives can be incorporated into sustained release formulations and those with low water solubility into therapeutically viable medication formulations thanks to drug delivery systems. The creation of novel medications will benefit greatly from the drug delivery technology. For the purpose of delivering medications

with diverse characteristics, several drug delivery methods must be devised.

Drug delivery system advancements are the outcome of many tries and failures, or an evolutionary process. It is necessary to test a wide range of medication delivery methods and to repeat the versions of the most promising ones. This procedure will never end unless a disease's appropriate cure is discovered. Instead than using the same strategy that others have been doing for ten or more years, trying a wide variety of ways demands a diversified range of ideas. For instance, several medication delivery systems based on nanoparticles have been created, although they all essentially take the same method and differ very slightly. Therefore, it is not shocking that this strategy has not produced any advancement. Why are nearly all nanoparticle systems designed for targeted delivery to tumors if nanoparticles are such an effective instrument for getting medications to the right places. Only a small number of the several other significant illnesses have been treated with nanoparticle formulations. We must thus use our creativity to think outside the box. The development of novel medication delivery methods will take longer if the next generation of scientists is kept inside the boundaries of present nanotechnology. It's time to experiment with new concepts and methods for a range of illnesses [45].

## CONCLUSION

In conclusion, controlled drug delivery systems have a rich historical background, with diverse formulation approaches and considerations. They hold great promise for optimizing drug therapy but require careful planning and development to harness their full potential.

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