ARTIFICIAL INTELLIGENCE IN CONTROLLED DRUG DELIVERY SYSTEM

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Abstract

Artificial intelligence (AI) has become more prevalent in a number of societal fields, most notably the pharmaceutical industry. In this review, we focus on how AI is being used in a variety of pharmaceutical industry fields, such as drug discovery and development, drug repurposing, increasing pharmaceutical productivity, and clinical trials, among others. This use of AI lessens the workload of human workers while also achieving goals quickly. We also talk about how various AI tools and methodologies interact, current problems and solutions, and the potential applications of AI in the pharmaceutical sector.

INTRODUCTION:

ARTIFICIAL INTELLIGENCE

Artificial intelligence has impacted every field of research during the past ten years. John McCarthy coined the phrase "A.I." in 1956. It is a subfield of computer science that has influenced everything from basic engineering to pharmaceuticals.

The use of artificial intelligence in drug discovery is crucial. In the field of drug discovery, many artificial network types, such as deep or neural networks, are used. In order to improve and provide a higher success rate for drug design, it is a fundamental technique to target the proteins utilised in drug design. Artificial intelligence is employed at every stage of the drug discovery process to improve the healthcare system and prevent health risks associated with pre-clinical testing. Additionally, it can lower costs more significantly. Numerous applications exist for predicting qualities or activities, such as physicochemical properties and (ADMET) Absorption, Distribution, and Temperature. Recently, there has been toxicity, excretion, and metabolism. The majority of the instances demonstrated the power of A.I. in this area. The features of the (ADME) Process and toxicity in the drug entity can be evaluated in silico, through virtual screening, De Novo design activity, and other AI-based methods. The A.I can use computer-aided design to produce a new chemical entity that will improve a molecule's stability while taking up less time. It can be used to improve diagnostic accuracy and work flow efficiency in clinical practise. The pharmaceutical industry has dramatically increased its data digitization during the last few years. The challenge of gathering,

examining, and implementing such knowledge to resolve complicated healthcare problems is nonetheless a side effect of this digitalization. Because AI can handle massive amounts of data with improved automation, this encourages its usage. Technology-based artificial intelligence (AI) systems can replicate human intelligence by using a variety of cutting-edge tools and networks. However, it does not pose a danger to totally replace human physical presence. AI makes use of hardware and software that can analyse and learn from input data to make independent judgments for achieving predetermined goals. As this review describes, its uses in the pharmaceutical industry are constantly expanding. The McKinsey Global Institute claims that the quick development of AI-guided automation will certainly radically alter society's work culture.

CONTROLLED DRUG DELIVERY SYSTEM

The phrase "controlled release" refers to the duration of a drug's prolonged activity. Additionally, it has an impact on the predictability and linearity of the pharmacokinetics profile of drug release, meaning that the free of drug ingredients from a controlled release drug delivery system moves toward the rate profile, which is not only predictable kinetically but also consistent from one unit to another.

For a long time, a controlled drug delivery system kept the medication level in the blood or tissue constant. Figure a shows pharmacokinetics curves for two types of delivery systems, conventional and regulated, showing changes in drug concentration in plasma over time.

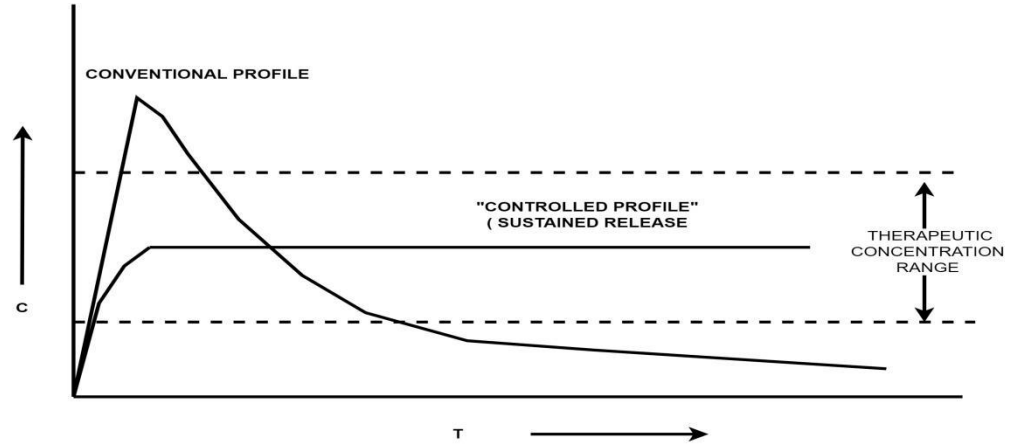

Fig.a (Conventional &Controlled drug delivery system)

In a regulated medication delivery system, the drug level varies for multiple tablet or injectable doses, above and below the maximum concentration bolus pk.

On the other hand, a controlled drug delivery system exhibits a zero order PK, where the drug level is kept constant while a therapeutic window and single dose formulations are used. The main idea behind controlled release drug delivery systems is to assess the biopharmaceutics, pharamacokinetics, and pharamacodyamic properties of a drug or entity in order to use the strength through the reduction of side effects and cure or control of control of disease in a very short amount of time while using the least amount of drug and introducing it via the

most suitable route. The instantaneous release of drugs lacks certain characteristics including dose maintenance, regulated release rate, and site selection or targeting.

A controlled release medication delivery system's main objective is to improve patient compliance while maintaining patient safety and enhancing the therapeutic activity of the drug. The ideal control delivery system is one that continuously or locally administers the drug at a predetermined rate for a predetermined amount of time. When a medication or other agent is carefully bonded to or mixed with a polymer—natural or synthetic—in such a way that the active agent is permitted to exit the substance in a predetermined manner, controlled-release drug delivery results. The release of the active agent must continue for a long time or it may be impacted by the environment or other factors.

Current Status

Recent developments in controlled drug delivery formulations and the polymer utilised in these kinds of systems allow them to do more than just lengthen a drug's successful release period.Contrary to standard dosage form, a controlled Release medication delivery method is capable of providing challenging forms of benefits.

Reduced dosing frequency, improved bioavailability, decreased drug level variability, maintained dose stability, and improved patient comfort.

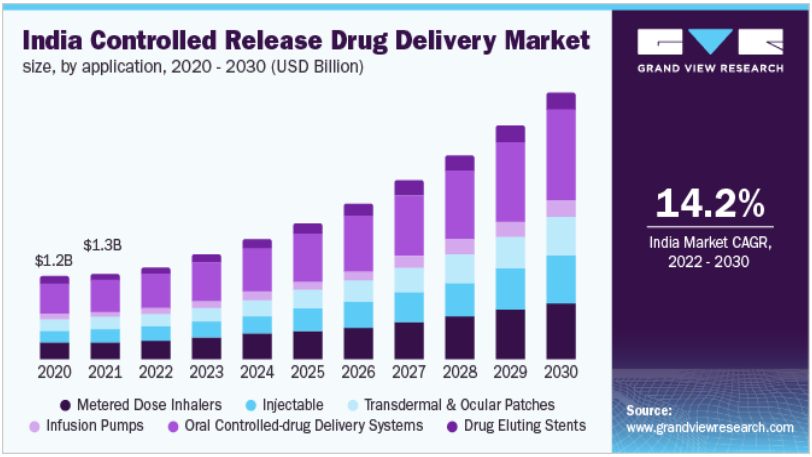

Fig.b(current status of controlled drug delivery system in India)

Characteristics feature of drug to design CDDS

For the designing of CRDDS product a variety of variables must be examined.

1. Drug properties: The physico-chemical characteristics of the medication, such as its solubility, stability, and protein binding, have a significant impact on how well CRDDS functions and is planned.

2. Route of Drug Delivery: Some routes of administration can have a negative impact on a medicine's efficacy, especially when they are used chronically during a drug delivery system. Therefore, diverse administration methods must also be taken into account.

3.Target Site: Some routes of administration can have a negative impact on a medicine's efficacy, especially when they are used chronically during a drug delivery system. Therefore, diverse administration methods must also be taken into account.

Factors affecting Oral Controlled Released Products: -

1. **Mechanism and site of Absorption:**Poor candidates for the CRDDS system are medications that are absorbed through the carrier mediated system.
   Eg: Vitamin B
2. **Dose size:**For single dosage medications, the greater range for oral drug delivery is typically 0.5–1 grm. In normal dosage, if a medicine is given in a high dose, it is less suitable for CRDDS candidates since it would grow to an excessive size and be delivered easily.
3. **Drug Stability:**Drugs in solid states degrade far more slowly than they do in suspensions or emulsions. When medications exhibit instability in the stomach, they are given in controlled doses such that their delayed release into the intestines. Drugs that are broken down in the intestine might potentially degenerate in this way. These medications are not appropriate for CR because they are unstable in combination.

4. **Solubility:** Medicines with poor oral bioavailability and low water solubility are more suited for regulated and sustained oral dose forms. Drugs that dissolve well in the stomach are not good choices. The medicine is a strong candidate for an oral controlled release dosage form if it is pH independent and has good water solubility. The drug's solubility may limit the CRDDS mechanism that can be used.

5. **Partition Cofficient**: The term "partition cofficient" refers to the ratio of a drug's oil phase to its aqueous phase. The biological membrane is used to regulate the drug particles. Drugs have a high partition efficiency, making them easily transverse biological membranes. The medication is essentially released upon partition cofficient during the drug's diffusion over the rate-regulating membrane. Less efficient drugs won't separate out of the lipid membrane once they enter it, making them unsuitable for oral control delivery systems.

6. **Drug pka:** Ionized drugs are not good candidates for the oral controlled release drug delivery system because their absorption rate is 3–4 times lower than that of unionised drugs. The optimal pH range for positive absorption is between 7.0 and 11.0 for acidic drugs whose ionisation is pH sensitive.

7. **Biologically Half- life:** For CRDDS drugs with a biological half-life of less than 2 hours, elimination, metabolism, and distribution are the most appropriate factors influencing the half-life of the drug.

Mechanism Aspects for oral Controlled release drug delivery formulation

1: Diffusion - controlled products

The water insoluble polymer controls the water circulation and subsequent release of the dissolved substance in these systems. Diffusion takes place when the CR system's component material passes through a medication. Diffusion must take place through the pores in the chains and matrix of the polymer.

They must be divided into two categories:

1 Reservoir Devices: This approach uses a water-insoluble polymer to surround the dry core. The medicine then exchanges the environment of the particles (or tablets) through the rate-limiting membrane. The rate of medication distribution in these systems is rather stable.

2Matrix Devices: When the medicine or active ingredient is spread throughout a polymer matrix in a homogenous system, the system is referred to as a matrix system. This sort of device usually reduces the rate of release since the active agent has a longer journey distance and takes longer to release when it leaves the polymer matrix and travels into the outside environment.

2: Dissolution Controlled Products

In these materials, a slow soluble polymer or microencapsulation is required to control the drug's rate of dissolution. The drug can be dissolved once the coating has broken down. The drug release rate can be controlled by modifying the coat's thickness and makeup. In order to deliver a pulse dosage shortly after administration as an immediate release portion, the majority of formulations include a fragment of the total dose.

3: Encapsulation Dissolution

It can also be described as a system that controls coating dissolution. The coating's durability and thickness must affect the rate of dissolution. By creating an appropriate salt or derivative, covering the medication with a slowly dissolving substance, or incorporating the drug slowly dissolved, controlled release products can be developed.

4: Matrix Dissolution System]]//////////////

It comes after the drug's initial release. It can also be described as a monolithic dissolution-controlled system. To manage it, you must change the porosity of the tablets and slow down the loss of moist ability. The rate of polymer dissolution can be calculated using drug release.

5: Osmotic pump

Solvent flow through semi-permeable from low to high concentration. With this technique, hydrophilic medicines can be released in zero order. a drug with an osmotically active salt combination (Eg.Nacl). Cellulose acetate is typically used to create semi-permeable membranes.

Osmotic pressure, caused by differing solute concentrations in a solvent in a space split by a semi-permeable membrane, is hydrostatic pressure.

6: Ion exchange resins:

Cross-linked water-insoluble polymers with ionizable functional groups are ion exchange resins groups. These resins are utilised to hide tastes , as well as a regulated release method. The compositions are created by integrating the medication molecules in the matrix of the ion-exchange resin and then a semi-permeable coating is applied to this core , a covering substance like cellulose acetate. This system decreased the rate of drug breakdown in the GIT. Divinylbenzene sulphonate is the most frequently used and secure ion-exchange resin on a tablet. Ion-exchange resins have been utilised in detergent compositions.

Application

AI in the pharmaceutical product lifecycle.

Because AI can help with rational drug design [16], decision-making, picking the best therapy for a patient, including personalised medicines, managing clinical data generated and using it for future drug development, and many other tasks, it is possible to imagine AI assisting in the development of a pharmaceutical product from the bench to the bedside. [17]. Eularis' E-VAI is a platform for analytical and decision-making AI that uses ML techniques. features a user-friendly interface for building analytical roadmaps based on stakeholders, competition, and other variables.

AI in Pharmaceutical Product Development

When a new therapeutic molecule is discovered, it must be included in a dosage form that has the appropriate delivery properties. In this case, AI can take the place of the previous trial-and-error method. With the use of QSPR, a variety of computational methods can be employed to resolve formulation design issues like stability, dissolution, porosity, and more. Rule-based systems are used by decision-support technologies to identify the kind, character, and severity of a problem. The physicochemical characteristics of the medicine dictate how much excipient is utilized, and feedback control is employed to continuously evaluate and improve the entire process. Guo et al. developed a hybrid approach using Expert Systems (ES) and ANN to create piroxicam direct-filling hard gelatin capsules in accordance with the specifications of its dissolution profile. The MODEL EXPERT SYSTEM (MES) decides and suggests formulation development parameters based on the input. While backpropagation learning is used by ANN to link formulation parameters to the intended result. In order to assure trouble-free formulation development, the control module cooperates.
The impact of powder flow property on the diefilling and tablet compression processes has been studied using a variety of mathematical tools, including computational fluid dynamics (CFD), discrete element modelling (DEM), and the Finite Element Method. The effect of tablet geometry on the dissolving profile can also be studied using CFD. The mass manufacture of drugs may greatly benefit from the integration of these mathematical models and AI.

Advanced AI-based application

1. **Nanorobots powered by AI for drug delivery**

Integrated circuits, sensors, power sources, and safe data backup are the key components of nanorobots, all of which are maintained utilising computational technologies like AI. They have been trained to recognise and attach to targets, avoid collisions, and then excrete from the body. Technological advances in nano- and microrobots give them the ability to go to a particular location depending on physiological parameters like pH, boosting effectiveness and minimising systemic adverse effects. Consideration of factors like dose adjustment, sustained release, and control release is necessary when developing implantable nanorobots for the controlled delivery of drugs and genes, and automation of drug release is required, controlled by AI tools like NNs, fuzzy logic, and reinforcement learning. Integrators Microchip implants are utilised for both implant detection inside the body and programmed release.

2. **AI in combination drug delivery and prediction of synergism/antagonism**.

Because they can have a synergistic effect for quick recovery, many medication combinations are approved and marketed to treat difficult diseases including cancer and tuberculosis. It takes a long time to screen a big number of medications using a high throughput method in order to choose the exact and potential drugs for combination. For instance, a regimen of six or seven medications is required for cancer treatment. The overall dosing regimen can be improved by screening drug combinations utilising ANNs, logistic regression, and network-based modeling. Rashid et al. developed a framework for quadratic phenotypic optimization to identify the most effective cancer combo therapy. Using FDA-approved medications to treat multiple myeloma that is bortezomib resistant The best two-drug combination for this design is Dec, MitoC, and mechlorethamine, whereas the best three-drug combination is Dec, MitoC, and mechlorethamine. If supported by information regarding the synergism or antagonistic effects of pharmaceuticals taken together, combination drug delivery may be more effective. 56% of synergism with "Mater regulator genes" was predicted using the Master Regulator Inference Algorithm. You could also utilise other strategies, such Network-based Laplacian Regularized Least Square Synergistic Drug RF and Combination. A model for predicting synergistic anticancer medication combinations was created by Li et al. using RF. 28 synergistic anticancer combinations were predicted by the authors using gene expression profiles and different networks. Although the remaining combinations might possibly be relevant, they have only reported three. Similar to this, Mason et al. employed ML to predict potential synergistic antimalarial combos using a data set of 1540 antimalarial medication molecules. This method is known as the estimation of Combination Synergy.

Conclusion

In addition to assisting in quick decision-making, AI can significantly contribute to the continued incorporation of the developed drug in its appropriate dosage form as well as its optimization, resulting in faster manufacturing of better-quality products and assurance of batch-to-batch consistency. Through thorough market analysis and prediction, AI can also

help establish the product's safety and efficacy in clinical trials, as well as ensure correct positioning and costing in the market. Although there are presently no pharmaceuticals on the market that were created using AI-based methods, and certain implementation issues still exist, it is expected that AI will soon become a priceless tool in the pharmaceutical business.

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