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Review Article

# A significant role of artificial intelligence in novel drug delivery system and drug design: A recent approach.

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ABSTRACT

Over the past five decades, the application of artificial intelligence in the pharmaceutical business has developed. The artificial intelligence of drug delivery systems is based on binary and therapeutic software science, which deals with problem-solving with the use of example programming. The article discusses drug delivery systems, AI tools, automated control systems, AI to anticipate new treatments, the creation of novel peptides from natural foods, the management and treatment of rare diseases, drug adherence and dosage, and barriers to AI adoption in the pharmaceutical industry.

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## INTRODUCTION

The artificial intelligence (AI) is the term used to describe the intelligence displayed by human-made machines. It is a broad field of study that covers computer science, cybernetics, neurophysiology, psychology, and linguistics. Its focus is on using symbolic programming to solve problems. It has significantly developed into a problem-solving science with several applications in business, engineering, and healthcare, including diagnosis, particularly to detect minute changes from the baseline, to spot pandemic disease outbreaks early on, and imaging diagnostics. The application of AI in medicine, such as IBM Watson in oncology, enables oncologists to offer their cancer patients the most appropriate and individualized treatment. The top oncologist's knowledge, clinical data, medical journals, textbooks, and IBM Watson's analysis of patient medical records are all sources of information [1-3]. In the past ten years, interest in the use of artificial intelligence (AI) technology for biological or genetic analysis and interpretation, expedited drug discovery, and the identification of rare or selective small-molecule modulators and behaviour prediction has grown. Treatment outcomes may be significantly enhanced by the use of automated workflows, databases, and artificial neural networks (ANNs) for the rapid analysis of massive amounts of data, the development of novel hypotheses and treatment strategies, the prediction of disease progression, and the assessment of the pharmacological profiles of drug candidates. By quickly predicting or identifying biological targets, target fishing (TF) may be highly helpful in tying targets to novel compounds, and the use of microfabrication technology to the creation of implantable microchips appears promising for regulated medication delivery [4]. A promising method to increase drug solubility, alter drug distribution in various tissues and organs, regulate drug release rate to achieve sustained release and controlled release profiles, and encourage drug aggregation in its target is the nano carrier-based drug delivery system (Micro/Nanorobots) [5]. With the ability to automatically adjust drug concentration and release timing, these multifunctional and sophisticated devices for controlled and targeted drug release have been used to address a variety of challenges associated with traditional delivery systems and improve effectiveness, safety, and patient compliance. This would be crucial in chronic disorders, which call for prompt treatment and ongoing observation [4]. The first artificial intelligence software, dubbed "Logic theorist," was developed by Herbert A. Simon and An Allen Newell in the year 1955. In addition to finding new and better proofs for some theorems, this programme proved 38 of 52 mathematical theorems. the 1956 year John McCarthy, a computer scientist from the United States, coined the term AI for the first time at the Dartmouth conference. AI was officially recognized as a field of study for the first time [6]. Since the 1950s, artificial intelligence has had a turbulent history. When IBM's Deep Blue computer beat chess champion Garry Kasparov in 1997, the perception that it was a field for dreamers began to alter. In 2011, IBM's brand-new Watson supercomputer was successful in taking home the $1 million prize on Jeopardy in the US. Since then, Watson has diversified into the healthcare and pharmaceutical industries, forming a relationship with Pfizer in 2016 to quicken the development of new immuno-oncology drugs. IBM Watson, a cloud-based platform for medical lab reports that gives researchers the capacity to find links across various data sets through dynamic visualizations, was unveiled in December 2016 in conjunction with Pfizer [2].

## Artificial Intelligence-Based Drug Delivery Systems

Pharmaceutical research and development have historically been a conservative area, favoring small-molecule medications that innately have (1) stability, (2) enough potency for therapeutic objectives, and (3) tolerable toxicity for the great majority of consumers [7]. The development of innovative technologies for efficient, targeted drug administration with little adverse effects has recently come under more and more scrutiny. In order to address issues with conventional drug delivery methods, such as their limited therapeutic index, systemic toxicity, and difficulty managing drug doses during long-term therapy, researchers have concentrated on controlled drug administration [8].

## Microchip

The best method for administering drugs for a long time without the patient to whom it is fixed is the microchip/Microfluidic chip drug delivery system. It consists of a variable number of drug-filled sockets (often 50–300) that release the medicine one at a time at predetermined intervals [9]. Silicon microchips have the capacity to store and emit a variety of substances. Future development of "smart" microchip implants or tablets that release medications into the body automatically as necessary could be facilitated by the inclusion of active control electronics, such as microprocessors, remote control units, or biosensors [10]. The microchip-based device can isolate and identify genetic changes in circulating tumor cells (CTC) from the blood of patients with solid tumors [11]. Microfluidic chips are a type of microfluidic device that allows for tiny amounts of liquids containing particles to be processed and visualized. The chips are a combination of micro-pumps, micro-valves, micro-mixers, micro-separators, and micro-sized channels (diameters ranging from 1 to 1000µm). The pumps move liquid within the channels in the chip at micro-level flow rates, allowing control over physical or chemical reactions. The liquids may contain either cells or nanoparticles. For example, microfluidic chips were used to study the migration of lung cancer cells under different cancer invasion microenvironments. Currently, microfluidics is most commonly used for the synthesis of LNPs for RNA/DNA delivery [12].

## Design and Components

Implanted microchips enable on-demand drug release. Solid silicon microchips consist of hundreds of reservoirs filled with up to 1 mL of drugs in an aseptic solid, liquid, or gel filling. The multi-reservoir microchips are hermetically sealed to avoid degradation and subsequently covered by an anode membrane which can be ablated electrothermally to release the reservoir contents (Fig.1).

Understanding the components, Microchips are fabricated using the same well-developed technology as used for microelectronic integrated circuits and microelectromechanical systems (MEMS), processes used to manufacture microdevices such as pressure sensors, accelerometers, flow sensors, inkjet printer heads, and micromirrors for projection. To allow for accurate control of surface microarchitecture, microchips are created using repetitive thin-film deposition, photolithography, and etching (removing) [13].

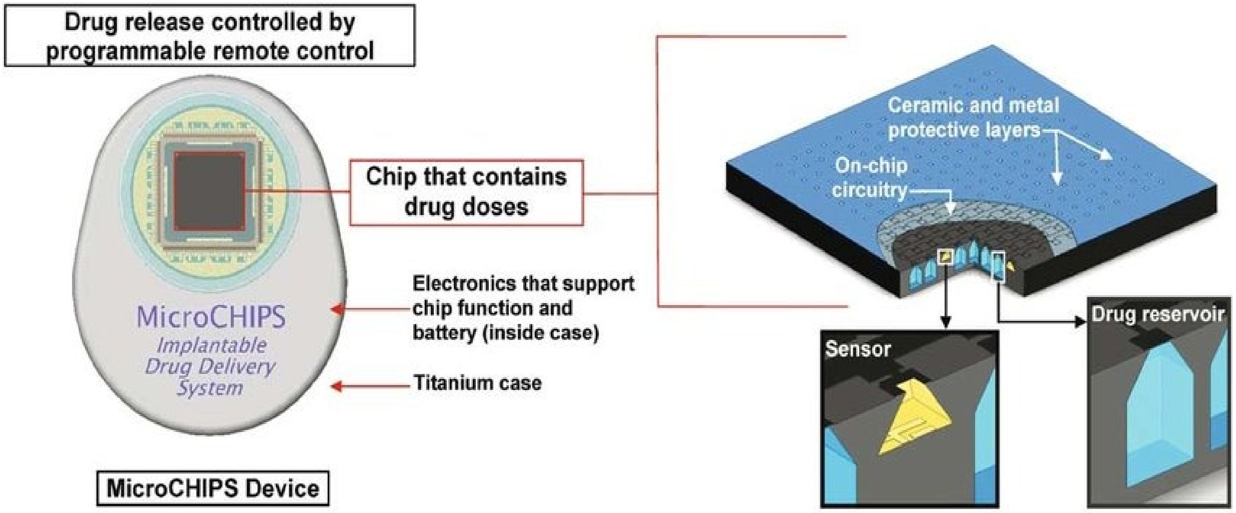


Figure 1. A schematic diagram of microchip.

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## Applications of Microchips in Drug Delivery System

- The use of microchips has been observed in the creation of artificial glands. and hormone regulation in the body.
- Microchip-based Medication is used in chronic depression (patients are liberated from taking the medicines for months or years).
- The microchip device can be made infinitesimal to enable local drug delivery so that high concentrations of the drug can be achieved at the site of application while keeping systemic concentrations low [14].
- Microchips (assembly consisting of two chips on the surface of a titanium housing that holds the electronics) may be implanted in women who are suffering from osteoporosis.
- The development of a microchip, especially for tuberculosis (TB) ELISA, is mainly responsible for detecting IgG responses against multiple types of antigens from plasma samples of active TB (ATB) patients in a rapid, and miniaturized detection system [15].

## Artificial Neural Networks

Artificial Neural Networks (ANNs) are artificial intelligence systems that are designed to simulate some functions of the human brain by using nonlinear processing units, which can learn from experience. ANNs are massively parallel-distributed processors made up of usually fully interconnected artificial neurons [16,17] The artificial neural network, first invented in the early 1960s, only started to expand progressively during the early-1980s along with the launch for modern neural network modeling & developments with computer technology [18].

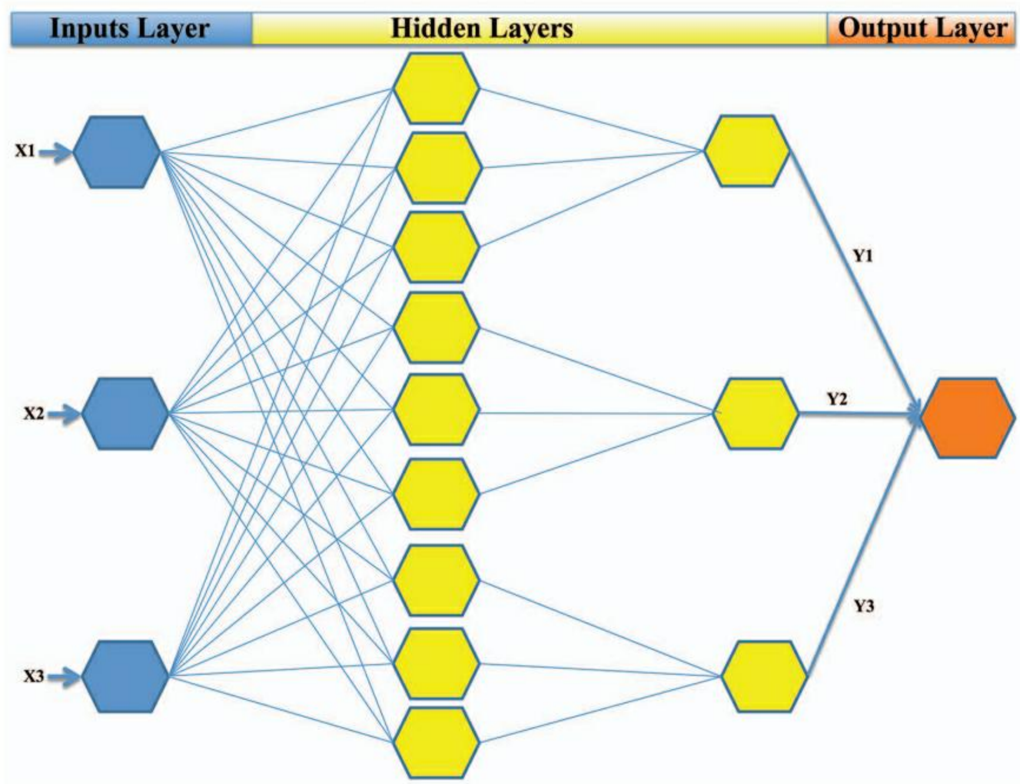


**Figure 2.** A schematic of the three-layered artificial network.

## Types and Design of ANNs

ANN models can be classified into three categories based on their functions first one is Associating networks, which are employed for data classification and prediction, and need input (independent variable) and correlated output (dependent variable) values to perform supervised learning. The second one is Feature-extracting networks, which are used for data dimension reduction and need only input values to perform unsupervised or competitive learning. And the third one is that non-adaptive networks need input values to learn the pattern of the inputs and reconstruct them when presented with incomplete data set. Among these three types of ANN models, associating networks can be employed to develop controlled-release drug delivery systems [16].

Input layer units (in blue) receive input signals (x1, x2, x3) and transfer the signal to the hidden layers via weighted connections. The output layer receives the signals (y1,y2,y3) and provides the representative output signal[19].

ANNs are usually characterized by their architecture using specific network topologies, it has been tried to enhance the robustness of traditional architectures. There are two types of neural networks including static and dynamic networks. The major difference between these networks is determined by the mechanism of signal transmission through the network in static networks, outputs are calculated based on their connection with feedforward inputs. Among various types of static networks, the multilayer perceptron (MLP) network (Fig.2) is the most commonly applied network that maps the input data sets. This neural network architecture includes multiple layers of nodes and each layer is fully connected to the next one leading to the recognition of particular elements. MLP has been used for designing controlled-release formulations, predicting drug dissolution profiles, and optimizing the formulations and drug release profiles. Due to the inner connectedness, dynamic networks are usually referred to as recurrent networks and various processing elements provide flexibility. In dynamic neural networks, past information is used to predict the present and future states of a system. This might be useful for characterizing or modeling drug release from controlled-release formulations[4]. The most commonly applied ANN layout is a forward propagating network trained by error backpropagation. The forward propagation network consists of three layers, the first one is the primary layer and called the input layer, the next one is the middle layer which includes several hidden layers, and the last one is the output layer (Fig.3). As the number of hidden layers grows, the capability of solving the problem accurately also increases [19,20].

## Applications of artificial neural networks in drug delivery systems

- Structure Retention Relationship (SRR) methodology in pharmacological research
- Quantitative Structure-Activity Relationships (QSAR) and Quantitative Structure-Property Relationships (QSPR)
- Pharmacokinetics and pharmacodynamics modeling
- Preformulation
- In-Vitro In-Vivo correlations
- Proteomics and genomics
- Diagnosis of disease
- Optimization of pharmaceutical formulations [21].

## Advantages of ANNs

- ANN does not require any assumption as to the significance of the links between the materials of the formulation, as well as the properties of the formulations.
- It does not require any previous knowledge of the problem's underlying mathematical nature.
- The Neural Network has a special ability to recognize a pattern.
- When the response variables are strongly nonlinear, ANN reliably forecasts outcomes [22].
- Once trained, neural networks are inherently fast and can lead to saving in both time and cost of product development.
- ANN requires no assumption to be made about the nature or significance of interconnections between formulation components or the relationship between the ingredients and properties of the formulation.
- An ANN model, unlike statistical models, operates upon the experimental data without data transformations [23].

## Disadvantages of ANNs

- The biggest limitation of ANN was how they are by default, computer systems; the Interaction which network gets cannot be readily represented in statistical format [22].
- ANN requires the use of sophisticated software whereas the (response surface methodology) RSM can be done using the earliest software such as EXCEL.
- The primary risk in developing a model is that of overtraining, a situation in which the neural network starts to reproduce the noise specific to a particular sample in the training data, which may cause it to lose its ability to predict accurately [23].

## Micro/Nanorobots

The first scientist to mention the term "nanobots" was the physicist Richard Feynman in 1959. The first study related to nanobots was made by Robert Freitas. It was related to medical nanobots called respirocytes; resembling red blood cells [24]. Nanorobotics is an arising field of nanotechnology which manages the planning and development of gadgets at a nuclear, atomic, or cell level. These theoretical nanorobots will be minuscule and would cross over inside the human blood. A nanorobot is a minuscule designed to carry out a specific task with nanoscale precision [25]. Development of the micro- and nano-electromechanical systems has provided the possibility of fabricating implantable robots for performing a variety of tasks including the controlled delivery of drugs or genes. Because of the remarkable advances in nanotechnology, increasing interest has been attracted to the development of nanorobots which are integrated with internal or external power supply, AI, sensors, actuating, signaling, processing information, or exhibiting swarm behavior [4,26]. Nanorobots depend on chemical sensors which detect the target molecules. It contains thousands of nanowires that help in the detection of proteins and other biomarkers that are left behind by cancer cells may help enable the detection and diagnosis of cancer in the early stages [27]. Nanorobots allow drugs of nano size (range from 1–100 nanometers) to be used in lower concentrations and have an earlier onset of therapeutic action. It also provides materials for controlled and targeted drug delivery by directing carriers to a specific location[26]. The various application of nanorobots in the fields of medical procedure, nervous system science, dentistry, hematology, microbiology, malignancy therapy, and quality treatment [25] such as targeting and early diagnosis of cancer, drug delivery, tissue engineering, gene delivery systems, cardiology, analysis of body vitals, monitoring of diabetes, minimally invasive brain surgery, and imaging and detection capabilities[26].

## Design and Component of Nanorobots

An ideal micro/nanorobot system is expected to be safely cleared by the body upon completion of the tasks. If micro/nanorobots were retained in the body after mission completion, they might accumulate in organs and cause chronic inflammatory reactions or other adverse effects. The solutions are broadly divided into three types: Manufacturing micro/nanorobots with safe and biodegradable materials; recycling micro/nanorobots through some technical methods; triggering their self-degradation through external stimuli[5]. Two types of nanorobots are most widely researched, organic and inorganic[28]. The nanorobot's design is based on organic microbe models[25]. Organic nanorobots, also called nanorobots, are manufactured using viruses and bacteria DNA cells. The such nanorobot is less toxic to the organism. Inorganic nanobots are created diamond structures, synthesized proteins, and others types of material. Nanorobotics and more generally, NEMS research involves design (which often is biologically inspired), prototyping, fabrication, programming, and applications such as biomedical nanotechnology[28]. Nanorobots can move uninhibitedly in the circulation system because of the Brownian movement[25]. Nanobots are designed to detect and mobilize a determined part of the body where the problem is located and, in the best scenario, send feedback. Because of these determinant tasks (detect and mobilize), two devices can be identified as essential: sensors and propulsion equipment. Sensors are one of the most important parts of nanobots. Mechanical, thermal, optical, magnetic, chemical, and biological sensors have been tested in nanobot applications. sensors provide two functions to the surface, detecting the presence of the target molecules and indirectly knowing the amount of damage that exists from the change in the functional properties of the nanobot. Propulsion is in charge of the movement of nanobots, Nanomotors can be defined as nanoscale devices with their propulsion, obtaining the energy by chemical reactions of the medium, electricity, magnetic or acoustic fields[24]. Magnetic propulsion is usually designed as a helical swimmer, flexible swimmer, or surface walker. The design of helical swimmers is to imitate bacterial flagella's rotary corkscrew motion. The combination of artificial bacterial flagella (ABF) and drug-loaded liposomes is often used. [5]. The ability to build nanorobots may be aided by the newest innovations and techniques in manufacturing, computation, transducers, and control. High precision and a business method for constructing early nanodevices and circuits are provided by CMOS VLSI configurations using profound brilliant lithography giving high accuracy and a business route for assembling early nanodevices and nanoelectronics frameworks [25].

## Application of Nanorobots in Drug Delivery

The main benefit of robotic devices is their controlled, precise, and site-specific drug delivery capability, compared to other conventional therapeutic delivery systems of smaller sizes. The micro-and nano-electromechanical systems have opened the door to the fabrication of implantable robots capable of performing a wide range of functions, such as controlled drug/gene delivery[29].

The potential use of bio-nano robots for drug delivery in cancer treatment has multiple advantages over current chemotherapy and radiation techniques. When chemotherapy drugs are ingested or injected, the drug travels throughout the body targeting fast-growing cells such as cancer cells and other healthy fast-growing cells. This can cause degenerative health effects such as damage to the digestive tract and heart as well as unfavorable side effects such as hair loss. The damaging side effects limit the dose of the drug administered effectively reducing the amount of the drug that reaches the tumor. In a targeted drug delivery system, the drugs are given directly to the tumor cells that are identified by the nanorobots. This would reduce the negative side effects and improve the patient's quality of life during and after the treatment [30].

A great advantage of using nanobots for drug delivery is that the amount and time of drug release can be easily controlled by controlling the electrical pulse. In recent years, increasing interest has been attracted towards the development of [4] Microbivores are drug-filled nanorobots utilized to digest stuck microorganisms[29], single-wall carbon nanotubes, and multiwall carbon nanotubes drugs effective to kill bacteria, Borondoped silicon nanowires were used to create highly sensitive, real-time electrically-based sensors for biological and chemical species, nano patch approach for directly targeting vaccines to thousands of viable skin antigen-presenting cells, Nanomagnets Remove Pathogens from Blood[31].

Advancements in nanotechnology may allow us to build artificial red blood cells called Respirocytes capable of carrying oxygen and carbon dioxide molecules (i.e., functions of natural blood cells). Respirocytes are nanorobots, small mechanical gadgets intended to work on the atomic level. respirocytes will truly change the treatment of coronary illness.

Respirocytes identify tumors and then allow the nanofiller to kill cancerous cells with a tiny but precise amount of a chemotherapy drug. It would not only find cancers in their earliest stages before they can do damage or spread but also deliver a small amount of a drug targeted directly at tumors, which would cause little or no side effects (Fig.3) [32]. On the other hand, nanobots that destroy brain cancer cells can detect cancer cells, destroy them, and emit an acoustic signal, and also the nanodevices can be used in the nervous system, specifically myelinated disorders [24].

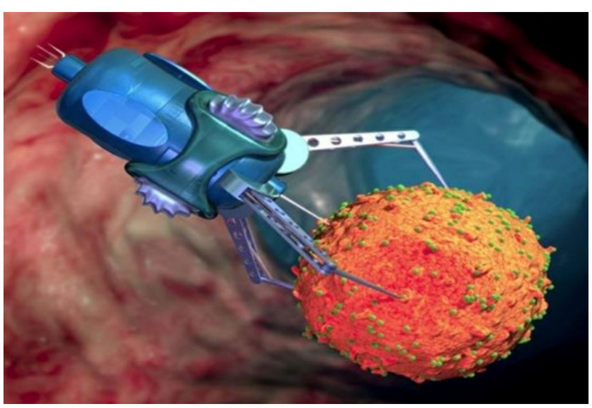

Fig.3 A Nanorobot used to kill the cancerous cell [32].

The gastrointestinal tract is relatively easier to access, thus there is more research on gastrointestinal tract drug delivery than other in other fields. In gastric tissue, the acidic environment is usually used to achieve drug delivery, such as promoting the movement of nanorobots by hydrogen produced by the reaction of metals and hydrogen ions to treat gastric infection[5].

The utilization of nanorobots in the field of dentistry such as the oral absence of pain, cleaning, beautifying, root canal fillings, dentine hypersensitivity, and orthodontics [25,33]. Micro and nanorobots are utilized for targeted drug delivery, and active drug targeting and also overcome limitations of passive targeted drug delivery [29]. Nanorobots face some limitations, including high design and development costs, high complexity, and difficulties with the interface. Due to the viscous nature of blood at the nanoscale, it is nearly impossible for the drug-carrying nanorobots to pass through blood vessels. The Brownian movement of the molecules causes collisions between molecules, and therefore the behavior of the nanorobot becomes unpredictable and uncontrollable. This instability has been one major limitation and a critical challenge that researchers are attempting to overcome [26].

### Drugs embedded with Sensors (Smart Pills)

Smart pills can be defined as ingestible capsules containing electronic or mechanical elements that traverse the gastrointestinal (GI) tract for purposes ranging from diagnosis, treatment, sampling, or surgery. These pills are easily swallowed by most people, thereby resulting in minimal discomfort, and greater patient acceptance, and can traverse the entire length of the GI tract. Diagnostically; these pills enable the use of novel sensors and imaging devices to improve our understanding of GI disease′s etiology with greater ease. From a therapeutic perspective, these devices open up the possibility of localized, targeted delivery of therapeutic agents to specific regions of the GI tract or systemic delivery of biologics through transepithelial delivery (Fig. 3) [34].

In general, the activation of a drug delivery system can be triggered by different types of parameters, such as temperature, chemical (i.e. pH), or electrical parameters (i.e. impedance), that are medical indexes for the detection of physiological conditions alterations [35]. From a historical perspective, research activities in the field of smart pills (in the following also called swallowable capsules) started in the 1950s. The first swallowable capsule was able to measure the pressure in the small intestine of patients suffering from dysentery [36]. The capsule body is 3D printed in acrylic resin. The total volume of the capsule is about 1300 mm3. The drug delivery system comprises two reservoirs, respectively for the drug and the electrolytic solution, separated by an elastic membrane. This solution eliminates the use of microvalves which are complex elements to integrate into the dome of the capsule and could be damaged by possible contact with the intestinal walls during the navigation. Bio-MEMS give the possibility to provide drug delivery with microchannels, microvalves, and micropumps for flow management at microscopic volumes, that can be used as active elements of smart pills. By their nature, pumps for biomedical applications have to comply with stringent requirements in terms of reliability and flow-rate control [35]. According to FDA, in 2017 Drug-loaded tablet-like device for monitoring medication adherence, is mainly intended for mental disorders and cancer [37].

### Application of Smart Pills in Drug Delivery System

Smart pills for drug delivery offer several significant opportunities for pharmaceutical industries because they may be used in a wide range of applications and enable therapies not possible with conventional means. For instance, they allow the treatment of locally active diseases along the gastrointestinal system, such as gastroesophageal reflux (GERD), esophageal cancer or inflammatory bowel diseases (IBD), intestinal cancer, and irritable bowel syndrome [35].

The advantages of using smart pills for drug delivery are well understood, as targeting diseased tissue is currently challenging, necessitating systemic treatment and consequently system-wide side effects. The utilization of drug-device combinations, specifically drug delivery capsules with integrated sensing or imaging capabilities, offers a means of potentially detecting and treating diseased GI tissue simultaneously, allowing targeted therapeutics and lower side effects in patients [34].

## CONCLUSION

Artificial intelligence is given a miracle revolution in the pharmaceutical field. The drug is given only based on therapeutic and their effect may be readily or simultaneously but with the revolution in the era of artificial intelligence, the drug reaches the target with the biodegradable based artificial vehicle to treat the specific disease with no side effects.

In many cases, AI is a boon in my opinion in diabetes mellitus type 2 where the insulin receptor isn′t bonded with insulin or we gave another kind of therapy to the patient rather than the disease did not cure or life going to suck and measurable. In this, all kinds of cases AI can do a miracle job reaching insulin at the targeted site where the glucose metabolism run for ATPs thus, we can cure diabetes 2 in a manner. It is an example to cure the many drastic and ghastly diseases cure based on artificial intelligence. Many surgeries can perform by artificial nanorobots by operating a super specialty doctor.

All of the above review battery of literature survey on miracles of pharmaceutical drug delivery dosage form to treat the world′s most ghastly diseases without any operation. It is a new boon for pharmaceutical industries.

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