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Review Article

INNOVATIONS IN PHARMA SECTOR: A REVIEW

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ABSTRACT

Innovation is one of the pharmaceutical industry's most defining characteristics. New medications can be crucial for maintaining the quality of human life, and may even affect its duration. The pressure to succeed is tremendous. Pharmaceutical innovation is hardly an orderly, predictable process. It follows a technology-push model dependent on a twisting route of scientific breakthroughs with uneven timing and hard to foresee outcomes. Drug innovation as a business process requires perception strategic, organizational, and managerial decisions. It is already enjoying intensive research coverage, giving rise to abundant but relatively dispersed knowledge of the mechanisms driving drug discovery and development. This will be a comprehensive impression of the process of drug innovation from a business and academic perspective. the evolving organizational forms and models for collaboration, summarize significant empirical regularities, and highlight differences in market positions related to firms' strategic orientation, innovation emphasis, attitudes to risk, and specialized resources. As a guide to future research, critical drivers and modes for drug innovation are systematized in a unifying framework of characteristics and process decisions. Because of its rich potential and high significance, research on drug innovation seems poised to gain increasing momentum in the years to come.

KEYWORDS: *Pharmaceutical Industry, Quality of Human life, Pharmaceutical innovation.*

INTRODUCTION

As biology and technology become ever more closely intertwined, new opportunities are emerging to improve healthcare through the use of innovative digital technologies. We live in an age in which technology is moving at a rapid pace, creating new fields and disrupting existing models and processes [1]. From a career standpoint, staying abreast of new innovations in Pharma can be extremely beneficial, helping you to adapt to change, seize new opportunities and focus on developing the skills that you will need in the future. New innovations in Pharma are proving to have great potential in pharmaceutical research and development of new drugs as well as improving patient outcomes and increasing patient access through reduced costs [2]. Five Innovations Pharma Sector Industry:

1. Precision Medicine
2. mhealth Sensors
3. Artificial Intelligence
4. Nano robot
5. 3D Printing

Introduction:

Precision medicine is an approach that integrates clinical and molecular information to understand the biological basis of disease. This information can be obtained by converting DNA into data through a process called genome sequencing. Researchers can use this data to identify specific gene abnormalities, or biomarkers, to understand which types of patients a drug will be most effective for, and who is likely to experience severe side-effects. This can aid in the development of new targeted therapies and the repurposing of existing drugs [3]. Targeted therapies are tailored to the genetic makeup of individual patients so genomic testing is required to ascertain the most effective therapy before it is administered. This understanding of the relationship between a drug and an individual's genes enables doctors to administer the right drug for the right patient at the right dose, first time – leading to better outcomes and reduced adverse effects [4]. In the UK, GlaxoSmithKline, Roche, AstraZeneca, Biogen, AbbVie and others are reportedly working with Genomics England on their project to sequence 100,000 genomes from 70,000 NHS patients with rare diseases and cancer, both Roche and Pfizer have also agreed deals with 23andMe to access their community of patients with Parkinson's and Crohn's disease respectively, to look for genetic clues to their causes [5].

Working:

- Identify the gene in which disease.
- Identify the protein associated with gene.
- Understanding the proteins structure and function.
- Replace the gene with another gene.

Fig. 1: Precision medicine

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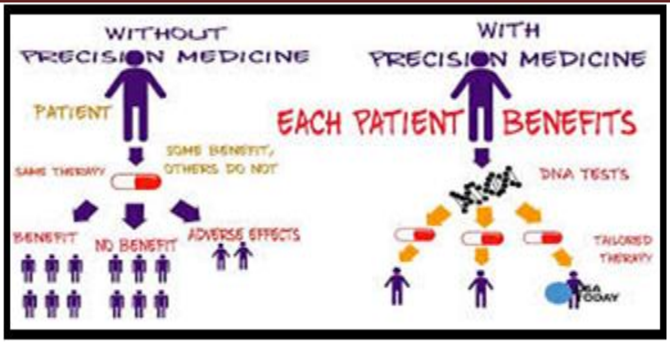

Fig. 2: Precision medicine

Applications:

***Get to optimal therapy more quickly**:* The use of diagnostic tests can help the health care provider to select a treatment option with the greatest probability of success at the outset, helping to reduce inefficient "trial and error" prescribing.

Use drugs more safely: Screening tests can identify patients who have an elevated risk for an adverse reaction to specific medicines. Also, individuals with uncommon variants of drug metabolizing enzymes and transporters may need a different dose, or may not benefit sufficiently or at all from certain medicines [6].

Increase patient compliance: The failure of patients to adhere to prescribed treatment plans exacerbates their medical condition and increases medical costs resulting from no treatment. When a therapy proves more effective or has a more favorable safety profile for a patient, the patient is more likely to adhere to the treatment.

Leverage "precision medicine" principles to increase the probability of success in R&D: Biopharmaceutical research and development focused on narrower, well-defined patient subpopulations has the potential to increase the speed of clinical trials and increase the probability of demonstrating clear clinical benefit.

Reduce inefficiencies in health care: Optimal practice of personalized medicine can help reduce many of the inefficiencies in the current health care system. Awareness of genetic risk factors encourages preventive care and early diagnosis, prevention of advanced disease states, reduction of ineffective treatment, and avoidance of additional care resulting from adverse drug reactions.

USES:

1. Diabetes
2. Arthritis
3. Depression
4. Cancer
5. Schizophrenia

Uses of precision medicine in cancer therapy:

Drug responsiveness of patients also diverge, resulting in poor therapeutic outcomes. Alternatively, targeted cancer therapies, although quite successful initially, frequently fail due to development of drug resistance and adverse side effects. Precision medicine involves a multitude of techniques and research forces like Epigenetics, Proteomics and Metabolomics, and research itself will generate new tools and technology, which will benefit our scientific society as a whole. Furthermore, precision medicine preludes the era of patient-informed therapy [7]. Revelation of patient's genome raises ethical issues of acknowledgement rights in compromise to psychological stress. It also raises political and legal issues regarding liabilities to clinical decision making. Implementations will also foster collaboration with the industrial and commercial sector, for example, pharmaceutical companies and medical device manufacturers that provide indispensable products and services. Lateral economic expansion, specifically, medical travel, is complimentary. Hence, the Precision Medicine Initiative collectively nurtures and coheres different social sectors on the path to success. In conclusion, the cancer precision medicine willleverage advances in biotechnologies, such as next generation sequencing, proteomics, transcriptome, epigenetics, pharmacology and bioinformatics, to identify precise causes for cancers and develop tailor-fit personalized therapies .As part of the Precision Medicine Initiative, this is an indispensable and near-term goal towards broader application on other diseases including diabetes, obesity, etc. Hence, the recent call for Precision Medicine Initiative rapidly went into spotlight throughout the world [8].

Precision medicine involves a multitude of technologies in order to gain success. The combination of genomics analysis and drug screening will yield unpredicted pharmacological outcome and reveal information for precise disease diagnosis and treatment [8].

Precision medicines in breast cancer:

Breast cancer is the most common cancer diagnosed in women, and one in eight women living in the United States has a lifetime risk of developing the disease. Breast cancer is also one of the most studied solid tumors and has the potential for being manageable with a precision medicine approach [9].

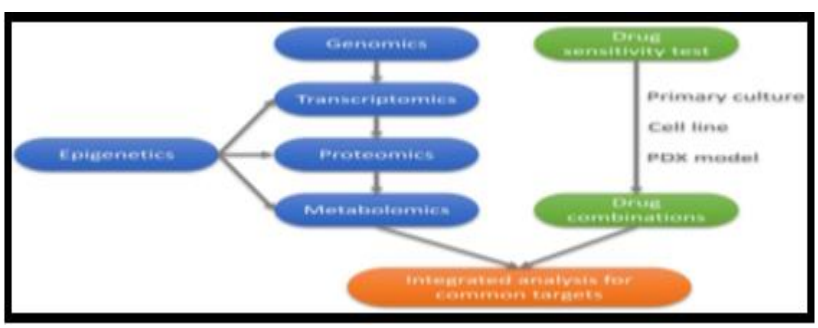

Fig. 3: Precision Medicine for Personalized Cancer Therapy.

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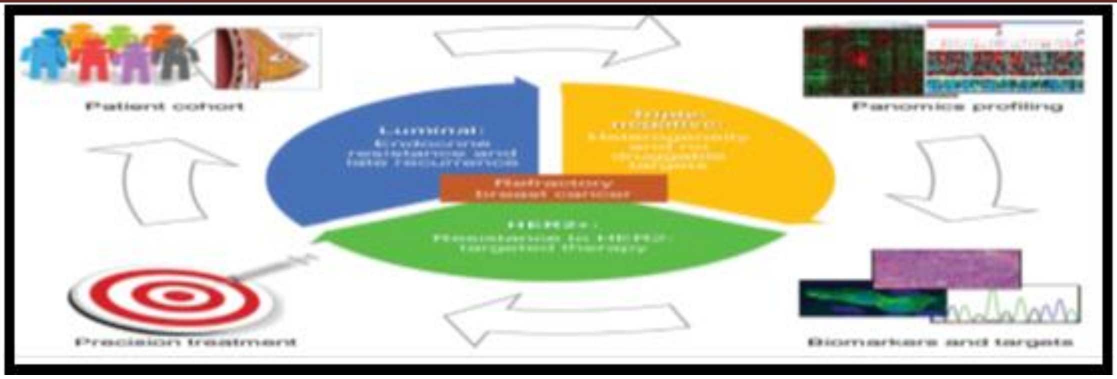

Fig. 4: Precision Medicine for Therapy.

NANOROBOTICS:

Introduction:

Nanotechnology is the study, design, creation, synthesis, manipulation, and application of Materials, devices, and systems at the nanometer scale. The application of nanotechnology in the field of health care, drug delivery has come under great attention in recent times. Using nanotechnology, quicker and much cheaper treatments can be developed. Therefore nanotechnology can help save the lives of many people. Nanotechnology, when used with biology or medicine, is referred to as nano biotechnology. A nanometer is one-billionth of a meter, too small to be seen with a conventional lab microscope. It is at this size scale about 100 nanometers or less that biological molecules and structures inside living cells operate. Nanotechnology involves the creation and use of materials and devices at the level of molecules and atoms [9].

Nano robots in drug delivery system:

Nanorobots are robots that carry out a very specific function and are just several nanometers wide. They can be used very effectively for drug delivery. Normally, drugs work through the entire body before they reach the disease affected area. Using nanotechnology, the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side-effects. Medical nano devices would first be injected into a human body, and would then go to work in a specific organ or tissue mass. The doctor will monitor the progress, and make certain that the progress, and make certain that the Nano devices have gotten to the correct target treatment region. The doctor will also be able to scan a section of the body, and actually see the Nano devices congregated neatly around their target (a tumor mass, etc.) so that he or she can be sure that the procedure was successful [10].

Robotic design in drug delivery:

Research in the design side of Nano robotics has determined information about their properties that will affect their use in drug delivery application. This has been accomplished by viewing the human body from a molecular standpoint, which provides a better understanding of what is required of Nano machines in that environment.

Size and volume:

Nano robot working in tissue could be as large as 50-100 microns, whereas one in the bloodstream needs to be 500-3000 nm. Injection of a dose of 3 cubic cm would be acceptable for the human body, since it has an average blood volume of 5400 cubic cm.

Acoustic power:

Another area to address is how the nanorobots are powered in the body. Some suggest that power be supplied by glucose and oxygen already present in the body. Alternately, external Acoustic power could be supplied. Some believe that energy storage devices are a necessary Supplementary supply. This will be an important area to further research, as onboard volume on the robots is limited. Acoustic signals sent back and forth between the nanorobots and the external source could theoretically provide steady communication. Communication will be necessary at least between nanorobots to pass sensory and control data for ensuring correct operation and monitoring progress. It will most likely also be used to transmit information to a human patient and medical personnel.

Surface:

The immune system will react to the presence of these devices is also being investigated. Since the immune system will attack any foreign objects present, it is proposed that the nanorobots be made with smooth, flawless, diamond surfaces. Experimental studies show that diamond exteriors may be ideal, because less leukocyte activity and fibrinogen adsorption occurs with these chemically inert surfaces.

Shape:

Another aspect for consideration is the shape of the device. While biological nanorobots can move freely with respect to one another, mechanical components are supported by stiff housing. Flexibility would make it much easier for the device to enter the cytoplasm, affect micro hydrodynamic stability and more.

Methods of navigation:

Two methods of navigation are currently being considered:
1) Positional: where the Nano robot knows its place in the body.
2) Functional: where the nanorobot detects subtle variations in the environment to compare to a set of predefined conditions.

A Fictitious Nano device:

The device is designed to travel to a site where it releases a short-lived drug molecule that has been converted onboard from a stable precursor. It is becoming clear how biological molecules, especially proteins, might be combined with other materials to make individual components of a device. But, it is not obvious how the complete device, or even a simplified version of it, might be assembled and integrated into a functional whole. Such a Nano device would also have to fight thermal motion and local flow to maintain its bearings. A fictitious Nano device is as shown in "Fig. 5" [11].

It consists of following parts:
1. Sensing device 2. Computing device 3. Shell

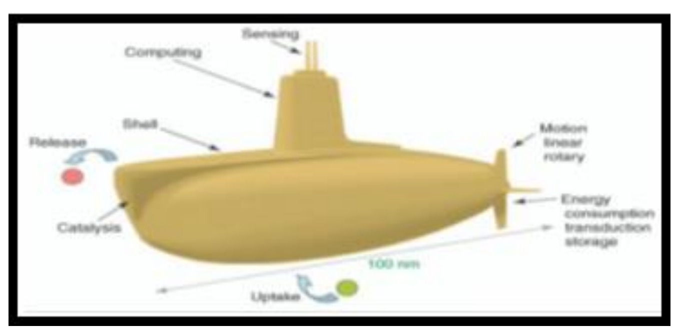

Fig. 5: Nano device

Mechanisms:

1. Uptake 2. Catalysis 3. Release 4. Energy consumption.

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Nano robot Locomotion:

Assuming the nanorobots isn't tethered or designed to float passively through the bloodstream, it will need a means of propulsion to get around the body. Because it may have to travel against the flow of blood, the propulsion system has to be relatively strong for its size. Another important consideration is the safety of the patient the system able to move the nanorobots around without causing damage to the host [12].

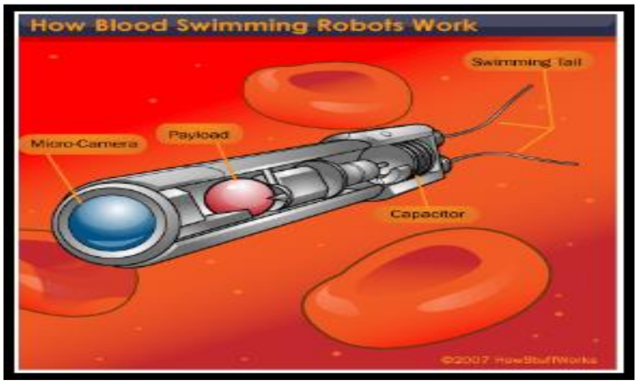

Fig. 6: Nano device

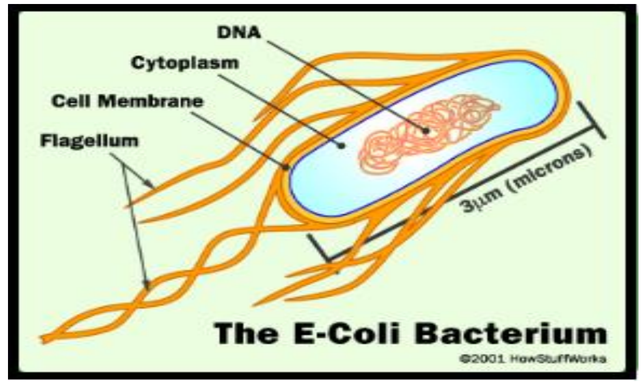

Fig. 7: Nano robot tools will have to be small enough to manipulate cells like RBC

APPLICATIONS:

Application in diabetes:

Nanorobots are considered a new possibility for the health sector to improve medical instrumentation, diagnosis, and therapeutic treatments. Patients with diabetes must take small blood samples many times a day to control glucose levels. Such procedures are uncomfortable and extremely inconvenient. To avoid this kind of problem the level of sugar in the body can be observed via constant glucose monitoring using medical nanorobotics. This automatic information can help doctors, specialists and professionals from formulation field to provide a real-time health care, improving the patient's medication regimen. Medical nanorobot manufacturing should include embedded and integrated devices, which can comprise the parts: 1. Sensing 2. Actuation Data transmission 3. Remote control uploading 4. Coupling power supply subsystems addressing the basics to biomedical instrumentation [13].

A) Nanorobots role through physiological point of view:

a) A multiplicity of blood-borne nanorobots should allow glucose monitoring not just at a permitting the physician to assemble a whole-body map of serum glucose concentrations.

b) Examination of time series data from many locations allows precise measurement of the rate of change of glucose concentration in the blood that is passing through specific organs, tissues, specific vessels.

c) Whole-body time series data collected while the patient performs at various activity levels (e.g., resting, postprandial) could have additional diagnostic value in assessing the course and extent of disease.

B) Mechanism of Nanorobots in glucose monitoring:

Glucose carried via the bloodstream is important to keep the human metabolism working Health fully, and its correct level is a key issue in the diagnosis and treatment of diabetes. The glycemic levels and parameters for an adult with diabetes should stay inside the pre-established target range. Normally persons with diabetes must try to keep their blood glucose levels (BGLs) between 90 and 130 mg/dL [14].

Hours after eating:

The nanorobots has embedded Nano bioelectronics as prototyping methodology for hardware architecture integration whether the nanorobots is invisible or visible for the immune reactions, it encounters no interference when detecting glucose levels in the blood stream. Because of its biocompatibility the nanorobot is not attacked inside the body by the white blood cells, making it invisible to the immune system. For glucose monitoring the nanorobotuses an embedded chemo sensor that involves the modulation of human sodium/glucose co- transporter type protein glucosensor activity. Using an embedded chemical biosensor the nanorobots can determine if the individual needs to drug release or not.

Amelioration of heart attack:

Nanorobots can also be used to prevent heart-attacks. Heart-attacks are caused by fat deposits blocking the blood vessels. Nanorobots can be made for removing these fat deposits. The nanorobots removing the yellow which is fat deposits on the inner side of blood vessels. From this hypothesis, such technology will help for delivery of drugs like lipid lowering substances such as lovastatin, simvastatin etc. These drug molecules will enter with nanorobots and give delivery at the site of action.

Tissue reconstruction:

Nanoparticles with nanorobots can be designed with a structure very similar to the bone structure. An ultrasound is performed on existing bone structures and then bone like nanoparticles are created using the results of the ultrasound. The bone-like nanoparticles are inserted into the body with the help of fins of nanorobots. When they arrive at the fractured bone, they assemble themselves to form an ordered structure which later becomes part of the bone. These applications will helpful in case of bone fractures, arthritic conditions etc [15].

Nerve regeneration:

Another key application for nanorobots is the treatment of injured nerves. Samuel Stupp and John Kessler at Northwestern University in Chicago have made tiny rod like nano-fibers which were incorporated in nanorobots called amphiphiles. They are capped with amino acids and are known to spur the growth of neurons and prevent scar tissue formation. Experiments have shown that rat and mice with spinal injuries recovered when treated with these devices.

Fig. 8: Working of miniature camera inside blood vessels

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Working of miniature camera inside blood vessels which are nearby to the nerves. Such camera gives pictorial view which in communication with communicating device and guides for further treatment [16].

Nanorobots in cancer therapy:

In Cancer Therapy, targeting and localized delivery are the key challenges. To overcome the Shortcomings of conventional methods, we have to selectively attack the cancer cells, while saving the non-malignant tissue from excessive burdens of drug toxicity. Theoretically, the proposed nanorobots should do the:

1. Nano-Sensors to sense the presence of malignant cells in body.
2. Nanocarriers to carry the combined NanoSensor-NanoDrug Encapsulate to vicinity of tissues.
3. Nano drug delivery particles to encapsulate drugs to be delivered at specific cancerous tissue sites and controlled drug-delivery at specific sites.
4. A Nano-Computer/Brain to integrate the above activities in a complex In-Vivo environment.

Functional components of nanorobots in cancer therapy which entailed as below:

A) Locomotion unit:

The primary purpose of NanoCarrier would be capability of automated navigation in the human body, to the vicinity of the organ/tissue where carcinogenic tissue issuspected. Understanding the motion of lower animal forms, such as bacterial flagella motion, can help to design and fabricate bio-inspired robots able to navigate in tortuous,slippery and difficult to access cavities of the human body. In general, such an approach is termed as Biomimetic.

Navigation technique:

a) Positional navigation: The first strategy is positional navigation, in which the nanorobot knows its position inside the human body to micron accuracy at all times in some clinic centered or body centered coordinate grid system. This method requires some onboard computation, at least a basic set of sensors (e.g., acoustic), and probably also a good clock (Nanochronometry). However, if the target coordinates are poorly specified, the system might fail or lead to positional errors [17].

b) Functional navigation: The second strategy is functional navigation, in which Nano devices seek to detect subtle variations in their environment, comparing diverse sensor readings with the profile of the target tissue or cell and congregating wherever this very precisely defined set of preconditions exists. These preconditions may be thermal, acoustic or barostatic, or immunochemical, mechanical or topological, or even genetic.

B) Nanosensors:

A specific bio molecular interaction between target and probe molecules alters the intermolecular interactions within a self-assembled monolayer on one side of a cantilever beam. This can produce a sufficiently large force to bend the cantilever beam and generate motion. The origin of this Nano mechanical motion lays in the interplay between changes in configurationally entropy and the intermolecular energetics.

C) Drug encapsulation and drug delivery:

Nano-enabled controlled drug delivery technology involves multidisciplinary scientific approach, and is very much essential in an effective Nano-enabled cancer therapy. These delivery systems offer numerous advantages compared to conventional dosage forms, which include improved efficacy, reduced toxicity and improved patient compliance and convenience. Here drug is attached to a carrier molecule such as a synthetic polymer, antibody, hormone or liposome [18]. As the absorption and distribution of the drug in such a system depend on the properties of the macromolecular carrier, parameters such as site specificity, protection from degradation and minimization of side effects can be altered by modifying the properties of the carrier. Nano shell combination with nanodevice in cancer therapy Nano device like as nanorobots if have been used in case of drug delivery along with Nano shell containing polymer and drug will give the better drug load at targeted site. It have developed a platform for Nano scale drug delivery called the Nano shell-dielectric metal (gold coated silica) Nano spheres whose optical resonance is a function of the relative size of the constituent layers. These nano shells, embedded in a drug containing tumor targeted hydrogel polymer, and then injected into the body, accumulate near tumor cells. When heated with an infrared laser, the Nano shells selectively absorb a specific Infrared frequency, melting the polymer and releasing the drug payload at a specific site [19].

Nanorobots in kidney diseases: Kidney stones can be intensely painful the larger the stone the more difficult it is to pass. Doctors break up large kidney stones using ultrasonic frequencies, but it's not always effective. Nanorobots could break up kidney stones using a small laser.

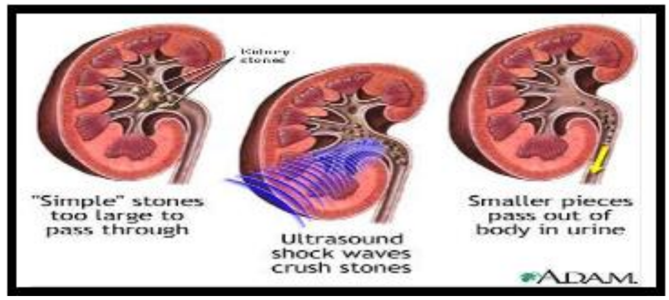

Fig. 9: Break up of kidney stones using a small laser

Treating arteriosclerosis: Arteriosclerosis refers to a condition where plaque builds along the walls of arteries. Nanorobots could conceivably treat the condition by cutting away the plaque, which would then enter the bloodstream.

Fig. 10: Treating arteriosclerosis

Gout:

In Gout, the kidneys lose the ability to remove waste from the breakdown of fats from the bloodstream. This waste sometimes crystallizes at points near joints like the knees and ankles. People who suffer from gout experience intense pain at these joints. Nanorobots could break up the crystalline structures at the joints, providing relief from the symptoms, though it wouldn't be able to reverse the condition [20].

ARTIFICIAL INTELLIGENCY:

Introduction:

Artificial Intelligence is advancing technology in healthcare. By providing rich and relevant information to patients and HCPs with on-demand medical and clinical confidence, AI can greatly advance healthcare professional (HCP) and patient communications [21]. Artificial intelligence is available today for HCP and patient use, and can even be tailored to personality profiles to support patients beyond disease. Artificial intelligence is well known for advancing precision medicine and more recently, genomic analytics. In Japan, doctors used IBM Watson to diagnose a patient with a rare form of leukemia [22]. Use of AI allowed them to diagnose the oncology patient and identify a lifesaving therapy much faster than if they had used traditional methods by manually examining the patient's genetic data. The researchers had to supply genetic data from the patient and then Watson crosschecked it with database of previous patients. Watson was then able to detect gene mutations that are unique to a particular type of leukemia [23].

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Applications:

- Artificial intelligence helps the HLI team identify patterns in huge data sets of genetic information and medical records [24].
- As is common with technologic advances, AI is replacing jobs that previously required humans with computers. It is being applied to repetitive types of jobs or actions in healthcare.
- It is also helping to speed up telemedicine. It is able to improve online consultations by recognizing patient history and symptoms more quickly, and recommending the best course of action [25].
- Cataloguing of medical knowledge.
- Produces new tools to support medical decision-making, training and research.
- Integrates activities in medical, computer, cognitive and other sciences [26].

D-PRINTING (3DP):

Introduction:

It is the art and science of printing in a new dimension using 3D printers to transform 3D computer aided designs (CAD) into life-changing products.

3D printing technology: It is a process of making three dimensional solid objects from a digital file. The creation of a 3D printed object is achieved using additive processes. In an additive process an object is created by laying down successive layers of material until the entire object is created. Each of these layers can be seen as a thinly sliced horizontal cross-section of the eventual object. It acquired an impact as standard tool in the automotive, aerospace, and consumer goods industries. More recently, 3D printing has gained interest in pharmaceutical manufacturing, with FDA's approval of a 3D-printed drug product in August 2015 [27].

History:

Early Additive Manufacturing (AM) equipment and materials were developed in the 1981. In1981, Hideo Kodama of Nagoya Municipal Industrial Research Institute invented two AM fabricating methods of a three-dimensional plastic model with photo-hardening polymer, where the UV exposure area is controlled by a mask pattern or the scanning fiber transmitter. July 16, 1984 Alain Le Méhauté , Olivier de Witte and Jean Claude André filed their patent for the stereo lithography process [28]. The application of French inventors was abandoned by the French General Electric Company (now Alcatel-Alsthom) and CILAS (The Laser Consortium).[28] Then in 1984, Chuck Hull of 3D Systems Corporation developed a prototype system based on a process known as Stereo lithography, in which layers are added by curing photopolymers with ultraviolet light lasers. Hull defined the process as a "system for generating three-dimensional objects by creating a cross-sectional pattern of the object to be formed". His contribution is the design of the STL (Stereo Lithography) file format widely accepted by 3D printing software as well as the digital slicing and infill strategies common to many processes today [29].

Working:

The different types of 3D printers each employ a different technology that processes different materials in different ways. A process polymer resin materials and again utilize a light/laser to solidify the resin in ultra-thin layers. Jetting of fine droplets is another 3D printing process, reminiscent of 2D inkjet printing, but with superior materials to ink and a binder to fix the layers. Perhaps the most common and easily recognized process is deposition, and this is the process employed by the majority of entry-level 3D printers [30]. There are many steps prior to pressing print and more once the part comes off the printer-these are often overlooked. Apart from the realities of designing for 3D printing, which can be demanding, file preparation and conversion can also prove time-consuming and complicated, particularly for parts that demand intricate supports during the build process [31]. There are continual updates and upgrades of software for these Layers by layer the printer will create the predetermined shape functions and the situation is improving. Furthermore, once of the printer, many parts will need to undergo finishing operations. Support removal is an obvious one for processes that demand support, but others include sanding, lacquer, paint or other types of traditional finishing touches, which all typically need to be done by hand and require skill and/or time and patience [32].

Advantages:

1. Ability to customize products.
2. Rapid production of prototypes.
3. Low cost of production.
4. Increased employment opportunities.
5. No storage cost.
6. Improves the safety, efficacy, and accessibility of medicine.

Disadvantages:

1. Intellectual property issues.
2. Unchecked production of dangerous items.
3. Limitations of size.
4. Limitations of raw material.
5. Cost of printers is high.

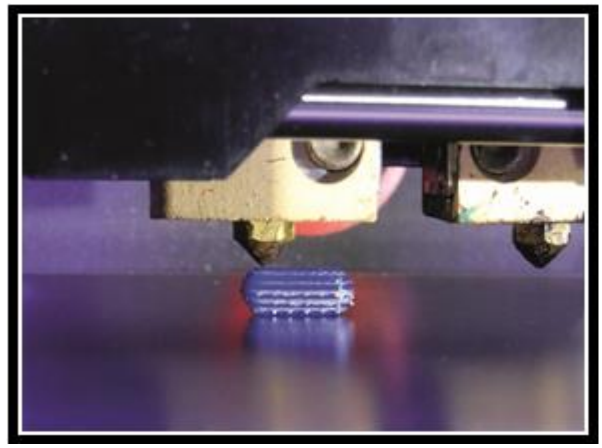

Fig. 11: 3D Printing

Working of 3D printing technology:

It starts with making a virtual design of the object to be created. This virtual design is made in a CAD (Computer Aided Design) file using a 3D modeling program or with the use of a 3D scanner. 3D designs are typically converted to the STL file format, which describes the external surface of a 3D model. 3D printing programs slice these surfaces into distinct printable layers and transfers layer by-layer instructions digitally to the printer. After printing, products may require drying, polishing or other post-processing steps [33]. Standard Terminology for Additive Manufacturing Technologies is as follows:

1. Material Jetting: It differs substantially from binder jetting, and can be challenging to implement. Advantage of material jetting over binder jetting and other methods is resolution; inkjet droplets are about 100 µm in diameter and layer thicknesses for material jetting are smaller than the droplet diameter. Commonly jetted materials include molten polymers and waxes, UV-curable resins, solutions, suspensions, and complex multicomponent fluids.

2. Binder Jetting: The primary 3D printing technology used for pharmaceutical production is inkjet deposition on powder beds. Inkjet printers spray formulations of drugs or binders in small droplets at precise speeds, motions, and sizes onto a powder bed. The liquidformulation inside the printer may contain a binder only, and the powder bed may contain the active ingredient (API) with additional excipients. Alternatively APIs can be jettedonto powder beds as solutions or nan particulate suspensions.

3. Material Extrusion: The material is extruded from robotically-actuated nozzles. Unlike binder jetting, which requires a powder bed, extrusion methods can print on any substrate. Common type of extrusion printing is fused filament fabrication (FFF), also known by the trademarked name: fused deposition modeling™ (FDM®) [34].

4. Powder Bed Fusion: It involves sintering (partial surface melting and congealing) or binding of high-melting-point particles with a low-melting-point binder.

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5. Photopolymerization: Also known as stereo lithography.involves exposing liquid resins to ultraviolet or other high-energy light source to induce polymerization reactions.

6. Directed Energy Deposition: Is a process where raw materials are melted by a focused energy source (ex: laser or electron beam) as they are being deposited. The method allows the use of powders or other raw materials that cannot be extruded [35].

7. Sheet Lamination: Automated laser-cutting and sheet-by-sheet assembly of products. This process is quick and inexpensive but also low-resolution and more wasteful than most printing methods.

Future of 3d printing:

Bioprinting is based on bio-ink, which is made of living cell structures. When a particular digital model is input, specific living tissue is printed and built up layer by cell layer. Bioprinting research is being developed to print different types of tissue, while 3D inkjet printing is being used to develop advanced medical devices and tools [36]. There is a growing trend towards personalized and customized medicines.

This technology may transform the pharmacy practice by allowing medications to be truly individualized and tailored to a patient [37]. Moreover the technology enables preparation of dosage forms with accurate deposition of materials, greater spatial control and geometric flexibility. There is a great hope of 3D bioprinting in producing reproducible biological constructs for producing structures for studies into implantation, regenerative medicine and automated assays for high throughput in vitro drug and toxicity studies in lab developed tissues [38].

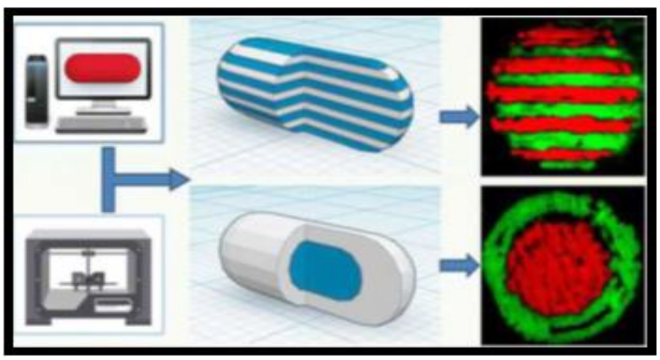

Fig. 12: SPRITAM it is an epilepsy drug 1st 3D printed drug approved by FDA

Use of 3d printing: [39]

1. Tissues with blood vessels
2. Low–Cost Prosthetic Parts
3. Drugs
4. Tailor-made sensors
5. Medical Models
6. Bone
7. Heart Valve
8. Ear cartilage
9. Medical equipment
10. Cranium Replacement
11. Synthetic skin
12. Organs

mHEALTH:

Introduction:

Pharma research institutes are already beginning to take advantage of mHealth technology to conduct clinical research. Smartphones with powerful processors and advanced sensors that can track movement, take measurements and record information are highly useful in post-market studies and allow people to participate in studies more easily. Mobile phone or smartphone becomes the most important communication device in people lives.. For now, mobile phones can use a variety of wireless communication techniques (GSM,Wi-Fi, Bluetooth and others). It allows to integrate mobile phones into existing healthcare services and also to create new services and applications in this area. Practical medicine and healthcare services supported by mobile devices are called mHealth solutions. This field is growing fast recently .mHealth applications are delivered via online stores, such as App Store, Google Play, Overstore and others that increase availability of mobile healthcare solutions. Another important factor, which determines applicability of mobile phones for healthcare purposes, is that a modern mobile phone is equipped with powerful embedded sensors, such as microphone, accelerometer, camera and others. There are surveys of mobile phone sensing applications, e.g., in variety of domains including healthcare, social networks, safety, environmental monitoring and transportation. Researchers notice that these sensors open new horizons for mobile healthcare applications, but they did not review a lot of such applications, so the main use cases of mobile phone sensors in mHealth were not disclosed. In this article we survey Health applications, which use embedded sensors and also demonstrate the main use cases for such sensors in these applications. The remainder of the paper is organized as follows. In Sec. II we present most popular sensors, which are used in modern mobile phones and discuss their general applications. In Sec. III we review existing mHealth applications, which use embedded sensors of mobile devices and discuss the main advantages of internal sensors usage.

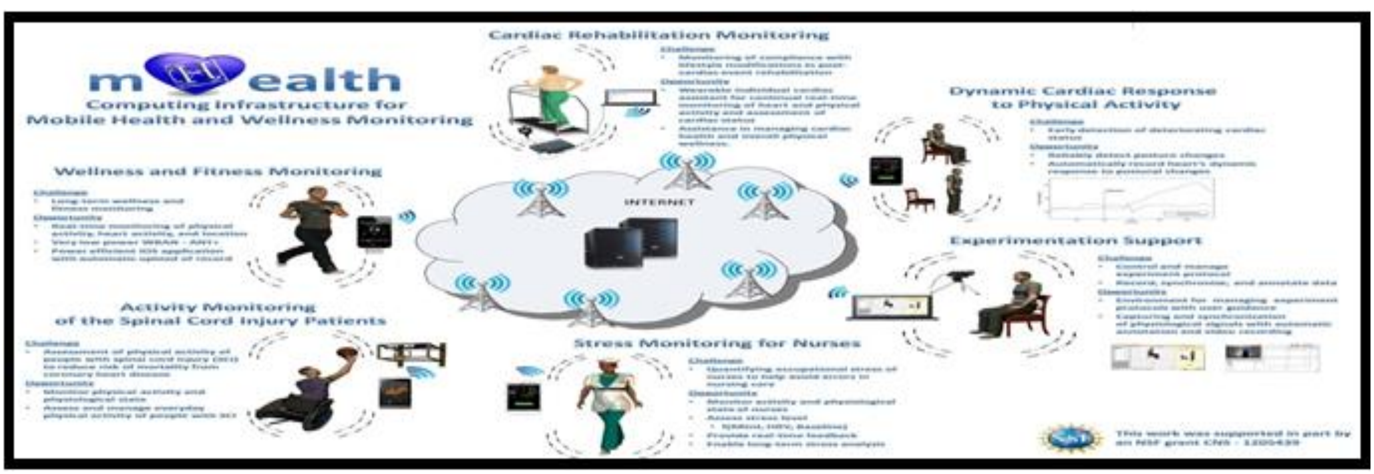

Fig. 13: m health activity

Mobile phone sensors:

All embedded sensors of a mobile phone can be subdivided into two categories. The first one includes environment sensors and the other contains position and orientation sensors. Environment sensors are used to measure different properties of the mobile phone environment. Microphone and camera are examples of the first sensor group. Such sensors as accelerometer, digital compass, gyroscope and GPS form position and orientation sensors group. They are used to

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determine orientation of the mobile phone in space and also device location. Camera is another very popular mobile phone sensor and its general task is photo taking and often video recording. The use of camera sensor can be extended to interact with real world objects, in this case a local analysis of photos or video stream is needed. For example, such analysis was proposed to read 2D codes. The other environment sensors are a light sensor and a proximity sensor. The light sensor measures intensity of ambient light and can be used to adjust brightness of the screen. The proximity sensor detects presence of nearby objects. When the user holds the phone close to his or her ear to answer the call, the screen is blocked to prevent accidental touch. Accelerometers and magnetometers are the sensors, which purpose is to determine a device orientation in space. Accelerometer measures acceleration across two or three directions. The resulted data are used to change screen orientation .Accelerometers can also provide a new way of interaction with the phone, e.g., in motion-sensitive mini-games to control a game process. Whereas the accelerometer in the mobile device allows measuring the linear acceleration of the device, a gyroscope helps to directly determine the orientation relative to the earth magnetic field. Generally, these sensors are used for navigation but also can be applied in new techniques to interact with mobile device using properly shaped permanent magnet.

MOBILE PHONE SENSORS IN HEALTHCARE APPLICATIONS:
Applications:

A. Microphone sensor:

There are several use cases of microphone in mHealth. In healthcare this sensor is obviously used for communication. It offers an effective means of bringing healthcare services to citizens that is extremely topical for developing countries. One of the key applications for mHealth in such countries are:

- Communication and training for healthcare workers;
- Disease and epidemic outbreak tracking;
- Diagnostic and treatment support.

In some cases the microphone can also be used to assess patient feels, e.g., it was shown for patients with the myotonic syndrome. Myotonia is a disorder characterized by slow relaxation of muscles after contraction, which may cause a difficulty to move. According the proposed method, within 8 weeks patients had to call to the data collection service and to talk about their health. Automated voice response system classified symptoms into the four categories: muscle stiffness, weakness, pain and tiredness. Thus the system allows reducing the number of the doctor visits because assessment can be done automatically and allows monitoring such patients without hospitalization [40].

B. Camera sensor:

The mobile phone camera sensor can be used to provide useful information about a patient images and videos that applies in such applications as remote doctor consultation. The more significant example of using mobile device camera in healthcare services is the teledermatology, where the patient skin images are used by the doctor to make a diagnosis. Teledermatology solutions exist in the market of healthcare services. For instance, one of them is provided by ClickMedix. The solution consists of the following parts: a mobile application, a data collection center and professionals in dermatology. To use this service a patient should be registered in the system. After registration the user is instructed on how to take photos of their skin correctly. Then, using the mobile application, the patient takes photos of his/her skin and sends them to the data collection server. The doctor gets access to these data and prescribes a treatment according to the analysis [41]. The service provider suggests using such a remote consultation when a patient cannot have recourse to qualified specialists for one of the following reasons:

1) Lack of access: patients cannot easily reach doctors;
2) Lack of funds: patients cannot afford the high cost of healthcare;
3) Lack of medical resources: most countries face the severe shortages of trained healthcare professionals, especially medical specialists, to perform an adequate diagnosis and quality treatment in rural areas. Another type of medical consultation involving mobile phone camera includes, for example, a remote doctor advising, which is used in Taiwan and China for teleconsultation and diagnostics of soft tissue injuries. Such applications decrease overall number of medical center visits by patient and eventually lead to the improvement of the healthcare. Several new applications in the cardiology field of mobile phone camera were proposed recently. There are two different ways to use phone camera in this field. The first one is to detect heart rate through human skin color analysis. It tracks color changes in the light that passes through a finger [42].

C. Accelerometer sensor and geolocation facilities:

The main application of accelerometers for healthcare purposes is to track a person's physical activity level. It is important as it allows reducing the risk of having many chronic diseases. There are specially designed accelerometer-based devices that measure activity level as a number of steps performed by the person. Such devices are called pedometers. To detect steps they capture readings from accelerometers and recognize the step pattern. Some pedometers can also calculate approximate number of burned calories. Embedded accelerometer of a mobile phone allows implementing the same functionality as pedometers provide. The main advantage of such a solution is that there is no need to have an additional sensing device. Several mobile pedometer applications are available for different popular mobile platforms. Although pedometer-like systems can be very useful for physical activity tracking, they are usually focused only on step counting and do not consider other daily activities, such as walking or running. For more accurate physical activity monitoring a system has to be able to detect different types of activity, including walking, running, bicycle riding, car driving and others. To recognize different activity patterns some studies use only a single accelerometer. For example, in the data were collected from tri-axial accelerometer worn on person's waist. The authors use Bayesian classification for activity recognition. As a result, approximately80% accuracy has been achieved using such activity classification technique. Similar studies have good accuracy in activity classification, but require additional equipment or use devices made only for research purposes. The requirement for additional devices makessuch systems inconvenient for a practical use [43].

Fig. 14: m health activity equipped in mobile phones

Recently mobile phones equipped with different embedded sensors have been used inseveral studies to collect data for activity classification. To create classification model some of these approaches use data from several internal modules, such as microphone, GPS and camera. The other approaches use only accelerometer data and aimed toachieve phone orientation independence along with high accuracy of activity classification. Accelerometer is also the central information source in human fall detection studies. In these studies fall detection is based on recognition of specific patters in accelerometer data. When the fall is detected, the system can send an emergency signal to the monitoring system. Such applications are very useful for elderly people monitoring. Unfortunately, the existing solutions for fall detection, for example Brick house, allows to detect falls only in limited environments, e.g., at home. Such systems are too expensive because they use special devices. They use accelerometer data from mobile phone built-in accelerometer and do not need any external devices. Such systems give an advantage over the other solutions to detect falls everywhere. Moreover, vast coverage of mobile phone communication services allows supplementing emergency call information with exact patient location determined using GPS module. Another useful application of mobile phone accelerometers has been proposed in projectm-Physicto provides rehabilitation service [44]. A patient using the system does not need to come to the rehabilitation center several times, but can perform rehabilitation exercises at home. To estimate training accuracy mobile phone with accelerometer is used. The first stage of the system usage is the system learning when patient perform exercise under specialist

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supervision. The second stage is a personal rehabilitation when the patients perform his/her rehabilitation exercises at home. During these exercises the systems captures the physical activity and classify it into four types: correct exercise, wrong exercise, exercise exceeds the maximum time, exercise does not exceed the minimum time. The system helps the patient to assess how accurately they perform exercises themselves. The experiments demonstrated that using this system the user constantly improves accuracy of personal rehabilitation exercises. Used with the help of: 1. Smartphones: (Samsung gear) 2.Fit ness band: (fit bit, jawbone) [45].

Summary:

- New innovations in Pharma can be extremely beneficial, helping you to adapt to change, seize new opportunities and focus on developing the skills that you will need in the future.
- Precision medicine is an approach that integrates clinical and molecular information to understand the biological basis of disease, hence it is useful in treatment of diseases like Parkinsonism, cancer etc.
- Using nanotechnology, the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side-effects.
- Artificial Intelligence is a rapidly advancing technology in healthcare, providing rich and relevant information to patients and HCPs with on-demand medical and clinical confidence, it can greatly advance healthcare professional (HCP) and patient communications.
- 3D printing or additive manufacturing is a process of making three dimensional solid objects from a digital file.
- There is an abundance of issues and themes that merit considerable research attention in the field of pharmaceutical innovation. This compilation will be a useful platform for many enthusiastic researchers to join in and contribute to the burgeoning stream of studies related to the discovery and development of efficacious novel drugs.

CONCLUSION

The world is becoming an increasingly more compact place, presenting ample opportunities for dispersed innovation and expedient collaboration. Continuous innovation is one of the pharmaceutical industry's most defining characteristics. New medications can be crucial for maintaining the quality of human life, and may even affect its duration. This is particularly evident to global pharmaceutical companies whose subsidiaries and research centers are already spread around the world. Future research could also look into the implications of using fundamental knowledge generated by nonprofit research institutions on the secrecy and proprietary rights demanded by private firms. The signaling value on industry participants of organizational changes enacted through partnerships such as licensing, co-marketing agreements, alliances, mergers, or acquisitions could constitute another fecund area of study. More research is needed to identify the environmental, structural, and strategic determinants that can affect drug innovation outcomes. Pharmaceutical innovation is hardly an orderly, predictable process. Drug innovation as a business process requires savvy strategic, organizational, and managerial decisions. It is already enjoying intensive research coverage, giving rise to abundant but relatively dispersed knowledge of the mechanisms driving drug discovery and development.

REFERNCES:

1. Chua CK, Leong KF, An J. Introduction to rapid prototyping of biomaterials. In: Rapid Prototyping of Biomaterials, Narayan R (Eds). Wood head publishing, **2014**;1-15.
2. United States Food and Drug Administration. Highlights of Prescribing Information Spritam. **2015**; http://www.accessdata.fda.gov/drugsatfda docs/label/2015/207958s000lbl.pdf.
3. Acemoglu D, Linn J. Market size in innovation: theory and evidence from the pharmaceutical industry. Quart J Econ **2004**;119(3):1049-1090.
4. Angell M. Excess in the pharmaceutical industry. Can Med Assoc J **2004**;171(12):1451-1453.
5. Arora A, Gambardella A, Magazzini L, Pammolli F. A breath of fresh air? Firm type, scale,scope and selection effects in drug development, working paper, **2007**.
6. Bottazzi G, Dosi G, Lippi M, Pammolli F, Riccaboni M. Innovation and corporate growth in the evolution of the drug industry. Int J Ind Organ **2001**;19:1161-1187.
7. Personalized Medicine Benefits - The Jackson Laboratory. jax.org.
8. Lu YF, Goldstein DB, Angrist M, Cavalleri G. "Personalized Medicine and Human Genetic Diversity". Cold Spring Harbor Perspectives in Medicine, 24 July **2014**.
9. Jump up Neergard, Lauran. "Obama Proposes 'Precision Medicine' to End One-Size-Fits-All". Drug Discovery & Development. Associated Press, 30 January **2015**.
10. Wang J. Nanomachines Compete with Nature Biomotors?. ACS Nano **2009**;3(1):4-9.
11. Drexler Eric. K. Nanosystems: Molecular Machinery, Manufacturing and Computation: John Wiley & Sons, **1992**.
12. Pardeike J, N. Schrodl, et al. Nanosuspensions as advanced printingink for accurate dosing of poorly soluble drugs in personalized medicines. Int J Pharm **2011**;420:93-100.
13. Amrute-Nayak M, Diensthuber RP, Steffen W, Kathmann D, Hartmann FK, Fedorov R, Urbanke C, Manstein DJ, Brenner B, Tsiavaliaris G. Targeted Optimization of a Protein Nanomachine for Operation in Biohybrid Devices. AngewandteChemi **2010**; 12(2):322-326.
14. Patel GM, Patel GC, Patel RB, Patel JK, Patel M. Nanorobot: A versatile tool in nanomedicine. J Drug Targeting **2010**;14(2):63-67.
15. Chawla JS, Amiji MM. Biodegradable poly (epsilon-caprolactone) nanoparticles fortumor-targeted delivery of tamoxifen. Int J Pharm **2002**;249:127-38.
16. Gates BD, Xu Q, Stewart M, Ryan D, Willson GG, Whitesides GM. New approaches to nanofabrication: molding, printing, and other techniques. Chem Rev **2005**;105:1171-96.
17. Deepak N Kapoor, AmitBansal, Ruchi Sharma, SanjuDhawan. Advanced nanomedicine: Present contributions and future expectations. Amer J Phytomed and Clin Therap **2013**;1(2):124-39.
18. Robert A, Freitas Jr. The ideal gene delivery vector: chromallocytes, cell repair nanorobots for chromosome replacement therapy. J Evolution Tech **2007**;16(1):1-97.
19. Abhilash P, Gregory A. Robotics technology: a journey into the future. UrolClin N Am **2004**;31:793-800.
20. Adriano C, Lior R, Luiz C, Kretly, Moshe R, Shmuel E. Nanorobotic challenges in biomedical applications, design and control. Tel-Aviv, Dec **2004**; Israel.
21. Haugeland J. Artificial Intelligence: The Very Idea. MIT Press, **1985**.
22. Kersting K, Raedt LD and Kramer S. Interpreting bayesian logic programs. In Proc. AAAI-2000 Workshop on Learning Statistical Models from Relational Data. **2000**.
23. Laird J, Newell A and Rosenbloom PS. SOAR: An architecture for general intelligence. AIJ **1987**;33(1):1–64.
24. McCorduck P. Machines who think: a personal inquiry into the history and prospects of artificial intelligence (Revised edition). A K Peters, **2004**.
25. McCarthy J, Minsky ML, Rochester N and Shannon C. E. Proposal for the Dartmouth summer research project on artificial intelligence. Tech. Rep., Dartmouth College, **1955**.
26. Nilsson, N. J. Problem-Solving Methods in Artificial Intelligence. McGraw-Hill, **1971**.
27. Hideo Kodama. "A Scheme for Three-Dimensional Display by Automatic Fabrication of Three-Dimensional Model," IEICE TRANSACTIONS on Electronics (Japanese Edition), April, **1981**; J64-C(4):237–241.
28. Kabsch W, Mannherz HG, Suck D, Pai EF, Holmes KC. Atomic structure of the actin: DNase I complex. Nature **1990**;347:37-44
29. Ueno T, Oosawa K, Aizawa S. Domain structures of the MS ring component protein (FliF) of the flagellar basal body of Salmonella typhimurium. J Mol Biol **1994**;236:546-55.

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30. Mendoza Hannah Rose. "Alain Le Méhauté, The Man Who Submitted Patent For SLA 3D Printing Before Chuck Hull", **2015**. 3dprint.com.
31. Moussion Alexandre. "Interview d'Alain Le Méhauté, 'impression 3D". Primante 3D, **2014**.
32. "3D-Printed Medical Devices Spark FDA Evaluation". LiveScience.com.
33. Hull CW. Apparatus for production of three-dimensional objects by stereolithography, US4575330, **1986**.
34. Jonathan and A. Karim. 3D printing in pharmaceutics: A new tool for designing customized drug delivery systems. Int J Pharm **2016**;499:376-394.
35. I. Gibson, D. Rosen, and B. Stucker. Additive Manufacturing Technologies: 3DPrinting, Rapid Prototyping, and Direct Digital Manufacturing, 2nd ed, New York: Springer, **2015**.
36. J. Norman, RD. Mudarawe, CMV. Moore, MA. Khan, A. Khairuzzama. A new chapter in pharmaceutical manufacturing: 3D-printed drug products, Advanced Drug Delivery Reviews **2016**. doi:10.1016/j.addr.2016.03.001.
37. Gupta MK, Meng F, Johnson BN et al. 3D Printed Programmable Release Capsules. Nano letters **2015**;15(8):5321-5329.
38. Schroder RR, Manstein DJ, Jahn W, Holden H, Rayment I, et al. Three-dimensional atomic model of F-actin decorated with Dictyostelium myosin S1. Nature **1993**;364:171-4
39. Water JJ, Bohr A, Boetker J et al. Three Dimensional Printing of Drug Eluting Implants: Preparation of an Antimicrobial Polylactide Feedstock Material. J Pharm Sci **2015**;104(3):1099-1107.
40. mhealth: New horizons for health through mobile technologies, World Health Organization, **2011**.
41. Westhead R. "How India's Health Care Woes Gave Birth to Private Medicine." Toronto Star. November 11, **2011**.
42. Bhatia Tej K and William C. Ritchie. Bilingualism in South Asia. In: Handbook of Bilingualism, Oxford: Blackwell Publishing, **2006**; pp. 780-807.
43. Patil AV, Somasundaram KV, Goyal RC. Current health scenario in rural India. Austral J Rural Health **2002**;10(2):129-35.
44. Tiwari P. Providing Healthcare Services in Rural India: Innovative Application of Mobile Technology. Healthcare and Informatics Review Online **2010**;14(2):3-9.
45. The world in 2010: ICT facts and figures. Geneva, International Telecommunications Union, **2010**. www.itu.int/ITU-D/ict/material/Facts Figures2010.pdf, accessed 13 May 2011).

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