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Abstract

In recent years there has been a rapid increase in nanotechnology in the fields of medicine and more specifically in targeted drug delivery. At present many substances are under investigation for drug delivery and more specifically for cancer therapy. Interestingly pharmaceutical sciences are also using nanoparticles to reduce toxicity and side effects of drugs. The potential to cross the Blood Brain Barrier (BBB) has open new ways for drug delivery into the brain. In addition, the nanosize also allows for access into the cell and various cellular compartments including the nucleus. Nanoparticles are also considered to have the potential as novel intravascular or cellular probes for both diagnostic and therapeutic purposes (drug/gene delivery), which is expected to generate innovations and play a critical role in medicine. Target-specific drug/gene delivery and early diagnosis in cancer treatment is one of the priority research areas in which nanomedicine will play a vital role. In conclusion nanoparticles for drug delivery and imaging have gradually been developed as new modalities for cancer therapy and diagnosis. This review illustrates the emerging role of nanotechnology in drug delivery.

Introduction

Nanotechnology is the disciple of science that deals with molecules of nanometeric size i.e. 10 power -9 of a meter[1].In the last few decades its benefits are being utilized for the betterment of human civilization. Discovery of nanomedicine has given rise to nanoparticles through which better target specific drug and gene delivery is possible[2]. Nanotechnology enables us to deliver drug in the form of dendrimers, liposomes, nanoshells, emulsions, nanotubes, quantum dots etc. for the manipulation of various diseases and their metabolic pathway[3]. It is of great importance in treatment and diagnosis of cancer. Some recent breakthrough in the form of drug delivery are effective target therapy used in pre-sympathomimetic & diagnosis technique[4].

Applications of Nanotechnology

At nanoscale, materials have novel properties like increased strength, resiliency, electrical conductivity[5,6]. One of the most common example of nanodevice is the iPod Nano which uses microscopic memory chips for increasing the storage capacity. Other example from our daily lives include use of nanoparticles in lotion which help in easy absorption[7]. A publication “Nanomedicine: Nanotechnology for Health” gives us an excellent overview for the products releated to health[5,6]. Silver nanoparticles can be used in eliminating fungus and preventing odours in shoes and refrigerators. These nanoparticles retain their infection-inhibition properties but at the same time allowing greater penetration into organic and inorganic molecules[6]. It is used to prevent infection in burn patient[7]. Life sciences combined with nanotechnology has given rise to nanobiotechnology that has been given insights in to disease processes, hence identifying more efficient biomarkers and understanding the mechanism of drug action[1]. Abraxane® a chemotherapic agent created by Abraxis is another lively example. Bioscience is used to destroy the tumor cells. The chemotherapy is delivered directly into tumour cells because tiny particles penetrate cell membrane easily[8]. Nanomaterials are used in treating glaucoma patients also. Many vaccines like hepatitis and malaria are also utilizing nanotechnology[9]. Nanomaterial vaccines are used to produce greater immunity to pathogens by delivering medications directly to specialized dendritic cells in the immune system[10]. Glucose level are being monitored with the help of patient monitoring devices. Miniature biochips detect increase in glucose level[11]. These particles are also helping epileptic individuals. Implants put in human body detect seizures activity before it is manifested and release medication to prevent the attack[12]. Nanomaterials are being used in regenerative science. It helps in creating artificial skin, cartilage and bone for human use[13]. Many chronic diseases like diabetes and neuro degenerative disease are being cured with this nanotechnology.
In the following paragraphs some of the applications are discussed in detail:

Nanodevices: Single walled carbon nanotubes are being used as a platform for investigating surface-protein and protein-protein binding and also to develop highly specific electronic biomolecule detectors[14]. The scheme combined with the sensitivity of nanotube electronic devices provides highly specific electronic sensors for detecting clinically important biomolecules like antibodies associated with human autoimmune disease.

Biosensors: These are currently used in areas of target identification, validation, assay development, lead optimization and absorption, distribution, metabolism, excretion and toxicity (ADME-box).

(a) Nanobiosensors: The nanosensors with immobilized bioreceptors probes which are selective for target analyte molecules are called nanobiosensors. These can be integrated into other technologies like lab-on-a chip to facilitate molecular diagnostics. Their applications include detection of microorganisms in various samples, monitoring of metabolites in body fluids and detection of tissue pathology such as cancer. Their portability makes them ideal for POC applications but they can also be used in laboratory settings.

(b) Nanowire biosensors: Surface properties of these can be easily modified therefore they can be decorated with virtually any potential chemical or biological molecular recognition unit, thus making the wires themselves analyte independent. Boron doped silicon nanowires are used to create highly sensitive, real time electrically based sensors for biological and chemical species.

(c) Viral nanosensors: Essentially the virus particles are called as biological nanoparticles. Herpes Simplex Virus (HSV) and adenovirus have been used to trigger the assembly of magnetic nanobeads as a nanosensor for clinically relevant viruses[15]. By using a magnetic field, as few as five viral particles can easily be detected in a 10 ml serum sample.

(d) PEBBLE nanosensors: Probes encapsulated by Biologically Localized Embedding (PEBBLE) nanosensors consists of sensor molecules which are entrapped in a chemically inert matrix by a microemulsion polymerization process that produces spherical sensors in the size range of 20 to 200 nm[16]. These are capable of real time inter and intracellular imaging of ions and molecules and are insensitive to interference from proteins.

(e) Optical biosensors: Many biosensors which are currently marketed rely on the optical properties of lasers to monitor and quantify interactions of biomolecules that occur on specially derived surface or biochips. Example: Surface plasmon.

(f) Laser nanosensors: In this laser light is launched into the fibre and the resulting evanescent field at the tip of the fiber is used to excite target molecules bound to the antibody molecules[17]. When laser falls on them, they release optical signals which are coded by photometric detection system. This system is used in analysis of proteins and biomarkers in human living cells.

Drug Delivery System

At present, 95% of all new therapeutic system have poor pharmokinetics and less developed biopharmaceutical properties[18]. There is no such medicinal system that delivers drug and distribute therapeutically active drug molecules to the site of action or inflammation without any side effects[19]. This problems are overcome by nanotechnology drug delivery system which possess multiple desirable attributes. Nanomedicine has a size such that it can be injected without occluding needles and capillaries which enables targeted drug delivery and medical imaging[20]. Thus nanosized liposomes, micelles, nanoemulsions, nanogels are used for this purpose.

Liposomes

Liposomes are used since 1960's[21]. They are single phospholipid membrane organelle with aquous centre inside.They are of different shapes and sizes ranging from 30nm to several micrometer[22]. Because of their size, hydrophobic, hydrophilic as well as biocompatibility, they are used as tool for targeted drug delivery[22,23]. Liposomes size is so small such that it can cross vascular pores to reach solid tumors[24,25]. Liposomes have been surface modified with active targeting ligands to improve delivery of therapautics to target cells[26-29]. Recently a multicomponent liposome consisting of doxorubicin and antisense oligonucleotide targeted to MRP 1 mRNA and BCL 2 mRNA to suppress pump resistance and non pump resistance have been developed[30].

Micelle for drug delivery

Micelle are self assemblies of amphiphiles that form supramolecular core-shell structure in aqueous environment. When the concentration exceeds CMC i.e. critical micelle concentration, hydrophobic interactions are predominant and provides a driving force in the assembly of amphiphiles in aqueous medium[31]. Now a days, micelle falls in the nanosize range that are formed with amphiphilic polymers. Most nanosized miceller delivery system are made up of amphiphilic polymers consisting of PEG and low molecular weight hydrophobic core forming block[32]. Due to their low monomer concentration in equilibrium with micelles, this system has advantage of reduce toxicity and are thermodynamically stable to dilution[33]. Micelle for drug delivery are of four types.

* Phospholipid micelles
* Pluronic micelles
* Poly (L-amino acid) micelles
* Polyester micelles

Dendrimers

It is known since 1980s, dendrimers are macromolecules constructed from the core of ABn (where n = 2 or 3) comprising a series of branches which are tree like around the core[34]. They are well suited for targeted drug delivery because of their nanosize, ease to prepare and functionalisation and polymorphism. Their structure is such that medicinally active therapeutic agent can be embedded in it[35-36]. Example: fluorouracil has antitumor activities, but also has side effects. PAMAM dendrimers after acetylation form dendrimer – 5 FU conjugates which after hydrolysis yields 5 FU., enabling the minimization of toxic effects[37].

Nanoemulsions for drug delivery

Nanoemulsions are dispersion of two immiscible liquids i.e. oil and water, where dispersed phase droplets are of the order of nanometeric size and is stabilized by surface -active films composed of surfactant and co-surfactant[38,39]. They tremendously gain importance because of their optical transparency thermodynamic stability and ease of preparation. Structure of nanoemulsion can effect the rate of drug release at the site of action. Due to their nanosize they provide much longer oil water contact area which facilitates drug release from the dispersed phase droplets. Sonication, high and low energy emulsification using homogenizers are required for its preparation. It has already been used in the i.v. injection of low dose amphotericin administered to mice, rats, dogs and monkeys and dose of 1.0 mg/kg[40].

Implications of nanotechnology

Implantations of nanotransmitters and nanosensors within individuals have opened gates for monitoring and treating them at the microscopic level with the use of nanodevices.But this crosses traditional bounderies of care in the hospitals as persons can get the treatment done while siting in their homes[41].Pateients at home could have access to date transmitted from biochips which will moniter the diseases like hypercholesterolemia, alerting them when critical levels are obtained. Education has increased individual responsibilities and provisions for safety are some of the implications of patients. Introduction of nanotechnology in daily life implies an entire role change for healthcare consumers. They will have powers of chosing their medication, but at the same time it will include responsibilities on their part. Some of the immediate implications for clinician’s role include changes in decision making and clinicians productivity. They may find their role changing into just participants, coordinators or coaches instead of experts. Diseases may also include those releated to softwares problems of nanodevices embedded in the human body. Highly individualized care may be needed. Patients and clinicians would need to have throughout knowledge of device interfaces as all body metabolism will be regulated by these devices. The day may not be far than insurance deny us as money due to monitoring our health at cellular level in early stages[42]. Nanotechnology will make us over dependent on devices. Inaccurate and errors with monitoring devices will be very challenging to detect. Advocates will be needed by everyone for safe and ethical use of nanomaterials[43]. Monitoring methods would be needed to assure that devices are checked and caliberated within safety limits. Hence if these implications can be managed nanotechnology is the biggest boon to mankind.

Conclusion(s)

Nanotechnology has brought a revolution in manufacturing materials, creating a vast number of new devices, drug delivery systems and monitoring and diagnosing systems. but the implications if this technology are very diverse, impacting consumers, clinicians and the practice of informatics. A major area of concern for health care providers is the ethical use of nanomaterials. If this technology will be wide spread and well accepted clinicians might find their roles as experts diminished. Nanotechnology has brought a new era in healthcare but the challenges is to develop it by overcoming various difficulties and implications. New opportunities have provide us with a powerful tool in the field of genomics, proteomics, molecular diagnostics and high throughout screening. Nanoparticles have the properties to become the most versatile materials for developing diagnostics. Advances in nanotechnology will provide a good inside view of our human systems. It has a bright future with the emergence of several promising approaches for delivery of therapeutics agent and imaging using the advantage of nanoscale carriers. Future studies will now be addressing a no. of challenges faced in nanomedicine application. Greater funds are being allocated for clinical and pre-clinical studies but still are studies are lacking in safety data that includes toxicity studies. Also the cost of nanomedicine should be in acceptable range so that it is successful in clinics. Nanotechnology is being applied at all stages of drug development, from formulations for optimal delivery to diagnostic applications in clinical trials. Actual utilization of nanotechnology novel drug delivery techniques lag behind because of perception that such technologies could delay products due to technical or regulatory reasons. So oral drug delivery remains a prefered option. Further the cost factor becomes a hinderance in its daily use. This review deals with promises and uses of nanotechnology in the field of pharmacy to its wide spread application in various fields of genomics, imaging, diagnosis, drug delivery and treatment of diseases.

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Illustrations

Illustration 1

Fig 1: Detailed structure of Liposome

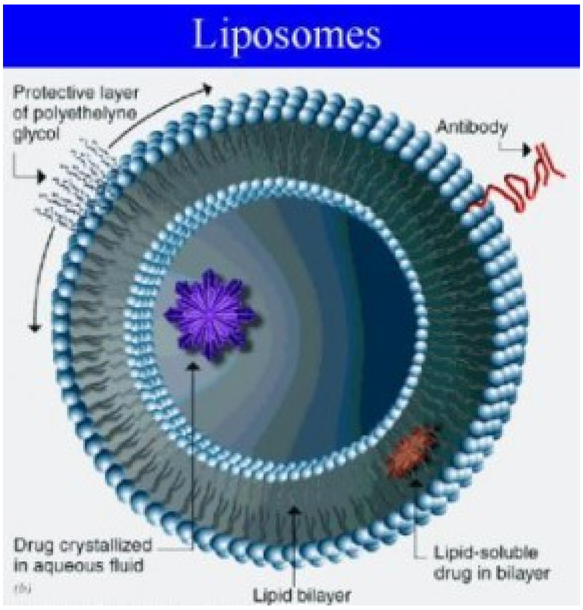


Illustration 2

Fig 2: Micelle containing active substance in the core

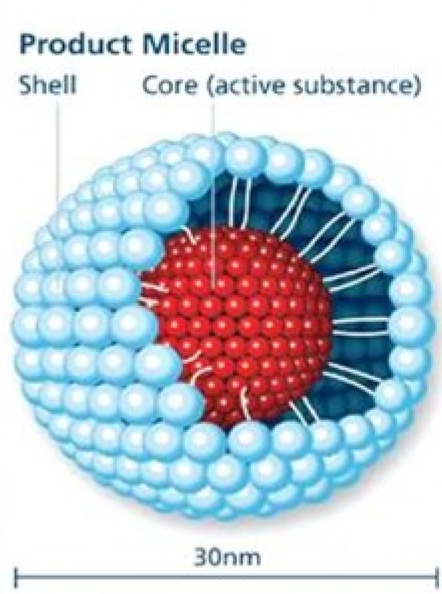
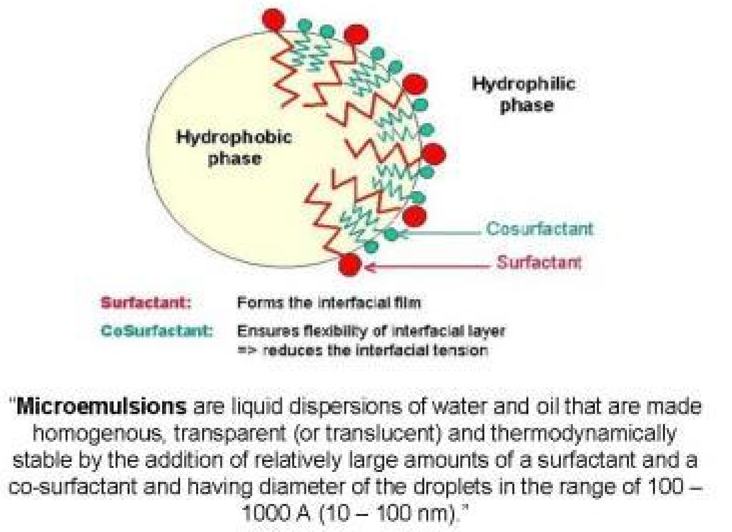


Illustration 3

Fig 3:Nanoemulsions for drug delivery



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