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A Review on Nanoparticle: Formulation Strategies, Characterization and Therapeutic Applications

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Abstract

Nanotechnology is the understanding and control of matter generally in the 1–100nm dimension range. The application of nanotechnology to medicine, known as nanomedicine, concerns the use of precisely engineered materials at this length scale to develop novel therapeutic and diagnostic modalities. Nanomaterials have unique physicochemical properties, such as ultra-small size, large surface area to mass ratio, and high reactivity, which are different from bulk materials of the same composition. These properties can be used to overcome some of the limitations found in traditional therapeutic and diagnostic agents. This review will discuss about methods and strategies used to formulation nanoparticles along with various characterization parameters. The review is also focusing on key therapeutics applications of nanoparticles in effective drug delivery.

Keywords: Nanoparticle; Nano suspension; Drug; Scanning Electron Microscopy

Abbreviations: PCS: Photon Correlation Spectroscopy; LD: Laser Diffraction; DLS: Dynamic Light Scattering Method; TEM: Transmission Electron Microscopy; SEM: Scanning Electron Microscopy; XRD: X Ray Diffraction; DSC: Differential Scanning Calorimetric.

Introduction

In Pharmaceutical development there are many drugs which are under research and development and have very low bioavailability due to low solubility and low dissolution. So for increasing bioavailability and solubility many approaches are used which are like use of cosolvent, forming complex, chemical approaches, weak acid weak base, micronization, emulsion formation etc. Nanonization is one of this approaches which is use to improve drug solubility and dissolution [1]. Nanoparticle is dispersed or solid particle which have size in range of 1billionth meter to 1000 billionthmeter from any dimension. By using simple method of nanoparticle preparation, more convenient formulation could be obtained compare to capsule, tablets, and pellets. They have nano size so they can use as Parentral formulation also and give 100% bioavailability.

Nanoparticle is formulated for BCS class II and IV drug which have law solubility problem. BCS class II drug have law solubility and have good permeability but they give law bioavailability because it have law solubility so it give law absorption of drug and thus it give law bioavailability. Same problem is occurring with BCS IV class drug which have law solubility with law permeability so by converting this type of molecules into nanoparticle we can remove this problem [2]. Nanoparticle has different chemical characterization than metal and their oxides, organic material, carbon material and other polymers. It also has different shape like sphere shape, tube shape, disk or hollow shape etc. it can be synthesis from solid, gas or liquid and nanoparticle have different surface properties than pure drug. Nanoparticle are chemically react

fast compare other drug. So we can said that nanoparticle have different biological, physical, chemical character than starting material [1].

Surface modification is applied on nanoparticle and which can use for many different action like for onset action, for sustained release, for controlled release, for targeted formulation, for improvement of dissolution of drug, for changing of chemical and biological characteristics. Surface modification can apply by different methods such as by using the polymer, by using the surfactant, by join with ligand, by applying coating on surface, by attached the particle with DNA or protein or any other bimolecular, by applying adsorbent like surfactant or polymer which adsorbed the particle and give action [3]. Nanoparticle is sometime surrounded by stabilizer or other exicipients. Metallic nanoparticles are also available in market which has different physical or chemical character from metal bulk. The example of this is nanoparticle of Au which has different color in different size formulation. Nanoparticles are used in medicine as well as other industries also like in rubber industry they use carbon black particle for fabrication of rubber.

Nanoparticle has different type like carbon-based nanoparticle which contains carbon nanotubes and fullerenes which are better compare to steel. Other type is ceramic nanoparticle which is inorganic solid made by carbides or carbonate or phosphate or oxides and use in drug delivery and photo imaging. other one type is metal nanoparticle which is made by using metal and use in formulation which need high surface energy and they also adsorbed little size molecules. Another type is semiconductor nanoparticle, particles use are like GaN, GaP, lnAs, Zns, Zno,Cdte etc. and they are used in electronic devices, water splitting etc. One type is polymeric nanoparticles which are also known as nanosphere in which active component is layered by polymer and use in pharmaceutical formulation for newer approaches like targeting controlled release. Lipid based nanoparticle is also available which have core in which nanoparticle is stabilize by using surfactant or emulsifier and it is used in cancer like disease condition [4].

Nanoparticle are small in size so they have special characteristics and the size of particle can be controlled by using surfactant and polymer and by controlling the size we can also controlled the absorption wavelength and emission wavelength. Transparency in nanoformulation can be attained if particle are below the light critical wavelength of light. In metal nanoparticle the melting point of metal is decrease and also gives better paramagnetic properties. Nanoparticle has different chemical nature so it gives different affinity to electron and which give different properties of electron transport.

Nanoparticle has more surface area so it cans high affinity to polymer matrix in which particle is incorporated. Surface modification in nanoparticle is used to give better stability to nanoparticle and it also use for improving the reaction and applications. Nano particles are used as smart drug for onset and fast result for disease like cancer, diabetes, artery blockage etc. Nanobots use for artery blockage and nanoparticles are also use in genetic problem and it also help in targeting the cell and it is also use for long lasting effect.

Nanoparticle is used in broad area. Most of nanoparticle is used in health and fitness maintenance. They are also used in food and nutrition, for electrical use, for home use etc. Example like Nano tooth cleaner, nanofilter use for air filtration, vitamin B-12 nanospray, nano cream as painkiller [2]. In market nanochips and nanobiosensor are available which medical device which is coated by Nano particulate.

Now a day nanoliposome is famous which have nanoparticle in it and coated by phospholipids and have size near to 25 billionths to 1000 billionth range. Generally liposome are used which have size between 50 billionth to 200 billionth range. Ambisome is product which is nanoliposome which contained particle of Amphotericin B into liposome which have size near to 65 nanometer and which is use for targeting the fungal infection. Daunorubicin is also capsulated into liposome and useful in targeting delivery in cancer tumor.

Some particles which have nanosize are coated by protein use for good effect. Example of it is PEGylated protein which has longer effect in blood. Some drug is also conjugated with protein like Paclitaxel drug is joined with albumin protein which have size near 131 nm. Some nanoparticles are converted into metal particle like Feridex is approved product of iron oxide which is nanoparticle and use in MRI of liver and spleen which is modified by surface. Superiority of this type of formulation are that it has particle size under 1 micron so have high solubility and dissolution power compare other dosage from and we can also produce 100% pure drug particle without using carrier [5]. There is some drawback like mass production is easily not done for nanoparticle and this need high cost for production and sometime need many techniques for production so it needs very long time.

Nanoparticle Formulation Strategies

Precipitation Method

This method is use from 1980 for production of nanoparticles. This is simple method in which API is solubilize in organic solvent and exicipients like polymer surfactant

and stabilizer are dissolved in a miscible inorganic solvent than with spontaneous agitation addition of organic solvent into inorganic solvent is performed and it give precipitation of particles.

This technology is simple and need law cost so compare with other techniques this process is easy and need less time for fulfillment. For performing this technique we require the solubility of API at least in one organic solvent and that organic solvent have properties to miscible with inorganic solvent so this is limits of this technique [1] . Carbamazepine and Greseofulvin are produce by applying this method.

Milling Method

This technology is developed in 1990. In this technique API and surfactant are charged with milling pearls and fill in chamber of milling and then high rotation is applied by using a motor and nanoparticles are form in suspension form. This process need long time for production because drug hardness and quantities like factor may affect this process. This technique needs high energy and sometimes erosion of pearls leads product degradation and give risk of bacterial and micro logical contamination. The media milling chamber is produce by using zirconium oxide, glass or polystyrene resin. The milling process is used for aqua and organic medium. It can use in both situation to produce diluted as well as concentrated suspension formulation. This method have disadvantage is it consume long time and milling may give instability to suspension [6].

Homogenization Method

This process is developed in 1990 for produce nanoparticles and nanosuspension. In this technique nanosuspension of API with excipients is passed from homonizer gap with high pressure which leads to cavitation and give nanoparticle by using high kinetic force. In high pressure homogenizer both pressure and mechanical force can apply for produce unique product.

Homogenizer also have option to change the force and pressure so one can adjust it for producing desire size of particle. It also has option for temperature changing. In hot homogenization process high temperature is used which melt the lipoids phase and give aqua phase. This method is not use for drug which can degreed at high temperature. For that type of drug we can use cold homogenization techniques. This technology is also use for Parentral formulation and in food and cosmetic production.

For this technique one should need to observe the cycle number applied for homogenization and temperature and pressure which is applied. For lab experiment 100 to 1500 bar pressure is used. Because of pressure small particle size is obtained which have better bioavailability and have large surface area so improvement of dissolution can be achieved. Albendazole, ibuprofen, Spironolactone, Nifedipine, Omeprazole are produce by using this strategies [7]. Fenofibrate nanoparticle use as tablet in Hypercholesterolemia condition which have brand name Triglide is produce by homogenization method.

Spray Drying Method

This method is used for tablets and powder production. First the macro suspension is produce which contained API and exicipients with proper solvent and then this suspension is passed from homonizer and it give nanosuspension. The second step is removing solvent. For solvent removing two methods are used like freeze drying and spray drying. The freeze-drying method is costly so spray drying method is first choice for industries and it give dry powder form nano powders and crystals [8]. The loading power of nanoparticle's powder is changed by changing the exicipients ratio and surfactant ratio with drug in suspension. At first time the spray drying have limitation and they are not use for nonproduction they give minimum 2 μm size in past but now a day this method is useful for produce 300 nm size and also give 90% yield. The principle of dryer is simple. First the drying gas is applied by heater in laminar air flow into system. Spray head spray the fine droplets of suspension and after drying of droplet it convert into solid particle. This type of powder can use for inhalation, for encapsulation, as drug carrier for suspension etc.

Production of Nanoparticle in Nonaqueous Media

This method is use to avoid removation of solvent after homogenization process. In this technique homogenization is applied into nonaqueous medium like PEG or self-emulsified drug delivery system and which is ideal for filling into soft or hard gelatin capsule [7].

Pelletization Method

Generally, nanosuspension are stable but in some cases like for oral administration and stability issue we need solid formulation so this technique is usable for this problem solution. Nanosuspension is converting into solid form by using methods like lyophilization or spray drying or extrusion and spheronization or layered on sugar pellets. In this method suspension is mixed with matrix exicipients and using extrusion process final product is obtained. The material is filling into pellet shape which is free flowing small spherical particle [8].

Emulsified Solvent Evaporating Technique

In this method drug and polymer is solubilize into aqua immiscible solvent and add this solvent into aqueous solvent in which surfactant is dissolved with drop wise and then homogenization is applied. Nanoparticles are obtained by lyphillization method after removation of solvent. In this method large amount of aqueous phase is added into solvent so it leads diffusion of organic solvent from internal phase to external phase. For some drug double emulsion method is also preferred. One should need to observe the duration and intensity of homogenization and type of drug and polymer for successfully follow this technique [8]. This method is also useful for water soluble drug by applying double emulsification method in which drug is solubilize into aqua and then applying of first emulsification method. The polymer used in method and type of solvent and intensity of homogenization may responsibly factor for affecting of this method.

Hot Melted Production Method

In this method melted material is used and homogenization is applied in hot temperature. Temperature is choosing by observing the melting point of material matrix used. Micro lab 40 homonizer is generally used for this method because this has temperature control jackets which cover the container. When desire size of particle obtained than solidification is next step for process and at room temperature solidification is done by using cooling [8].

Direct Compression Method

The nanoparticle powder is obtained from nanosuspension by using spray drying or any other method and which can use orally by filling it into capsule. In case of acid sensitive drug nanoparticle are fill into hard gelatin capsule. The other way of applying nanoparticle as orally is convert it into tablet formulation. For that drug nanosuspension is mixed with matrix forming material like micro size polymer powder or lipid and lactose powder and then spray drying is apply. By this process the liquid phase is go into API-matrix compound and convert into free flowing powder than direct compression is apply and which give long release tablet formulation [8].

Characterization of Nanoparticles

Nanoparticle Size

The size detection of nanoparticle is important to observe the dissolution, saturation solubility, physical and biological stability. The mean size of particle is detected by using photon correlation spectroscopy (PCS). Coulter counter miltisizer and laser diffraction (LD) is also use for checking of this property. PCS method is also useful for measurement of width of particle. Dynamic light scattering method (DLS) is also used in industry for measurement of size of nanoparticle and it can also measure the size of particle have size under 10 nm. In this technique the liquid colloid sample is undergo for Brownian motion and give information about diffusion coefficient by using scattering of light. This method measures the size between 2 nm to 2000 nm and gives result in 1 to 10 minutes. For this method small quantity of sample need and give result fast and give facility of measuring of particle diameter and polydispersity index [9].

Shape and Morphology

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) can use for checking of this property. For TEM liquid or wet sample is need and for SEM solid sample is require. Sometimes SEM is used to detect the nanosuspension size so for that one need to remove solvent from suspension so lyphillization or drying methods are used. Agglomeration and sticking is problem in this method so cryoprotectat or other exicipients are added before this method performance. Like mannitol is used in lyophilization it performs it work by covering the nanoparticle so no agglomeration take place. Sometime x ray diffraction (XRD) also use for detection of polymorphic change due to pressure and homogenization [10].

Zeta Potecial

This measurement is useful to detect the stability of colloidal dispersion after storage. As per literature zeta potecial between ± 20 mv to ±30 mv is give desirably stable nanoparticle into suspension [11].

Differential Scanning Calorimetric Studies (DSC)

This method is used to detect the drug and exicipients interaction. By using thermogram of pure API and mixture of exicipients with API one can give result on interaction and melting point [1].

Dissolution Velocity and Saturation Solubility

This character provides information about solubility with comparison to microparticles and also gives information about in vivo performance. For study this nanosuspension is first convert into solid form and then by using proper media of dissolution saturation study is performed at different temperature and time according by following the pharmacopeial methodology.

Saturation solubility is generally depending on API and the media use for dissolution and temperature used for same. The saturation solubility increases if substance have law melting point. Kelvin Oswald equation said that saturation

Solubility is increase when we decrease the size of particle. The Oswald equation is as under.

$$LogCss/logC=2\sigma v/2.303RT\rho r \text{ ..... (1)}$$

Where, Css is saturated solubility and C is solubility of large particle and V is volume of particle and T is temperature, is tension between interfacial and is solid density and r is radius of particle.

By this equation it can be interpret that saturation solubility is increase when particle size is decrease because the size of particle is inversely proportional to saturated solubility.

The dissolution is also increase when particle size is become small.it is explained by Noyes-whitney equation [5].

$$dc/dt=DA/H(Cs-C) \text{ ..... (2)}$$

Where,

$\frac{dc}{dt}$ Is dissolution rate of drug.

D is rate constant for diffusion
A is surface area
H is distance of diffusion
is saturated solubility
C is concentration around particle.

In nanosize particle have larger surface area so it can increase the dissolution because surface area is directly proportional to dissolution rate. Decrease in size also increases the saturation solubility which gives beneficial effect in dissolution [12].

Therapeutic Application

Dermal

Dermal use means drug is apply on skin and absorption of drug is occur from skin by intercellular route of lipid, by transcellular route and by using the follicular penetration. Fluconazole nanoparticle into NLCs and SLNs are used into fungal disease which gives better penetration compare to simple drug. The transdermal penetration is increase by nanoparticle by increasing the gradient of concentration between skin and nanoformulation. Like hesperidin and lutein anti-ageing nanoformulation is use to increase the solubilizing power of hesperidin. Other example is diclofenac drug when it administered orally it give severe gastric problem but this problem is overcome by converting diclofenac into nanosuspension (solid in oil) type which increase diclofenac sodium flux into skin of pig 3.8-fold. As nanoparticle has law size compare to microparticles so it lead to better solubility and penetration into skin and give more activity. On mucosal layer nano spray can also useful and local action is also available by converting nano formulation into lotion or cream form [13].

Novavax Company producing topical formulation of liposomal nanoparticle for drug Micellular Estradiol under trade name of Estrasorb which is use for menopausal therapy. Diclofenac diethylamide drug solid lipid nanoparticle is incorporate into transmucosal patch and which is use for sustained release of diclofenac after surgery into tooth.

Ointment of nanoparticle of gold which is attached with Ribonucleic Acid is used for cancer of skin in which Ribonucleic Acid is joining with the infected cell and inhibits the protein synthesis into cell so it inhibits the growth of tumor cell indirectly.

Ocular

Nano ointment or suspension is prepared for using it into eye for poor soluble drugs. The advantage of this is it give long time effect and give great performance but it have disadvantage is that most of drug have law solubility in lachrymal fluid so it give law concentration of drug at desire site. Nanoparticle can convert into slaw release formulation so it can use for long period and it also reduces the drug loss in lachrymal fluid. Like ibuprofen nanosuspension nanoparticles are use as safe drug formulation for 24 hr. usage [14].

Hydrogel, Dendrimers and polymeric nanoparticle are also used in eye for various diseases. Mucoadhesive nanoparticle loaded with drug is used into contact lenses which can improve patient compliance and increase the bioavailability. Example of this is lenses loaded with timolol drug nanoparticle are given better bioavailability compare to simple eye drops in glaucoma disease and it also need law dose compare to eye drop. In cornea the eye drop is also used but they have disadvantage of drainage and have law penetration affinity so nanoparticle are developed which have Mucoadhesive force so give higher effect than eye drops.

PLGA nanoparticle coated by eudragit surfactant gives good effect into eye of mice compare to non-coated particle of PLGA. Liposome is one of nanomedicine which can be used. Samolin '*et al*' developed the idoxuridine liposome which improve the penetration of drug into cornea with compare to simple solution and used into herpes simplex keratitis

disease. Aclon Pharma also nanoparticle of Brizolamide which is use as suspension for Glaucoma disease and have Trade name is Azopt.

Parenteral

0.1μm to 0.3 μm size nanoparticle are used to increase the retention and penetration of drug into tumor. Some drugs which are use into cancer like mycoepoxydine are available in market as IV formulation. For reduce the opsonin attack nanoparticle are coated with other exicipients so it can give long time effect into tumor. Example is PEG coated nanocrystal; it gives long time circulation into blood compare to other coated nanoparticles.

By altering the surface of nanoparticle, it can be used in severe disease like HIV and tuberculosis by altering the protein of plasma. 1, 3-dicyclohexylurea is use to control blood pressure and available as infusion apply as IV.

The Enzon company producing drug for fungal infection with trade name abelcet is containing liposomal nanoparticle of drug amphotericin B given as IV. The other example is liposomal IRIV vaccine produce by berna biotech Company under trade name of Epaxal use as IM formulation for hepatitis A. Johnson and Johnson company produce aprepitant drug particle under Trade name of Sustenna which is use as intramuscular injection and have appetite stimulant effect.

Samyang Company produces IV polymeric nanoparticle formulation of drug Methoxy-PEG-poly (D, L-lactide) for metastatic breast cancer under trade name of Genexol-PM. Other example is albumin bound Paclitaxel nanoparticle formulation which is use in metastatic cancer as IV formulation under trade name of Abraxane produce by Abraxis Bioscience Company. The drug name Cytarabine liposomal nanoparticle produce by company Skyepharma under Trade name of Depocyt used as Intrathecal route for malignant lymphomatous meningitis [15].

Palmitate drug is use as IV formulation for treating eye infection and cataract surgery which is produce by Aclon Pharma Company under Trade name of llevro. Janssen Pharma also developed intramuscular injection of Acetate for disease condition like schizophrenia under name as Sustenna.

Oral

On concentrate of issue like safety and cost oral route is first choice for patient. Nanoparticle is administered orally as nanosuspension form, as capsule form, or as direct compressing tablet or other type of tablet form. For good action of drug, we need to focus on solubility power of drug and then power of absorption into gastric juice which give absorption into blood and then give needed effect of drug. Some factor is observed for oral usage is like PH of GIT tract, solubility of drug, dose of drug, food interaction etc. [15].

Nanoparticle is used in oral delivery so it increases the patient compliance compare to injection. This technology is very useful for patient who received medicine for daily usage so instead of injection pill give better compliance in disease like Cholesterol problem, Diabetes etc. Antiemetic drug name aprepitant produce by Elan company under trade name of emend use orally and company also producing oral formulation fenofibrate drug under trade name of Tricor used as anti hyperlipidemic drug. Wyeth pharmaceutical company produce immunosuppressant drug name sirolimus under trade name of Rapamune used as oral formulation of nanoparticle. Some research also suggests that oral delivery of insulin as nanoparticle give same efficiency as Parentral formulation. Some nanoparticle is used for delivery of protein, Hormones and Peptide delivery into body, for this process nanoparticle are used as carrier. Example of this is Apollo company developed nanoparticle for use as orally for insulin and anti-inflammatory protein which is known as TNF blocker and this is in category of protein based drugs and antibodies.

In market there some nanoparticle which is use in several diseases is like Greseofulvin tablet which is made from Greseofulvin and PEG for treating fungal infection and which have Trade name is Gris-PEG. Schwarz Pharma also produce nanoparticle of verapamil HCL which is given as capsule under Trade name of Verelan PM and use to treat arrhythmia. Several research are also in pipeline which is based on subject of chemotherapy and for deliver the medicine which is use in cancer to directly in targeted part.

Subcutaneous

Subcutation means administered drug under the layer of skin. This process is use when intravein usage of drug is not possible or costly. Drug is given in fatty tissue which is located under the skin. The common sites are thing, arm and abdomen. Amgen Company producing nanoparticle use as SC formulation by using PEG with Granulocyte Colony Stimulating Factor under trade name of Neulasta used in chemotherapy of neutropenic cancer. TEVA Pharmaceutics Company also produce SC polymeric nanoparticle for multiple sclerosis disease under trade name of Copaxone which contained L-Glitamic acid, L-tyrosine copolymer, L-alanine, L-lysine. PEG-Hepatocyte Growth Factor combination also in market for disease acromegaly produced

by Pfizer Company under trade name of Somavert which is use SC polymeric nanoparticle form [16]. Bioengineering and Nanotechnology institute developed the Nanohydro gel of drug herceptin which is injected under skin layer and give release of drug till a week and decrease the size of tumor into mice. Nanoparticles are also use as adjuvant to increase the immune response into vaccine preparation. Subcutaneous route is preferred for lymphatic drug delivery also so particle which have size less than 1 micrometer are use directly. The example of this is PMMA nanoparticle which is used as adjuvant in HIV 2 [17].

Targeted Delivery

Nanoparticle of Fe2O3 is used for upgrade the Magnetic Resonance Imaging of tumor. Peptide coated nanoparticle of Fe2O3 is attached with infected cell and improve the MRI scanning property [18]. Some nanoparticle is also used to detect the cancer cell into blood which have special sensor so they are used to detection of cancer at first stage [19-25]. Nanoparticle also used for develop the nanospray which is useful for detection of Deoxy Ribonucleic Acid and gene protein sequence (Tables 1&2).

Organic nanoparticle	classification and type Advantages	Recent studies focused on the application of organic passively drug targets for cancer treatment.		
		PS	Cancer type	Reference
Silica	Surfaces can be easily modified	Protoporphyrin IX	In vitro cervical cancer	Silica-based platform carriedand released PS in intracellular reducing environment with improved phototoxic effect [21].
Alumina	Highly stable [22]	Pheophorbide-loaded polymeric micelles stabilized with alumina.	In vitro colon andsquamous cell carcinoma.	Significantly reduce cell viability in a dose- and time-dependent manner [23].
Magnetic		Superparamagnetism, high field irreversibility, high saturation field, ability to target specific locations in the body guide by	Dimercaptosuccinic acid-coated superparamagnetic iron oxide NPs.	Effectively targeted breast cancer cells with significant cell death induction [25].

NPs, Nanoparticles; PS, Photosensitizer.

Table 1: Applications of Organic Nanoparticles in Photodynamic Therapy.

Name (company)	Particle type/drug	Investigated application/indication	ClinicalTrials.gov identifier (phase)
ND-L02-s0201 (Nitto Denko)	siRNA lipid nanoparticle conjugated to Vitamin A	Hepatic fibrosis	NCT02227459 (Ph I)
ARB-001467 TKB-HBV (Arbutus Biopharma)	Lipid particle containing three RNAitherapeutics that target three sites on the HBV genome	Hepatitis B	NCT02631096 (Ph II)
RGI-2001 (Regimmune)	Liposomal formulation of a-GalCer	Mitigating graft versus host disease following stem cell transplant	NCT01379209 (Ph I/II)
ThermoDox® (Celsion)	Lyso-thermosensitive liposomal doxorubicin	Temperature-triggered doxorubicin release: Breast cancer recurrence at chest wall (microwave hypothermia) Hepatocellular carcinoma (radiofrequency ablation) Liver tumors (mild hypothermia) Refractory solid tumors (magnetic resonance high intensity focused ultrasound)	NCT00826085 (Ph I/ II) NCT02112656 (Ph III) NCT02181075 (Ph I) NCT02536183 (Ph I)

Table 2: Summary of current clinical trials of intravenous nanoparticles [26].

Conclusion

The application of nanotechnology to drug delivery has already had a significant impact on many areas of medicine. Currently, more than 20 nanoparticle therapeutics are in clinical use, validating the ability of nanoparticles to improve the therapeutic index of drugs. In addition to the already approved nanoparticles, numerous other nanoparticle platforms are currently under various stages of preclinical and clinical development, including various liposomes, polymeric micelles, Dendrimers, quantum dots, gold nanoparticles, and ceramic nanoparticles. With continued research and development efforts, nanotechnology is expected to have a tremendous impact on medicine for decades to come.

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