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# Review on Polymeric Micelles; A Nanotechnological Carrier for Smart Drug Delivery

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**ABSTRACT**

The drug delivery system is most essential topic that related to the medicinal science for administration of drug in our body with different complication. For oldest day to now a day several drug delivery systems will discovered, at first various conventional drug delivery (oral, parenteral, local or topical) continuing but now a day's several smart or developed technologies should discovered for delivery of drug for their advantageous like site specific, target specific, prevent wastage of drug, patient more compliance, improve bioavailability, good appearance, controlled release, sustained release, long circulation etc for that's why nanotechnological novel drug delivery system are approaches. In this review explains about the nanotechnology that help with drug delivery with advanced system like nano base liposomes, niosomes, nanoshells, nanosystem, carbon nanotube, nanowires, polymeric micelles and different nanoparticles. Most of these polymeric micelles are briefly described with their characteristic of advanced nano technological carriers for drug delivery system and also described about the some other drug delivery system with advanced technology.

## INTRODUCTION:

Nanotechnology is a science that deal with the formulation, developed and characterizations of molecule or any device which a size ranges nanometres that help to controlling drug delivery system in modern decades [1, 2]. The term “nano” is obtained from the Greek word for “dwarf” one nanometer is equal to one-billionth of a meter or regarding the breadth of six carbon atom or 10 water molecules. Atoms and molecules are very small in size like blow nm or similar to nm or larger [3]. Presently several nanotechnological approaches showing in medical science i.e. several number of nanotechnological systems showing their physiological, therapeutical and diagnostic activity and their viability have been established [4]. In this nanotechnology based drug delivery system is preferred because of their active realistic activity that should be developed. In the starting polymeric drug delivery system several polymeric complex and polymeric micelles are developed to the delivery of drug with their suitable formulation should studied in different clinical trial [5]. Including different nanotechnological drug delivery system polymeric micelles is one of the most developed carrier-mediated drug delivery systems. Polymeric micelles contain composite core-shell like structure in which core contain a hydrophobic or lipophilic chamber containing lipid soluble drug are outer surrounded shell are hydrophilic in nature that contain several polymers like poly-ethylene-glycol that have a good compatibility to circulated blood and produced therapeutically action when consume to the tumour effected cell[6-8]. These polymerics are more preferable now days for their several advantages like easy to prepare for drug delivery, control and targeted drug delivery system, encapsulation of appropriate drug without any interaction with other substances [9-12].

## SEVERAL APPROACHES FOR DRUG DELIVERY SYSTEM:

Different particular system are available as a carrier media for deliver a particular therapeutically active agents in the conventional route, as example liposomes drug delivery ystem that are also nano system help for deliver antidiabetic drug insulin by the oral route [13]. Liposomes are lipid bilayers containing vesicle drug delivery system that encapsulated lipid-soluble drug with in lipid bilayer and water soluble drug with in aqueous core in a suitable condition that there will be no lost of any drug due to decomposition or any other chemical reaction for their encapsulating periods [13-14]. In that case preparing liposomes are disrupted in intestinal bile component and degraded due to the presence of phospholipids of intestine for that why premature release conducted of this liposomal encapsulating drug in

GI fluid [15-16]. Another colloidal system like emulsion, microemulsion, nanoemulsion is also effective for oral drug delivery with their suitable solubility of bio-fluid [17-18]. Advance different new drug delivery systems are discovered with their advanced technology such as nanoparticles with their size in several nanometer like nanosphere, nanocapsule, hydrogels, nanotube, nanosystem, nanoshell, or any other silica particle encapsulating various decomposed drug, labile drug, hormone, protein, peptide containing nanoparticle (nanotechnological drug delivery system) [19-25]. Different polymer that are used to nano-carrier for oral drug delivery system like poly-alkyl-cyano-acrylate, tetra polymer of methyl-metha-crylate, 2-hydroxy-ethyl methacrylate, n-butyl-acrylate etc [22, 26]. These approaches are generally used to conventionally oral drug delivery systems with modifying their characteristic in nanotechnology but optimum achieving their therapeutical and pharmacological response to different parenteral routes available because these routes for novel drug delivery are active for their control, targeted, sustains release.

**MICELLES:**

In past decade micelles have shown greater affinity as a medium for drug delivery system for their characteristic like controlled release and god therapeutical activity [27-28]. Micelles are formed while amphiphles property showing in water as containing hydrophobic internal core carrying lipid-soluble drug and outer hydrophilic layer are aqueous in nature to maintain their stability with consisting with each other [29]. Micelles forming carrier mediated drug delivery system depend upon various factors like their shape, size, surface area, charge activity etc and these also depend upon various formulating methods of polymeric micelles with addition of some other ingredients like amphiphiles and non ionic surfactants (sodium lauryl sulphate) to improve their quality and highly advanced carrier mediated delivery in pharmaceutical field [30-35]. In the different field different micelles group act as a carrier for drug delivery systems with great potency by forming hydrophilic and hydrophobic core interaction and outer surface containing polymeric layer. This polymer like poly-ethylene-glycol (PEG) having greater affinity for producing layer with highly hydration property that's why they form repulsion charges and these repulsion charge help to prevent aggregation and floats or circulate separate entity for a long lime and maintain their stability [36-39]. Micelles having other different qualities like different block-forming hydrophobic characteristic improved their formulation maintaining stability and their core structure prevent the phagocytizes activity in reticuloendothelial system that can help to reduce quick elimination and circulate long time in our systemic circulation [40-42].

**POLYMERIC MICELLES:**

Polymeric micelles are low molecular weight containing amphiphilic co polymer consisting of hydrophobic core containing lipophilic drugs and surface block hydrophilic polymeric chain that have a great stability in our body fluid [43]. Polymeric micelles are applicable in this situation when drug are unstable in physiological fluid, show low solubility, interact with other body parts, and have insufficient pharmacokinetics activity. This hydrophilic cell are helped cannot interact with the drug and intercellular protein and peptide molecules that increase the stability of this dosage system. The approximate size of polymeric micelles is 10 to 100 nm and this small size is distributed effectively drug delivery system [43]. The most suitable route for delivery of polymeric micelles is parenterally, most of the low water soluble drug like several steroids indomethacin, amphotericin-B, adriamycin, hydrocorticosteron etc are effectively encapsulated hydrophobic core and effectively deliver as a safe and stable carrier mediate system [44-48]. Here the most important base is that polymeric micelles for oral drug formulating delivery system prepared by the assemblage of Kabanov [49-54]. The basic of these fundamentals these polymeric micelles are prepared by using pluronic-tri-block copolymer (as well called poloxamer; poly-ethylene-oxide$_x$-b-poly-propylene-oxide$_y$-b-poly-ethylene-oxide$_x$ ; PEO$_x$-b-PPO$_y$-b-PEO$_x$) and additional some block isomeric form are organized as a carrier-mediated drug delivery system for DNA[55].

So, our attempt to delivery of drug through orally is design for chemical modification and structurally modification of different amphiphilic polymer that helps to formulating a carrier mediated polymeric micelle vesicles. To achieve our goal we have to select different new polysaccharides materials that are not harmful (non-toxic, non-irritant, chemically stable) like hydroxyl-propyl cellulose (HPC), water soluble cellulose derivatives, dextran ( DEX) a glucose polymer 1, 6 α-glycoside-linkage, [56] these all are effectively used in the manufacturing of dosage form (e.g.; DEX since plasma substitute as locally and systematically [57] and HPC use as a oral tablet preparation [58-59] and also used as a binding agent or disintegrating agent for tablet granulation process of their biological adhesivity characteristic). In serially showing moreover DEX or HPC with their amphiphilic property we connected a cetyl hydrophobic group in their frame structure are depict under the explanation of DEX, we select to connect the hydrophobic part to the hydrophilic polysaccharides frame structure through a small PEO linkage, producing DEX grafting through PEO$_{10}$-C$_{16}$ (DEX-g-PEO$_{10}$-C$_{16}$ or HPC-g-PEO$_{10}$-C$_{10}$); these number nest to PEO indicate to the number of ethylene-oxide grouping in PEO, and the number next to the carbon

indicate to the number of carbon in the chain of alkyl group; and to develop the solubility prospective of this co-polymer throughout the badly aqueous soluble drug. Some time in aqueous solution containing polymer like hydrophobically modified polysaccharides (HM) show great compatibility and effective, stable drug delivery system when above their critical association concentration (CAC) when polymeric micelles are to be formed[58, 60].

**PHYSICOCHEMICAL PROPERTIES OF POLYMERIC MICELLES:**

As early describe the polymeric micelles having their great ability to act as a carrier mediated controlled drug delivery system depending upon their size and critical association concentration (CAC), concentration of copolymer that exist lower level of polymeric single chain. This explanation helps to define the polymeric micelles are interrelated with the critical micelling concentration (CMC) of surfactant micelles so their micellization process not only depends for amphiphilic polymer and surfactant [61-62]. The determination of critical association concentration of different copolymer depends on different factor like the nature and diameter of the hydrophobic coaring chamber and outer hydrophilic chain. Amphiphilic copolymeric series having greater hydrophobic value decrease the critical association concentration value with water followed by those involving lowering hydrophobic value. In favour of the group of copolymer when core forming chain is remain constant then elevate the molecular weight of hydrophobic coating chamber that decrease the critical association concentration [63]. In a small degree when diameter of core forming chamber is retain at a stable diameter and also elevated the diameter of the hydrophilic chain then also elevated the value of critical association concentration [64-65]. The determination of critical association concentration of polymeric micelles is obtained by fluorescence spectroscopic method using pyrene. A suitable hydrophobic fluorescence probe that completely involving the micelles containing a hydrophobic coreing chamber. Due to presence of photo physical characteristic pyrene undergoes changes as a result of converting the nano polarity that help to expend to diffuse the water from hydrophilic chaining portion to hydrophobic core [66-67]. In generally two methods are available to determination of critical association concentration of polymeric micelles using of pyrene fluorescence spectroscopy [68]. The main method explained by kalya nansundaram et al. [69]., taking merit of converting the vibronic fine configuration of this pyrene discharge and observing the modify the proportion of the intensities.

## CLASSIFICATION OF POLYMERIC MICELLES:

Polymeric micelles are mainly classified into three types depending upon their intermolecular interaction conducted by segregation of aqueous layer containing segments, these are conventional polymeric micelles, polyion complex forming polymeric micelles and noncovalently connecting polymeric micelles.

### 1. Conventional Polymeric Micelles

It is the most important type of polymeric micelles generally produces by hydrophobic interaction in between the aqueous coring environment and their coring segment. Poly(ethylene oxide)-b-poly(propylene oxide)-bpoly(ethylene oxide) is the most important example of block-forming amphiphilic copolymer are u8sed for the preparation of this type of polymeric micelles with the help of hydrophobic interaction [70].

### 2. Polyion Complex Forming Polymeric Micelles

This type of polymeric micelles is formed with the help of electrostatic interaction in-between different polyelectrolyte. Generally polyion complex are formed while two alternative charges polymer are added to a solution and alter charge containing polyelectrolyte are interact with each other and incorporated to aqueous coring segment and this type of formation are called as polyion complex forming polymeric micelles. The structural integrity and charging liability depend upon two force that is electrostatic interaction force and van der Walls interaction force. this type of polymeric micelles are prefer for their advantageous activity like easy to prepare, long stability, easy to drug encapsulating and also highly targeting throughout the long circulation in our body. It also prevents toxic activity because of their preparation are conducted by taking of aqueous solvent that are less toxic than organic solvent. This type of polymeric micelles are easy to encapsulate various therapeutically active components, it may be aqueous soluble or oily soluble or any other having different electrostatic interactions with in coring chamber. That's why it help for easy to release of drug like charge molecule containing protein, enzyme, genetics materials etc[71-72]. In recent times, Jung *et al.* formulated methoxy poly(ethylene glycol)-grafted-chitosan loaded polymeric micelles of all-trans retinoic acid through the formation of a polyion complex among the chitosan containing amino group and all-trans retinoic acid containing carboxylic group. This type of system is developed for targeting of

brain tumour. This type of polymeric micelles has very small size ranges 50 to 150 nm and drug encapsulation is greater than 80% [73].

**3. Noncovalently Connecting Polymeric Micelles**

This type of polymeric micelles is called as metal complexation polymeric micelles, it also called as "block copolymer free" polymeric micelles because they are prepare by interpolymeric hydrogen bonding complexation or metalic complexation by taking of self combinant homopolymer, graft copolymer, and random copolymer. This is called as noncovalently connecting polymeric micelles because this type of polymeric micelles containing core and shell are noncovalently attached homopolymeric hydrogen and or metal ligand complex bonded formatted structure [74].

**TYPE OF POLYMER USES IN POLYMERIC MICELLEES:**

Mainly two types of copolymer bloc (di, tri, and tetra) copolymer and graft copolymer that are ampiphilic in nature used for the preparation of polymeric micelles. Graft copolymer containing two part one is called as structural backbone and also another play an important role like called side grafted chain, so that play an combination role of structural backbone and grafting combination. Graft copolymer is prepared to ‘click’ reaction in between structural polymeric backbone and side chain [75]. An example of different ampiphilic copolymer with their structure is given to the following Table 1. In generally spherical type of polymeric micelles are prepared in an aqueous solution by adding of different di-block and tri-block amphiphilic copolymers, in that case hydrophilic block may be slightly larger than the hydrophobic block. However when the hydrophilic block are more large then the hydrophobic block then copolymer exist as a unimers in water and when hydrophobic block are more larger then produces another structure. For the formulation of polymeric micelles by using different amphiphilic copolymers are given in Table 2.

| Table: 1 Example of Amphiphilic Copolymer with their structure | | | |
|---|---|---|---|
| Type of Polymer | Structure | Example | Reference |
| Block Copolymer | di - block<br>AAAAAAABBBBBB | Poly(styrene)-b-poly(ethylene oxide) | [76] |
| | tri - block<br>AAAABBBBBAAAA | Poly(ethylene-oxide)-b-poly(propylene-oxide)-b-poly(ethylene oxide) | [77] |
| Graft Copolymer | AAAAAAAAAAAA<br>B B<br>B B<br>B B<br>B | N-phthaloylchitosan-g-polycaprolactone | [78] |

| Table: 2 Example of Polymer Used in Polymeric Micelles | |
|---|---|
| Example | Reference |
| N-phthaloylcarboxymethylchitosan | [79] |
| Poly(2-ethylhexyl acrylate)-b-poly(acrylic acid) | [80] |
| Poly(tert-butyl acrylate)-b-poly(2-vinyl pyridine) | [81] |
| Poly(ethylene oxide)-b-polycaprolactone | [82] |
| Poly(e-caprolactone)-b-poly(ethylene glycol)-b-poly(e-caprolactone) | [86-84] |
| Poly(e-caprolactone)-b-poly(methacrylic acid) | [85] |
| Poly(ethyleneglycol)-b-poly(e-caprolactone-co-trimethylenecarbonate) | [86] |
| Poly(aspartic acid)-b-polylactide | [87] |
| Poly(ethylene glycol)-block-poly(aspartate-hydrazide) | [88] |
| Poly(N-isopropyl acrylamide-co-methacryl acid)-g-poly(D,L-lactide) | [89] |
| Stearic acid-grafted chitosan oligosaccharide | [90] |

## PREPARATION METHOD OF POLYMERIC MICELLES:

Very commonly two methods are used for the preparation of polymeric micelles. Firstly dissolution method by using low molecular weight and a small size of block copolymer by using suitable solvent with the help of suitable stirring, heating and sonication method for easy to dissolving. That maintain the characteristic of polymeric micelles by tapping of micelles within the solvent that play a nonsolvent that are sensitive to core. Another method is used for the preparation of micelles that is non dissolution with in a non specific solvent. For particularly micellization of a combination of block forminging copolymer or specific particular solvent or may be change in ph, temperature or any other factor [91].

### Formulation of drug encapsulating polymeric micelles:

Three technique are generally applied for formulating drug encapsulating polymeric micelles that are direct dissolution, solvent evaporation and dialysis. Among this direct dissolution is the simplest method for the formulation of micelles by directly dissolving of polymer and drugs in a solvent. Drug-polymer combination to form micelles when the critical micelling concentration is at fixed or elevated in this solution. Drug encapsulating efficiency is very low by using this method. To overcome this problem this method are alter by increasing temperature or primarily prepare an evaporating thin drug layer before the addition of polymeric solution. Generally volatile organic solvents are used for dissolving the polymer or drug molecules to formulate polymeric micelles by solvent evaporating techniques. When the solvent are evaporated then produces a thin layer of drug polymer combination after that thin layer containing combination are introduced in water then producing polymeric micelles with loaded drug. These two methods are not applicable when block copolymeric chain are larger and hydrophobic in nature. In this case, polymeric micelles are prepared by taking of large quantity of low aqueous soluble drug in this polymeric solution and the method is used as a dialysis. Firstly taking of drug – polymeric mixture in an organic solvent in the form of small pouch or bag after that replace the solvent like water and introducing the drug- polymer loaded bag then after some time producing drug encapsulating polymeric micelles[92-93]. Although this method having some demerits like unwanted action of taking organic solvent in the time of preparation and also taking more than 35 hours for their preparation. However to overcome this problem lyophilization technique are used by taking mixture of water and tert-butanol with addition of drug and polymer to form a very economical and simplify

combinated product after that lyophilized product are redispersed in a solvent then produces drug encapsulating polymeric micelles[94-95].

## SIGNIFICANCE OF POLYMERIC MICELLES IN DIFFERENT FIELD:

### BIOLOGICAL DISTRIBUTION

The main objective to deliver of drug throughout the different sector in our body by using a suitably carrier-mediated polymeric micelles having greater affinity to decompose the drug with perfect therapeutical and pharmacological activity. To achieve targeted drug delivery throughout the body is essential to conduct these polymeric micelles very suitably because their small nanosize carrier-mediated structure help slow and sustained circulation for a long time to the different tissue containing circulating system. However, there will be some difficulties produces for the long circulation of polymeric micelles, first of its glomerular excretion through the kidney and also appreciation through the reticuloendothelial system when presence in the liver, lung and spleen [96]. This glomerular excretion can be prevented by applying size modification of carrier-mediated polymeric vessels with their normal size. And another difficulty should be prevented by applying aqueous polymer like poly-ethylene-glycol that help to long circulation due to the presence of effective repulsion activity [97] on their surface to easy movement these nano scale carrier containing polymeric micelles throughout the circulation of blood and these properties maintain the stable and stealth polymeric micelles. Polymeric micelles are considered by a critical association concentration (CAC) that describe about the overhold concentration of assemblage polymeric micelles not easily separate after quickly dilution followed by injection into our body for the reason that lowering critical association concentration like $10^{-6}$ to $10^{-7}$ meter that is lowering to the surfactant micelles as comparison to below 1000 folds and dissociation constant is pharmacokinetic ally low this character help for long circulation and finally decomposited to the targeted tissue.

A suitable example for the biological distribution of polymeric micelles is combination of polymeric micelles with poly-ethylene –glycol-block-poly-D, L lactide (PEG-b-PDLLA) copolymer considered with $^{125}$A. This PEG-b-PDLLA containing polymeric micelles shows great blood circulation (half life near about 18 hour) behind injectable supply and circulate about 24 hour of 25% dose of the drug in their injection. Then calculate the compartmental modelling with the help of central and peripheral compartmental model like their plasma drug concentration of polymeric micelles with the plasma blood proportion and plasma volume

space determine the volume of distribution, this assembly help for the determination of polymeric micelles that are suitably distributed to the blood section and complete interact with the blood cell after their completely supply. These circumstances of polymeric micelles are identified by gel chromatographic method. These polymeric micelles prevent the reticuloendothelial system problem as well as the encapsulation by hepatic sinusoidal capillaries considered as a long inter endothelial junction also lacking of basement surface, showing the comparatively small size of the polymeric micelles. However polymeric micelles was release the block copolymer through the urinary excretion as molecular weight comparison due to glomerular filtration , which give an clear idea of polymeric micelles having their safety, efficacy and low risk of distribution and storage in different targeting cell or tissue in our body.

**DISTRIBUTION TO TUMORS TISSUE:**

Polymeric micelles have a greater affinity to deposition of drug in different tumors tissue due to their long circulation and targeting property. This mechanism is described by the microvascular hyperprmeability to macromolecular circulation and lymphatic system containing deposited to the tumors tissue, this is called a ‘permeability enhancer’ and ‘effect of retention’ [98-99]. These types of microvascular hyperpermeability tumors recommended to showing of vascular endothelial growth factor or vascular permeability factor [100], also depending upon the other factor like basic friboblast growth factor [101], nitric oxide, bradykinin, peroxinitrate, etc [99]. Especially vascular permeability factor or vascular endothelial growth factor, a protein secreted by tumors showing main activity in the process of angiogenesis involving cell division of vascular endothelial system, specifically degraded the membrane of vascular basement and nearest extracellular matrix and endothelial cell migration so that elevation level of microvascular permeability [100].

**DISTRIBUTION FOR CANCER CHEMOTHERAPY:**

Polymeric micelles act as a smart drug delivery system containing hydrophobic drug for the treatment of cancer chemotherapy. Normally amphiphilic block forming copolymer having their suitable core-shell structure and several hydrophobic nano size potent drugs (anticancer drug) are encapsulated with suitable outer hydrophilic cell and their having good nano carrier structures that help for suitable storage and targeted specific cancer cell. Poly-ethylene-glycol-block-poly(aspartic acid) [PEG-b-P(Asp) as a polymer are incorporating anticancer drug doxorubicin to form polymeric micelles having diameter 10 to 50 nm, this is suitably

polymeric micelles that encapsulated doxorubicin in their hydrophobic core and to optimized of these formulation name as NK911 in a hospital of a national cancer centre in Japan for phase II clinical trial of drug delivery studies [6, 102]. In this case doxorubicin are coagulated in the surface of the polymeric micelles that produces instability but maximum supplying of drug to the core with the help of $\pi$-$\pi$ interaction of the cyclic structure of doxorubicin are help to the stability for maintaining long circulated release of the drug and produces therapeutically activity. So it is essential that the relation between drug and core forming block co polymer for maintaining their loading of drug and also their circulation releasing capacity. Whereas, it is easy to observed that various hydrophobic drugs such as Amphotericin-B, Spicamycin containing their long fatty acid chain easily encapsulate polymeric micelles as exemplified by fatty acid ester containing side chain derivatives of poly-ethylene-block-polymer containing aspartic acid [103], their structure look like compatibility of drug and copolymer, here also determine that the loading capacity of drug that help for release rate of drug. If the loading of the drug is very high then the excessive drug are conjugated to form a crystalline structure inside the core that decrease the release rate of drug [104-105]. This property of polymeric micelles like internal core is separated due to highly rigidities polymeric composition effect the drug loading and their biological distribution for their encapsulation. Now a day's Paclitaxel are encapsulated with polymeric micelles formulate the [PEG-b-P (Asp)] altering 4-phenyl-1-butanolate and this is called as NK105 [106]. In that case activity of drug loaded complex is more efficient to the tumor area. These NK105 serve as a good antitumor's action in human beings due to the significantly experiment conducted by taking a mice in a national cancer centre in Japan with their phase-I clinical trial and obtaining a great successfully achievement [106].

**SITE SPECIFIC SMART DRUG DELIVERY:**

Recently there have been several momentums for the delivery of polymeric micelles as a smart functional activity for their targeting to the specific site of our body tissue [107, 108, 109, 8]. The main objective to developed smart polymeric micelles to improve the specificity and also increased the delivery of high amount of drugs to the specific targeted tissues for producing great pharmacological activity and also decrease the adverse effect so site specific delivery for polymeric micelles is great novel technology for their long circulation and specific action depending upon their composition and formulation characteristic. To ensure the leakage of drug from carrier-mediated polymeric micelles throughout circulation to

developed the carrier mediated polymeric micelles and check out for supplying drug encapsulated carrier mediated polymeric micelles intracellularly for their efficiency and release overall the leakage characteristic during their therapy, for that several parameters are check inside the cell like their ph modules and enzyme activity [110, 108, 109, 8, 111, 112]. Now a day's several ph-sensitive polymeric micelles are discovered for introducing doxorubicin to the site-specific chain containing polymeric coring chamber also involvement in between acid-labile hydrogen bond [109, 110, 8]. Several enzyme activities are also help for the development of polymeric micelles to site-specific targeting and produce active pharmacological activity. So, the distribution of drug to the specific site of our body are are developed to ph sensitive polymeric micelle for their long systemic circulation, low leakage of drug and targeted to the highly amount of drug to specified tissue like tumors. That should be check a ph sensitive polymeric micelles are given to a tumors containing mice and showing a great tumor-preventing activity as comparison to the free delivery of doxorubicin [109].

**SIGNIFICANCE OF NANOTECHNOLOGY IN DRUG DELIVERY SYSTEM:**

These modern days drug delivery through nanotechnology is greatly famous for their advanced technology in developed medical science. Nanotechnology define the any nano size device or nano carrier mediated structure that help transporting of nano size dosage form with their great biological significance and achieving all about your response in modern platform [113-116]. There are several mild application and utilization for their active performance and reduce their other complication throughout the continuing conventional drug delivery technology in medical history. In few past discursion many pharmaceutical scientist described about the different pharmaceutical development technology of drugs substances and also their suitable drug delivery system will be observed, however all this system maintaining their all pharmacokinetics like their ADME and also improved their stability for maintaining the active concentration of drug to active target site that means prolong duration of the release of the drug to specific site [117-118]. For decrease the dosing frequency and improve patient compliance generally, nanotechnologically novel drug delivery system will developed for that drug that have an very short half life and not biodegradable and not biocompatible with conventional drug delivery system [119]. In different pharmaceutical company there having a large scope for new drug delivery technology of different dosage form with suitable methodology for their marketing and also improvised their reasonable generic expression, near about 15% of the modern pharmaceutical company are selling their

product depending upon the drug delivery system [120]. Today day the main application of nanotechnology bases for pharmaceutical development yet there having amazing series of outgoing significance [121-122]. These significance help for changing the characteristic of novel drug development like nanoparticles or any other with their modification of drug development for improving response to target tissue for maintain their bioavailability and bioequivalence. The most important example is polymeric nanocapsule prepared in this condition that easy to break and controlled release to the targeted site and also behaves differently in different body environments such as acidic and basic and also presents different complicated conditions. There also important to observation of polymers and the combination of polymeric components that help of this type of novel drug delivery in nanotechnology [123-124].

Nanotechnology is also help gene delivery for the treatment of several genetic disorders by helping to alter the defected gene or to prevent the harmful gene [125-128]. The technique for changing the defective gene are introduce of a good and healthy gene to an earmarked genomic place to alter the abnormal defective gene and also using homologous recombination technique or specific reverse mutation for altering of the abnormal gene to normal functionalised gene [129-131]. There are several gene delivery nonotechnoly are available like viral vector, non viral vector and normally injected some genetic material to targeted tissue (gene guns) having their several advantages less producing disadvantages [132, 125, 126, 133, 134]. So, there are also described about the different nanotechnological drug delivery systems.

**LIPOSOMES:**

Liposomes are small spherical vesicles act as a carrier mediated drug delivery system made by lipid bilayer generally composition of phospholipid and cholesterol are help for encapsulating drug [135].these liposomes are available in different nano eter ranges for highly specific delivery of drug, in that case liposomes are effective for gene delivery due to their small size and presence of lipid bilayer that are structural similarly to the cell membrane and also circulate long time in our blod due to presence of hydrophilic polymeric layer and also surface attaching to the genetic material (DNA, RNA) or any other type of ligand or any substances that help suitable targeting particularly parts, cell or tissue in our body [136-137]. Cationic liposomes contain a positive charge in their surface are combined with negative charge DNA molecule and formed lipoplexes (cationic liposomes –S-DNA-

complex) produced in the procedure of electrostatic force and hydrophobic attraction are used as a non viral vector in-vivo delivery of genetic component in cultural boddy [134,138, 139]. This lipoplexes are generally engulfed through the endocytosis procedure for releasing of endosomal compartment. Liu et al [140] express that combining liposomes holding poly-cationic-lipid and cholesterol illustrate more transportation to the liver then loss DNA molecule, this type of work helps lipoplexes , cholesterol and DNA are injectabally inputted to the circulation with defective of hepatectomy. However, this nanotechnical novel system are help for the transporting of nano size drug with highly frequency targeted and also help for the chemotherapeutical, radio graphical activity for the treatment of cancer with their modern advantages[141-144].

**NANOPARTICLES:**

Nanoparticles are polymeric-based colloidal dispersed particles with size ranges in between 10-1000 nm [145]. These nanoparticle are similar to microparticles except of microparticles are may be slightly larger then nanoparticles and these are prepared by using of PLGA and PLA polymeric composition act as a non viral gene delivery system due to their biocompatibility, biodegradability and capable for preventing the degradation of DNA in endolysosomal system [146]. However, these polymeric containing nanoparticles show their great ability to transport drug and protein molecules. Newly it was observed that quick displace of nanoparticles from the endolysosomal chamber tocytoplasomic chamber due to their intracellular uptake by the endocytosis process, this quick displace of nanoparticles from the endolysosomal chamber should protect the nanoparticls and also their engulfing DNA from endolysosomes due to their degradative pathway [147]. These nanoprticle are basically two type like nano-sphere and nano-capsule are suitably prepare by different mechanical method for encapsulating drug also genetic materials with different fraction of nanoparticles having their great transportation and releasing activity in specific and targeted area in our body (gene therapy: ) [148].

**NANOSHELLS:**

Nanoshells are also nontechnological developed nanoparticulate system for treatment and diagnosis of cancer type of disease. The composition of nanoshells is metallic having silica gel core are coated with gold metallic component [149]. The main mechanism for treatment of cancer or tumor cell without effecting any other cells by using nanoshells to alter the density of gold layer taht enhances the optical absorption capability of nanoshells closed to

the far-IR range and this radiating light are fallen to tissue to reflecting to absorbing the nanoshell and generated heat to destroy the cancer cells [150]. This nanoshell has a great power to targeting the specific effected body organs like cancer cell or tumors tissue by attaching of anticancer agent on their surface [151]. This gold coated nanoshell also play an important role in our body through drug delivery like treatment of breast cancer, detection of immunological assays and determine the analyte with biological medium due to absence of any sample.

**NANOWIRES:**

Nanowires are very fine nanoscale silica wire, covering with single strand of human hairs. Nanowires are effective with their characteristic like they are very very small as compare to any pathological virus and these wires very powerful as also comparison to spider silk [151]. These nanowires have a great function in detecting and treating cancer cells. These nanowires are also effective for the determination of analyte like cancer biomarker and study of kinetics of bimolecular science [152]. For determination of different types of cancer like prostate cancer, breast cancer and ovarian cancer, these nanowires are most effective when they are combined with proteinous materials as a carrier.

**CARBON NANOTUBES:**

Carbon nanotubes are also effective nano carrier mediated system generally comprises carbon atom are attached with condensed benzene structure showing in the structure of tube. Fullerenes is the main type of carbon nanotubes, they are used in the treatment of cancer therapy by a combination of graphite and diamond with third allotropic form of carbon in this carbon nanotubes [153]. Carbon nanotubes are generally prepared by several number of specific monoclonal antibody, chelating radiating ions and different fluorescent probes are used to treat tumors cells [154]. For easy to endocytosis of cell the surface layer of nanotube are made by proteinous component. After that these carbon nanotubes are heated near IR wavelength range by absorption and reaching of this range they release the heat or energy (~70ºC) to destroy the cancer cells [155]. The most important technique for determination of breast cancer cells act as a biological sensor for the layering of carbon nanotubes with monoclonal antibodies that are conducted by carbon nanotubes containing antibody have the power of specific sensitivity of receptor-containing cancer cell.

**DENDRIMERS:**

Dendrimers are internally coring nanomolecular components that are prepared by branching of several polymeric component [156]. Dendrimeric polymer has great capability for gene delivery as well as drug delivery. They form very small particle as like nanometer range for conjugation of DNA molecule and also drugs [157-158]. The forming dendrimers –DNA conjugation different from engulfing in such a way main interact produces gene retension is occurred by electrostatic interaction with in the negatively phosphate groups in DNA framework and positive charge amino group-containing polymer structure [159-160]. These formations occur during the mixing of normally in aqueous solution. Generally poly-amides-amines are used for the formation of dendrimers for genetic delivery and nowadays also several another groups are attached to developed the standard delivery of dendrimers.

Maksimenko et al express that developed transfection applying poly-amide-amine conjugation [160], this explanation shows that transfection in the different lining of cell by plasmid cytomegalovirus β-galactoside plasmid dendrimers complex was improved by the occurrence of anionic oligomer involving oligonucleotides or dextran sulfate.

**CONCLUSION:**

Nanotechnology including polymeric micelles has great characterization for modern advantageous drug delivery system. It also shows better opportunities for novel drug therapy with decreasing site effect benefited for easy to formulate, drug loading efficiency and targeting is highly achieve. It also effective for some transporting deeply complicated tissue or cell in our body like immunological substances, proteins, enzyme, antibody, and or any other biological active agent to treat several complication mostly tumor, cancer, inflammation etc. In this review article expresses about the all important developed and prospectors meteorology for developing of drug delivery system as a novel carrier mediated drug delivery and in future also discover several approaches in polymeric micelles.

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