IJBPAS, December, 2022, 11(12): 5728-5744

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

SYNTHESIS CHARACTERIZATION AND APPLICATION OF NANOPARTICLES IN THERANOSTICS AND POLYMER COATING: A REVIEW

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Received 6th Feb. 2021; Revised 25th March 2022; Accepted 12th May 2022; Available online 1st Dec. 2022

https://doi.org/10.31032/IJBPAS/2022/11.12.6632

ABSTRACT

From many years drug delivery systems have become so important and having ability of combining therapeutic action from a drug with some techniques like magnetic resonance imaging (MRI), magnetic particle imaging (MPI), near infrared (NIR), and photoacoustic imaging (PAI), etc. Theranostics is combination of the imaging with therapy and its increasing the efficacy of treatment with accurate direction. For the preparation of theranostic drug delivery carrier we need to developed a single model which kept the capacity of adsorption, releasing property of drug and imaging properties which can enhance the action. This is very much favorable thing that combine form of polymer with magnaticnano particles gives such a very good platform and also provide use full information. Polymers work as a reservoir for drugs, during this magnaticnano particle using for MRI, MPI and treatment for cancer. For the cancer and different disease therapies and its diagnosis there are several articles, reviews published in the duration of last five years on the topic of coated nanoparticles dependent on bifunctional proteins and conducting polymers, biopolymers, etc .Polymer coated magnetic NP models showed a meaning full consent because of their collective functions and balanced magnetic properties. Apart from these very informative reviews something is missing and there is a little gap so that it's important to understand the applicability of theranostic propertiesfor real life applications.

Keywords: Polymer, NanoParticle, Drug, Coating

1. INTRODUCTION

1.1. Surface Modification of Magnetic nanoparticles1 (functionalization in detail)

Indeed, magnetic nanoparticles have great potential for biomedical applications, but they also possess some drawbacks such as, high tendency of agglomeration, high surface energy, prone to oxidation and high chemical reactivity. As a result, magnetite nano particles may suffer a great loss in their biocompatibility and performance. The presence of a molecule with appropriate functionality on the surface of magnetite nanoparticles results in a great change in their physical, chemical and biological properties. Broadly speaking, functionalization of magnetite nanoparticles can be carried out using two strategies **(see Figure 1(a))**:

(i) The functionalization agent may be added into the reaction system during thee synthesis of magnetite nanoparticles **[15]**, and

(ii) Once the nanoparticles have been synthesized, their surface can be modified chemically using some chemical approach **[18]**.

The type of chemical interaction, taking place between the magnetite nanoparticles (MNPs) surface and the functionalizing reagent (FR) may also a basis for categorization. The interaction may be a non-covalent or covalent type, depending on the chemical nature of the modifying agent.The non-covalent attachments **[22]** usually consist of electrostatic interactions, attachment of modifying agent with some film or sheet covering the nanoparticles surface or π-π stacking etc. In some cases, a non-specific adsorption of functionalizing agent on the MNPs surface can yield a conjugation, but with less stability. However, if the sorption is chemical in nature then formation of covalent bond is highly probable. Here, there may be sharing of electrons from similar or non-similar atoms, thus resulting in non-polar or polar bond formation respectively. The Covalent type of bonding between the MNPs surface and FR results from a variety of chemical reactions that may take place between the two. These reactions include electrophilic/nucleophilic substitution and addition reactions, oxidation, reduction, polymerization, esterification etc. Sometimes, a desired molecule is conjugated on the surface of MNPs using intermediary linkers such as oleic acid, aminoproliltriethoxysilane, etc. Finally, formation of a metallic shell over the surface of magnetite nanoparticles may also be treated as functionalization. The studies

related with formation of metallic bond between Fe atoms present on the surface of magnetite nanoparticle and some other metal have been reported rarely. In this way, core-shell structure can be made with a metallic shell and magnetitebased core.For example, Tomotaka *et al*. **[1]** have synthesized core/shell magnetite/gold nanoparticles and investigated their dynamic magnetic properties and Magnetic particle imaging (MPI) performance. They found a great difference in the AC hysteresis loops obtained with native magnetite and magnetite/gold core/shell nanoparticles, thus indicating that core-shell interface influenced their dynamic magnetic properties. Similarly, Faaliyan and co-workers **[2]** synthesized magnetite nanoparticles by co-precipitation method, followed by immediate formation of silica shell over magnetite nanoparticles surface via sol-gel technique. The TEM analysis confirmed a total diameter of around 25 nm, with average core and shell size around 20 and 2.5 nm respectively. The high core size to shell thickness ratio (i.e. 20/2.5 =8.0), the magnetic saturation was quite significant. Nonmetal such as Carbon has also been used to prepare magnetite/carbon core/shell nanoparticles with fluorescent property. Recently, Wang *et al* **[3]**. have reported a single pot solvothermal approach to prepare core/shell magnetite/carbon nanoparticles , having a core size of 9.1 nm and shell thickness of 3.4 nm respectively. These nanoparticles exhibited near IR fluorescence property, coupled with super paramagnetic behavior, and had potential to be used in imaging guided photothermal therapy.

In the following sections, some major strategies regarding functionalization of organic groups onto the surface of magnetite nanoparticles shall be discussed.

1.2 Functionalization with organic molecules/groups

Magnetic nanoparticles have a wide range of applications which include water purification, biotechnological field, targeted drug delivery, hyperthermia treatment **[4]**, etc. However, MNPs, when functionalized with a proper organic compound, have shown great enhancement in their water de-contamination efficiency **[5]**. And therapeutic efficacy in drug delivery **[6]** and other biomedical applications **[7]**. Moreover, functionalization also results in increase in the stability of the MNPs against aggregation.Aggregationofthe nanoparticlescancausevenousemboli.

1.2.1 Polysaccharides functionalized MNPs

The agglomerating tendency of MNPs exhibits adverse effects on their physico-chemical and magnetic properties. This also reduces the effective surface area of nanoparticles. Therefore, attempts have been made to functionalize the surface of MNPs with suitable functionalizing agent (FA). In a study, Robinson *et al*. **[8]** synthesized starch @MNPs by oxidation-precipitation of $FeSO_4$ solution in the presence of gelatinized starch, with variation in starch to iron mass ration between 0.05 to 10.The TEM analysis revealed that bare MNPs (no starch) had an average diameter of 66±5 nm while the particles , synthesized with starch to iron ratio of 10, had diameter of 12±4 nm, indicating that smaller particles were produced in the presence of starch due to non-aggregation of MNPs. Following the similar procedure, Verma and co-workers **[9]** used s-Fe_3O_4 nanoparticles as catalyst to synthesize biologically potential Imidazopyrimidine derivatives via an ecofriendly one-pot multicomponent synthetic procedure. The catalyst s-Fe_3O_4 provided greater surface area to the reactants and the yield was as high as 98% with the advantage that catalyst s-Fe_3O_4 could be re-used. Starch-functionalized MNPs have also been reported **[10]** for purification of bacterial amylase from fermented broth.

Chitosan, a semi-synthetic biopolymer , has fair reputation as a biocompatible, environment friendly, polysaccharides and it is obtained from chitin, a fully naturally occurring polysaccharide via controlled acetylation.Chitosan-coated MNPs have been widely exploited for binding of drugs andbiomolecules, e.g. enzymes, proteins and antibodies **[11]**. **[12]** Recently, Piosik *et al*., **[13]** have reported functionalization of MNPs with aminated chitosan, having three long distanced free amino groups, using in-situ approach and investigated their interactions with a model biological membrane made of dipalmitoylphosphatidylcholine(DPPC).The chitosan solution, containing Fe(II) and Fe(II) ions, was precipitated by NH_4 OH, followed by treatment with epichlorohydrin and periodate. The FTIR spectroscopic analysis confirmed the generation of three long-distanced amino groups on MNPs **(see Figure 1(b)**. In another work by Nehra *et al* **[14]**. reported synthesis of chitosan-coated MNPs using post-synthesis method.They had an average diameter of 11.4 ± 5.2 nm and showed strong antimicrobial action against *Escherichia coli* (*E. coli*), *Bacillus subtilis, Candida albicans, Aspergillus niger and Fusarium solani*.

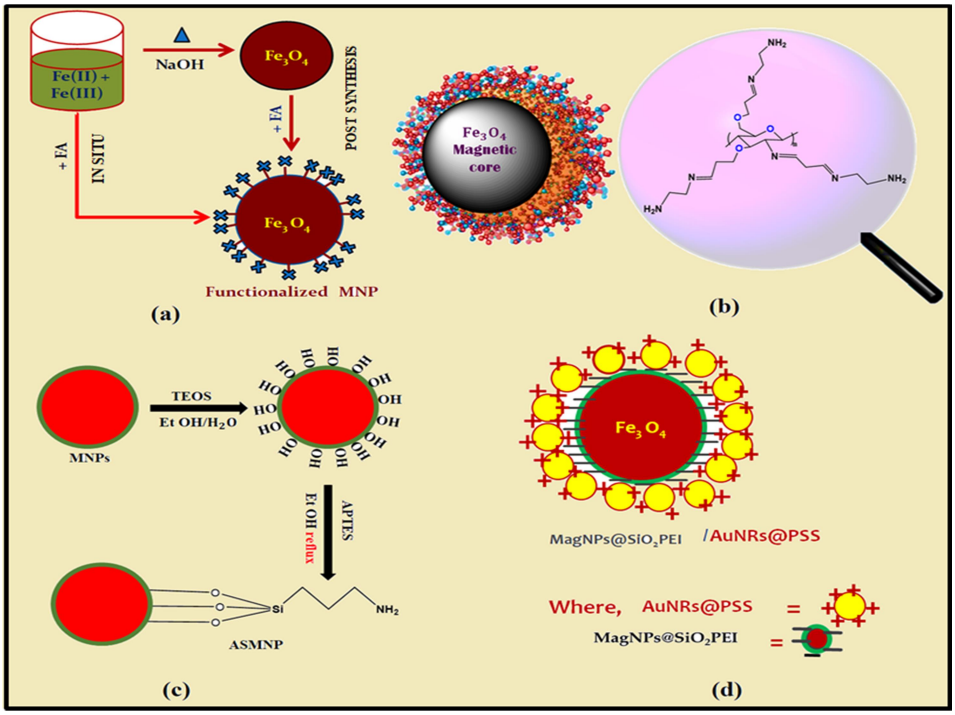

Figure 1 a: Functuonalized MNP, Fig.1 b:Magnatic core, Fig.1 c:ASMNP, Fig.1 d:silica nano particle

MNPs have widely been used as contrasting agent (CA) in magnetic resonance imaging (MRI) applications due to their superparamagnetic nature, biocompatibility and non-toxicity. However, due to large surface area to volume ratio and magnetization, this contrasting agent has fair tendency of aggregation which is a serious drawback. Therefore, MNPs have been functionalized with a suitable polymer like dextran to achieve excellent dispersion.Hong *et al*. **[15]** prepared ferrofluid, comprising of water and dextran coated MNPs, using an in-situ approach. A mixture of dextran, Fe(III) and hydrazine sulfate(reducing agent) was kept under stirring, followed by sequential addition of Fe(II) and the precipitating agent NH_4 OH. With the increase in the dextran contents in the reaction mixture, size of the dextran @MNPs decreased from 352.2 to 23.84 nm, thus indicating a fair dispersion ability of dextran coated MNPs as compared to native MNPs. Indeed, the solvent based functionalization or coating is the most widely adopted strategy among researchers. However, recently solvent free functionalization of magnetite nanoparticles with dextran has also been reported. In a very interesting work, Sakaguchi *et al*. **[16]** carried out functionalization of MNPs by dextran using a unique approach which consisted of vibration ball-milling of Fe_3O_4

with dextran in the solid state under vacuum. It was reported that ionic scission of Fe-O bond of Fe_3O_4 resulted in loss of electron pair and mechano-cation Fe_3 O_4 was formed. Similarly, ionic scission of C-O bond of dextran resulted in formation of dextran mechano-anion. Later on, an unique covalent bond formation took place by electron pair donation by 'naked' O^- and its acceptance by naked Fe^+.

1.2.2 Amino/carboxylic groups functionalized MNPs

MNPs have excellent biocompatibility and magnetic property, but in most of the cases they require to be attached covalently with an appropriate biomolecules for biomedical applications. This is usually achieved by functionalization of amino groups onto the surface of MNPs. These amino groups, present on the surface of MNPs, can be attached covalently with the biomolecules. Therefore, a number of studies have been reported which describe different strategies for functionalization of amino groups. This strategy is very useful for immobilization of enzymes onto the MNPs. In a recent study **[17]**, silica coating on MNPs was done by their reaction with Tetraethyl orthosilicate (TEOS), followed by their reaction withN-2-aminoethyl-3-aminopropyltriethoxysilane (APTES) for introduction of amino groups on to the surface of MNPs. Finally, these amino-functionalized MNPs were attached covalently with the enzyme 6-phosphogluconate dehydrogenase. The functionalization onto surface of synthesized MNPs may schematically be shown in **Figure 1(c)**. L-Cysteine (L-Cys) is a versatile zwitterionic amino acid which contains amino, carboxylic and thiol groups and therefore its functionalization onto the surface of magnetite nanoparticles has great potential for using in glycoproteomics research, i.e. L-Cys functionalized MNPs can be used for enrichment of glycopeptides. In a significant work, Feng and co-workers **[18]** proposed a post-synthesis method to functionalize L-Cys onto MNPs. The MNPs, prepared using a previously reported hydrothermal method **[19]** were dispersed with L-Cys in phosphate buffer medium using ultra sonication at 60^oC for 3h. The well dispersed Fe_3O_4/L-Cys nanoparticles had an average diameter of 200 nm and were almost spherical. The Fe_3O_4/L-Cys nanoparticles were characterized by XRD, TEM and mass spectroscopic analyses and subsequently used for glycoprotein enrichment process. In order to use MNPs for targeted delivery of anticancer drugs such as doxorubicin, 5-fluorouracil, dexa-methasoneetc., it is essential to conjugate

these anti-cancer agents onto the surface of MNPs. This is usually achieved by generating amino/carboxylic functionalities on their surface, followed by attachment of these groups with desired anticancer agent that is to be delivered. In a study by Rehana *et al*. **[20]**, post synthesis procedure was applied to functionalize MNPs with, L-arginine, L-cysteine and some carboxylic acids. The functionalized MNPs were spherical in shape and had cubic spinal structure. The anticancer drug Paclitaxel loaded L-arginine coated MNPs showed enhanced cytotoxic affect, thus leading to apoptosis. FinallyDNA fragmentation was observed in case ofL-arginine coated iron oxide nanoparticles. This showed that amino acid coated MNPs had potential for cancer treatment. Amino groups functionalized MNPs have shown excellent performance in enhancing the production of a biologically potential compound Menaquinone-7 (MK-7) which plays a key role in treatment of Alzheimer's disease, and liver, blood and prostate cancers **[21**, **22]**, MNPs were functionalized with L-lysine using in-situ approach. In brief, Fe(II), Fe(III) and L-lysine were taken in 1:1.75:4 molar ratio and precipitated with NH_4OH under normal stirring at 70^{o}C.The *Bacillus subtilis natto cells* were cultured and attached to L-lys@IONs. These nanoparticles were transferred in to fermentation media to produce Menaquinone-7. The amino-functionalized MNP is a versatile material for various biomedical applications. Therefore, it has been a focus of research for Nano chemists to develop different methods for preparation of amino-functionalized MNPs. In a report, Songvorawit and co-workers **[23]** prepared amino-functionalized MNPs by Polyol technique at low temperature (121^{o}C) in an Autoclave, in the absence of any inert gas. Ethylene diamine was used as source of amino groups. The adhesion of bacteria on the surface of these functionalized nanoparticles was investigated by Trujill *et al*., **[24]**.

2. Polymeric Component

2.1 Coating of Magnetic NPs with a Polymer

At the particular time of coating of magnetite NPs with polypyrrole as well as poly(3,4-ethylenedioxythiophene):poly(4-styrenesulfonate; PEDOT:PSS; an *in-situ* surface polymerization is developed **[25]**. NIR absorbance is allowed here by a conjugated polymer. NPs has very useful multimodal imaging capabilities which is utilizing by PAI and MRI these technics used during the surgery of mice to tumor during hyperthermia. Polycarbic acid facilitates

penetration into the cell membrane and it's a biochemical that is a major component of gum acacia. For the fabrication of Doxorubicin loaded Polyarabic acid coated magnetite NPs.Doxorubicin loaded Polyarbic Acid Coated magnetite Nano Particle is designed for theranostic nano system because its penetrating capacity is very good. Doxorubicin is highly pH sensitive that's why it is released in breast cancer tumor cell **[26]**. Additionally, the nanoparticle proves that it has very good biocompatibility, least cytotoxicity, and it can differentiate to trading agents. Coating with poly(ethylene glycol) (PEG), dextran, and chitosan increases the usefulness of nanoparticle over polymer as well as it increases the usefulness of both MRI and hyperthermia applications **[27]**. On the basis of conjugation of magnetite NPs and cyclodextrin polymer nanosponges are originated and it's a novel nanotheranostic platform which are active with folic acid (FA) **[28]** curcumin was loaded into the lipophilic central cavity of cyclodextrins and applied to the magnetic field that released the drug because of acidic pH of tumor.

2.1.1. pH responsive coating

Stimuli-responsive nanocarriers including liposomes, polymeric micelles, polyplexes and lipoplexes are having great importance in considering this situation of triggered release of drugs **[29, 30]**. They are capable of responding to environmental changes like temperature, pH, biomaterials, solvent, ionic strength, light, chemical agents, electrical fields and magnetic fields. Among these pH-responsive nanocarriers have unique importance for the triggered release of drugs at the targeted sites by responding to the different pHs in various parts of the body **[31]**. The main disadvantage of conventional chemotherapy is that it cannot apply the drug specifically to the cancer cells and thus leads to damage of normal living cells. The extracellular pH is 7.4, while in the tumor cells the pH is 5–6 because of the rapid and frequent cell proliferation and lactic acid accumulation **[32]**.

2.1.2. Conventional coating

To increase the quality of cancer treatment, targeted nanoparticles have been employed by conjugating targeting ligands that covalent to cell receptors which are very much expressive in tumor cell (10-13) **[33]**, Theranostic nanoparticles with controlled release of gemcitabine for targeted therapy and MRI of pancreatic cancer. ACS Nano. This is the proof that targeted delivery of nanoparticle-drug enhance drug cumulating in tumors and therapeutic effects during minimizing systemic toxicity. Tumor cells

and active stromal cells **[34]** are expressing that Urokinase plasminogen activator receptor (uPAR) some of the cancer expressing high levels of plasminogen activator receptor like 70% of pancreatic **[35]** 80% of ovarian **[36]**, and 37% of gastric cancers **[37]**. As rapid increase of tumor edge and in metastatic tumors uPAR expression also increased **[38]**. This is previously explained that uPAR targeting increased internalization of nanoparticles by tumor cells which are making uPAR a feasible target for effectual drug delivery into peritoneal metastatic tumors along with a condensed upper layer of stromal barrier **[39]**. Moreover Ning Gao *et al* showed the therapeutic effectiveness with that magnetic resonance imaging (MRI) ability of uPAR targeted theranostic iron oxide nanoparticles (IONPs) which carries gemcitabine in a human pancreatic cancer xenograft model following intravenous (i.v.) administration.

Peritoneal tumors and delivery in an orthotopic mouse pancreatic tumor (PANC02) model explained by Ning Gao *et al*. In this work they investigated and compared targeting effectiveness and bio distribution of uPAR targeted delivery of iron oxide nano particles with or without cancer treatment drugs and medicinal effectiveness of delivery of uPAR targeted theranostic nanoparticles was explained in this highly aggressive tumor model.

3. METHODS

3.1. Mouse peritoneal tumor model

Ning Gao *et al* firstly verified the PANC02 cells morphology and this cell line (24) provided to him by Dr. Keping Xie (M.D. Anderson Cancer Center, Houston).firstly they anesthetized orthotopic pancreatic tumor model, 6 to 8 week-old female, C57BL/6 mice (Harlan Laboratories, IN) by intramuscular injection of a mixture of 95 mg/kg ketamine hydrochloride and 5 mg/kg xylazine of body weight in sterile saline.there after shaving of mice and incision employed to show the spleen and the pancreas.Mixture of BD Matrigel and PANC02 cells (5x105) injected directly into the pancreas.With the help of surgical clamp and suture incision wound can be closed. After surgery, the mice was put on for two days to recover with pain medication.

3.1.1Production of targeting ligand conjugated nanoparticles

Ning Gao *et al* used Magnetic IONPs with 10 nm core size functionalized with an amphiphilic copolymer containing carboxyl groups which was prepared by Ocean Nanotech, LLC (San Diego, CA) using an established protocol **[40]**. Amine PEG carboxyl (MW2000, Biomatrik, Zhejiang,

China) was conjugated to the surface carboxyl groups of the amphiphilic polymer coating to generate PEG-IONPs with surface carboxyl groups in order to avoid non-specific uptake by macrophages present within the peritoneal cavity.

3.1.2. Theranostic applications of magnetic nanoparticles in cancer

This the opportunity of novel physical and chemical properties of magnetic IONPs has been used to developed new and improved theranostic IONPs in preclinical studies **[41]**. Tumor present in human body have highly heterogeneous tumor blood vessel distributions and stromal drug delivery barriers for that nanoparticle-mediated drug delivery is preferred on individual patients and easily its accessible of effectiveness of intratumrol drug delivery. For cancer patients with the help of this oncology approach using this theranostic nanoparticles can allow adjustment of treatment strategies. In addition to the reliable imaging property, theranostic nanoparticles have been brought to carry a single therapeutic agent or the combination of two or more drugs **[42]**, including chemotherapy drugs, small-molecule agents, photosensitizers and siRNAs. Significant benefits of nanoparticle-loaded drug delivery added: first, rising the useful drug dose by targated delivery of a heavy amount of drug molecules, notably highly insoluble drug-loaded nanoparticles, into the tumor during reducing systemic side effects **[43]**; second, Securing the drug to avoid breaking the drug before it reaches the targeted cell and third, selective delivery over cell receptors that ignore multidrug-resistant mechanisms on the tumor cell membrane **[44]** For example, gold-coated IONPs with cisplatin were used to treat human ovarian cancer cell lines and tested for the drug delivery effectiveness.

4. DISCUSSION

Ning Gao etal shows the result according to them in this study they used a mouse pancreatic tumor model with both orthotopic and s. c. tumors offers a novel opportunity to compare the effectiveness of uPAR-targeted delivery of theranostic IONPs following i.v. or i.p.

4.1. Temperature responsive coating

Temperature sensitive polymer have long been studied for drug delivery applications due to their attractive temperature-dependent drug release behavior. Thermo-responsive like Poly (*N*-isopropylacrylamide) (PNIPAAm) and its copolymers are using in this application **[45]**. At a characteristic lower critical solution temperature 32°C Poly(*N*-isopropylacrylamide) (PNIPAAm) showing a reversible phase-transition (10-

12) **[46]**. Polymers getting hydrophilic and swell due to absorption of water at below the LCST and at higher temperature than LCST hydrophobic groups are going to increase and this fashion convert nature of polymer in hydrophobic because of shrinking and releasing the payload. Hydrophilic monomers like acrylamide increased the LCST above body temperature and PNIPAAm is mostly copolymerized with this monomer and it is using for the controlled drug delivery applications. Some other monomer like allylamine (AH) also polymerized with PNIPAAm and with the help of this co-polymerization it's providing amine functional groups forbioconjugation applications **[47]**. Although PNIPAAm's huge possibility in the field of drug delivery and biomedical sciences, it has some harmful effect like non-degradability which can create inflammation and toxicity due to the prolonged presence of the polymer in the body **[48]**. The limitation is providing information of group which can developed biodegradable and temperature sensitive PNIPAAm-based copolymers for drug delivery applications **[49]**. In this current study Nikhil Pandey etal synthesized a copolymer of PNIPAAm, AH, and a previously synthesized water soluble biodegradable photoluminescent polymer (WBPLP) **[5]** to form a unique thermo-responsive fluorescent polymer (TFP), and parallel formulated the nanoparticles (TFP NPs).

4.2. Synthesis of fluorescent polymer

Nikhil Pandey *et al* synthesized WBPLP by their previously developed methods. In brief they used equimolar ratio of citric acid and 1,8-octane diol mixed with L-cysteine(0.8).At 160°C mixture were melt for 20 min. parallel going down tem at 140°C than reacted for an additional 75 minutes to form BPLP-Cysteine oligomers this compound is collecting by precipitation method using water/1-4 dioxane mixture there after freeze dried and mixed with polyethylene glycol and amino acids to form water soluble BPLP (WBPLP)

4.4. Copolymerization of WBPLP and AH

By carbodiimide chemistry WBPLP with AH going to conjugated. Briefly WBPLP (45 mg) was dissolved in 2-(N-morpholino) ethanesulphonic acid (MES) buffer (5 ml), simultaneously with the addition of 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and *N*-Hydroxy Succinimide (NHS) (1:1) than completion of 30 min of the above process mixed on a rotator, AH (18.75 µl) was added and the reaction was continued for 12 hours at room temperature than WBPLP-AH copolymer was dialyzed using 500 Da

molecular weight cut-off dialysis membranes (Spectrum Laboratories Inc, Rancho Dominguez, CA) for 24 hours to remove the unreacted chemicals.

4.5. Synthesis of TFP NPs

Nikhil Pandey *et al* generate TFP NPs, WBPLP-AH then copolymerized with *N* isopropylacrylamide (NIPAAm) by radical polymerization in the presence of a crosslinker. Later they described the method in brief, the purified WBPLP-AH solution (5 ml) and NIPAAm (45 mg) were dissolved in deionized (DI) water (25 ml). Crosslinker, *N,N'*-Methylenebisacryamide (BIS, 5.85 mg) and surfactant, sodium dodecyl sulphate (SDS, 17.4 mg) were added to the mixture, while continuously stirring for 30 minutes. Ammonium persulphate (APS, 52.48 mg) and tetramethylethylenediamine (TEMED, 69 µl) were then added to initiate the radical polymerization, and the reaction was stirred for 4 hours under nitrogen at room temperature. With the help of dialysis process formed nano particle carried out dialysis using 3500Da dialysis membrane till 24 hours to remove free surfactants and unreacted chemicals.

4.6. Synthesis of TFP-MNPs

Silanefunctionalized MNPs used as template for TFP conjugation and synthesized TFP-MNPs.By soncation method TFP-MNPs were synthesized by dispersing MNPs in 99% ethanol and simultaneously addition of 2mL acetic acid than again repetition of sonication after 5 min reaction mixture transferred and added 0.49mL vinyltrimethoxysilane after that reaction is continued at room temp up to 24 hours than Nikhil Pandey etal used 99% ethanol to wash Silane-MNPs and collect it by magnet.For the synthesis of TFP-MNPs Nikhil Pandey *et al* used silane-MNPs (10 mg) and sonicated with 25mL distilled water at 50W up to 10 minutes. During the sonication purified WBPLP-AH (100 mg), NIPAAm (45 mg), BIS (5.85 mg) and SDS (17.4 mg) was added there after reaction mixture transferred in a stir plate and while vigorous stirring APS (52.48 mg) and TEMED (69 µl) were added.Now reaction will be under in nitrogen up to 4 hours at room tem than TFP-MNPs were collected by a magnet and with the help of distilled water washed it many times and remove extra chemicals **[49]**.

CONCLUSION

In this review article we conclude the study of polymer coating and different nano particle for theranostic applications of magnetic nanoparticles in cancer.

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