

## A Review on Magnetically Loaded Drug Delivery System

Anushka V. Suroshe, Prof. V. V. Deshpande

<sup>1</sup>B.pharma student Ishwar deshमुख institute of pharmacy, Digras , Maharashtra, India

<sup>2</sup>Professor, Department of Pharmaceutics, Ishwar deshमुख institute of pharmacy, Digras ,Maharashtra, India.

Submitted: 01-07-2022

Accepted: 14-07-2022

**ABSTRACT:** Magnetic drug targeting is a method by which magnetic drug carriers in the body are manipulated by external magnetic fields to reach the target area. This method is potentially promising in applications for treatment of diseases like cancers, nervous system diseases, sudden sensory neural hearing loss, and so on, due to the advantages in that it can improve efficacy, reduce years. Successful magnetic drug targeting requires a good magnet system to guide the drug carriers to the target site. A well-designed controlled drug delivery system can provide a therapeutic amount of drug to the proper site in the body and then maintain desired drug concentration for the specific period of time. A number of approaches are available in delivering therapeutic substance to target site in a sustained style and controlled release fashion. One such approach is using magnetic microspheres as carriers for drugs. Microsphere drug delivery system has gained vast attention due to its diverse applications that range from targeting the drug to specific site to imaging and helping the diagnostic features.

**KEYWORDS:** Magnetic microspheres, Magnetic drug delivery, Magnetic field, micro carriers.

### I. INTRODUCTION:

Magnetic drug delivery by particulate carriers is a very efficient method of delivering a drug to a localized diseased site. Very high concentrations of chemotherapeutic or radiological agents can be achieved near the target site, such as a tumor, without any toxic effects to normal surrounding tissue or to the whole body. Magnetic microspheres are spherical particles, composed of metallic iron which serves as delivery vehicle for the site specific targeting, retention and release of pharmaceuticals. Magnetic microspheres are very much important which localize the drug to the disease site. In this respect, larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug.

Microspheres are characteristically free flowing small spherical particles consisting of proteins or synthetic polymers, which are biodegradable in nature and having a particle size ranging from 1-1000 nm. They are considered as one of the important approaches in delivering therapeutic substance to the target site in a sustained and controlled release fashion.

Encapsulated magnetic particles in the range of 10-500 nm are usually called magnetic Nano spheres and any magnetic particles of just below 1-100 nm are magnetic microspheres. In general, magnetic liposomes are also included when speaking about magnetic carriers.

The principle of magnetic targeting by comparing systemic drug delivery with magnetic targeting. In magnetic targeting, a drug or therapeutic radioisotope is bound to a magnetic compound, injected into a patient's blood stream, and then stopped with a powerful magnetic field in the target area. The magnetic fields are believed to be harmless to biological system and adaptable to any part of the human body. Up to 60% of an injected dose can be deposited and released in a controlled manner in selected non reticuloendothelial organs. Magnetism has application in numerous fields like diagnostics, drug targeting, molecular biology, cell isolation, cell purification, hyperthermia and radio immunoassay.

Magnetic drug delivery by particulate carriers is an efficient method of drug delivery to a localized disease site. A drug or therapeutic radioisotope is encapsulated in a magnetic compound; injected into patient's blood stream & then slowly released from magnetic carriers or confers a local effect, thus it reduces the loss of drug as freely circulating in body. Drug targeting is a specific form of drug delivery where the drug is directed to its site of action or absorption.

The development of new delivery systems for the controlled release of drugs is important in order to increase patient compliance through prolonging drug action and reducing adverse effects by lowering peak plasma concentration. Microspheres can be used for the controlled release of drugs, vaccines, antibiotics, and hormones and are easily administered through a syringe needle. Microspheres could provide a larger surface area and possess an easier estimation of diffusion and mass transfer behaviour also the encapsulated small molecules could diffuse out of the body fluid. They are generally biocompatible, can provide high bioavailability, and are capable of sustained release for long period of time. Several commercial products are based on polymer microspheres including Lupron Depot and Nutropin Depot.

Magnetic microspheres are an alternative to traditional radiation methods which use highly penetrating radiation that is absorbed throughout the body. Its use is limited by toxicity and side effects. Magnetic radioactive microspheres are applied in methods similar to non-radioactive spheres. A magnet, placed outside the body, is directed to the target site. The magnet can be a rod shaped permanent magnet of any size or can be contained in equipment that looks like an open magnetic resonance imaging scanner. The loaded microspheres are introduced into a blood vessel, and in as little as half an hour, they gather at the target site to emit radiation that kills surrounding cancer cells. The therapeutic action usually a couple of days or weeks, depending on the material used. If necessary, the treatment can be repeated. Spheres need to be peppered with microscopic magnetic particles, such as iron, so they will be attracted to the magnet for applications requiring in vivo magnetic targeting.

Magnetic drug delivery by particulate carriers is a very efficient method of delivering a drug to localized disease site. Magnetic drug transport technique is based on the fact that the drug can be either encapsulated into a magnetic microsphere or conjugated on the surface of microsphere. When the magnetic carrier is intravenously administered, the accumulation takes place within area to which the magnetic field is

applied and often augmented by magnetic agglomeration. The accumulation of the carrier at the target site allows them to deliver the drug locally. Very high concentration of chemotherapeutic agents can be achieved near the target site without any toxic effect to normal surrounding tissue or to whole supposable to replace large amounts of drug targeted magnetically to localized disease site, reaching effective and up to several fold increased drug levels.

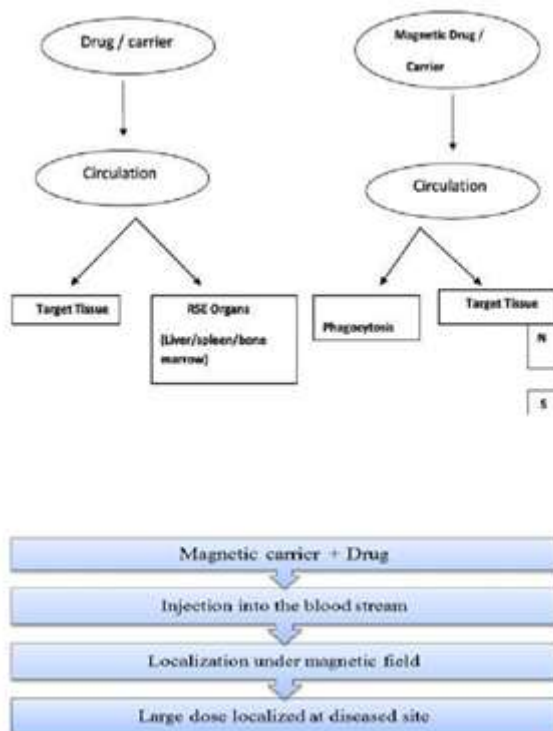
#### PRINCIPLE OF MAGNETIC MICROSPHERE DRUG TARGETING :

Drug targeting is a specific form of drug delivery where the drug is directed to its site of action or absorption. This could be a particular cell, organ structure or tissues. The aim of the specific targeting is to enhance the efficiency of drug delivery and at the same time to reduce the toxicity & side effects. Magnetic drug transport technique is based on the assumption that the drug can be either encapsulated into a magnetic microsphere or conjugated on the surface of the microsphere. When the magnetic carrier is intravenously administered, then accumulation takes place within the area to which the magnetic field is applied and often augmented by magnetic agglomeration. The accumulation of the carrier at the target site allows them to deliver the drug locally.

#### Magnetic Properties Of Microspheres:

Magnetic particles for bio separation consist of one or more magnetic cores with a coating matrix of polymers, silica or hydroxyl apatite with terminal functionalized groups. The magnetic core generally consists either of magnetite ( $\text{Fe}_3\text{O}_4$ ) or magnetite ( $\gamma\text{-Fe}_2\text{O}_3$ ) with super para magnetism is when the dipole moment of a single domain particle fluctuates rapidly in the core due to the thermal excitation so that there is no magnetic moment for macroscopic time scales. Thus, these particles are non-magnetic when an external magnetic field is applied, but no develop a mean magnetic moment in an external magnetic field.

**Fig.1.1: Mechanism of Targeting**



Flowchart of principle of magnetic targeting:

1. By magnetizing the spheres to saturation levels prior to vascular targeting.
2. By clustering magnetite at the centre of each sphere to produce large macro domains.
3. By substituting one of the newer ferromagnetic materials that as higher susceptibility than Fe<sub>3</sub>O<sub>4</sub>.

Micro carriers includes :-

- A. Magnetic microspheres
- B. Magnetic liposome
- C. Magnetic nanoparticles
- D. Magnetic resealed erythrocytes
- E. Magnetic emulsion
- F. Bio modulators
- G. Magnetic neutrophil

**A. Magnetic microspheres:**

Magnetic microspheres are supramolecular particles that are small enough to circulate through capillaries without producing embolic occlusion but are sufficiently susceptible (ferromagnetic) to be captured in micro vessels and dragged in to the adjacent tissues by magnetic fields of 0.5-0.8 tesla (T). Magnetic microspheres

were prepared by mainly two methods namely phase separation emulsion polymerization (PSEP) and continuous solvent evaporation (CSE). The amount and rate of drug delivery via magnetic responsive microspheres can be regulated by varying size of microspheres, drug content, magnetite content, hydration state and drug release characteristic of carrier. The amount of drug and magnetic content of microspheres needs to be delicately balanced in order to design an efficient therapeutic system. Magnetic microsphere are characterized for different attributes such as particle size analysis including size distribution, surface topography, and texture, etc. using scanning electron microscopy (SEM), drug entrapment efficiency, percent magnetite content and in vitro magnetic responsiveness and drug release.

**B. Magnetic Liposome:**

Liposome are simple microscopic vesicles in which lipid bilayer structures are present with an aqueous volume entirely enclosed by a membrane, composed of lipid molecule. There are a number of components present in liposomes, with phospholipids and cholesterol being the main

ingredients but in case of magnetic liposome's magnetite is one of the components of the liposomes. Generally, these are magnetic carrier which can be prepared by entrapment of Ferro fluid within core of liposomes. Magnetic liposome can also be produced by covalent attachment of ligands to the surface of the vesicles or by incorporation of target in the matrix of structural phospholipids.

**C. Magnetic nanoparticles:**

Magnetic nanoparticles (MNPs) possess unique magnetic properties and the ability to function at the cellular and molecular level of biological interactions making them an attractive platform as contrast agents for magnetic resonance imaging (MRI) and as carriers for drug delivery. Recent advances in nanotechnology have improved the ability to specifically tailor the features and properties of MNPs for these biomedical applications.

**D. Magnetic resealed erythrocytes:**

Resealed erythrocytes have various advantages as drug carriers such as it is biodegradable, biocompatible, large quantity of variety of material can be encapsulated within small volume of cell and can be utilized for organ targeting, etc. Due to these advantages of resealed erythrocytes, magnetic resealed erythrocytes came into existence which contains Ferro fluids (magnetite) along with loaded drug within the cell.

**E. Magnetic emulsion:**

Magnetic emulsion was also tried as drug carrier for chemotherapeutic agents. The emulsion is magnetically responsive oil in water type of emulsion bearing a chemotherapeutic agent which could be selectively localized by applying an external magnetic field to specific target site.

Akimoto and Meri moto prepared magnetic emulsion by utilising ethyl oleate based magnetic fluid as the dispersed phase, casein solution as the continuous phase and anticancer agent, methyl CCNU trapped in the oily dispersed phase as active chemotherapeutic agent.

**F. Bio modulators:**

Biological response modifiers (BMRs) alter host,tumor as well as microbial responses in four ways.

1. Augmentation of host effectors mechanisms directed against tumour cells or microorganisms.
2. Decrease in host response that interferes with tumour resistance by a quantitative increase in endogenous effect resistance by an increase in endogenous effect resistance by molecules or redirecting their sites and duration of action.
3. Augmentation of tumoursensitivity to host cells by dedifferentiating tumour cells.
4. Increase in host tolerance of conventional cancer treatment.

**G. Magnetic neutrophils:**

In certain clinical conditions, where patient sera contains chemotactic factor in activators and neutrophils directed inhibitors of chemotaxis, an indirect approach of targeting white cells by chemo attraction fails. These disorders include chronic lymphocytic leukaemia, alcoholic cirrhosis, crohn's disease, haemodialysis sarcoidosis and Hodgkin's disease. Even though failure of chemotaxis is not observed in all patients, such conditions are life threatening. Therefore, a means of making neutrophils ingest magnetite base system ought to be developed, so that the sites of severe infection can be selectively approached for therapy.

**Materials used in preparation of magnetic carriers:**

Sr.No.	Materials used	Types	Examples
1.	Synthetic polymer	a)Biodegradable b)Non biodegradable	Glycolides, Epoxy polymers, Polyanhydrides, Lactides, Acrolein
2.	Natural polymer	a)Proteins b)Carbohydrates c)Chemically modified carbohydrates	Albumin, Gelatin, Collagen, Agarose, Starch,

			<b>Chitosan, Polydextran, Polystarch</b>
--	--	--	--

**Table: List of materials used in preparation of magnetic microspheres**

**Drugs and polymers used in preparation of magnetic microspheres**

Sr.No.	Drug	Polymer
1.	Dexamethasone	Albumin
2.	Indomethacin	Methylmethacrylate
3.	Oxantrazole	Chitosan
4.	Diclofenac sodium	Ethyl cellulose
5.	5-fluorouracil	Eudragit L-100
6.	Doxorubicin	Poly((N-isopropylacrylamide)
7.	Nimesulide	Polyvinyl alcohol
8.	Ganciclovir	Poly(d,L-lactide-co-glycolide)
9.	Methotrexate	Calcium pectinate
10.	Doxorubicin	Poly(acrylic acid)

**Table: List of Drug and Polymers used in preparation of magnetic microspheres**

**List of drugs, polymers, use and their respective methods for which magnetic microspheres have been formulation**

Drug	Polymer	Use	Method	Reference
Amphotericin B	Albumin	Treatment of leishmaniasis	Spray drying	(Sánchez-Brunete JA , 2004)
Aztreonam	Dextran	Antimicrobial activity	Continuous solvent evaporation	(Kang et al.1987)
Adriamycin	Albumin	Cytotoxic effect on tumor cells.	Heat stabilized protein methods	(Tao K et al.,1999)
Mesalamine	Chitosan, Eudragit, Ethyl cellulose	Ulcerative colitis	Phase separation emulsion polymerization	Satinder kakkar et al. 2014
Dexamethasone	Albumin	Lymphocytic tumors	Modified phase separation emulsion technique	(Sussan et al.1996)
Azithromycin	Dextran	Potentiator effect on antimicrobial activity against S.aureusand P.aeruginosa reference strains	Continuous solvent evaporation	(Grumezesce et al.2012)

Diclofenac sodium	Gelatin	Reduced joint swelling	Emulsification and cross linking	(Saravanam and M et al.208)
Vancomycin	Starch	Cytotoxic effect on cancer cells	Continuous solvent evaporation	(AM (Grumezesce, 2012)
Cisplatin	Albumin	Anticancer activity	Phase separation emulsion polymerization	(Vyas MB 2012)
Insulin	Feridex	Diabetes	Invasive method	(Vijaya Ganapathy Vaithilingam, 2016)
6-thoguanine	Polylactic acid polyethylene glycol co polyester	Anticancer	Continuous solvent evaporation	(Kakar and Singh, 2014)

**List of drugs, polymers, use and their respective methods for which magnetic microspheres have been formulated.**

❖ **Methodology and Experimental work**

**Preparation of Magnetic microspheres:**

**Solvent Evaporation Method:**

Polymer encapsulated microspheres are synthesized by continuous solvent evaporation technique. A solution of polymer, drug and magnetite is added to the volatile organic solvent, which forms auxiliary solution on stirring. The resulting solution is then homogenized and stirred at a temperature in the range of 22-30°C. The formed magnetic microspheres are separated by centrifugation. The product is then freeze-dried and stored at 4°C.

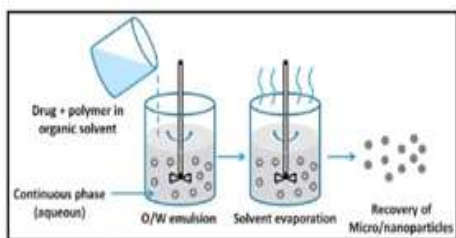


Figure 1: Solvent evaporation technique.

**II. EXPERIMENTAL WORK:**

❖ **Preformulation Study:**

Preformulation can be defined as investigation of physical and chemical properties drug substance alone and combined with excipients. Preformulation studies are the first step in the rational development of dosage form of drug substance. The objectives of preformulation studies

are to develop a portfolio of information about the drug substance so that this information is useful to develop formulation. Preformulation investigations are designed to identify those physicochemical properties and excipients that may influence the formulation design, method of manufacture and pharmacokinetic biopharmaceutical properties of the resulting product.

The goals of the program therefore are:

1. To establish the necessary physicochemical characteristics of a new drug substance.
2. To determine its kinetic release rate profile.
3. To establish its compatibility with different excipients. Hence, a preformulation study on the obtained sample of drug includes physical test determination and compatible studies.

❖ **Organoleptic properties:**

Organoleptic properties are sensory experiences of the distinctive attributes or qualities of a thing. For example, cannabis organoleptic properties include but are not limited to terpene profile, sweetness, pungency, flavour and quality of experience. The drug powder was analyzed for colour, odour and taste.

❖ **Descriptions:**

Physical appearance testing can be the most subjective but important tests performed on drug substances. The polymorphous form can provide information regarding the solid state of the material. The colour can be an indication of purity



and means to identify contamination that occurred during the synthesis process. The drug sample was analyzed for physical appearance and powder nature.

❖ **Melting point:**

Melting point of the drug sample was determined because it is a good first indication of purity of the sample since the presence of relatively small amount of impurity can be detected by lowering as well as widening in the melting point apparatus veego (VMP) and the temperature at which the drug melts was noted. Average of triplicate readings was taken.

❖ **Solubility Analysis:**

The solubility of the selected drug was determined in ethanol, Distilled water and methanol by following procedure. The solubility analysis was also done to select a suitable solvent system to dissolve the drug and also to test its solubility in the dissolution medium was to be used.

• **Evaluation and characterization of magnetic microspheres:**

**1) Particle size and shape:**

The most widely used procedures to visualize microspheres are conventional light microscopy and scanning electron microscopy (SEM). Both can be used to determine the shape and outer structure of microspheres. LM provides a control over coating parameters in case of double walled microspheres. The microspheres structures can be visualized before and after coating and the change can be measured microscopically. SEM provides higher resolution and contrast to the LM. SEM allows investigations of the microspheres surfaces and after particles are cross sectioned, it can also be used for the investigation of double walled systems. Confocal fluorescence microscopy were used for the structure characterization of multiple walled microspheres. Laser light scattering and multi size coulter counter other than instrumental methods, which can be used for the characterization of size.

**2) Flow properties:**

**a. Bulk density:**

It is determined by pouring a sample of microspheres of known weight into a measuring cylinder without tapping and measuring its volume, then dividing the weight by the volume. It is determined by pouring a sample of microspheres of

known weight into a measuring cylinder & thoroughly tapping it and measuring its volume, then dividing the weight by the volume.

**b. Hausner's ratio:**

Hausner ratio is the ratio of the tapped density to the bulk density of microspheres and can be used to predict of microspheres flow. Low Hausner ratio of <1.2 indicates free flowing microspheres.

**c. Angle of repose:**

It is defined as the maximum angle to the horizontal that is attainable by a heap of microspheres. The angle of repose is the angle made by material, with respect to the horizontal when piled.  $\tan^{-1}(2h/d)$  is formula used to calculate angle of repose where h is height of pile of powder and d is the diameter. High angle of repose indicates poor flowing microspheres, while low angle indicates free flowing microspheres.

**d. Drug release rate:**

In vitro drug release kinetics study used to study the drug release profile of the synthesized doxorubicin loaded Fe<sub>3</sub>O<sub>4</sub> magnetite nanoparticles modified with PLGA-PEG co polymers, 3 mg of drug loaded nanoparticles were dispersed in 30 ml of phosphate buffered solution (pH 7.4) and acetate buffer. Samples were incubated at various temperatures from 37° C to 40° C. At designated time intervals, a 3 ml sample was removed and same volume was reconstituted by adding 3 ml of fresh phosphate buffered solution and acetate buffer to each sample. After the experiment, the samples were analyzed using ultraviolet spectrophotometry to determine the amount of doxorubicin released.

**III. RESULT :**

• **Preformulation results:**

Organoleptic characterization and melting point determination.

Sr.No.	Test	Observation
1.	Colour	Bright Red
2.	Odour	Odourless
3.	Melting point	205° C

**Table : Preformulation results**

The organoleptic character and melting point was found to be as per standard drug so the

formulation was found to be pure according to IP specification.

• **Solubility Analysis:**

The solubility analysis was found to be as per standard drug so the formulation was found to be pure according to IP specification.

Sr.No.	Solvent	Solubility
1.	Distilled water	Freely Soluble
2.	Alcohol	Sparingly Soluble
3.	Normal saline	Slightly Soluble

**Table : Solubility Analysis**

• **Particle size and shape determination:**

The particle size and shape was determined to be as per standard drug so the formulation was found to be pure according to IP specification.

<b>Particle Size</b>	Less than 200 um
<b>Particle Shape</b>	Spherical

• **Flow properties determination:**

The flow properties was determined to be as per standard drug so the formulation was found to be pure according to IP specification.

<b>Bulk density</b>	0.08-1.7g/cm <sup>3</sup>
<b>True density</b>	2.6-3.6 g/cm <sup>3</sup>
<b>Hausner's ratio</b>	<1.2
<b>Angle of repose</b>	>40

• **Drug release profile:**

The in vitro doxorubicin in release profile were obtained by representing the percentage of doxorubicin release with respect to the amount of doxorubicin encapsulated. The magnetic microspheres were used to encapsulated doxorubicin, a drug model. In vitro experiments revealed that the drug release from the microspheres is pH-dependent.

**IV. SUMMARY AND CONCLUSIONS:**

It has been observed that magnetic microspheres are among the best novel drug delivery systems, as it has the advantage of target

specificity and better patient compliance. Its applications are enormous as they are not only used for delivering drugs but also for imaging tumors, detecting bio-molecular interaction etc. So in future by combining various other strategies, magnetic microspheres will find the central place in novel drug delivery, particularly in diseased cell sorting, diagnostics, gene & genetic materials, safe, targeted and effective in-vivo delivery and supplements as miniature versions of diseased organ and tissues in the body. Characteristic of magnetic microspheres particle size of drug carrier, can effect the degree of drug entrapment. In targeting, using the magnetic content of carrier & the magnitude of applied magnetic field are important. If a high magnetic content is incorporated thus amount of magnetic fields needed is reduced but the space available for drug entrapment decreases. Drug incorporation and magnetite has to be delicately balanced. Optimum magnetic content would be between 22-50% of drug weight in the drug carrier complex. Microspheres are one of the most promising controlled and targeted drug delivery systems.

**REFERENCES**

- [1]. Zhu KJ, Henderson RW, Jensen K, Pitt CG. Synthesis, properties and bio degradation of poly (1,3-trimethylene carbonate). *Macro molecules* 1991;24(8): 1736-1740.
- [2]. Patil SA, Suryavanshi HP, Bakliwal SR, Pasar SP. Ferro fluids: a promising drug carrier-a review. *Int J Pharma Res Dev* 2001;2(10):25-28
- [3]. Vyas SP, KharRk. Targeted & controlled drug delivery. New Delhi: CBC Publisher & distributors; 2004, p.459-463.
- [4]. Agarwal A, Chhajer P, Maheshwari S. Magnetic drug delivery in therapeutics. *Int J Pharm Sci Res* 2012; 3(2): 4670-4680.
- [5]. <https://www.chemicell.com/products/magnetic-particles/magnetic-particle-separation.htm> accessed on 17/01/2011
- [6]. Lokwani P. Magnetic particles for drug delivery: an overview. *Int J Res Pharm Boomed Sci* 2011;2(2): 465-473.
- [7]. Langik C, Schumer D. Biogenic nanoparticles: production, characterization and application of bacterial magnetosomes. *Phys J Concerns Matter* 2006;18: 79-86.
- [8]. Weckler B, Lutz HD. Solid State In org.Chem. *Eur J Mol Structure* 1998;35:531-544.



- [9]. Mukherjee S. Magnetic microspheres: latest approach in novel drug delivery system. *J Pharm Sci Innovation* 2012;
- [10]. Berensmeier S (2006) Magnetic particles for the separation and purification of nucleic acids. *Applied Microbiology and Biotechnology* 73(3):495-504.
- [11]. Harshad P, Sunil B, Nayan G, Bhushan R, Sunil P (2010) Different Method of Evaluation of Mucoadhesive Microsphere. *Internationale Journal of Applied Biology and pharmaceutical Technology* 1(3): 1164-1165.
- [12]. Agusundaram M, Madhu SC, Umashankar K, Vankata AB, Lavanya C, et al.(2009) Microsphere As A Novel Drug Delivery System A Review. *International Journal of Chem Tech Research*(13)
- [13]. A.K. Gupta, M. Gupta (2005), "Synthesis and Surface Engineering of Iron Oxide Nanoparticles for Biomedical Applications", *Biomaterials*26(18): 3995-4021.
- [14]. Akbarzadeh A, Samiei M, and Davaran S. (2012), "Magnetic Nanoparticles Preparation, Physical Properties, and Applications in Biomedicine", *Nanoscale Research Letters* 7(1): 144.
- [15]. Akhtar J, Chaturvedi R, Sharma J, Mittal D and Pardhan P. (2009), "Magnetized Carrier as Novel Drug Delivery System", *International Journal of Drug Delivery Technology*1(1):28-35.
- [16]. Balaita L and Popa M. (2009), "Polymer Magnetic Particles in Biomedical Application's", *Revue Roumaine de Chimie* 54(3), 185-199.
- [17]. Batra D, Kakar S, Singh R and Nautial U. (2012), "Magnetic Microspheres as a Targeted Drug Delivery System: An Overview", *Journal of Drug Delivery Research*1(3):10-17.
- [18]. Cao Y, Bai G, Chen J, Tian W, Wang S and Yang W. (2006), "Preparation and Characterization of Magnetic Microspheres for the Purification of Interferon a-2b", *Journal of Chromatography B* 833: 236-244.
- [19]. Duguet E, Vasseur S, Mornet S and Devoisselle JM. (2006), "Magnetic Nanoparticles and their Applications in Medicine", *Nanomedicine* 1 (2): 157-168.
- [20]. Garabi M, Yamini Y and Rezaee M. (2010), "Magnetic Nanoparticles: Synthesis, Stabilization, Functionalization, Characterization and Applications", *Journal of the Iranian Chemical Society*7(1): 1-37.
- [21]. Green M. (2005), "Organometallic Based Strategies for Metal Nanocrystal Synthesis", *Chemical Communications*24: 3002-3011.
- [22]. Gupta AK, Naregalkar RR, Vaidya VD and Gupta M. (2007), "Recent advances on Surface Engineering of Magnetic Iron Oxide Nanoparticles and their Biomedical Applications", *Nanomedicine* 2(1), 23-39.
- [23]. Gupta PK, and Hung CT. (1989), "Magnetically controlled targeted micro carrier systems", *Life Science* 44, 175-186.
- [24]. Hafeli U, Achuty W, Teller J, Zborowski M. (1997), "Scientific and clinical applications of Magnetic Carriers", First ed. Plenum Press, New York.
- [25]. McCarthy JR, Kelly KA, Sun EY and Wessleder R. (2007), "Targeted Delivery of Multifunctional Magnetic Nanoparticles", *Nanomedicine* 2 (2): 153-167.