# A REVIEW ON MAGNITICALLY MODULATED DRUG DILIVERY SYSTEM.

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**ABSTRACT**

*Magnetic microcarriers are one of the innovative drug delivery technologies that have surfaced, including many routes of administration to provide targeted and controlled drug delivery. These microcarriers include magnetic emulsion, magnetic resealed erythrocytes, magnetic liposomes, magnetic nanoparticles, and magnetic microspheres. Due to their special qualities, magnetic particles can undergo magnetic polarization and magnetophoretic mobility. As a result, these carriers could be suitable for the delivery of medications to particular parts of the body. Other applications, like those in magnetic separation, hyperthermia, and magnetic resonance imaging, are made possible by their unique qualities. The principles of magnetic targeting, the mechanism of magnetic targeted drug delivery, the advantages and disadvantages of magnetic targeting, magnetic microcarriers, the use of magnetism in targeted drug delivery, and other related topics will all be covered in these projects. magnetically oriented medication delivery via particle carriers is a successful technique for reaching specific disease locations, including tumour. It is possible to obtain high concentrations of radioactive or chemotherapeutic chemicals close to the target region without endangering the healthy surrounding tissue. Magnetic microspheres and nanospheres can be used as contrast agents and drug reservoirs that are activated by an external magnet application, among other non-targeted applications.*

**KEYWORDS:** *Targeting, Microsphere, Nanosphere, Neutrophiles, Liposomes, Emulsion.*

## INTRODUCTION:

The biggest drawback of the conventional drug delivery system is that anti-cancer drugs administered intravenously may accumulate in cancerous cells, which may contain many leaky blood vessels. As a result of this accumulation, the drug may also negatively affect healthy tissue and exhibit numerous side effects. One of the biggest challenges in developing a site-specific drug delivery system is selective targeting of therapies, wherein medications must accumulate at the precise spot for their pharmacological impact. A variety of chemical parameters are changed, such as the partition coefficient, ligand attachment, changed charge density, and the synthesis of alternative biodegradable polymers, to get around such issues with site-specific targeting**.** Magnetic responsive drug delivery systems, which apply an external magnetic field to enhance drug concentration at the tumour location following the introduction of magnetic particles, are intended to target specific sites for medication delivery without interfering with RES. By manipulating a drug with magnetic moment in a magnetic drug delivery system, we may prevent the drug from acting on healthy tissue and only act on malignant cells, improving the treatment's efficacy and requiring less dosage. A magnetic drug delivery

system can be utilized to treat a variety of conditions, including gene therapy, abrupt sensorineural hearing loss, nervous system problems, and malignancies. An alternative to these systems has been discovered to address these issues, namely magnetizing the carriers to enable the retention or guidance of these particles at the intended location with the use of an external a suitable strength magnetic field [7].

## HISTORY:

Drug delivery via magnetically modulated systems is a relatively new field. Gilchrist, a surgeon, wrote a seminar paper on selective inductive heating of lymph nodes following the injection of magnetite particles with a size range of 20–100 nm into the lymph nodes close to the surgically excised malignancy. Turner & Rand paired this radiofrequency heating technique with embolization therapy later in 1975. Gilchrist was unaware that his magnetic particles might be directed and delivered to certain locations by magnetic means [1].

Meyers (1963) reported their ability to use a horse shoe magnet to increase the amount of tiny iron particles injected intravenously into the veins of dogs' legs externally [3]. Hilal developed magnetically endowed catheters in 1974 and explained how small magnets may be utilized to deposit and selectively embolize arterio-venous lesions [4].

Dr. Kenneth Widder & Associates created the first spherical magnetic microspheres with greater definition in 1979. They created albumin microspheres that contained magnetite (Fe3O4) and medications Although their magnetic albumin microspheres were not investigated in human trials, they performed effectively in animal studies for tumour therapy and as magnetic resonance agents' number five. Magnetic particles were utilized by Wu et al. (1995) and Jones and Winter (2001) for liver cancer embolization therapy [5,6,7].

## PRINCIPLE:

Particulate carriers using magnetic drug delivery is an effective way to deliver medication to a specific disease site. It is possible to obtain extremely high concentrations of radioactive or chemotherapeutic agents close to the target site, such as a tumour, without endangering healthy surrounding tissue or the body as a whole.

Magnetic microspheres and nanospheres have non-targeted uses such as MRI contrast agents and drug reservoirs that are activated by magnets applied externally to the body.

The physiological parameters, such as particle size, surface characteristics, field strength, and blood flow rate, among others, influence the efficiency of magnetic carriers. It is believed that the process of extrusion by magnetic targeted carriers is connected to some type of channel that is opened by the magnet's force.

## ADVANTAGES OF MDDS:

- Therapeutic responses in the target organs at only one tenth of the free drug dose.
- Controlled drug release within target issues for intervals of 30 min to 30 hrs.
- Avoidance of acute drug toxicity directed against endothelium and normal parenchymal cells.
- Adaptable to any part of the body.
- This drug delivery system reduces circulating concentration of free drug by a factor of 100 or more.

## DISADVATAGES OF MDDS:

This novel approach suffers from certain disadvantages also as given below: -

- Magnetic targeting is an expensive, technical approach and acquires specialized manufacture and quality control system.
- Its needs specialized magnet for targeting, advanced techniques for monitoring, and trained personnel to perform procedures.
- Magnet must have relatively constant gradients, in order to avoid focal over dosing with toxic drugs.
- A large fraction (40-60%) of magnetite, which is entrapped in carriers, is deposited permanently in target tissues.
- Drug cannot be targeted to deep seated organs in the body, so this approach is confined to the targeting of drugs [8].

**MECHANISM OF ACTION:**

The foundation of the magnetic drug transport method is the drug's ability to be either magnetically microsphere-encapsulated or free of them.

↓

The accumulation occurs within the region where the magnetic field is applied when the magnetic carrier is administered via the IV route.

↓

To move and concentrate the drug, an external magnetic field is applied at the desired location.

↓

Blood flow rate, surface morphology, and particle size are examples of physiological factors that affect the accumulation of magnetic carriers.

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One of the main advantages of this approach is that it can reduce the drug's systemic distribution while targeting a specific area, so avoiding ADME. and generates the therapeutic benefit at a low dosage.

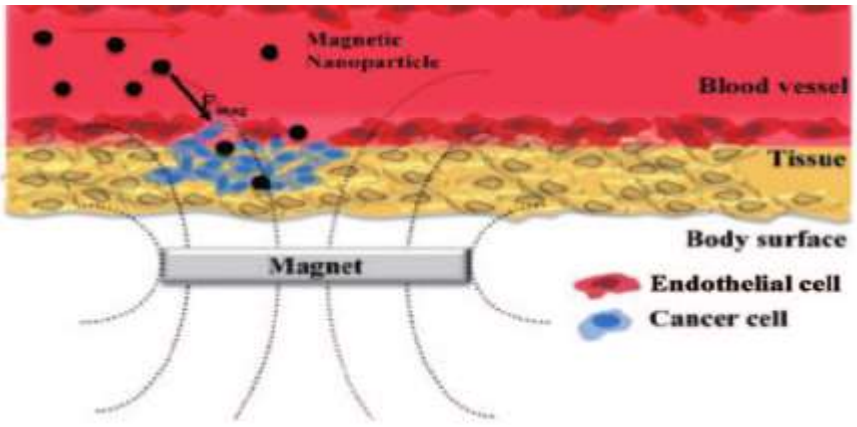


**Fig.** mechanism of magnetically modulated drug delivery system

**MAGNETICALLY MODULATED MICROCARRIER:**

Because magnetic microcarriers are site-specific, the issue of their quick clearance by RES is also resolved by placing these microcarriers in the intended area. Blood lines because the velocity in capillaries is 300 times slower than that of arteries, or 0.05 cm/sec, they have a much smaller magnetic field (6–8 KOE), which is sufficient to keep them within the target area's capillary network10.An important substitute for the bimolecular malformation (i.e., composition, inactivation, or deformation) seems to be magnetic carrier technology. Among these microcarriers are:

1. Magnetic microsphere
2. Magnetic nanoparticles
3. Magnetic liposomes
4. Magnetic resealed erythrocytes

5. Magnetic emulsion
6. Magnetic neutrophils [8].

1. **MAGNETIC MICROSPHERE**:

Supramolecular particles known as magnetic microspheres are <4 m in size, which allows them to pass through capillaries without causing embolic occlusion prone (ferromagnetic) to being drawn into micro vessels and into nearby tissues by magnetic fields between 0.5 and 0.8 Tesla (T).

Two main techniques were used to prepare magnetic microspheres: continuous solvent evaporation (CSE) and phase separation emulsion polymerization (PSEP). By adjusting the size of the microspheres, the drug content, the magnetite content, the hydration state, and the drug release characteristic of the carrier, the amount and rate of drug delivery via magnetically responsive microspheres can be controlled. The microspheres' magnetite and medication contents must be magnetite content, phase behaviour of drug release, quantitative measurement of phospholipids, entrapped volume lamellarity using P-NMR and freeze fracture microscopy and analysis of cholesterol [8].

2. **MAGNETIC NANOPARTICLES:**

The field of magnetic nanotechnology has shown a wide range of applications in recent decades, expanding to include neurological, cardiovascular, and oncological disorders. Because of their physical characteristics, they have been the subject of intense investigation in several fields as next-generation drug carriers. Because of their intrinsic magnetic core capabilities and effective coating, magnetic nanoparticles have demonstrated significant promise in drug loading efficiency. These particles, which are smaller than 100 nm, are used in conjunction with a magnetic field to altered by various substances, including cobalt, nickel, and iron. Better performance is provided below their size's critical value, which is approximately 10–20 nm. These above the blocking temperature, nanoparticles exhibit super magnetic behaviour and behave like paramagnetic atoms with reduced resonance. They can be applied in a variety of ways, such as cell tracking, tissue engineering, magnetic resonance imaging, vascular contrasting agents, diagnostic tools, and theragnostic in the targeting of genes for cancer treatment. Over extended periods, though, intrinsic instability issues may arise because of their propensity to oxidize in air and lose their magnetic properties.

Various substances such as cobalt, nickel, iron, ferrous oxides, ferrites such as MFe2O4 (where M can be Cu, Mg, Mn, Ni, etc.) and sulphur have been used to prepare magnetic nanoparticles metal mixtures. Several techniques, including co-precipitation, thermal decomposition, and the micro-emulsion method, can be used to synthesize them [9].

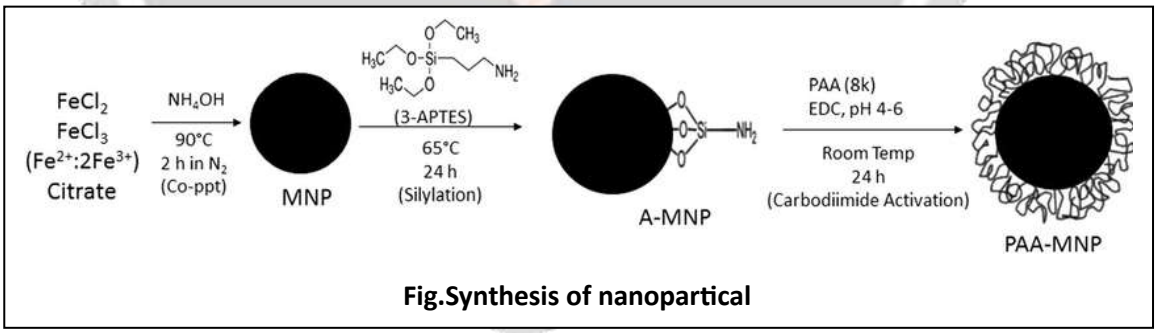


**Fig.Synthesis of nanopartical**

3. **MAGNETIC LIPOSOMES:**

The compositional structure of magnetic liposomes is bilayer, with the lipid and aqueous layers having different designs. These are hydrophobic and hydrophilic medicinal agents are encapsulated in a biocompatible, nanometric-sized vesicular structure. The aqueous layer of magnetic liposomes contains water-soluble active ingredients, while the lipid layer of magnetic liposomes contains lipid-soluble active drugs (Martin, 1989). There are typically two types of magneto liposomes: those with metal oxides in the aqueous layer and those with meta oxides encased in a layer of lipid following lauretha stabilization [8].

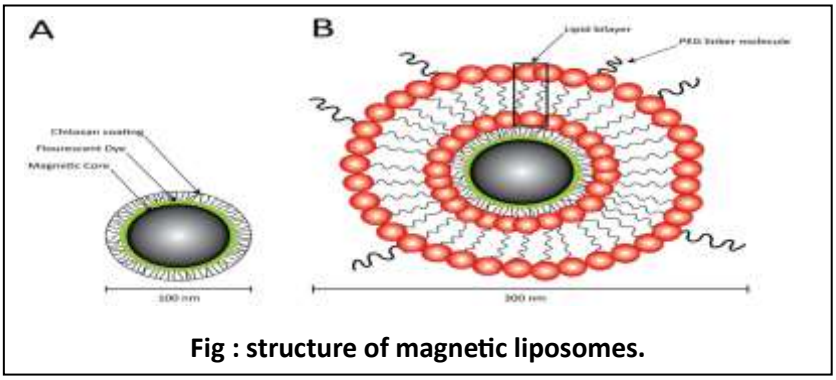


**Fig : structure of magnetic liposomes.**

4. **MAGNETIC RESEALED ERYTHROCYTES**:

Resealed erythrocytes are advantageous as drug carriers because they can encapsulate a wide range of materials and are biodegradable and biocompatible tiny cell volume and can be applied to organ targeting, among other things. Owing to these benefits, magnetic resealed erythrocytes which include ferrofluids, or magnetite as well as drugs loaded within the cell were created. Ibuprofen-loaded magnetically responsive erythrocytes were created and evaluated in vitro. The erythrocytes that were press-well loaded with ferrofluids (magnetite) and ibuprofen18. An external magnetic field was effectively sensed by the loaded cell. Numerous process variables that could impact the loading of drugs and magnetite were examined, such as drug concentration, magnetite concentration, and ferrofluid sonication. The morphology, osmotic fragility, haemoglobin release, and in vitro drug efflux of the loaded erythrocytes were all assessed percentage of cell recovery and magnetic responsiveness. Diclofenac sodium-bearing erythrocytes were produced using the press well technique and evaluated for a number of in vitro characteristics as part of the ongoing investigation. Magnetically sealed erythrocytes loaded with aspirin prevent arterial thrombosis. Aspirin is also released in the vicinity of thrombosis (thrombolytic effect), and thrombosis is absorbed or flushed due to the force exerted by the flow of magnetic erythrocytes under a magnetic field. Local thrombosis in animal arteries was prevented by magnetic targeting of red cells loaded with aspirin.

Through surgery, a vascular wall flap was inverted into the lumen of the arteries in eighteen dogs and sixteen rabbits, causing thrombosis in each case. A totally obstructive red thrombus was formed inside the vessel in 80% of cases after 4 to 5 hours. One of the arteries had an external SmCo5 magnet attached to it.

The magnet's steady magnetic field had no effect on the formation of the clot. Following intravenous administration of autologous red blood cells loaded with ferromagnetic colloid compound and aspirin, there was a complete abortion of arteriothrombotic on the magnet application side and no deterioration of clot formation in the control artery [8].

5. **MAGNETIC EMULSION**:

The emulsion is an oil in water type that responds to magnetic fields and contains a chemotherapy agent that can be localized by putting a particular target site under an external magnetic field. It seems to have the ability to give some chemotherapy agents site specificity. Using casein solution as the continuous phase, ethyl oleate-based magnetic fluid as the dispersed phase, and methyl CCNU (1-(2-chloroethyl)-3-(trans-4-methylcyclohexyl)-1-nitrosourea) trapped in the oily dispersed phase as an active chemotherapeutic agent24—Akimoto and Morimoto prepared an emulsion of magnetic materials. In vitro, the emulsion demonstrated good magnetic field retention [8].

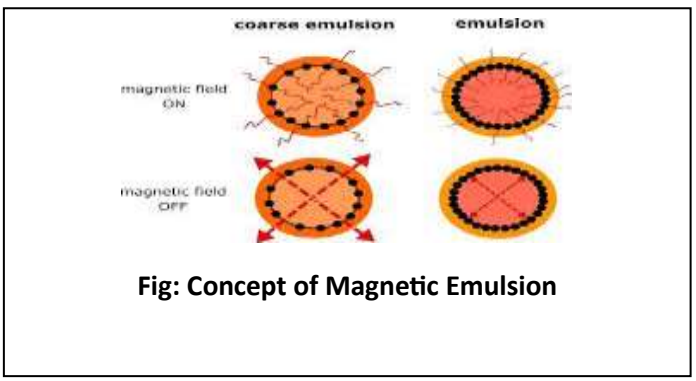


**Fig: Concept of Magnetic Emulsion**

## 6. MAGNETIC NEUTROPHILS:

In certain clinical conditions, where patient sera contain chemotactic factor in activators and neutrophils directed inhibitors of chemotaxis, an indirect approach of targeting chemoattraction of white cells fails. These illnesses include Crohn's disease, alcoholic cirrhosis, and chronic lymphocytic leukaemia, illness, sarcoidosis, hemodialysate, and Hodgkin's disease.

Although not all patients experience chemotaxis failure, these conditions can be fatal. Thus, a method for causing neutrophils to consume the magnetite base system should be created in order to target therapy specifically at the sites of severe infection [8].

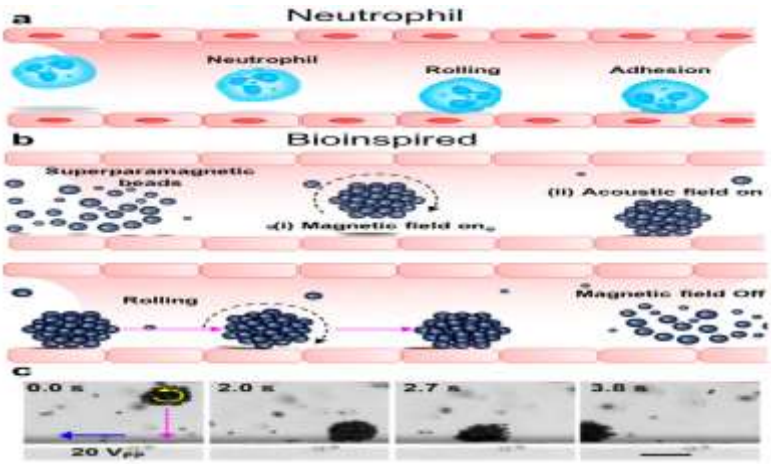


**Fig:Concept of Magnetic Neutrophile**

## APPLICATION:

Since its inception, magnetic drug delivery systems have demonstrated remarkable potential in the biomedical and biophysical sciences. Here, we'll talk about a few of its principal contributions to the delivery of drugs today:

1. Treatment of Tumours

Magnetic microspheres can be utilized in chemotherapy to deliver anti-cancer medications, such as doxorubicin, to tumours. Magnetically modulated drug targeting systems have proven effective in this type of site-specific targeting. In these situations, a magnetic field is used to concentrate the medication at the tumour site, preventing systemic side effects. Following the administration of both free doxorubicin and doxorubicin combined with magnetic microspheres, various rats with sarcoma were evaluated. Rats administered free doxorubicin were found to have larger tumours, whereas rats treated with magnetic microspheres had a noteworthy 83% reduction in tumour size.

2. Targeting of Radioactive compounds

Target tissues can receive the delivery of therapeutic-range radioisotopes under a magnetic field. An increase in dose can result in damage to normal tissues while improving anti-tumour activity. Targeted tissue selective radiation is conducted with the aid of magnetic particles coupling with various isotopes and binding them with the application of an external magnetic field. Radiolabelling has been successful in recent years using isotopes like 188Re, 90Y, 111ln, and 125I.

3. Magnetic system for the diagnosis of diseases

As a contrast agent for magnetic resonance imaging (MRI), one of the most significant uses of magnetic particles is in the diagnosis of illnesses. For the first time, 0.5–1 micrometre sized ferrite was tested in vivo by Saini et al. (1987) 29. Since then, efforts have been made to develop smaller superparamagnetic iron oxides (SPIOs) into unimodular nanometre sizes. Superparamagnetic Fe3O4 is the most widely used material; it can be coated with silicone, polymers, and dextran. The primary uses of SPIOs have been as an

intravenous liver-specific contrast agent, for the detection of metastases in non-enlarged lymph nodes, and for the distinction of intestinal loops from other abdominal structures.

4. Magnetic Hyperthermia

Because diseased tissues are more sensitive to temperature than healthy tissues, it has been demonstrated that magnetic hyperthermia can help destroy the diseased tissues by raising the temperature tissues. Another benefit is that it is limited to the tissues that are diseased. This mechanism has led to the recent establishment of liposomal nanoparticles as a successful cancer therapy approach. Using magnetic particles coated in phospholipids, magnetic liposomes have also been created and investigated for the treatment of cancer through hyperthermia.

Diagnostic Applications

The diagnostic uses of magnetic delivery systems include the following contemporary and practical uses:

* In-vivo Applications: With the advancement of NMR.

* In-vitro Applications: Magnetic solid phase extraction method is used in the isolation and determination of components and impurities from testing samples in large volume as opposed to conventional extraction processes which are more time consuming. This is a new pharmaceutical class known as magneto pharmaceuticals [9].

## CONCLUSION:

In many scientific fields, magnetic vesicular systems have proven to be incredibly beneficial carrier systems. Magnetic microcarriers have been studied over the years for specific medication administration in particular magnetic targeted chemotherapy because of its improved tumour targeting, therapeutic efficacy, reduced toxicity, and adaptability to be used for a variety of intended goals. Despite certain limitations, such as the need for a strong magnetic field to deposit magnetite and ferrofluid, magnetic microcarriers remain crucial for controlled and selective targeting delivery of different medications. Future drug research in this challenging area will require more studies, long-term toxicity testing, and characterization to guarantee the enhancement of the magnetic medication delivery method. Drug release from implants that is magnetically modulated compensates for release decay over time. Additionally, it reduces the size, cost, and complexity of devices that are implanted. However, the irreproducibility of magnetic modulation and the need for surgery to replace such implants following full drug release have compromised the usefulness of such implants. An externally programmable infusion pump that only requires a small amount of magnetic modulation to activate radiometry circuits to enable bidirectional information transfer [8].

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