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Resealed Erythrocytes as an Innovative Drug Delivery System: A Comprehensive Review

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ABSTRACT: -
The search for novel ways to administer therapies has been continuous throughout the large field of ,while lowering potential adverse effects. A innovative strategy that has attracted attention for its potential to revolutionize medicine administration is the interesting idea of resealed erythrocytes.
Simply explained, resealed erythrocytes act as little messengers in our bloodstream. They are altered red blood cells, which are also in charge of transporting oxygen throughout our bodies. However, scientists have discovered a technique to change these organic carriers of oxygen into amazing medication delivery systems. These altered cells are comparable to small delivery vans that carry drugs exactly to the locations where they are required throughout the body.
These drug carriers are rapidly taken up from blood by macrophages of reticuloendothelial system (RES) present in liver, lung and spleen of the body. Wide varieties of drugs like Anti-inflammatory, steroidal and chemotherapeutic agents are seen to have reduced side effects upon incorporation into these carriers. The morphology, isolation techniques, properties and methods of drug loading are highlighted in this paper along with the characterization and applications of resealed erythrocytes, which hopefully put some light for researchers working in this area.

I. INTRODUCTION: -

In the vast realm of medical science, the quest to develop innovative methods of delivering treatments has been ongoing. Scientists are continuously seeking ways to make medications more effective while reducing potential side effects. Enter the intriguing concept of resealed erythrocytes, a novel approach that has garnered attention for its potential to revolutionize drug delivery. To put it simply, resealed erythrocytes are like miniature couriers within our bloodstream. They are modified red blood cells, the same ones responsible for carrying oxygen throughout our bodies. However, researchers have found a way to transform these natural oxygen carriers into something extraordinary – drug delivery vehicles. These modified cells can be likened to tiny delivery trucks designed to transport medications precisely where they are needed in the body. Consider our bloodstream as a complex network of highways, with medications as essential cargo that must reach specific destinations within our body. Resealed erythrocytes act as expert drivers of these drug delivery trucks. By carefully removing their original cargo, oxygen, and replacing it with medications or therapeutic agents, scientists have harnessed the potential of these cells to deliver treatments to specific sites with remarkable precision. In this review, we embark on a journey to uncover the inner workings of resealed erythrocytes and understand why they hold such promise for improving the delivery of medical treatments. We will explore the methods used to create these specialized cells, delve into the types of medicines they can carry, and learn about the mechanisms that allow them to release these medicines at the right time and place. Additionally, we will discuss the crucial safety considerations that must be addressed when using resealed erythrocytes as drug delivery carriers. As we venture deeper into the world of resealed erythrocytes, we hope to shed light on the tremendous potential they offer in the field of medicine, potentially reshaping the way we administer treatments and enhancing patient care. Different carriers have been utilized for drug delivery, but cellular carriers have the most potential benefits because to their biodegradability, biocompatibility, and self-degradability. They also have a large drug loading capacity.The development of drug delivery system in future will be aimed to maximize therapeutic performance.

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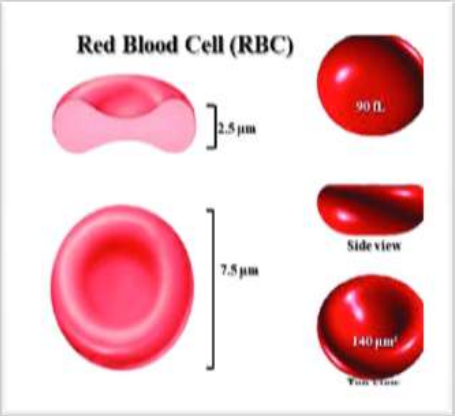
Anatomy, Morphology and Physiology of Erythrocytes: -[1]

(Fig.No.1)-Reasealed Erythrocytes



(Fig.No.2)-Reasealed erythrocytes

Red Blood Cells have shapes like biconcave discs with a diameter of 7.8 µm and thickness near 2.2 µm. Mature RBCs have a simple structure. It is also in elastic in nature.. Because of the strength and flexibility of their plasma membrane, cells can squeak through tiny capillaries without rupturing. RBCs are unable to proliferate or engage in complex metabolic processes because they lack a nucleus and other organelles. Because mature RBCs lack a nucleus and have a completely open interior, they are highly specialized for the oxygen transport function. The permeability properties of the cells of different cations (Na+, K++) and anions (Cl- HCO3-) are maintained by the red blood cell membrane, a dynamic, semi-permeable component of the cell connected to energy metabolism. Hemoglobin makes up about 280 million molecules per RBC[1]

A protein termed globin, which is made up of four polypeptide chains, and a ring-shaped non-protein pigment called heme,is bound each of the four chains. Hemoglobin, an iron-containing molecule that can bind to oxygen and give blood its red colour, is abundant in these cells.

The body naturally produces erythrocytes, which can biodegrade in its nature, erythrocyte solation is simple and involves a lot of medication is able to be loaded into tiny cells, non-immune-stimulating and capable of targeting diseased tissue.Any organ, continue the drug's systemic action while it's there

During an extended period of time within the body, prevent early deterioration,proteins and enzymes become inactive and excrete as a carrier for several medications, focus on the medications inside the

both non-RES and the reticulo-endothelial system (RES) sites/organs. They are able to transport substantial volumes of Drugs may function as long-acting, slow-release systems.280 million hemoglobin molecules are contained in each RBC.

5.4 million cells/mm3 blood in a healthy male and 4.8 million cells/mm3 blood in a healthy female.

Electrolyte composition of Erythrocytes:-[2]

Na+ is more concentrated in plasma and K+ is more concentrated in erythrocytes.

When the internal osmotic pressure of erythrocytes equals that of plasma, it is referred to as isotonic (0.9% NaCl or normal physiological saline).

The morphology of red blood cells changes when the osmotic pressure of the medium in which they are suspended changes.

Water diffuses into the cells in a hypotonic medium, causing them to swell, lose all of their hemoglobin content, and possibly burst.

Additionally, they will contract and take on an uneven form if the medium is hypertonic, defined as having an osmotic pressure greater than 0.9% NaCl. Erythrocytes are treated with balanced ion solutions, such as Ringer's and Tyrode's solutions, which are both isotonic and contain ions in the right amounts.[3]

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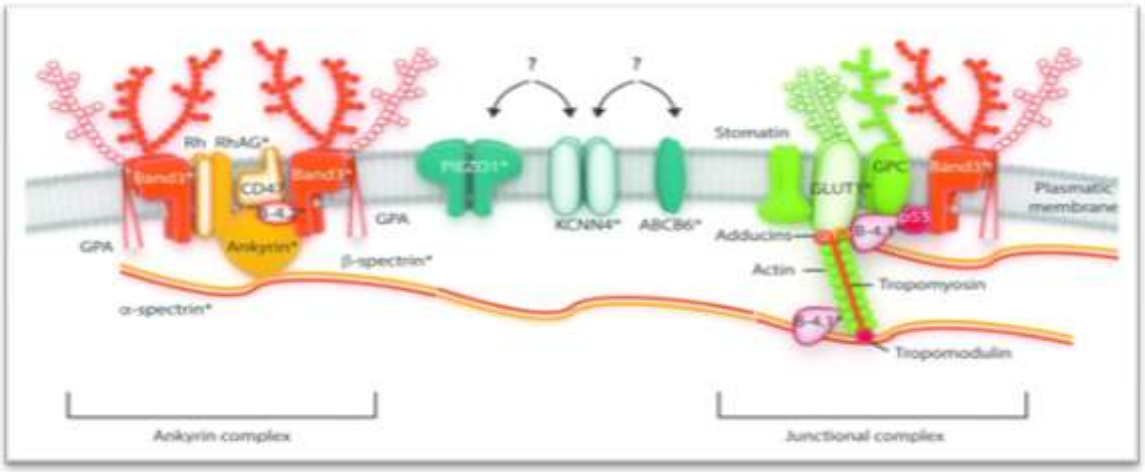

(Fig.No.3):- Erythrocytes Membrane

Erythrocyte Membrane:-[3]

Proteins and lipids are almost of equal weight. The net negative charge on the membrane's outermost surface is mostly caused by the carboxylic groups of sialic acid. Red blood cells are protected from one another and are able to keep a sufficient distance from one another to prevent IgG from readily attaching to them because of their negatively charged surfaces. The isoelectric point rises to pH 4-5 following neurallaminidase's quantitative removal of sailic acid. N-acetyl nuraminic acid is found in roughly 2.4 107 residues per human red blood cell. Nearly half of the membrane's total lipid content is made up of phosphoglycerides. The other major lipids in the membrane are sphingomyline and cholesterol. Red blood cells are incapable to synthesize lipids.

Composition of erythrocytes:-

Blood contains about 55% of fluid portion (plasma) 45% of corpuscles or formed elements.

Normal blood cells have extensile, elastic, biconcave and non-nucleated configuration with a diameter ranging from 6-9microns and the thickness is nearly 1-2microns.

Erythrocytes have a solid content of about 35% most of which is Hb and rest 65%being water.

Source of erythrocyte:-

Different mammalian erythrocytes have been used for drug delivery, including erythrocytes of mice, rats, rabbits, monkeys, chicken and sheep,pigs.[4]

Erythrocytecan beusedascarriersintwoways:-

Targeting particular tissue/organ:-

Only erythrocyte membrane is used with this approach.

This is accomplished by dividing the cells in a hypotonic solution, administering the medication, and letting the cells to redesign as spheres. Such erythrocytes are called as red cell ghost.

For continuous or prolonged release of drugs:-

Additionally, they can be utilized in continuous or prolonged release systems, which prolong the effects of the medicine. There are numerous ways to encapsulate medicines into erythrocytes.

They stay in the bloodstream for a very long time. (Up to 120 days) and withdraw the medication gradually.

Resealed Erythrocytes:[5] -Such drug-loaded carrier erythrocytes are made by simply taking a blood sample from the target organism, separating the erythrocyte from the plasma, inserting the drug, and then resealing the cellular carriers. These carriers are also known as Resealed Erythrocytes as a result.[30] The overall procedure is dependent on how these cells react to osmotic pressure. The drug-loaded erythrocytes target the pharmaceuticals to a reticuloendothelian system upon reinjection by severing as slow circulating depots. (RES). Released erythrocytes have a long circulation half-life, are biocompatible, biodegradable, and can be loaded with a variety of active ingredients. The negative

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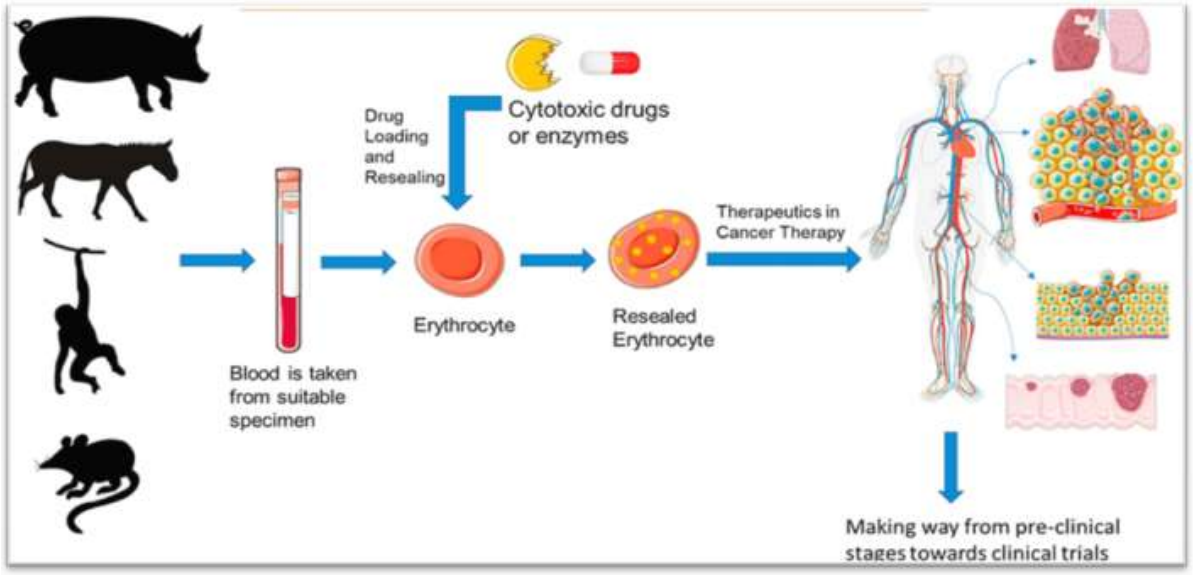

(Fig.No.4)- Reasealed Erythrocytes

Effects of numerous medications, including aspirin, steroids, and cancer treatments, are reduced by resealing erythrocytes.

Properties of resealed erythrocyte: -[6]

Minimize the pre-release of medication before reaching the intended destination.
The drug should be dispensed at the target site in a controlled and gradual manner.
The drug should possess an ideal size and shape, allowing it to traverse capillaries with minimal drug seepage.
It should exhibit the capacity to transport a wide range of drugs.
It should be blood-compatible and have minimal toxicity.
The carrier system should exhibit notable storage stability and possess specific physicochemical attributes that enable recognition by the desired target site.

Criteria for selection of erythrocytes as drug carrier:-[7]

1. In order to facilitate their passage through the capillaries, they should have the proper size and shape.
2. They ought to possess particular physicochemical characteristics that would enable the identification of the intended target site.
3. They should have the least amount of toxic side effects while still being biocompatible.
4. The breakdown products ought to be compatible with human health.
5. Before the goal is accomplished, there should be the least amount of drug leakage or leaching from the erythrocytes.
6. They should be qualified to transport a wide range of medications with various characteristics.
7. They ought to work well with medications in terms of physicochemistry.
8. During storage, the carrier system ought to exhibit notable stability.
9. The drug release pattern should be controlled at the site of action.
10. They ought to be heavy drug users.

ISOLATION OF ERYTHROCYTES:-

Blood is collected into heparin-zed tubes by vein-puncture. Blood is extracted using a syringe that contains an anticoagulant drop via a cardiac or splenic puncture in small animals and veins in large animals.The whole blood is centrifuged at 2500 rpm for 5 min at 4+/-10 degrees in a refrigerated centrifuse. The serum and buffer coats are carefully removed and packed cells are washed three time with phosphate buffer saline (PH= 7.4). The washed erythrocytes are diluted with PBS and stored at 40 degrees centigrade for as long as 48 hrs before use. Mammalian erythrocytes from a variety of species, including mice, cattle, pigs, dogs, sheep, goats,Rabbits, rats, chickens and primates, have been used to deliver drugs.

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Advantages and Disadvantages of Reasealed Erythrocytes:-[9-34]

Sr.no	**Advantages**	**Diadvantages**
1.	They are inert, biodegradable, and compatible.	Since they degrade, the RES removes them in vivo. Although this increases their ability to target drugs, it severely reduces their usefulness as long-acting drug carriers and, in some situations, may create toxicological issues.
2.	They play a Significant role in defense of the organism against the harmful effects of the medicine that is entrapped. such as antineoplasms.	Compared to other carrier systems, entrapped erythrocytes may exhibit variability and less standardization in their preparation due to their biological origin.
3.	They having a very lengthy lifespan.	Compared to other carrier systems, entrapped erythrocytes may exhibit variability and less standardization in their preparation due to their biological origin.
4.	The desired size range and the remarkably consistent shape and size.	The inaccessibility of numerous significant therapeutic targets, including the central nervous system, extravascular tissue components, and solid malignancies.
5.	The potential for specific medication administration to the RES organs.	Their ability to transport non-phagocyte target tissue is restricted.
6.	The potential for perfect zero-order drug release kinetics.	Cell clumping and dosage dumping are potential risks
7.	A large range of substances that can ensnare erythrocytes and have a comparatively high dosage ofmedication.	Even though this strengthens its ability to target medications, it severely limits its useful life as long-circulating medication carriers and, in certain cases, may result in toxicological problems.
8.	Chemical alteration of medicines is not necessary for drug entrapment	Since entangled erythrocytes are natural, their therapy may be more variable and less standardized than that of other carrier systems
9.	The potential to use artificial erythrocytes, or synthetic erythrocyte equivalents.	.A number of substances have the potential to alter the erythrocyte's physiology
10.	The possibility of utilizing synthetic erythrocytes or their equivalents in artificial form.	.Compared to other carrier systems, entangled erythrocytes may have more variability.
11.	to enhance the pharmacokinetic and pharmacodynamic properties of the medication.	Many important therapy targets are unachievable, such as solid tumors, extravascular towel factors, and the central nervous system.
12.	A notable decrease in fluctuations in steady-state concentrations relative to conventional methods of drug delivery	Concerns regarding the technological factors and safety of preserving erythrocytes that are loaded
13.	they minimized the undesirable effects of the drugs.	Several compounds may change the erythrocyte's physiology
14.	Easy management over a duration of minutes to months	The quick leakage of some encapsulated chemicals from the loaded erythrocytes.
15.	The availability of information, techniques, and resources for handling, transferring, and utilizing erythrocytes.	Responsible for biological damage because of the blood's origin.
16.	The absence of any unwanted	The handling and collecting of erythrocytes

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	immunological reaction to the drug contained.	require strict and particular procedures
17.	A significant increase in the amount of time between treatment doses, with the drug remaining in the therapeutic window region for longer	When compared to alternative carrier systems, encapsulated erythrocytes may exhibit certain inherent differences in their loading and release characteristics.
18.	It protect organism against toxic effect of drug (e.g. antineoplastics).	• Another issue with carrier erythrocytes for potential usage in rectifiers is the storage of the filled erythrocytes.

(Table No.1)

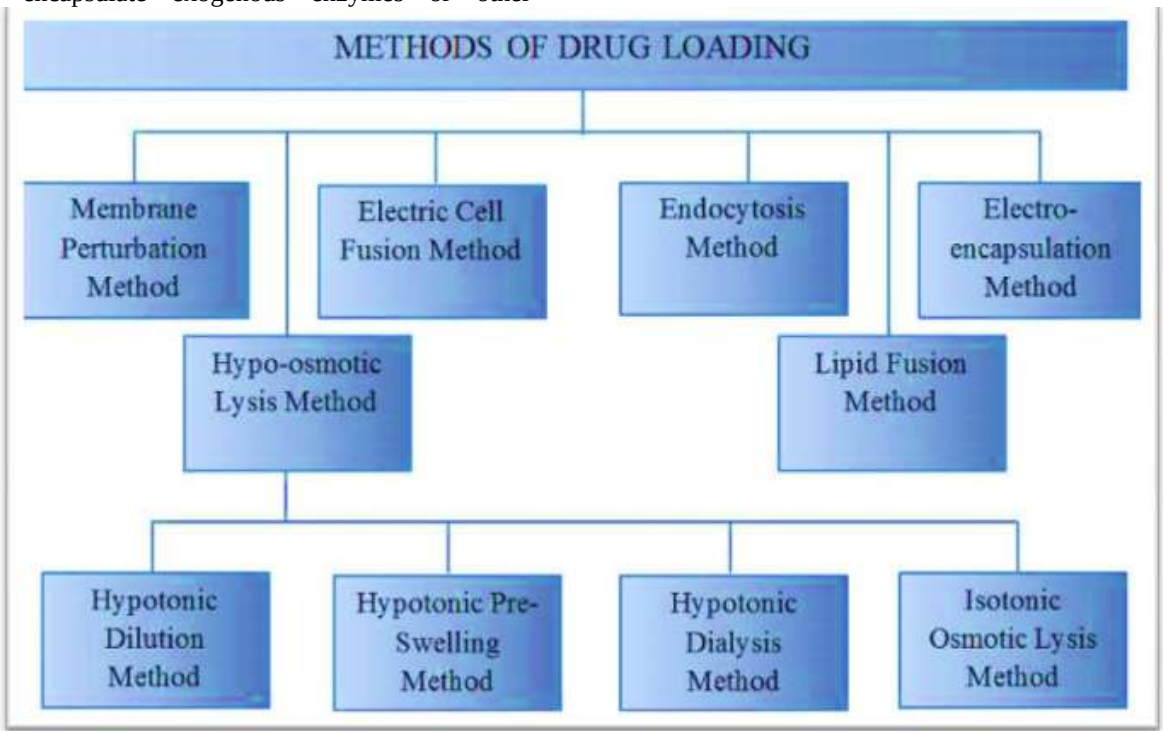
Encapsulation of Resealed Erythrocytes:-

Drugs and other bioactive substances can be loaded into erythrocytes using a variety of techniques, such as chemical perturbations of the erythrocyte membrane or physical osmosis-based systems like electrical pulse methods.

The drug must have a significant amount of water solubility, resistance against degradation within erythrocytes, lack of physical or chemical interaction with erythrocyte membrane, and well-defined pharmacokinetic and pharmacodynamic properties for the compound to be successfully entrapped, regardless of the method employed.

Techniques for loading drugs into erythrocytes:-

In most cases, the ability of erythrocytes to encapsulate exogenous enzymes or other compounds inside erythrocytes determines their potential usage.Drugs or other bioactive substances can be loaded into erythrocytes using a variety of techniques, such as chemical modifications of the erythrocyte membrane, osmosis-based systems, and physical techniques like the electrical pulse approach. Whatever the technique, the drug must possess the following ideal qualities in order to successfully entrap the compound: a high degree of water solubility, resistance to erythrocyte degradation, no chemical or physical interaction with the erythrocyte membrane, and clearly defined pharmacokinetic and pharmacodynamic properties. The medicinal substance is entrapped into erythrocyte.



(Fig.No.5)

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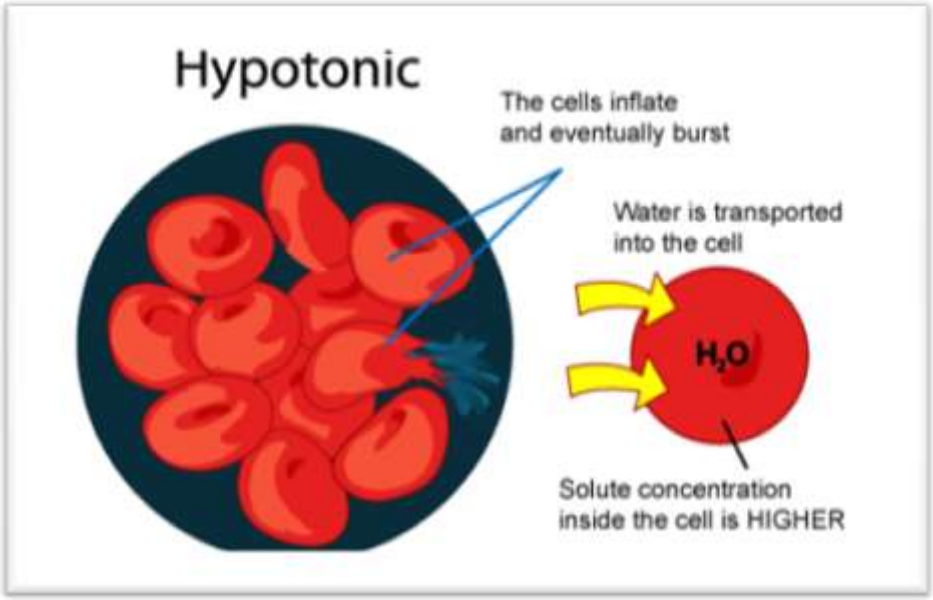
They having four main types,such as followed:-
[A] Osmosis based methods
1] Hypotonic Hemolysis
2] Hypotonic Dilution
3] Hypotonic Dialysis
4] Hypotonic Pre-Swelling
B] Chemical perturbation of the membrane
C] Electro-insertion or electro encapsulation
D] Entrapment by endocytosis

A) OSMOTIC BASED METHOD:-

(1)Hypotonic hemolysis-[35,36,37]

Hypotonic dilution was the earliest, easiest, and fastest technique to load compounds into erythrocytes that was studied.This technique is predicated on erythrocytes' reversible swelling in a hypotonic solution, as illustrated in figure. Erythrocytes possess a remarkable capacity for reversible deformation under the cells and reversible shape changes with or without corresponding volume changes. The cells are able to maintain their integrity up to a tonicity of 150 mosm/kg, above which the membrane bursts, releasing the contents of the cells. Just prior to cell lysis, a few transitory pores on the membrane stress measuring 200–500 Å are created at this time.



(Fig.No. 6):-Hypotonic hemolysis

Advantages:-[38]

Achieved good ruse effectiveness
There is a significant decrease in the volume of superfluous cell product that equilibrates with the erythrocyte's intracellular space during lyses.

Disadvantages:-[38]

system that is difficult to finish.
Research using a hydro stably fastening flyspeck analyzer revealed that the laden ghosts' size distribution isn't uniformly distributed.

2)Hypotonic Dilution:-

Hypotonic dilution was the first and most straightforward method for loading composites into erythrocytes that was studied.

The stages in this method are to lace a volume of packed erythrocytes with 2–20 volumes of a waterless pharmaceutical result and maintain the tonicity of the result by adding a hypertensic buffer.

Furthermore, the combination undergoes centrifugation, the supernatant is extracted, and isotonic buffer is used to irrigate the bullet.

This method's primary disadvantage is its low overall effectiveness and significant hemoglobin and other cell component loss, which decreases the rotation
The cells' half-life after loading. These can be employed to target organs within the RES after being phagocytosed by RES macrophages.

3)Hypotonic dialysis:-

This technique was first reported by Klibansky in 1959, and Deloach and Dale used it to load lipids and enzymes in 1977.

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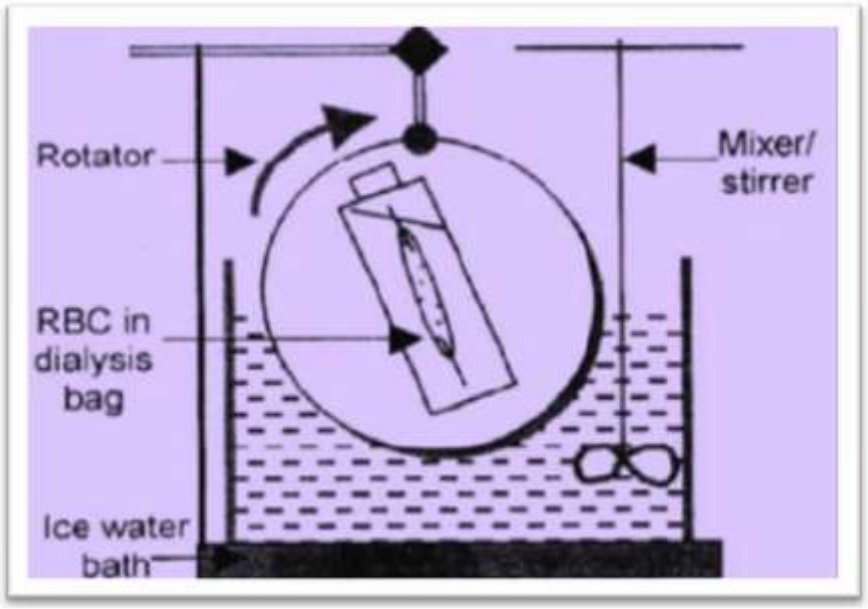
The idea of a semipermeable dialysis membrane that maximizes macromolecule intracellular extracellular volume rate is the foundation for a number of lysis and resealing procedures.
In this procedure, pharmaceutical outcomes and erythrocyte suspense are combined to obtain the requisite hemocrit.
After that, the slurry is inserted into dialysis tubing that has been threaded on both ends.
There remains in the tube an air bubble the size of a fourth of the internal volume.
The 100 ml swelling result container is filled with the tube.
The vial is maintained at 4 degrees Celsius for the desired lysis duration.Klibansky originally described this technique in 1959



(Fig.No. 7) Hypnotic dialysis

4) Hypnotic preswelling:-[39,40]

Its foundation is the first, carefully regulated swelling in a buffered, hypotonic solution. Low g values are used to centrifuge this combination. Once the cell fraction reaches the lysis point, 100–120 µL quantities of an aqueous solution containing the medicine to be encapsulated are added. The supernatant is disposed of. The mixture is then centrifuged in between each phase of the medication addition process. When a cell combination reaches the lysis point, a calculated amount of hypertonic buffer is added to restore its tonicity. The loss of a clear separation between the cell fraction and the supernatant after centrifugation indicates the lysis point. The cell suspension is then incubated at 37 0C to cause the erythrocytes that have been resealed to anneal.

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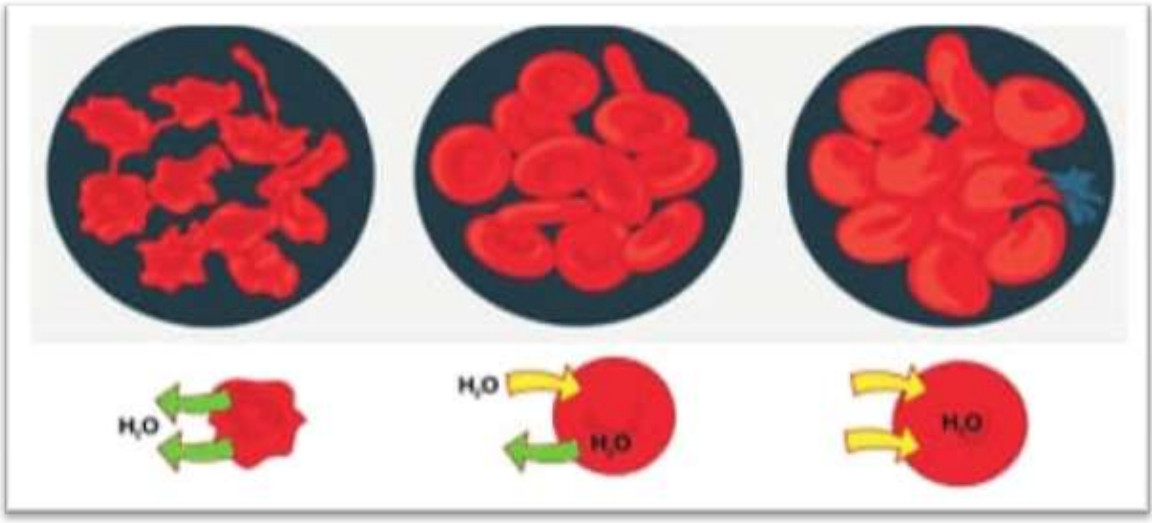

(Fig.No.8):-Hypnotic Preswelling

B) chemical membrane perturbation method:-

Based on the fact that erythrocytes' membrane permeability increases in response to specific chemical exposure, it is hypothesized that polyene antibiotics, like amphotericin B, also increase the permeability of erythrocytic membranes. Kitao and Hattori successfully employed this technique in 1980 to entrap the anticancer medication daunomycin in human and animal erythrocytes. Halothane was also used for the same reason. Nevertheless, these techniques are not well-known as they have caused the cell membrane to undergo irreversible, damaging alterations.

C)Electro encapsulation:- [41]

The technique, often referred to as electroporation, is predicated on the use of transient electrolysis to create pores that result in the desired membrane permeability for drug loading into erythrocytes. In an electrical discharge chamber, erythrocytes are suspended in an isotonic buffer. It uses a capacitor in an external circuit that is charged to a specific voltage and discharged through cell suspension within a specific time frame to create a square-wave potential. The anticancer medication daunomycin was effectively entrapped in human and animal erythrocytes in 1980. This procedure is not very well-liked since it also causes irreversible, damaging alterations in the cell membrane.

It uses a capacitor in an external circuit that is charged to a specific voltage and discharged through cell suspension within a specific time frame to create a square-wave potential. The anticancer medication daunomycin was effectively entrapped in human and animal erythrocytes in 1980. This procedure is not very well-liked since it also causes irreversible, damaging alterations in the cell membrane.

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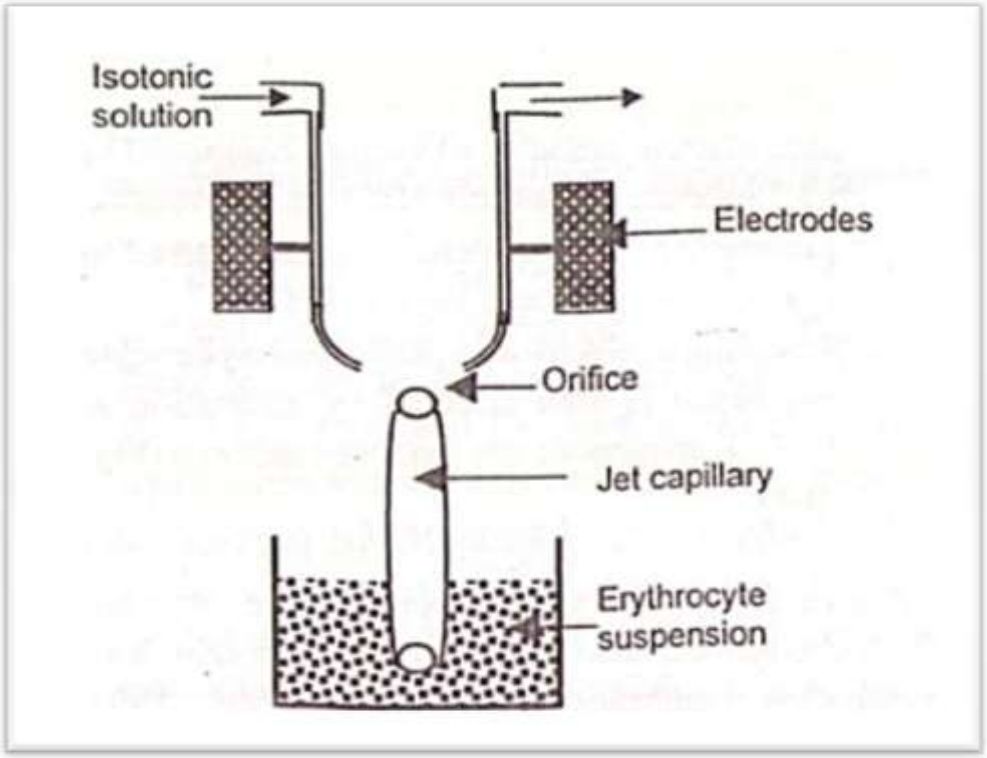
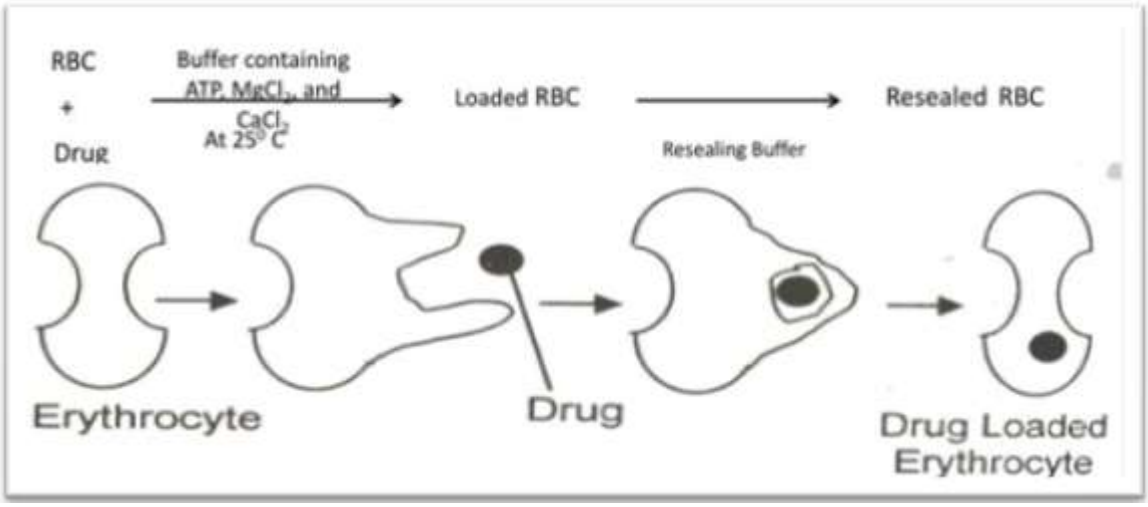


(Fig.No.9):- Electro encapculation methods

D) Entrapment by endocytosis:-[42,43,44]

Schrier published a study on it in 1975. One volume of washed and packed erythrocytes is added to nine volumes of buffer containing 2.5 mM ATP, 2.5 mM MgCl2, and 1 mM CaCl2, and endocytosis is performed by letting the mixture sit at room temperature for two minutes. After incubating at 37°C for two minutes with 154 mM of NaCl, the pores produced by this technique are shut again. Endocytosed material is separated from the cytoplasm by the vesicle membrane, which also shields it from the erythrocytes. Primine, eight aminoquinolones, vinblastine, chlorpromazine, phenothiazine, hydrocortisone, tetracaine, and vitamin A are among the medications utilized in this proceure.



(Fig.no.10):-Entrapment by endocytosis

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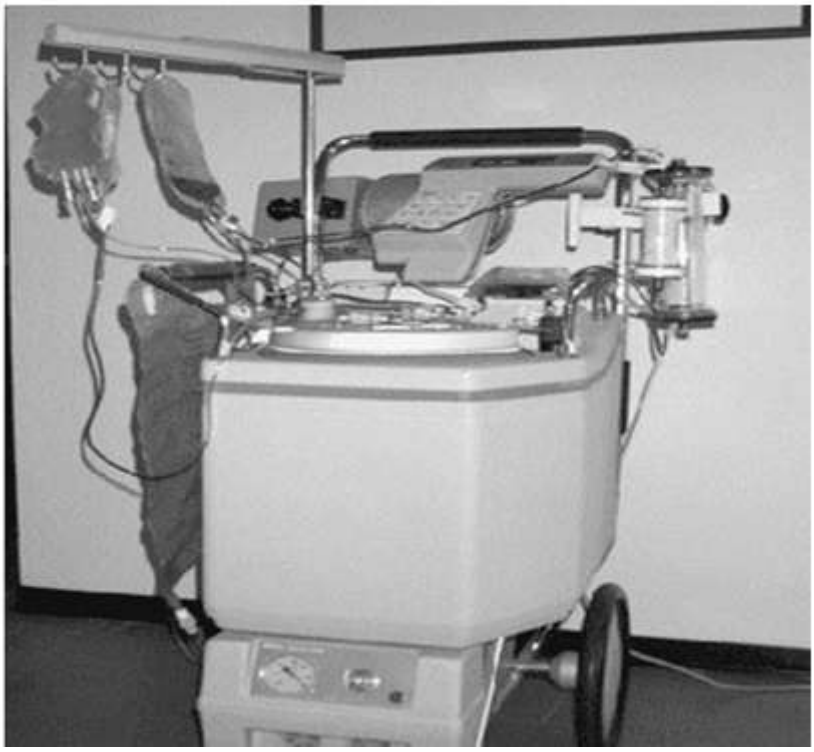
Storage:-

Maintain the prepared encapsulation intact for two weeks at 40 degrees Celsius in Hank's balanced salt solution (HBSS). employing batches of blood for transfusion and the preswell or dialysis procedure, as well as group "o" (universal donor) cells. A regular blood bag can be used to store and encapsulate bath samples.



(Fig.N0.11):-Red Cell Holder

Evaluation parameters of Reasealed Erythrocytes:-

Following the administration of a therapeutic drug to erythrocytes, the carrier cells undergo physical, cellular, and biological assessment.

1. Shape and Surface Morphology: An erythrocyte's life span following administration is determined by its morphology. Transmission electron microscopy (TEM) or scanning electron microscopy (SEM) are used to compare treated and untreated erythrocytes in order to characterize the morphology of the erythrocyte. You can also employ other techniques, such as phase contrast microscopy.

2. Drug Content: The amount of drugs in the cells affects how well the technique of entrapment works. Centrifugation at 2500 rpm for 10 minutes is followed by the deproteinization of packed, loaded cells (0.5 ml) with 2.0 ml acetonitrile. Spectrophotometric analysis is used to determine the drug concentration of the clear supernatant.

3. Turbulance fragility: This is assessed by shaking the cell suspension ferociously or passing it through needles with a smaller internal diameter (such as 30 gauges). Haemoglobin and medication discharged following the surgery are identified in both scenarios. It is discovered that resealed cells have a higher turbulent fragility.

4. Cell Recovery and Counting: This process counts the number of red blood cells per volume of whole blood, usually using an automated machine. The number of intact cells per cubic of packed erythrocytes is counted both before and after the medicine is loaded.

5.Erythrocyte Sedimentation Rate (ESR): This measures how stable an RBC suspension is in plasma and is influenced by the quantity, size, and relative concentration of the cells.

6.Determination of Entrapped Magnetite: An article describes using an atomic absorption spectroscopy approach to ascertain the amount of a specific metal present in a sample. A fixed amount of erythrocytes containing magnetite are treated with HCl, heated at 600°C for two hours, and then treated with 20% w/v trichloroacetic acid. The supernatant obtained after centrifugation is then

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utilized to measure the magnetite concentration using atomic absorption spectroscopy.
7. In vitro stability: The cells are cultured in autologous plasma or an iso-osmotic buffer with hematocrit levels between 0.5 and 5% at temperatures between 4 and 370 degrees Celsius in order to evaluate the stability of the loaded erythrocytes.
8. Haemoglobin release: Changes in permeability may result in a decrease in the amount of haemoglobin in the erythrocytes.

Applications of Reasealed Erythrocytes:-
1)In-Vitro application-[35,46]]

To aid in the uptake of enzymes, phagocytosis cells have been employed in vitro. Cytological method could be used to visualize the enzymes within the carrier red blood cells. Defects like the insufficiency of glucose-6-phosphate dehydrogenase (G6PD) can be helpful in identifying the process that ultimately results in these effects. Micro-injection is the most common method of RBC administration in vitro. Through the fusion process, a protein or nucleic acid was introduced into eukaryotic cells. Similar to this, antibody molecules disperse throughout the cytoplasm right away when injected via the erythrocytic carrier system. The place of action of a toxin fragment has been verified by auto-injecting antibody RBC into living cells. RBC-mediated microinjection of antibodies has been shown to prevent their entry into the nucleus.

2) In-Vivo application:-[45,47,48]
The following are the In-Vivo Applications:
a. Bioactive drugs are targeted against the RE System:

Damaged red blood cells are quickly removed from the bloodstream by the spleen and liver's phagocyte Kuffer cells. Thus, resealed erythrocytes can be directed against the spleen and liver by changing their membranes. The surface properties of erythrocytes can be altered using a variety of techniques, such as gluteraldehyde, antibodies, and carbohydrates like sulphydryl and sialic acid.
b. Designating certain websites as non-RES Structure:
It is possible for resealed erythrocytes to transport an enzyme or medication to the macrophage-rich area. Recently, resealed erythrocytes have been used to target organs other than RES. A quick discussion of a few of the representative approaches is given.

C. Going after the liver: enzyme replacement or deficient treatment. By injecting these enzymes, numerous metabolic diseases associated with absent or insufficient enzymes can be addressed. However, allergic responses, toxicity, and a shorter half-life of the enzymes in circulation are the drawbacks of exogenous enzyme treatment. By taking the enzymes exactly as they are sealed, these issues can be resolved.Glycosidase, glucoronidase, and galactosidase4 are the enzymes that are utilized. Treatment options for the condition brought on by a buildup of glucocerebrosides in the liver and spleen include glucocerebrosidase-loaded erythrocytes

d. Hepatic tumor treatment :

Hepatic tumors represent one of the most common forms of cancer worldwide. Erythrocytes have been successfully used to deliver antineoplastic medications such methotrexate, bleomycin, asparginase, and adriamycin. Agents that load quickly, like daunorubicin, diffuse out of the cells and cause issues. Using gluteraldehyde or cisaconitic acid to covalently attach daunorubicin to the erythrocytic membrane, this issue can be resolved. The carboplatin-loaded resealed erythrocytes exhibit liver localization.

e. Treating illnesses caused by parasites:

Resealed erythrocytes are a helpful method for delivering antiparasitic medicines because of their capacity to preferentially accrete into RES organs. This approach is effective in controlling parasitic disorders involving the harboring of parasites in the RES organs. The outcomes of experiments involving animals were positive.

f.Removing the excess iron from RES:

Erythrocytes laden with desferrioxamine have been used to treat individuals with thalasseemia who have acquired too much iron from repeated transfusions. It is highly advantageous to target the RES with this medication since the RES organs accumulate iron due to the destruction of elderly erythrocytes in these organs.

g. Get rid of harmful substances:

Bovine rhodanase and sodium thiosulfate-containing mouse carrier erythrocytes were shown by Cannon et al. to reduce cyanide poisoning. It has also been observed that resealed erythrocytes

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harboring a recombinant phosphodiestrase can antagonize organ phosphorus poisoning.

3)Resealed erythrocytes can also be used for the following purposes:-

* Antibody attachment to erythrocyte membrane to obtain specificity of action of enzymes;
* Surface modification with antibodies;
* Surface modification with gluteraldehyde;
* Surface modification with carbohydrates, such as salicylic acid;
* Drug-entrapment of paramagnetic particles;
* Entrapment of photosensitive material;
* Delivery of antiviral agents, such as azidothymidine, azathioprene, etc.;
* It is used for Enhancement of oxygen delivery to tissues;
* It is used for Microinjection of macromolecules.

II. CONCLUSION:-

In the past decade, resealed erythrocytes have shown great promise as carriers for drugs and therapies, both for passive and active targeting. While this approach has significant potential, it requires further optimization before becoming a routine drug delivery system. Additionally, the concept can be extended to deliver biopharmaceuticals, and there is much to explore in this regard. Most research in this area has focused on in vitro studies, and ongoing projects aim to progress to preclinical and clinical studies to prove the capabilities of this promising delivery system. In the near future, therapeutic applications using red blood cells as drug carriers in humans are likely to become a reality, with potential benefits such as reducing side effects and improving targeted drug delivery. The focus of future studies will include enhancing the properties of erythrocytes, understanding the biology of red blood cells and their membranes, developing control systems, and delivering drugs selectively to the central nervous system. Overall, resealed erythrocytes are seen as "golden eggs" in the realm of novel drug delivery systems due to their tremendous potential.

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