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"A REVIEW ON RESEALED ERYTHROCYTES AS DRUG DELIVARY SYSTEM"

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ABSTRACT:

The primary goal of this study is to look into the unique characteristics, medical loading technology, and biomedical operation of resealed erythrocytes. Because of its capacity to circulate throughout the body, biocompatibility, zero order release kinetics of medicines, repeatability, and convenience of administration, resealed erythrocyte is becoming more popular. Erythrocytes are biocompatible, biodegradable, and have long rotation half-lives, allowing them to be loaded with a variety of physiologically active composites in a number of chemical and physical forms (hypotonic dilution, hypotonic hemolysis, electro- insertion, ruse by endocytosis, hypoosmotic lysis). These drug carriers are quickly taken up from the circulation by reticuloendothelial system (RES) macrophages found in the liver, lung, and spleen.When anti-inflammatory, steroidal, and chemotherapeutic drugs are objectified into these carriers, they are shown to have less negative effects. To make carrier erythrocytes, take a blood sample from the organism and separate the erythrocytes from the tube. The cells are shattered and the medicine is entangled into the erythrocytes by using colourful styles; they are eventually resealed, and the ultimate carrier is referred to as

" Resealed Erythrocytes ". This research emphasises the morphology, insulation methods, packaging, and styles of medication loading, as well as the characterisation and operations of resealed erythrocytes, which should help experimenters working in this area.

Introduction:

At the moment, there are 30 different types of drug delivery products on the market. The total annual income for all of these is around US$ 33 billion, with a 15 percent annual growth rate (grounded on global product profit). The growing demand for safe medicines that can reach their goal while causing minimal side effects is one of the reasons for this growing interest in drug delivery. In fact, the bio-distribution of medicinals throughout the body is one of the most significant issues with systemic medicine administration. This uneven distribution means that in order to get the desired therapeutic attention, a significant amount of medicine must be given, with the majority of it being squandered in regular apkins. A "perfect" medicine, on the other hand, should only exert its pharmacological effort when it is absolutely necessary at the target region, with the least amount of attention and no negative effects on non-target chambers.

The current delivery systems matriculate carriers that are more complex multicomponent structures (microcapsules, Micro patches, cells, cell ghosts, lipoproteins, liposomes, erythrocytes) or simple, answerable macromolecules (monoclonal antibodies, answerable synthetic polymers, polysaccharides, and particulate biodegradable polymers) (JaitelyV. et al 1996). Unfortunately, the body gradually perceives the medicine targeting mechanism as non-self, and unexpected venom could obstruct its utilisation. This was the situation with the initial generation of monoclonal antibodies that were combined with cytotoxic drugs or other answerable carriers in a preclinical setting.It has been proposed that optimal medicine delivery systems consist of a tone-powered, computer-controlled medical nanorobot system known as pharmacyte, which is capable of precision transport, timing, and targeted distribution of pharmaceutical drugs to specified targets in the body.

Although this perfect medication delivery system is not yet accessible, tremendous progress has been made in recent years over traditional medicine formulations, particularly in the area of

1. Transduced cells, which are capable of expressing pharmaceutically applicable substances.
2. Medicines or rectifiers could be loaded into cell carriers. The carrier cells may release the medicinal content in this order in rotation or at specific locations, or they could target the medicine to other cells in the body.

The inherent carrier capacities of erythrocytes, often known as red blood cells, for the transport of medications and medicine-loaded microspheres have been extensively researched. Such medicine-loaded carrier erythrocytes can be made by taking blood samples from the organism of interest, extracting the erythrocytes from the tube, enmeshing medicine in the erythrocytes, and resealing the cellular carriers. Be a result, these carriers are referred to as resealed erythrocytes.

CLASSIFICATION OF DRUG DELIVARY SYSTEMS:

Drug targeting system required system are required for targeting drugs to specific sites, and maintaining relevant drugs levels at the site for

a period required for desired therapeutic action.
Soluble carries:- monoclonal antibiotic, soluble synthetic polymers, modified plasma proteins.
Particulate carrier :- liposome, Microparticles, Nanoparticles, Microspheres. Target specific recognition moieties:- Monoclonal antibodies, Carbohydrate, lectins.

ANATOMY, PHYSIOLOGY & COMPOSITION OF ERYTHROCYTE :

Red blood cells (also known as erythrocytes) are the most frequent form of blood cells and the invertebrate organism's main mechanism of providing oxygen (O2) to the body apkins via the circulatory system's blood influx. The cells grow in the bone marrow and circulate throughout the body for around 100 to 120 days before being recovered by macrophages. It takes roughly 20 seconds to complete each turn. Red blood cells make up around a quarter of the cells in the human body. RBCs are biconcave discs with a perimeter of 7.5 m and a consistency of about 2.0 m. The structure of mature RBCs is basic. It's also pliable by nature. They have a robust and flexible tube membrane that permits them to twist without rupturing as they squeeze through capillaries with a tiny diameter. RBCs require a nexus as well as other organelles in order to multiply and maintain extensive metabolic conditioning. RBCs are primarily used for oxygen transport, and because adult RBCs lack a nexus, all of their internal space is available for this purpose. The permeability characteristics of the cells of colourful cations (Na, K) and anions are conserved by the red blood cell membrane, a dynamic, semi-permeable factor of the cell, which is associated with energy metabolism in the conservation of the permeability characteristics of the cells of colourful cations (Na, K) (Cl- HCO3-). About 280 million haemoglobin motes are found in each RBC. A haemoglobin patch is made up of a protein called globin, which is made up of four polypeptide chains, each of which is bound by a ring-like non-protein colour called a brim.

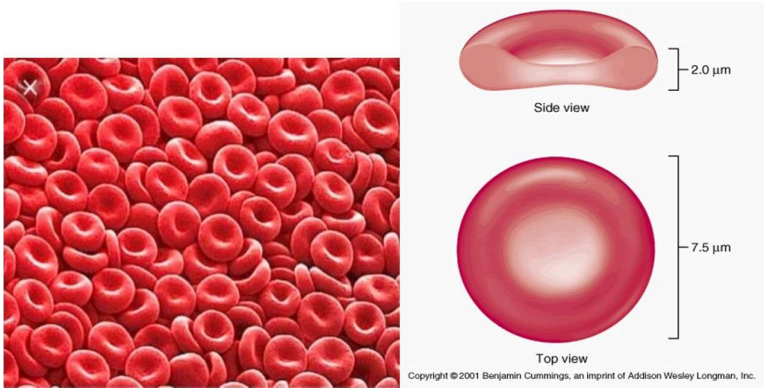

Fig. No.1- ERYTHROCYTES

Erythrocyte Membrane:

Because of the carboxylic groups of sialic acid, the membrane has a net negative charge. This negative face charge protects RBCs from colliding with other RBCs, allowing them to maintain a sufficient distance between themselves so that they are not easily scattered by IgG. After quantitative removal of the sailic acid by neurallaminidase, the isoelectric point is elevated to pH 4- 5. Per deadly erythrocyte, there are roughly 2.4 107 N-acetyl nuraminic acid residues. The membrane's phosphoglyseride content accounts for around half of the overall lipid content. Sphingomyline and cholesterol are the membrane's other colourful top lipid elements. Erythrocytes do not have the ability to synthesis lipids, however they do have the potential to develop lipids and the use of tube lipids for alleviation.

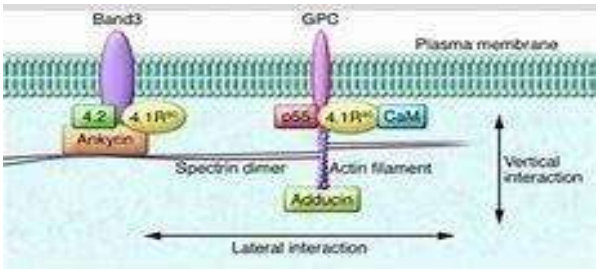

Fig. No.2 - Erythrocyte membrane.

RESEALED ERYTHROCYTES:

To make drug-loaded carrier erythrocytes, just take a blood sample from the organism of interest, separate the erythrocytes from the plasma, entrap the drug in the erythrocytes, and reseal the cellular carriers. Be a result, these carriers are often referred to as Resealed Erythrocytes. The overall process is predicated on the osmotic responses of these cells. Drug-loaded erythrocytes function as slow circulating stores and target the medications to a reticuloendothelian system after reinjection. (RES).

Released erythrocytes are biocompatible and biodegradable, have a long rotating half-life, and can be loaded with a range of active compounds. Resealed erythrocytes diminish several characteristics with numerous negative effects, such as aspirin, steroid, and cancer treatments.

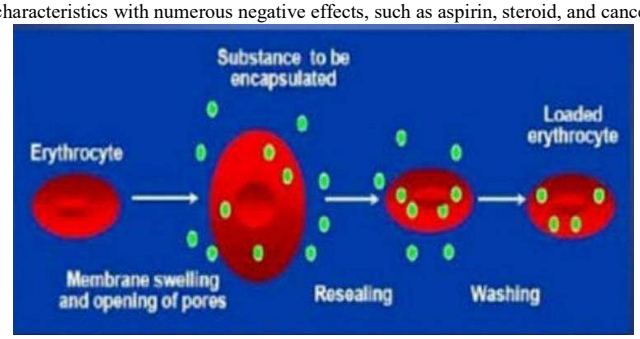

Fig. No. 3-Drug loading in Erythrocyte

Criteria for selection of erythrocytes as medicine carrier

1. 1.They should have specified specific-chemical packages that can be used to honour a requested target point.
2. 2.They should be biocompatible, with as little toxic side effects as feasible.
3. 3.Biocompatible declination products are required.
4. 4.Before the aim is attained, there should be minimal or no leakage or filtration of drugs from the erythrocytes.
5. 5.They should be able to transport a wide range of medications in a variety of packages.
6. 6.They must be physically and chemically compatible with pharmaceuticals.
7. 7.During storage, the carrier system should be remarkably stable.
8. 8The medicine should be released in a controlled manner at the point of action.
9. 9.They should be able to maintain high medicine loading effectiveness for a wide range of .medicines with various dosages parcels.
10. 10.There should be no danger of an immune response being triggered accidentally.
11. 11.The inability of RBCs to maintain their shape and morphology when put in isotonic saline also contributes to their suitability as drug and enzyme transporters.

Properties of resealed erythrocyte of novel drug delivery carrier

1. The drug should be released in a regulated manner at the target spot.
2. It should be the right size and shape, and it should be suitable to flow through capillaries and modes.
3. medicine leakage should be kept to a minimum.
4. It should be biocompatible and have a low position of toxin.
5. It should be suitable to transport a wide range of specifics.
6. It should have unique physiochemical features that allow it to honour the needed target size.
7. After the drug is released at the chosen place, the carries system's declination product should be biocompatible.
8. It needs to be physically and chemically compatible with the drug.
9. During storehouse, the carrier system should maintain a reasonable position of stability.

- **Advantages & Disadvantages of Resealed Erythrocytes**
- **Advantage**

1. Biocompatibility, biodegradability, and indolence are all terms that can be used to describe a substance.
2. There are no unfavourable vulnerable responses to the entangled medicine.
3. Significant protection of the organism against the entangled medicine's poisonous goods, similar as ant neoplasms.
4. Exceptionally long lifetime.
5. A desirable size range and a size and shape that is fairly invariant.
6. Targeted medicine delivery to the RES organs is a possibility.
7. Possibility of ideal zero- order medicine release kinetics.
8. A wide range of composites containing a significant quantum of medicine and able of being entangled within erythrocytes.
9. Synthetic erythrocyte counterparts are a possibility (artificial erythrocytes).
10. medicine ruse does not necessitate medicine chemical revision.

Disadvantage

1. The RES removes them in vivo since they are biodegradable.
2. Although this increases its medicine targeting power, it oppressively restricts its useful life as long- circulating medicine carriers and, in some situations, may beget toxicological issues.
3. Because entangled erythrocytes are natural, they may have further variability and lower standardisation in their medication than other carrier systems.
4. Several chemicals have the eventuality to change the erythrocyte's physiology.
5. Because entangled erythrocytes are natural, they may have further variability and lower standardisation in their medication than other carrier systems.
6. numerous essential treatment targets, similar as solid tumours, extravascular towel factors, and the central nervous system, are inapproachable.
7. enterprises about the safety and technological aspects of storing laden erythrocytes

Limitation

1. They have little implicit asnon-phagocyte target towel carriers.
2. It's possible that cell cementing and lozenge jilting will do.

APPROCHES FOR DRUG DELIVARY :

Erythrocytes can be employed as a carrier in two different ways:
1.targeting a specific towel or organ For targeting, only the erythrocyte membrane is used. This is accomplished by hypotonically dividing the cell and inserting the drug into the cells, allowing them to reseal into spheres. Erythrocytes are similar to red cell ghosts. Erythrocytes can be utilised in a nonstop or prolonged release system for medicines, allowing the drug to be delivered over a longer period of time. There are a few options.
2. for encapsulation that can last for over to 120 days and deliver the encapsulated drug sluggishly and steadily. insulation of erythrocytes Venepuncture is used to collect blood into heparinized tubes. In a hype containing a drop of anticoagulant, blood is withdrawn from a heart or splenic perforation (in small creatures) or modes(in large creatures).
The entire blood is spun at 2500 rpm for 5 twinkles at 4 10 °C in a chilled centrifuge. Packed cells are irrigated three times with phosphate buffer saline (pH = 7.4) after the serum and Buffy coats have been carefully removed. The cleaned erythrocytes are contaminated with PBS and stored at 40 °C for up to 48 hours before use. For drug administration, a variety of mammalian erythrocytes have been used, including those from mice, cattle, gormandizers, tykes, lamb, scapegoats, primates, fowl, rats, and rabbits.

No.	Species	Washing buffer	Centrifugal force(g)
1	Rabbit	10mmolKH_2PO_4/$NaPOH_4$	500-1000
2	Dog	15mmolKH_2PO_4/$NaPOH_4$	500-1000
3	Human	154mmol NaCl	<500
4	Mouse	10mmolKH_2PO_4/$NaPOH_4$	100-500
5	Cow	10-15 mmolKH_2PO_4/$NaPOH_4$	1000
6	Horse	2mmol$MgCl_2$,10mmol glucose	1000
7	Sheep	10mmolKH_2PO_4/$NaPOH_4$	500-1000
8	Pig	10mmolKH_2PO_4/$NaPOH_4$	500-1000

Table no. 2 – Isolation of Erythrocyte.

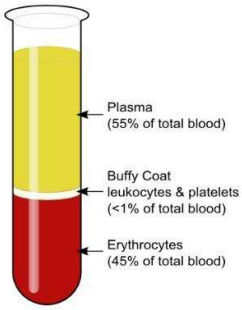

Fig.No.4-separation process

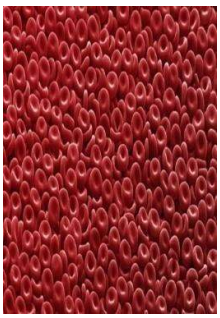

fig.No.5- Isolated erythrocyte

fig.No.6-resealed erythrocyte

ERYTHROCYTE ENCAPSULATION :

Demand for encapsulation

1. Erythrocytes can entrap a wide range of biologically active substances (5000- 60000 Dalton).
2. Non-polar motes can come entangled in erythrocytes when they are exposed to mariners.
3. illustration, Tetracycline, can be significantly entangled in bovine RBC.
4. In general, polar motes should be entangled, stillnon-polar motes can also be entangled.
5. By absorbing over other motes, it can be locked in erythrocytes.
6. Charged motes are retained longer than uncharged motes once enclosed.
7. When the patch is lower than sucrose but larger than B – galactosidase, the size of the patch entangled is a significant determinant.

METHOD OF DRUG LOADING :

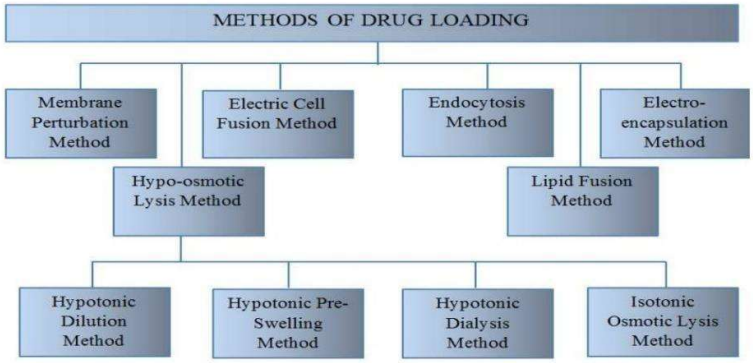

fig.no.7- method of drug loading

1.Hypo-osmotic lysis method

Their Four types are as follows-

a) Hypotonic Dilution system
b) Preselling system
c) Dialysis system

d) Bibulous lysis system

a) Hypotonic Dilution-

The first and simplest approach for loading composites into erythrocytes that was investigated was hypotonic dilution.
Lacing a volume of packed erythrocytes with 2–20 volumes of a waterless medicinal result and maintaining the tonicity of the result by adding a hypertonic buffer are the steps in this method.
In addition, the mixture is centrifuged, the supernatant is removed, and the bullet is irrigated with isotonic buffer.
The main drawback of this method is its low overall efficacy and high loss of haemoglobin and other cell components, which reduces the rotation half-life of the laden cells. These are phagocytosed by RES macrophages and can be used to target RES organs.

Advantage

1. Good ruse effectiveness is attained
2. The volume of redundant cellular result that equilibrates with the intracellular space of erythrocyte during lyses is vastly reduced.

Disadvantage

1. System that takes a long time to complete.
2. Studies with a hydro stoutly fastening flyspeck analyser indicated that the size distribution of laden ghosts isn't set up to be homogeneous.

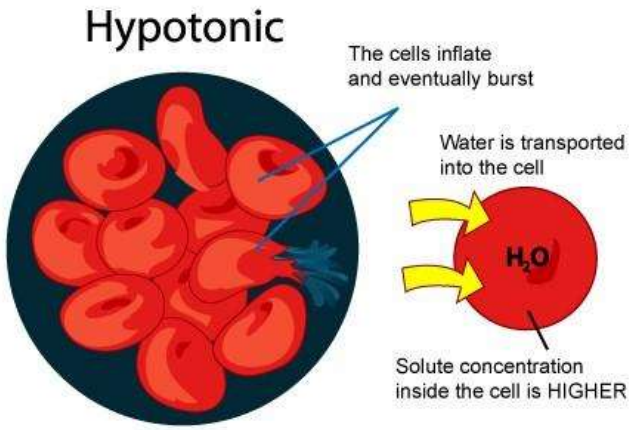

Fig .No.8- Hypotonic dilution.

b) Hypotonic dialysis system

In 1959, Klibansky described this method, and in 1977, Deloach and Dale utilised it to load enzymes and lipids.
Several techniques to lysis and resealing are based on the concept of a semipermeable dialysis membrane that maximises macromolecule intracellular extracellular volume rate.
To get the required hemocrit, erythrocyte suspense and medication results are blended in this technique.
The slurry is placed into dialysis tubing that is threaded on both ends afterward.
An air bubble the size of a quarter of the interior volume has been left in the tube.
The tube is inserted into the swelling result container, which holds 100 ml.
For the requested lysis time, the vial is held at 4 degrees Celsius.

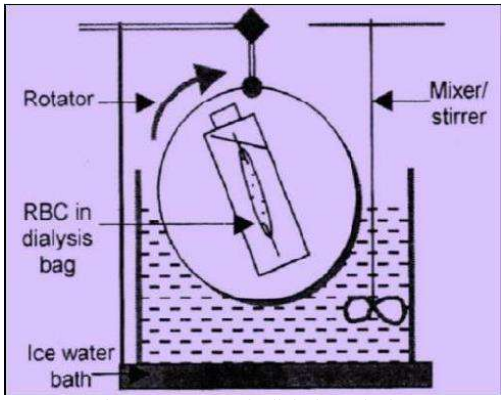

Fig.No.9- Hypotonic dialysis method.

C)Osmotic lysis method:

The osmotic pulse method is another name for it.
The solute diffuses into the cells due to the concentration gradient, followed by an influx of water to maintain osmotic balance, when erythrocytes are incubated in solutions with a high membrane permeability.
Chemicals including urea solution, polyethylene glycol, and ammonium chloride have been used to achieve isotonic hemolysis.
Finally, cells were detached and resealed at 370C after being diluted with isotonic-buffered drug solution.

D)Hypnotic Preswelling method:

It works by inducing controlled swelling in a hypotonic buffered solution at first.
Low g values are used to centrifuge this combination.
By adding 100–120 L sections of an aqueous solution of the medicine to be encapsulated to the cell fraction, the supernatant is removed and the cell fraction is brought to the lysis point.
Between the drug addition processes, A centrifuge is used to separate the components of the mixture.To restore the tonicity of a cell combination, a certain amount of hypertonic buffer is introduced during the lysis process.
A distinct boundary between the cell fraction and the supernatant vanishes when centrifugation is used to detect the lysis point.Finally, the erythrocytes that have been resealed are reannealed by incubating the cell suspension at 37°C.

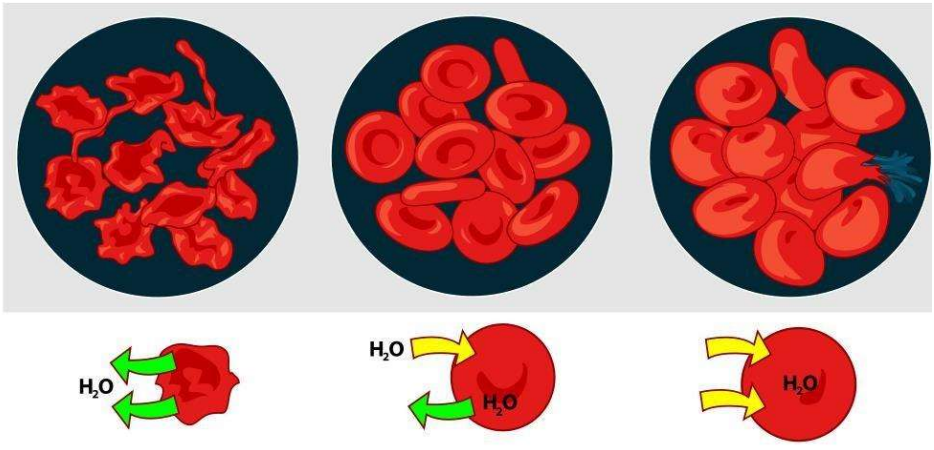

Fig.No.10– Hypotonic Preswelling

2.Membrane perturbation method:

When cells are exposed to polyene antibiotics like amphotericin B, the permeability of the erythrocytic membrane rises, which is based on the increase in membrane permeability of erythrocytes when the cells are exposed to specific chemicals.
In 1980, Kitao and Hattori effectively entrapped the antineoplastic medication daunomycin in human and animal erythrocytes using this approach. They did the same thing with halothane.
These techniques, however, are not commonly known since they inflict irreparable damage to the cell membrane.

3.Electro-encapsulation method:

It's also Called as the electroporation method, and it works by using transient electrolysis to create pores with the necessary membrane permeability for drug loading into erythrocytes.
In an electrical discharge chamber, erythrocytes are suspended in an isotonic buffer.
It has an external capacitor that is charged to a specific voltage and subsequently discharged through cell suspension over a certain amount of time to produce a square wave potential.
In 1980, it was the first time it was utilised to entrap the anticancer drug daunomycin in human and animal erythrocytes.
This method also damages the cell membrane irreversibly, which is why it is not commonly employed.

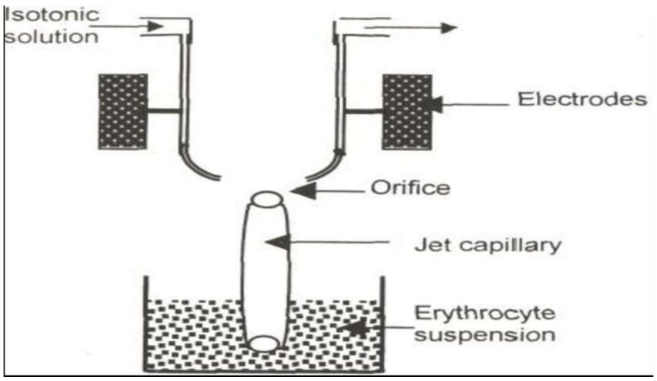

Fig.No.11- Electro-encapsulation method.

4.Entrapment by Endocytosis:

Schrier first reported it in 1975.
Endocytosis is accomplished by combining two minutes at room temperature using one volume of washed packed erythrocytes in nine volumes of buffer containing 2.5 mM ATP, 2.5 mM $MgCl_2$, and 1 mM $CaCl_2$.
With 154 mM NaCl and a 2-minute incubation at 37°C, the pores created by this method are resealed.
The vesicle membrane separates endocytosed material from cytoplasm and shields it from erythrocytes.
The drugs used in this procedure include primaquine, 8-aminoquinolones, vinblastine, chlorpromazine, phenothiazine, hydrocortisone, tetracaine, and vitamin A.

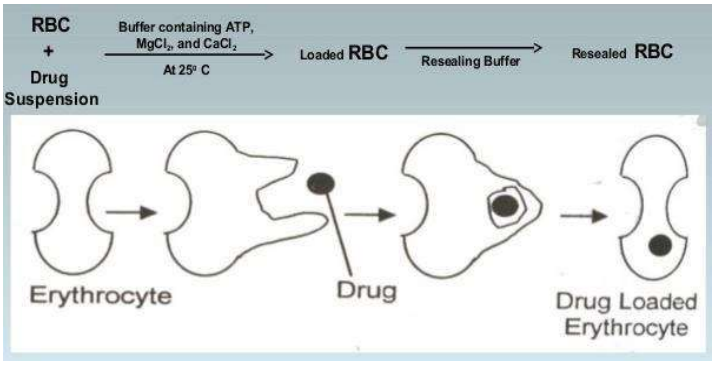

Fig.No.12- Entrapment by Endocytosis.

5. Lipid fusion method:

A drug-containing lipid vesicle is fused directly to human erythrocytes in the process of fusion, resulting in a drug exchange with a lipid-entrapped drug. As a result, this method is used to entrap inositol monophosphate, which helps to increase RBC O2 carrying capacity.

6.Electric cell fusion method:

It begins with drug molecules being loaded into erythrocyte ghosts, followed by these cells adhering to target cells.
By causing an imprisoned molecule to be released, an electric pulse is employed to speed up the fusion process.
The loading of a cell-specific monoclonal antibody into an erythrocyte ghost is a better illustration of this method.
An antibody against a specific surface protein of target cells can be cross-linked with a drug-loaded cell, prompting the target cells to seek out the drug.

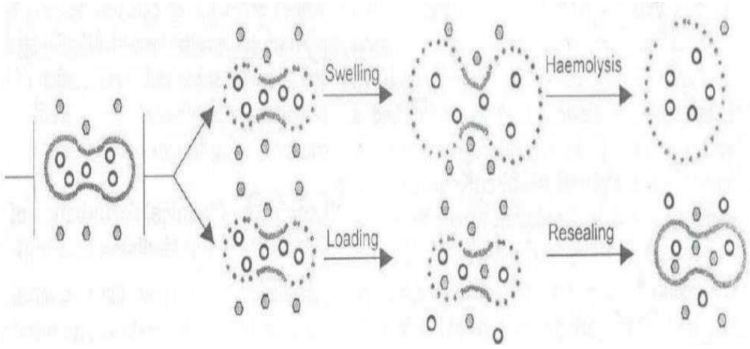

Fig.No.13- Electric cell fusion method.

STORAGE:

The encapsulate d preparation maintained its integrity after being suspended in Hank's balanced salt solution (HBSS) at 40°C for two weeks.
Transfusion batches employing group 'o' (universal donor) cells with the preswell or dialysis procedure.
A regular blood bag can be used for bath encapsulation and storage.

EVALUTION OF RESEALEE:

After the therapeutic drug is loaded onto erythrocytes, the carrier cells are tested physically, cellularly, and biologically.

1. Surface Morphology:

The shape of erythrocytes following injection determines how long they live.

Erythrocytes are morphologically characterised by comparing them to untreated erythrocytes using transmission or scanning electron microscopy
Other techniques, such as phase contrast microscopy, can be employed.

2.Drug Content:

The entrapment efficiency of the procedure is determined by the drug content of the cells.
The process involves deproteinizing packed, loaded cells (0.5ml) with 2.0 ml acetonitrile and centrifugation at 2500 rpm for 10 minutes.
The drug content of the clear supernatant is determined spectrophotometrically.

3.Turbulance fragility:

The passage of cell suspension through needles with a smaller internal diameter (e.g. 30 gauges) or s evere shaking of the cell suspension determines it.
Haemoglobin and medication discharged after the surgery are measured in both circumstances. The resealed cells' turbulent fragility is shown to be increased.

4.Cell Counting and Cell Recovery:

The number of red blood cells per unit volume of whole blood Before and after loading the drug, the number of intact cells per cubic of packed erythrocytes is counted, usually with automated equipment

5.Erythrocyt Sedimentation Rate(ESR):

It's a metric for RBC suspension stability in plasma, and it's linked to cell quantity and size, as well as relative plasma protein concentrations, particularly fibrinogen and globulins.
The rate of sedimentation of blood cells in a standard tube is measured in this test.
A normal blood ESR ranges from 0 to 15 mm/hr; a higher rate indicates active but unidentified illne ss processes.

6.In vitro stability:

The stability of the loaded erythrocytes is determined by incubating the cells in autologous plasma o r an iso-osmotic buffer with a hematocrit of 0.5 to 5% at temperatures ranging from 4°C to 370°C.

7.Osmotic shock:

For the osmotic stress experiment, the erythrocyte solution (1 ml 10% het) was diluted with distilled water (5 ml) and centrifuged for 15 minutes at 3000 rpm.
The percent haemoglobine release in the supernant was estimated using analytical methods.

APPLICATION OF RESEALED ERYTHROCYTE:

1.In-Vitro Application: To aid in the uptake of enzymes in vitro, phagocytosis cells were utilised. A cytochemical approach was used to visualise enzymes within carrier RBC.
Defects like glucose-6-phosphate dehydrogenase (G6PD) deficiency can help researchers figure out what's causing these symptoms.
Micro-injection is the most common in vitro application of RBC.

The fusion method was used to introduce a protein or nucleic acid into eukaryotic cells.

When antibody molecules are delivered by the erythrocytic carrier system, they disperse rapidly throughout the cytoplasm.

2.In-Vivo Application

a)Targeting of bioactive agents to RE System: Damaged erythrocytes in the liver and spleen are quickly removed from circulation by phagocyte Kuffer cells.

By altering the membranes of resealed erythrocytes, they can be used to target the liver and spleen. Surface modification with antibodies, gluteraldehyde, carbohydrates such as sialic acid, and sulphydryl are some of the methods used to change the surface properties of erythrocytes.

b)Targeting to sites as other than RES Organ: The ability of resealed erythrocytes to transport a medication or enzyme to a macrophage-rich environment.

Resealed erythrocytes have lately been used to target organs other than RES. A few representative approaches are briefly examined.

c)Treatment of parasitic diseases: Resealed erythrocytes' ability to selectively accusmulate into RES organs makes them a promising instrument for antiparasitic drug delivery.

This approach can successfully manage parasitic infections that involve parasites being harboured in the RES organs.

Animal trials using erythrocytes laden with antimalarial, antileishmanial, and antiamoebic medicines yielded positive results.

d)Removal of toxic agents: Cannon et colleagues. found that murine carrier erythrocytes containing bovine rhodanase and sodium thiosulfate inhibited cyanide poisoning.

The use of resealed erythrocytes with a recombinant phosphodiestrase to block organ phosphorus poisoning has also been described.

3.Other applications of resealed erythrocytes include :

* Antibody attachment to erythrocyte membrane to get specificity of enzyme action
* Surface adjustment with gluteraldehyde
* Surface adjustment with carbohydrates such as salicylic acid
* Entrapment of paramagnetic particles along with the drug
* Entrapment of photosensitive material
* Antibody attachment to erythrocyte membrane to get specificity of enzyme action * It is used for Delivery of antiviral agents such as azidothymidine, azathioprene, etc.

RECENT DEVELOPMENT :

Nanoerythrosomes are vesicles generated by the ejection of RBC ghost and have an average diameter of 100 nm.

The method produced tiny vesicles around the size of liposomes.

Nanoerythrosomes are spherical particles that appear to be durable and maintain daunorubicin (DNRcytotoxic)'s and anticancer activity in mice with P338-D-cell leukaemia. Antiviral drugs can be manufactured in such a way that they directly reach macrophages.

Erythrosome:

Erythrosomes are specially constructed vesicular structures in which the cytoskeletons of chemically cross-linked human erythrocytes serve as a substrate for a lipid bilayer.

This can be accomplished using a process similar to that used for reverse phase evaporation. Erythrosomes have been proposed as a potential drug delivery encapsulating technology, particularly for macromolecular medicines.

CONCLUSION & FUTURE PERSPECTIVES:

Several applications for the use of resealed erythrocytes as carriers for medications, enzyme replacement treatment, and other therapies have been developed in the last decade.

Resealed erythrocytes technology will remain an active sector for additional study until alternate carrier systems mature.

A newly founded firm that is developing items for human usage is currently testing the commercial medicinal applications of carrier erythrocytes in Europe (Deloach and Way, 1994).

Commercial applications will be investigated in the following years, which will be a vital moment in this subject.

Several therapeutic uses involving red blood cells as drug carriers are predicted to develop in humans in the near future.

Some researchers have shown that such modified red blood cells can be used in blood transfusions.

Initial tests with a variety of cross linking agents have shown promise, but more research is needed with lower concentrations of cross linkers and the encapsulation of a diffusible medicine to thoroughly evaluate the system.

Through its biannual meeting, the International Society for the Use of Resealed Erythrocytes provides an excellent place for scientists in this exciting and satisfying field of research to exchange knowledge.

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