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ROLE OF POLYMERSOMES IN THERAPEUTICS: CURRENT ASPECTS

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Abstract: Nanotechnology has recently received a lot of attention, leading to the development of new methods for medical cures. Nanotechnology is involved in solubilization of drug, targeting of anti-cancer drugs as well as diagnostic applications. Polymersome nanoparticles, which are synthetic amphiphilic vesicles composed of various chemical polymers, are currently being investigated for delivering various probes for imaging target tissues/organs, targeting cytotoxic drugs to tumor cells, and gene therapy. Polymersomes have gained prominence as flexible transporters in recent years due to their colloidal stability, tunable film properties, and ability to move a wide range of medications and particles in the body.

Different polymersomes has been planned and made in the lab for extra opportunities and applications in drug transport, clinical imaging, hardware and nanoreactors.

Polymersomes can be self-assembled from amphiphilic macromolecules and their structural characteristics such as vesicle shape, size, and membrane thickness, their mechanical and transport properties too as their combination conduct can be fluctuated by changing the trial conditions.

The polymersome, due to its amphiphilic nature has the capacity to hold water soluble and insoluble substances (like medications and imaging tests).

In view of this, polymersomes have enormous potential as nanostructured biomaterials for applications such as symptomatic imaging and in vivo medication delivery.

Index Terms -Polymersomes, cancer diagnosis, block copolymer, electroformation, drug delivery

I. INTRODUCTION

Polymersomes are self-assembled vesicles whose building blocks are amphiphilic copolymers. They have a radius that varies from 50 nm to at least 5 µm. Many polymersomes have a watery mass in their centre that can be used to cover and safeguard sensitive to cargo including drugs, catalysts, proteins and peptides, and DNA and RNA fragments. Polymersomes display expanded dependability and diminished porousness as compared to regular liposomes. Properties such as porosity, discharge rates, steadiness can be controlled through controlled engineering.

A variety of naturally decomposing and reactive block copolymers can be used to successfully alter the overall characteristics, medicament epitome, and drug delivery capabilities of polymersomes, which are remarkably responsive and naturally stable structures.

Because of these advantages, polymersomes rank among the most appealing supramolecular structures for potential use in the delivery of therapeutics, diagnostics, and proteins in the rapidly developing fields of nanomedicine and nanobiology.

Polymersomes simulate liposomes in capacity and morphology but have increased stability and reduced permeability (Rideau E, Dimova R, Schwille P, et al,2018)It's interesting to note that using synthetic polymers allows designers to change the membrane's properties, controlling the polymersome's permeability, release rates, stability, and other aspects. (Xiao-ying ,et al,2017)

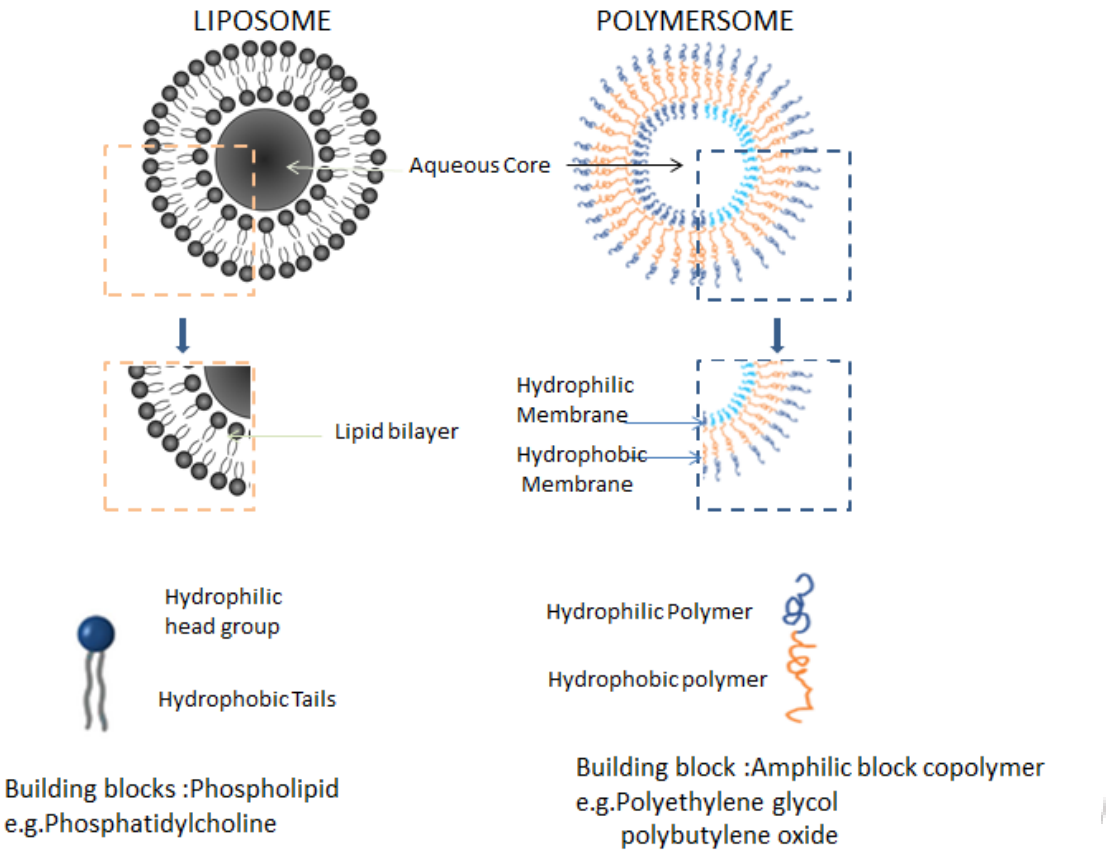

Figure 1. The structural similarities and differences between the liposome and polymerosome

PREPARATION OF POLYMERSOMES

Solvent-free and solvent displacement methods are two main groups into which methods of preparation can be divided. (Lefley, J.,et al,2020)

Solvent free methods

Film rehydration and electroformation, which develop the amphiphilic block copolymers in aqueous solution, are examples of solvent-free processes.

Solution displacement methods

When using solution displacement techniques including direct injection, emulsion phase transfer, and microfluidics, the block copolymers are dissolved using organic solvent. (Wong, C.K.,et al,2019)

Solvent free methods:

1. Film Rehydration

The most popular, cost effective preparation method is rehydration of thin polymer films. An organic solvent is used to dissolve the block copolymer. (Rideau, E., et al,2018) The organic solvent must effectively dissolve both the copolymer's hydrophilic and hydrophobic building units. The solvent is then evaporated from this polymer-solvent mixture by exposing it to the atmosphere on a glass or metal plate. When rehydrated, the polymer layer allow water molecules to pass through and swells. The vesicles separate from the polymer sheet as a result of the expansion caused by polymerosome production (Figure 2). The range of vesicle sizes produced by this method is very wide. Formed polymerosomes are then forced through a filter with predetermined pore widths to reduce the size of the dispersed vesicles. (Sui, X. et al. 2015), (Fetsch, C. et al.2016)

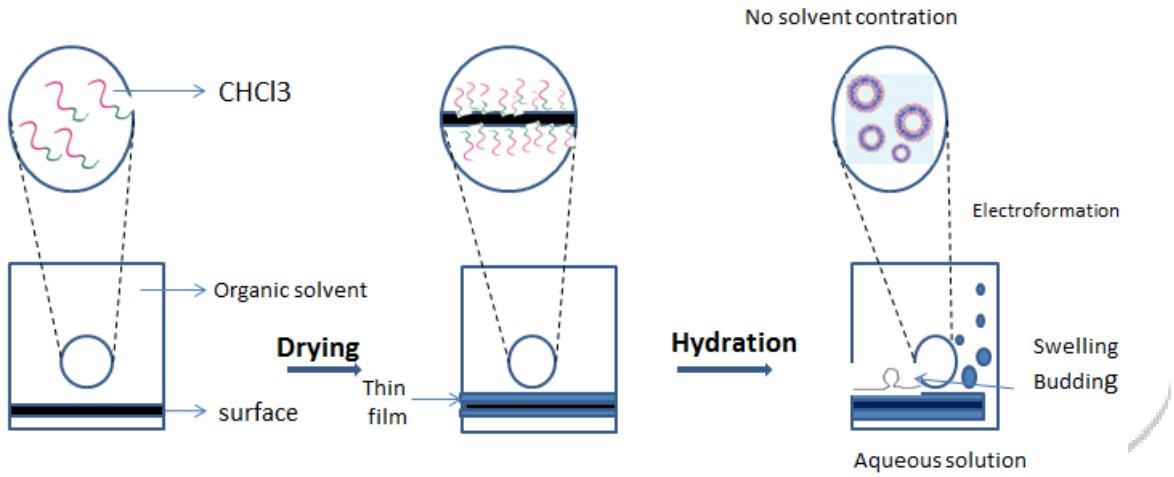

Figure 1. A diagram of the electroformation and film rehydration processes used to create polymersomes .(Rideau, E., et al,2018)

2. Electroformation

Another method of preparation without the use of solvents is electroformation, which uses a supported film rehydration technique. In this case, block copolymers are placed onto indium-titanium oxide (ITO) glass, gold, or platinum anodes. A regulated rotating flow is given to the cathodes, resulting in the formation of a polymeric film. To ensure a precise distribution of polymersome sizes, the amount of vesicle swelling and partition can be adjusted. (E. Ibarboure ,et al 2020).

Solution displacement methods

1. Direct injection

Direct injection based method considers the difference between the polymer's solubilities in a fluid arrangement and in its original soluble state. (K. Vijayakrishna, et al 2009) The block copolymers are dissolved in suitable solvent(s). The polymer solution is then introduced dropwise into an aqueous medium with the help of a syringe and needle assembly. Upon injection of the organic solution into water, the increase in interfacial tension and vigorous agitation leads to precipitation of the hydrophobic polymer in the form of polymerosomes. [E. Rideau et al 2018]

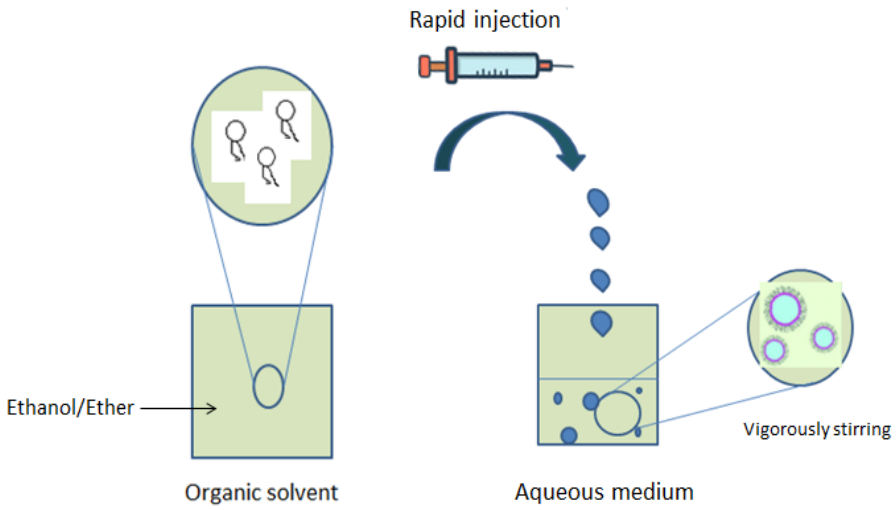

Figure 3. Polymerosomes prepared by direct injection method

2.Emulsion Phase Transfer

Vesicles of the same size are produced via the emulsion phase transfer technique. (M. R. Kim et al,2016) An oil-in-water biphasic system is combined with an emulsion of water-in-oil droplets. A water-in-oil-in-water (w/o/w) double emulsion is created as a consequence. Hydrophobic medications are found in the oil layer, while hydrophilic pharmaceuticals are confined in the watery core. A w/o/w double emulsion is used to stabilize the complete vesicular system.(N. Soomherun, et al 2017)

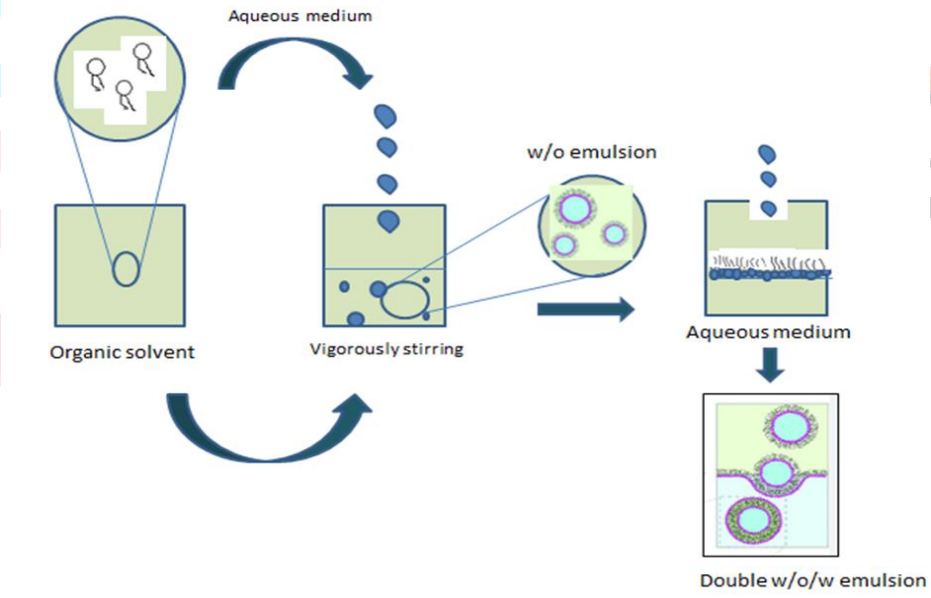

Figure 4. Emulsion Phase transfer method (E. Rideau *et al.*, 2018).

APPLICATIONS

1. POLYMERSOMES FOR CANCER DIAGNOSIS AND THERAPY

Currently i) surgery, ii) radiation therapy and iii) chemotherapy are the three therapeutic approaches used most frequently to treat cancer patients. Surgery is the quickest method, but it has disadvantages, such the inability to finish the entire course of therapy if the tumour is found close to a sensitive location or if it has already developed a metastasis. Radiation therapy, is non selective and damages nearby healthy cells or tissue in addition to the tumor. Chemotherapy prevents the body's cells from growing or kills them if they divide too quickly. However, undesirable side effects are commonly encountered.

The effectiveness of chemotherapeutic agents has recently been enhanced by encapsulating them inside nanocarriers, which prolongs action by preventing renal uptake. The blood arteries that provide blood to tumorous areas are very permeable to macromolecules. These macromolecular substances remain inside the tumour tissue for a long time after entering the tissue. This phenomenon can be enhanced by using polymerosomes as carriers for the anti-cancer drugs. Based on this principle, poly(2-

methacryloyloxyethylphos-phorylcholine)-poly (2-(diisopropylamino)ethyl methacrylate) (PMPC-PDPA) polymerosomes were utilized as carriers for doxorubicin. Doxorubicin was reported to have a strong cytotoxic effect on both healthy and cancerous cells, but when encapsulated it had a preferential effect on melanoma cells indicating that this formulation can be used to achieve an enhanced drug delivery to cancerous cells rather than to the healthy surrounding cells. (Levine DH, et al ,2008)

2.POLYMEROSOMES FOR DRUG DELIVERY

Drug delivery systems that specifically target certain regions within the human body are a challenge for modern researchers. Most presently approved drugs lack a reliable method of focusing on certain tissues or cells. Drugs that target specific areas of the body may be able to lessen or completely eliminate adverse effects and need lower doses, all of which will save costs, improve therapeutic effectiveness, and improve patient compliance. (Meerovich I,et al 2019)

Synthetic liposomes known as polymerosomes have the ability to carry either hydrophilic molecules in the aqueous core or hydrophobic molecules in the membrane bilayer, or a mix of both. These block copolymer vesicles can be used for drug targeting through surface functionalization with ligands for specific cell receptors (e.g., proteins, carbohydrates, or small molecules). Also, controlled drug release can be achieved through the incorporation of stimuli-responsive moieties. Polymersomes are now widely used in several biological applications, including medication administration, gene delivery, protein delivery, imaging, and diagnostics. [Jung Seok Lee,et al,2012]

Applications in both diagnosis and treatment involve functionalized polymersomes. Targeted medication delivery to different organs is one of the applications, with a focus on neurological illnesses, cancer, sensorineural hearing loss, infection and inflammation found in the CNS, brain, tumor cells, cochlea, and macrophages**.** (Collins J, et al 2017)

Simultaneous administration of drugs acting on different targets increases the probability of effective therapy in cancer. However, combination therapy using medications that have different physicochemical properties requires the use of different carriers/solvents and advanced knowledge of formulations. As against this, use of biodegradable polymerosomes for the administration of cocktail of anti-cancer drugs is a simplistic approach to a complex problem. Polymer-based shells were reported to be used to efficiently transport both hydrophobic and hydrophilic medicines, paclitaxel and doxorubicin, respectively to the site of action. The dual medication combination had a higher maximum tolerated dosage than the free drug cocktail and reduced tumors more efficiently and sustainably than the free drug cocktail. (Ahmed, F. et al. 2006)

Block copolymers have been successfully employed to encapsulate gold nanorods and doxorubicin (DOX) to produce nanomaterials with potential use as dual stimuli-sensitive drug delivery systems for combination anticancer therapy. When the pH was lowered7.4 to 5.8, release rate of doxorubicin was increased. Also, when the polymerosomes were irradiated with NIR laser, an increase release rate was reported. (DiazDuarte-Rodriguez, M. et al. 2019)

1. Due to their large drug loading capacity and capacity to transport both hydrophilic and hydrophobic molecules, polymersomes have gained significant interest for use in drug delivery applications. Examples of ligands conjugated onto polymersome surfaces to achieve targeted drug delivery. The ligand receptor and corresponding site of action are noted. (K. Kiene,et al 2017)(Abolfazl Akbarzadeh ,et al 2013)

ligands	Receptor	Target/Pathology
Small molecules		
Vitamin B7	Biotin Receptor	Cancer
Selegiline	Amyloid-beta peptide	Neurodegenerative diseases
Selectin	Activated endothelium	Inflammation
Carbohydrates		
Glucose/Lactose	Protein Receptor	Bioadhesion
Hyaluronan	CD44	Cancer
Antibodies		
OX26	Transferrin Receptor (TfR)	CNS
Epidermal Growth Factor	EGF Receptor	Cancer
Anti Aβ1–42 MAb	Aβ1–42 Peptide	Alzheimer's disease
Peptides and Proteins		
Tet1	Neuronal trisialoganglioside (GT1b) clostridial toxin receptor	Sensorineural Hearing Loss
Lactoferrin (Lf)	Lf Receptor	Brain
Insulin	Insulin Receptor	CNS

SUMMARY AND CONCLUSION

Delivery of drug preferentially to target sites is one of the major objectives of formulation development. In case of therapies that require simultaneous administration of drugs, developing such formulations and ensuring the availability of the drugs at the site of action remains one of the biggest hurdles to be overcome. Polymerosomes are vesicles that can be used to advantage because of their structural complexity that allows them to hold hydrophilic as well as hydrophobic moieties and deliver them to the desired site. Studies in this field have helped to develop a fundamental understanding of the physicochemical properties of polymerosomes and apply this knowledge in the design of targeted dosage forms. A more systematic study

of polymerosomes and their role in targeting as well as diagnostic imaging applications needs to be carried out for establishing conclusive evidence of its potential.

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