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# THERAPEUTIC APPLICATION FOR DRUG DELIVERY USING NEW BIOMIMETIC POLYMERSOMES

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**Abstract:**

*Biomimetics has resulted in a significant increase in advanced particle systems that imitate biological cells. Polymersomes are amphiphilic block copolymers that allow for the controlled release of hydrophilic and hydrophobic drug molecules. The surface modification allows for targeted drug administration, protein transport, medical imaging, nanoreactors, artificial organelles, and biosensors. The self-assembling process and size are affected by factors such as polymer content, temperature, and shear pressures. They provide highly specific and customizable biologic responses with little toxicity, making them a safe and effective delivery option for the future creation of efficient therapeutic vectors.*

**Keywords:** *Polymersomes, cancer drug delivery, vaccine delivery, nucleic acid delivery*

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## INTRODUCTION:

Polymersomes are spherical nanostructured entities having a hollow aqueous compartment encased by a bilayer membrane of synthetic amphiphilic block copolymers, similar to polymer vesicles. Polymersomes, which are made of synthetic polymers rather than natural polymers, are presently being developed to perform some of the same roles as strong viral capsids, such as carrying, targeting, and releasing medications. Then there are liposomes, which are polymersomes with a variety of features that are mostly used in biomedicine and biotechnology. The properties of its membranes can be modified thanks to their high stability and chemical diversity [e.g. selective permeability].

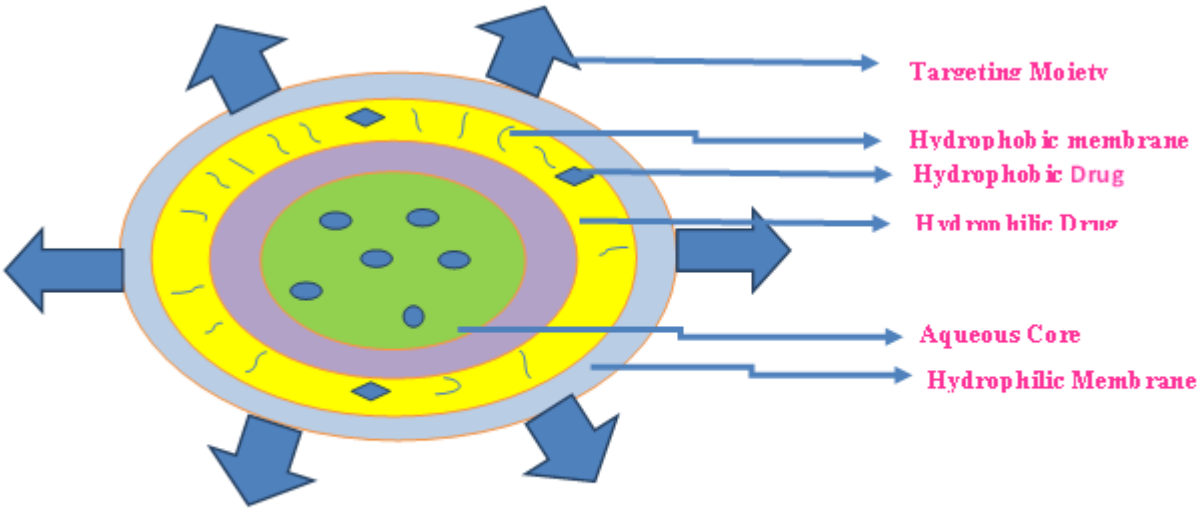


Figure 1: polymerosomes

Because of the increased molecular weight of the amphiphiles and the entangled nature of the copolymers, the critical aggregation concentration of the forming amphiphilic block copolymers is lower[1,2]**.** In practice, this means that the constituent polymers can be chemically modified and functionalized to a much greater extent without compromising their self-assembly capabilities.It also produces stable dispersions that are less prone to fusion and aggregation, which reduces the shelf life of liposomes[3]. Drug delivery, gene therapy, protein delivery, medical imaging, nanoreactors, and artificial organelles are just a few of the applications where their potential has been proved[4,5,6]. Polymersomes [also known as polymeric vesicles] have gained a lot of attention in the last decade because of their similarity to biological compartments, and they've seen a lot of use in medicine and biotechnology, such as medication or gene delivery and nanoreactors.

Polymersome Self-Assembly and Fabrication from Amphiphilic Block Copolymers Polymersomes are nanoscale devices with an aqueous compartment enclosed by a bilayer membrane. They self-assemble from a variety of synthetic amphiphilic block copolymers, such as diblock copolymers[7,8], triblock copolymers, grafted polymers[9], and dendritic polymers, in a dilute aqueous solution[10]. Polymersomes can also be easily created to improve mechanical stability, bestow stimuli responsiveness, or introduce desired functionality due to the chemical diversity of polymers[11,12].

**Need and importance:**

The field of biomimetics has experienced a significant increase in the creation of advanced particle systems, owing to a desire to mimic nature's assemblages using synthetic components. These biomimetic techniques can be used to create particulate systems that imitate the structure of biological cells. Because of their unique sub compartmentalized structure, cells are self-contained living organisms that can undertake complicated chemical reactions and various, connected cellular functions inside spatially defined settings. The main emphasis of this feature article is the creation of multicompartment particle systems, which has been the subject of additional research. Formulating carriers that mimic the compartmentalized structure of biological cells allows for the encapsulation of a wide range of

[bio]molecules that can be spatially confined, as well as the incorporation of stimuli for regulating enzymatic reactions and controlled simultaneous and/or subsequent release of the encapsulated [therapeutic] molecules.

**Therapeutic applications:**
Polymersomes are potential entities for a variety of applications, including drug delivery, gene therapy, protein delivery, medical imaging, nanoreactors, artificial organelles, and biosensors, because they can carry both hydrophilic and hydrophobic loads. Much research has also focused on examining and changing their permeability by introducing channel proteins like OmpF, thereby turning them into simple cell models. [13-16]The following is a brief overview of polymersome uses identified in the literature, as well as some instances.

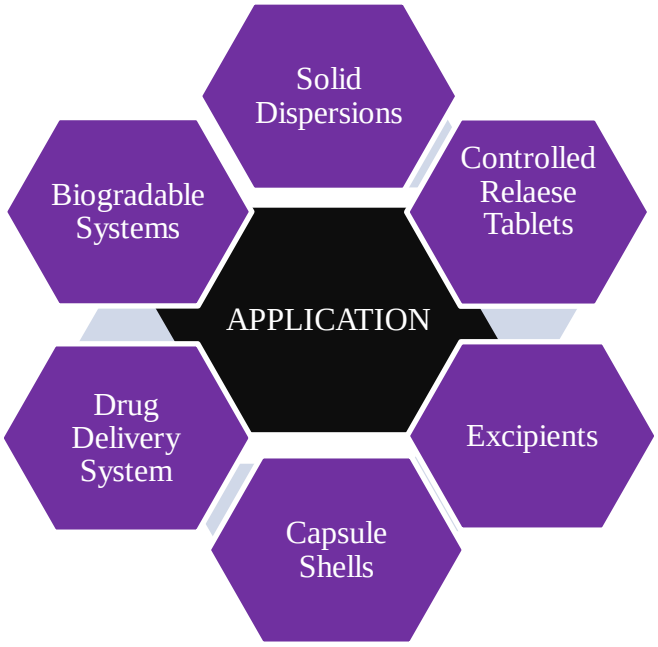


Figure 2: Application of polymerosomes

**Medical applications of polymersomes:**
Various research has proven the potential utility of polymer vesicles for medical applications such as medication administration, gene therapy, and protein delivery. Discher et al., for example, produced polymersomes that can load and deliver functional siRNA and antisense oligonucleotides [AON] into cells. These degradable carriers were generally taken up non-specifically by grown cancer cells, which eventually turned them into micelles, allowing endolysosomal escape and administration of either siRNA into the cytosol for mRNA knockdown or AON into the nucleus for exon skipping within the mRNA[17]. When injected into tumor-bearing animals, biodegradable polymersomes comprised of PEG-PLA loaded with two anticancer medicines, paclitaxel [TAX] in the membrane and doxorubicin [DOX] in the lumen, demonstrated fast shrinkage in the tumors[18-20]. Polymersomes encapsulating fluorescent compounds were produced and researched for optical imaging in diagnostics. When encapsulated inside PBD-PEO polymersomes, Hammer's group created porphyrin-based near-infrared fluorophores that can generate a signal strong enough to penetrate 1 cm of a solid tumor. The near-infrared [NIR]-emissive polymersome may be followed in vivo using non-invasive optical imaging after being injected into the tail vein of mice[21].

**Delivery of cancer drugs:**
Several studies have revealed the anticancer potential of polymersomes in vitro, which has broadened the possibilities of polymersomes for therapeutic protein delivery. Nonspecific dispersion of protein-loaded polymersomes has been avoided in order to increase their delivery to their target region. TNF-encapsulated PEO-b-PBD-based vesicles with a surface decorated with PR-b, an effective 51 targeting peptide, were

created[21]. Galactose-decorated and GrB-loaded chimeric polymersomes made from galactose-b-PEG-b-PCL [Gal-b-PEG-b-PCL], asymmetric PEG-b-PCL-b- poly[2-[diethylamino]ethyl methacrylate] [PEG-b-PCL-b- PDEA], and PEG-SS-PCL for improved intracellular protein delivery[22].

Multi-stimulus-responsive carriers have also been designed to boost the therapeutic potential of polymersomes. In this regard, dual-bio responsive polymersomes were developed for efficient encapsulation and triggered the release of proteins such as fluorescein isothiocyanate [FITC]-labeled BSA [FITC-BSA] and CC [FITC-CC] into cells cytosol, which were highly sensitive to both intracellular pH and reductive environment[23].

**Vaccine distribution:**

Polymersomes' aqueous interior allows for the safe delivery of antigens and adjuvants without the need for chemical modification. Designing innovative adjuvant formulations and antigen delivery systems could help match target recipients' specific demands. Polymersomes offer potential benefits by encapsulating unmodified protein antigens with small molecule adjuvants due to their increased stability and customizable features. The association of antigen with polymersomes as hybrid assemblies was the focus of early research. The antigen immunogenicity of the polypeptide-b-peptide copolymer-based vesicles loaded with influenza hemagglutinin [HA] was improved in vivo, with polymersomes functioning as an adjuvant. Endocytic delivery of antigenic protein or TLR agonist adjuvants into dendritic cells was produced using stimuli-responsive oxidation-sensitive polymersomes based on PEG-b-PPS to generate antigen-specific cell-mediated immune responses[24]. Due to antigen cross-presentation through MHC I, encapsulation and release of the model antigen ovalbumin from these vesicles resulted in activation of splenic dendritic cells [DCs] and priming of OT-I CD8+ T lymphocytes in vitro. The platform's in vivo potential was studied in order to better understand the nature of the immune response[25].

**Nucleic acid delivery:**

The delivery of nucleic acid-based compounds into target cells has been hailed as an innovative illness treatment approach. Polymersomes have piqued interest in this respect because of their empty, hydrophilic inner core for efficient encapsulation, and hydrophobic membrane for greater protection and controlled release, depending on the component polymers. They also allow sensitive payloads to enter cells and be released intracellularly. In recent years, polymersomes have been used to distribute a variety of nucleic acids macromolecules [pDNA, AON, and siRNA] in vitro and in vivo. DNA-polycation polyplexes influenced the first designs of polymeric vesicles for DNA delivery[26]. Poly[amino acid] [poly[AA]-based polymer vesicles produced by covalent modification of poly-L-lysine and poly-L-ornithine with palmitoyl and methoxy PEG [MPEG] were found to be effective in vivo gene delivery vehicles in one study [to lungs and liver][27]. When a galactosamine targeting ligand was attached to PEO chains, increased luciferase expression was seen when pCMVluc was delivered to HepG2 cells[28]. An amphiphilic polymer PEG-b-PEI-b-PA was generated after a similar modification using polyethyleneimine [PEI], which formed vesicles and mediated GFP transgene expression in the liver after intravenous administration[29].

For effective encapsulation and delivery of siRNA, polymer vesicles made of peptide-functionalized PBD-b- PEO were reported[30]. Simultaneous delivery of multiple therapeutics is a successful technique for overcoming the limitations of single therapeutic delivery platforms. Polymersomes [CPSomes] based on diblock copolymer [MPEG-b-PLA] were created and explored for code delivery of Bcl-xL siRNA and doxorubicin [DOX][31]. Polymersomes based on the triblock copolymer PEO-b-poly[2-[diisopropylamine]- ethyl methacrylate]-block-poly[acrylic acid] [PEO-b-PDPA-b- PAA] were able to deliver anticancer drug [doxorubicin]and siRNA [FITC-siRNA] to overcome self-renewal and tumor producing capabilities of CSCs by decreasing expression of cell promoting oncogene miR-429. pH-responsive diblock copoly- peptide-based vesicles were also reported for codelivery of chemotherapeutic drugs and siRNA[32].

## CONCLUSION:

The following criteria are envisioned for an ideal nanocarrier for efficient delivery of macromolecules to cells:

a) deliver the macromolecule in an inactive conformation
b) provide sufficient protection from harsh environments encountered in vivo, such as degradation by proteases and nucleases during circulation
c) demonstrate limited toxicity to cells
d) accumulate and deliver the therapeutic at the target site
e) enable efficient escape from endo/endo/endo/endo/endo/end Extensive research and significant advancements in building

polymeric vesicles for intracellular delivery of protein and nucleic acid macromolecules have occurred over the last decade.

Highly specific delivery to target cells is required for therapeutic effectiveness. Although various studies have addressed these elements individually or in combination in recent years, achieving all of these characteristics in a single formulation remains an unattainable aim. To that end, more effort should be put into developing carriers using repeatable formulation methods, fully biocompatible polymers, developing nonspherical polymersomes, designing and developing hybrid polymer/lipid vesicles, understanding biological fate, leveraging techniques for endosomal escape and biological interactions, and resolving clinical trial challenges.

The accompanying safety difficulties and additional intracellular barrier of nuclear entrance for DNA-based vesicles must be properly examined and overcome. We feel that cytotoxicity, drug loading efficiency, and long-term stability of polymersomes must be thoroughly explored and understood before they may be used in pharmaceuticals in the future. New ways for producing polymersomes on an industrial scale that are simple and cost-effective must also be investigated.

## BIBLIOGRAPHY:


1. Tanner, P., Baumann, P., Enea, R., Onaca, O., Palivan, C., & Meier, W. [2011]. Polymeric vesicles: from drug carriers to nanoreactors and artificial organelles. *Accounts of chemical research*, *44*[10], 1039-1049.
2. Taubert, A., Napoli, A., & Meier, W. [2004]. Self-assembly of reactive amphiphilic block copolymers as mimetics for biological membranes. *Current opinion in chemical biology*, *8*[6], 598-603.
3. Discher, D. E., & Eisenberg, A. [2002]. Polymer vesicles. *Science*, *297*[5583], 967-973.
4. Meng, F., Zhong, Z., & Feijen, J. [2009]. Stimuli-responsive polymersomes for programmed drug delivery. *Biomacromolecules*, *10*[2], 197-209.
5. Blanazs, A., Armes, S. P., & Ryan, A. J. [2009]. Self-assembled block copolymer aggregates: from micelles to vesicles and their biological applications. *Macromolecular rapid communications*, *30*[4-5], 267-277.
6. Massignani, M.; Lomas, H.; Battaglia, G., Polymersomes: A Synthetic Biological Approach to Encapsulation and Delivery, Adv. Polym. Sci., **2010**, 229, 115-154.
7. Van Dongen, S. F., Nallani, M., Schoffelen, S., Cornelissen, J. J., Nolte, R. J., & van Hest, J. C. [2008]. A block copolymer for functionalization of polymersome surfaces. *Macromolecular rapid communications*, *29*[4], 321-325.
8. Meng, F., Zhong, Z., & Feijen, J. [2009]. Stimuli-responsive polymersomes for programmed drug delivery. *Biomacromolecules*, *10*[2], 197-209.
9. Discher, B. M.; Won, Y. –Y.; Ege, D. S.; Lee, J. C. –M.; Bates, F. S.; Discher, D. E.; Hammer, D. A., Polymersomes: Tough Vesicles Made from Diblock Copolymers, Science, **1999**, 284, 1143-1146.
10. Lee, H. J.; Yang, S. R.; An, E. J.; and Kim, J. –D., Biodegradable Polymersomes from Poly[2-hydroxyethyl aspartame] Grafted with Lactic Acid Oligomers in Aqueous Solution, Macromolecules, **2006**, 39, 4938-4940.
11. Discher, D. E., & Ahmed, F. [2006]. Polymersomes. *Annu. Rev. Biomed. Eng.*, *8*, 323-341.
12. Meng, F., Engbers, G. H., & Feijen, J. [2005]. Biodegradable polymersomes as a basis for artificial cells: encapsulation, release, and targeting. *Journal of Controlled Release*, *101*[1-3], 187-198.
13. Onaca, O., Nallani, M., Ihle, S., Schenk, A., & Schwaneberg, U. [2006]. Functionalized nano compartments [Synthosomes]: Limitations and prospective applications in industrial biotechnology. *Biotechnology Journal: Healthcare Nutrition Technology*, *1*[7-8], 795-805.
14. Malinova, V., Belegrinou, S., Bruyn Ouboter, D. D., & Meier, W. P. [2009]. Biomimetic block copolymer membranes. *Polymer membranes/biomembranes*, 87-111.
15. Nallani, M., Benito, S., Onaca, O., Graff, A., Lindemann, M., Winterhalter, M., ... & Schwaneberg, U. [2006]. A nanocompartment system [synthosome] designed for biotechnological applications. *Journal of Biotechnology*, *123*[1], 50-59.
16. Nardin, C., Widmer, J., Winterhalter, M., & Meier, W. [2001]. Amphiphilic block copolymer nanocontainers as bioreactors. *The European Physical Journal E*, *4*[4], 403-410.
17. Kim, Y., Tewari, M., Pajerowski, J. D., Cai, S., Sen, S., Williams, J., ... & Discher, D. E. [2009]. Polymersome delivery of siRNA and antisense oligonucleotides. *Journal of Controlled Release*, *134*[2], 132-140.
18. Ahmed, F., Pakunlu, R. I., Brannan, A., Bates, F., Minko, T., & Discher, D. E. [2006]. Biodegradable polymersomes loaded with both

paclitaxel and doxorubicin permeate and shrink tumors, inducing apoptosis in proportion to the accumulated drug. *Journal of Controlled Release*, *116*[2], 150-158.

19. Ahmed, F., Pakunlu, R. I., Srinivas, G., Brannan, A., Bates, F., Klein, M. L., ... & Discher, D. E. [2006]. Shrinkage of a rapidly growing tumor by drug-loaded polymersomes: pH-triggered release through copolymer degradation. *Molecular Pharmaceutics*, *3*[3], 340-350.
20. Discher, D. E., Ortiz, V., Srinivas, G., Klein, M. L., Kim, Y., Christian, D., ... & Ahmed, F. [2007]. Emerging applications of polymersomes in delivery: From molecular dynamics to shrinkage of tumors. *Progress in polymer science*, *32*[8-9], 838-857.
21. Levine, D. H., Ghoroghchian, P. P., Freudenberg, J., Zhang, G., Therien, M. J., Greene, M. I., ... & Murali, R. [2008]. Polymersomes: a new multi-functional tool for cancer diagnosis and therapy. *Methods*, *46*[1], 25-32.
22. Wang, X., Sun, H., Meng, F., Cheng, R., Deng, C., & Zhong, Z. [2013]. Galactose-decorated reduction-sensitive degradable chimeric polymersomes as a multifunctional nanocarrier to efficiently chaperone apoptotic proteins into hepatoma cells. *Biomacromolecules*, *14*[8], 2873-288.
23. Zhang, J., Wu, L., Meng, F., Wang, Z., Deng, C., Liu, H., & Zhong, Z. [2012]. pH and reduction of dual-bioresponsive polymersomes for efficient intracellular protein delivery. *Langmuir*, *28*[4], 2056-2065.
24. Scott, E. A., Stano, A., Gillard, M., Maio-Liu, A. C., Swartz, M. A., & Hubbell, J. A. [2012]. Dendritic cell activation and T cell priming with adjuvant-and antigen-loaded oxidation-sensitive polymersomes. *Biomaterials*, *33*[26], 6211-6219.
25. Stano, A., Scott, E. A., Dane, K. Y., Swartz, M. A., & Hubbell, J. A. [2013]. Tunable T cell immunity towards a protein antigen using polymersomes vs. solid-core nanoparticles. *Biomaterials*, *34*[17], 4339-4346.
26. Arigita, C., Zuidam, N. J., Crommelin, D. J., & Hennink, W. E. [1999]. Association and dissociation characteristics of polymer/DNA complexes used for gene delivery. *Pharmaceutical Research*, *16*[10], 1534-1541.
27. Brown, M. D., Schätzlein, A., Brownlie, A., Jack, V., Wang, W., Tetley, L., ... & Uchegbu, I. F. [2000]. Preliminary characterization of novel amino acid-based polymeric vesicles as gene and drug delivery agents. *Bioconjugate Chemistry*, *11*[6], 880-891.
28. Brown, M. D., Gray, A. I., Tetley, L., Santovena, A., Rene, J., Schätzlein, A. G., & Uchegbu, I. F. [2003]. In vitro and in vivo gene transfer with poly [amino acid] vesicles. *Journal of controlled release*, *93*[2], 193-211.
29. Brownlie, A., Uchegbu, I. F., & Schätzlein, A. G. [2004]. PEI-based vesicle-polymer hybrid gene delivery system with improved biocompatibility. *International journal of pharmaceutics*, *274*[1-2], 41-52.
30. Pangburn, T. O., Georgiou, K., Bates, F. S., & Kokkoli, E. [2012]. Targeted polymersome delivery of siRNA induces cell death of breast cancer cells dependent upon Orai3 protein expression. *Langmuir*, *28*[35], 12816-12830.
31. Kim, H. O., Kim, E., An, Y., Choi, J., Jang, E., Choi, E. B., ... & Haam, S. [2013]. A biodegradable polymersome containing Bcl-xL siRNA and doxorubicin as a dual delivery vehicle for a synergistic anticancer effect. *Macromolecular bioscience*, *13*[6], 745-754.
32. Li, Z., Li, J., Huang, J., Zhang, J., Cheng, D., & Shuai, X. [2015]. Synthesis and Characterization of pH-Responsive Copolypeptides Vesicles for siRNA and Chemotherapeutic Drug Co-Delivery. *Macromolecular bioscience*, *15*[11], 1497-1506.