CRIMSON PUBLISHERS
Wings to the Research

Research & Development in Material Science

ISSN: 2576-8840

Mini Review

Supramolecular Gel-Based Pluronic-Cyclodextrin Inclusion Nano-Micelles Engineered for Targeted Drug Delivery

Dhruvi Patel[1], Manjusha BS[2] and Ketan K[1]*

[1]*Applied Chemistry Department, India*

[2]*Department of Applied Science, India*

***Corresponding author:** Ketan K, Applied Chemistry Department, India

Submission: November 06, 2018; **Published:** November 30, 2018

Abstract

Cyclodextrins (CDs) are studied extensively as drug delivery carriers through "host–guest" interactions and have gain huge research attraction. In addition, CDs based self-assembled poly-pseudo rotaxane (PPRTx) in Pluronic's® solutions containing CDs has captured an eye for the researchers to develop supramolecular biomaterials by improving the solubility and stability of drugs in aqueous and gel medium by Pluronic's®-CDs inclusion complexation.

Keywords: Supramolecular; Pluronic's®, Cyclodextrins (CDs), Inclusion complex; Gelation

Introduction

Block copolymer sequences based on poly (ethylene oxide)-poly (propylene oxide)-poly (ethylene oxide) (PEO–PPO-PEO) are commercially available triblock copolymers with the following trade names: Pluronic's® or Poloxamer. It consists of two or more distinct chains (or blocks) that are covalently linked together (Figure 1a). This system exhibits a sol-gel transition below or close to the physiological temperature which may be due to the 3-dimensional packing of the micelles due to the hydrophilic-hydrophobic balance (HLB), increasing micellar volume and provoking micelle packaging during gelation. However, this balance can be modulated by incorporating the side chains with hydrophilic/hydrophobic segments. Amongst several known Pluronic's®, F-127 is a non-toxic PEO-PPO-PEO based surface- active block polymer (average molecular weight of 11500g/mol). It has been FDA and EPA approved and so is used widely as food additives, drug delivery carriers, in pharmaceuticals, tissue engineering processes, etc. Thermo-reversible gelation is one of the significant characteristics of this compound in aqueous solutions, i.e. it exhibits gelation above 18% at 4-5 °C and remains highly clear viscous gels at room temperature. This aqueous transparent gel is typically used in drug delivery systems, in treatment of burns/wound healing applications [1,2]. These amphiphilic Pluronic's® aggregate to form micelles at the critical micelle concentration (CMC) in an aqueous solution where the hydrophobic chains tend to collapse, while the hydrophilic chain show affinity towards solvent and gets solvated. Here at a very low concentrations, the block copolymers exist as individual micelles or unimers. When the CMC exceeds, these unimers undergo aggregation to form micelles where the insoluble core-domain gets surrounded by a soluble "corona" or "shell" better known as spherical "core-shell" micelle (Figure 1b). As the two blocks PEO and PPO in Pluronic's® are incompatible with one another, they undergo phase segregation, thereby forming a wide range of nanostructure assemblies with intricate morphologies. In addition to the typical and preliminary spherical micelles in Pluronic's®, vesicles have grabbed significant attention due to their hollow structures in drug delivery applications.

However, such self-assemblies rely on the co-operation of van der Waals, electrostatic, hydrogen bonding, and hydrophobic interactions [3,4]. Studies have shown a fascinating type of self-assembly process as "host-guest" interactions class of materials: cyclodextrins (CDs). CDs are cyclic oligosaccharides consisting of six, seven, or eight glucopyranose units (α, β, and γ-CDs) linked by 1,4-R-glycosidic bonds (Figure 2). Considering the terminal hydrolysis–triggered drug incorporation into the CDs cavity, β-CD is much preferable amongst its several units because the size of β-CDs is suitable for drug molecules. They are all characterized by a toroidal shape with a hydrophobic cavity which imparts them the ability to form inclusion complexes through non-covalent interactions with a variety of molecular guests that can fit into their cavity or could be threaded onto long polymeric chains, forming so-called "(pseudo)-polytrioxanes (PRTx)". The hydrophilicity of the outer rims and the relative hydrophobicity inside the cavities render CDs

to form stable inclusion complexes in presence of organic additives (flavours, pigments, vitamins and drugs). This CDs have been extensively used due to their high improving and enhancing drug solubility characteristics and controlling drug release profiles. Thus, these supramolecular structures have been extensively explored as Nano-scale molecular devices in the biomedical field to encapsulate drugs, in gene delivery and their reversible thermal gelation [5,6].

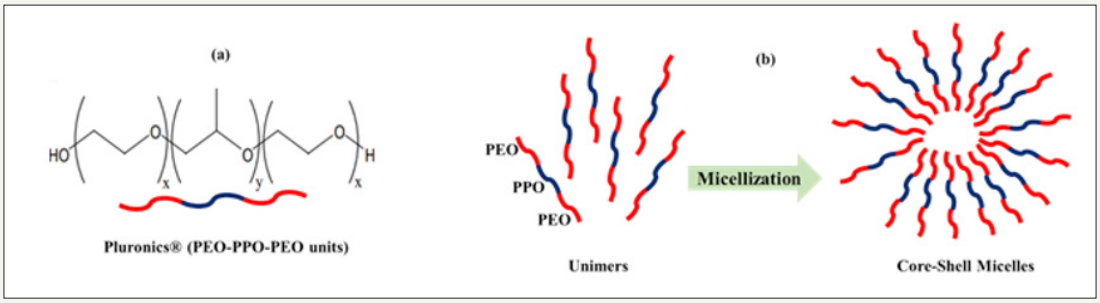

Figure 1:

1a: Chemical structure

1b: Micellization phenomenon in Pluronic's®.

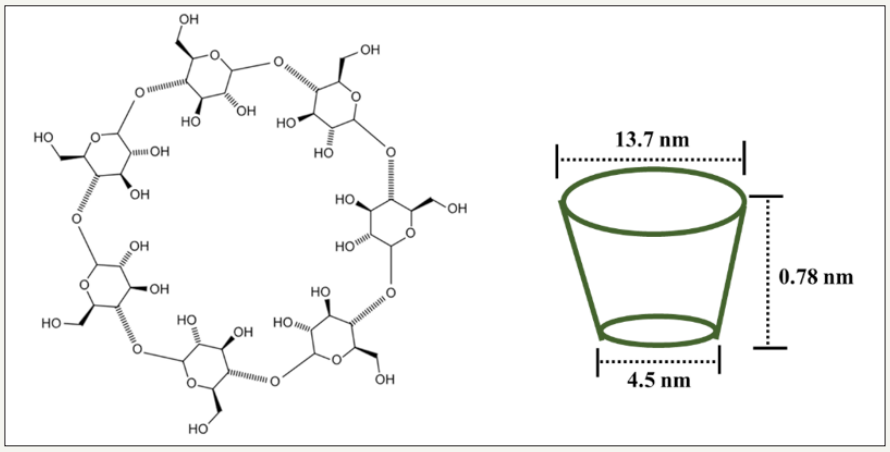

Figure 2: Chemical structure of β-CDs.

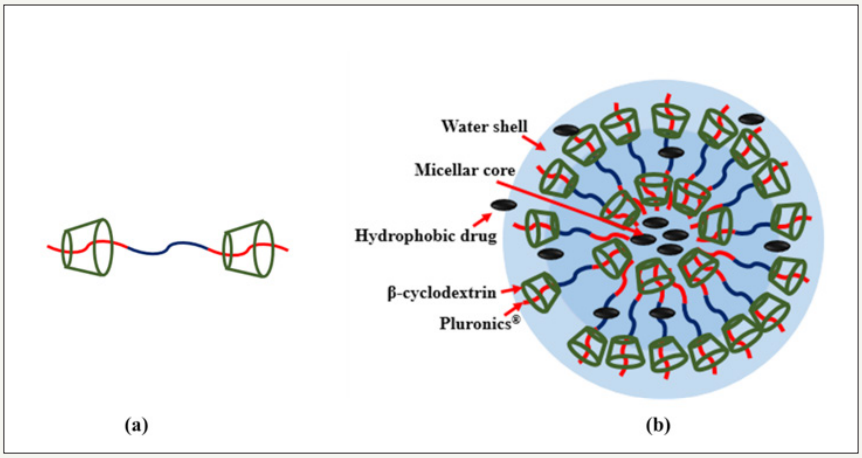

Figure 3: Pseudo-polytrioxanes (PRTx) supramolecular assemblies leading to Pluronic's®-CDs inclusion complexation.

CDs based PRTx derivatives are well reported where the polymeric cores could be polyesters, polyamides, poly (ethylene glycol) (PEG), poly (propylene glycol) (PPG), and many di- and triblock copolymers (Figure 3). Studies have shown the hydrophobic inter-

How to cite this article: Dhruvi P, Manjusha BS, Ketan K. Supramolecular Gel-Based Pluronic-Cyclodextrin Inclusion Nano-Micelles Engineered for Targeted Drug Delivery. Res Dev Material Sci . 9(2). RDMS.000707.2018. DOI: 10.31031/RDMS.2018.09.000707

action between these polymers and CDs cavities, hydrogen-bonding among the rims of the neighbouring CDs on the same polymer chain as the driving forces resulting in various nano-structures self-assemblies like growing micelle, hollow sphere, rod-like and platelet structures [6-8]. Poly (ethylene oxide) (PEO) chains enhance the drug solubility in water. It is biocompatible and the PEO chains with low molecular weight possess excellent flexibility, while those with high molecular weight are rigid. Moreover, the resultant PEO hydrogels formed are extensively researched as drug delivery vehicles. Recent studies have shown a great emphasis of CDs/PEO-based PRTx as they led to interesting micellar architectures widely applicable in the biomaterials field. Such evolution of the fine structures of self-assembled PRTx in Pluronic's® (F108) solutions containing dilute to highly concentrated β-CDs was first illustrated by Kuo shih et al. [8] Cecile et al investigated the associative structures formed by the complexation of various β-CDs derivatives to encapsulate the local anaesthetics in F127 micelles [9]. Jie Qin concluded the strategy for fabricating hollow spheres by supramolecular inclusion forming coil–rod complexes [10]. Tarimci N has shown the improvement in the solubility and stability of drug in aqueous typical dosage environment employed in the derivative of β-CDs (2-hydroxypropyl-β-cyclodextrin) [11]. Dreiss et al. [5] showed the interaction of heptakis (2,6-di-O-methyl)-β-cyclodextrin (DIMEB) with Pluronic's® F127 in solutions above the CMC leading to its complete disruption in the polymeric micelles. Perry et al. [11] reported the kinetics and structural observations of the self-assembly behaviour in inclusion of Pluronic's® F-68 and native β-CD in water. Collins J et al. [12] used Pluronic's® based β-CDs PRTx for treatment of Niemann-Pick Type C (NPC) disease. Marin et al. [13] attempted to deliver Doxorubicin (DOX) drug in Pluronic's® micelles and showed the effect of high-frequency ultrasound on drug release from micelles and intracellular uptake. Valero et al. [5] inferred the competitive and synergistic interactions between polymer micelles, drugs and CDs and noted the importance of drug solubilization locus.

Conclusion

Biomaterials based on CDs and Pluronic's® have received an increasing attention in recent years for controlled drug delivery due to their ability to form inclusion complexes and hydrogels (gelation) as these supramolecular structures can optimize and tune their performance as biocompatibility, flexibility, and stability. CDs as individualized components is undoubtedly paving an advantageous option to the clinical trials in therapeutics. Knowledge about the stability of these supramolecular entities after drug administration and their performance regarding drug targeting and release is thus becoming mandatory for the correct designing of CDs-based carriers using Pluronic's®-CDs inclusion complexes. Thus, the involved "host-guest" interactions in Pluronic's®-CDs is opening an unexpectedly wide range of advanced biomedical applications.

References

1. Arimci N, Kilin T, Ermis D (1996) The effect of 2-hydroxypropyl-β-cyclodextrin on release of naproxen from pluronic F-127 gel. Proceedings of the Eighth International Symposium on Cyclodextrans, Kluwer Academic Publishers, USA, pp. 453-456.
2. Aguilar M, Elvira C, Gallardo A, Vázquez B, Román J (2007) Smart polymers and their applications as biomaterials topics in Tissue Engineering. Biomaterials 3(1): 1-27.
3. Zheng Y, Wyman I (2016) Supramolecular nanostructures based on cyclodextrin and poly (ethylene oxide): syntheses, structural characterizations and applications for drug delivery. Polymers 8(5): 198-204.
4. Simões S, Rey RA, Concheiro A, Alvarez LC (2015) Supramolecular cyclodextrin-based drug nanocarriers. Chem Commun (Camb) 51(29): 6275-6289
5. Castiglione F, Valero M, Dreiss C, Mele A (2011) Selective interaction of 2,6-di-o-methyl-β-cyclodextrin and pluronic F127 micelles leading to micellar rupture: a nuclear magnetic resonance study. J Phys Chem B 115(29): 9005-9013.
6. Valero M, Castiglione F, Mele A, Silva M, Grillo I, et al. (2016) Competitive and Synergistic interactions between polymer micelles, drugs, and cyclodextrins: the importance of drug solubilization locus. Langmuir 32(49): 13174-13186.
7. Collins C, Cauliff L, Hyun S, Zhang Z, Paul L, et al. (2013) Synthesis, characterization, and evaluation of pluronic-based β-cyclodextrin polyrotaxanes for mobilization of accumulated cholesterol from niemann-pick type c fibroblasts. Biochemistry 52(19): 3242-3253.
8. Shih K, Li C, Li W, Lai H (2014) Fine structures of self-assembled beta cyclodextrin/pluronic in dilute and dense systems: a small angle X-ray scattering study. Soft Matter 10 (38): 7606-7614.
9. Dreiss C, Nwabunwanne E, Liu R, Brooks N (2009) Assembling and de-assembling micelles: competitive interactions of cyclodextrins and drugs with Pluronics. Soft Matter 5(9): 888-1896.
10. Qin J, Meng X, Li B, Ha W, Yu X, et al. (2010) Self-assembly of β-cyclodextrin and pluronic into hollow nano-spheres in aqueous solution. J Colloid and Interface Science 350(2): 447-452.
11. Perry C, Hebraud P, Gernigon V, Brochon C, Lapp A, et al. (2011) Pluronic and β-cyclodextrin in water from swollen micelles to self-assembled crystalline platelets. Soft Matter 7(7): 3502-3512.
12. Collins C, Loren B, Alam M, Mondjinou Y, Skulsky J, et al. (2017) pluronic based β-cyclodextrin polyrotaxanes for treatment of niemann-pick type c disease. Scientific Reports 7: 46737-46750.
13. Marin A, Sun H, Husseini G, Pitt W, Christensen D, et al. (2002) Drug delivery in pluronic micelles: effect of high-frequency ultrasound on drug release from micelles and intracellular uptake. J Controlled Release 84(1-2): 39-47.