General Introduction

1.1: Block Copolymers (BCs)

Block copolymers have engaged in research with a promising role in the advanced development of polymer science with numerous pivotal contributions. BCs are the class of smart materials technologically exploits in a myriad of ways in the fields of chemistry, physics, material sciences, and biological sciences including medical sciences [1-6]. With fascinating features, research on BCs has long been a popular topic worldwide. Fig.1.1 shows the number of research publications at *Web of Science* with the topic "*block copolymer*" since the year 1990.

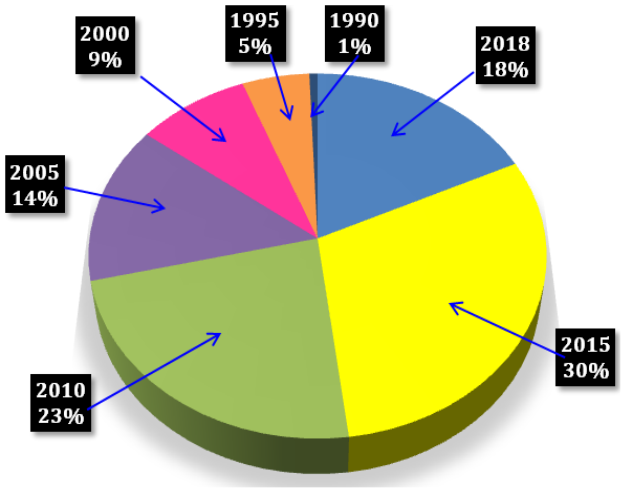

Fig.1.1: The number of publications with block copolymer as topic against year. The data were obtained from the Web of Science (2018 Clarivate Analytics)

Not only in the academic interest, but the scope of applications for BCs has been expanding to the various important fields of advanced materials, drug delivery, patterning, porous materials, etc over the last twenty years [7]. Advanced materials like thermoplastic elastomers showed great advantage of the combination of rubbery segments and rigid segments within BCs. The encapsulation of drug and delivery at target are well facilitated by the amphiphilic nature of BCs in solutions. Various nanoscale morphologies induced by self-assembly of BCs found the applications in soft lithography and synthesis of porous materials [8].

The block copolymer is a polymer consisting of multiple sequences, or blocks, of the same monomer alternating in series with different monomer blocks. The monomer blocks are covalently linked to each other. BCs are classified according to the number of blocks present and its arrangement in the Structure of BC structure. For example, BCs with two blocks are known as diblock copolymers AB; those with three blocks are triblock copolymers and those with more than three blocks are called segmented or multi-block copolymers. Nonlinear BCs are often called star-block copolymers. The various types of BCs are schematically represented in Fig.1.2.

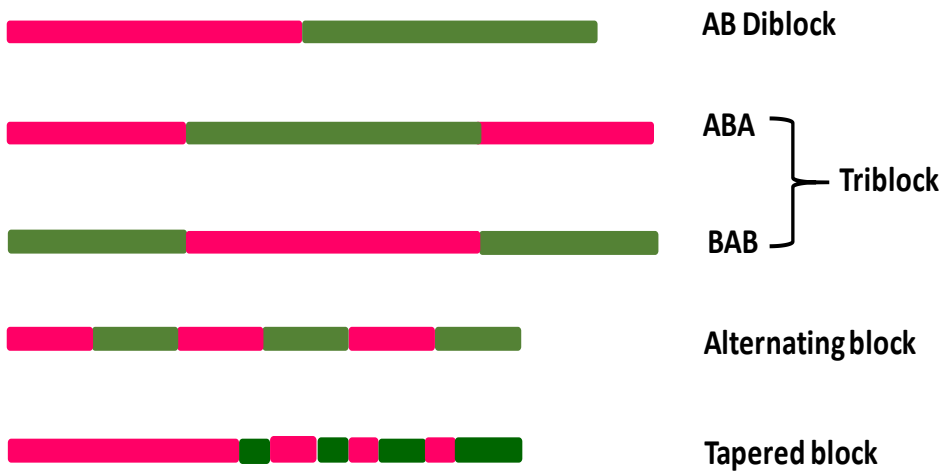

Fig.1.2: Types of block copolymers

As BCs are a specific class of copolymers in which distinct monomers are chemically joined in discrete blocks along the polymer chain and arranged with different architectures [9], Fig.1.3 shows the linear, branched (graft and star), and cyclic molecular architectures.

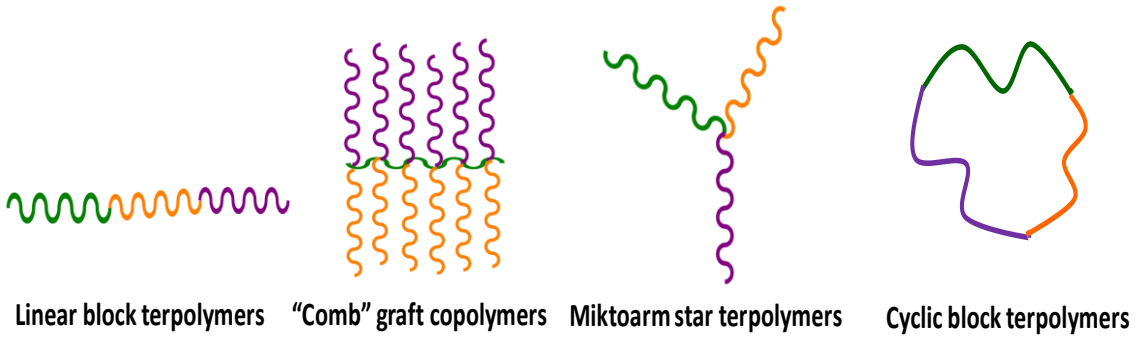

Fig.1.3: Linear, branched and cyclic molecular architectures of block copolymers

The unique structural architecture by two different blocks in BCs makes them behave like amphiphiles or surface active agents (Surfactants). It means that they are self-assembles into the medium.

1.2: Self-assembly of Block copolymers (BCs)

Self- assembly of BCs is a very broad and active area. In a selective solvent, i.e., good for one block and poor for the other block, BCs assemble to form stable aggregates/micelles with a variety of structures. BCs with hydrophilic and hydrophobic blocks behave like amphiphiles and form micelles in water similar to conventional surfactants with some unique characteristics. As seen in Fig.1.2, the hydrophilic (A) and hydrophobic (B) blocks can be from different monomers as AB diblock, ABA and BAB triblock and even star and radial BCs. For ABC triblock copolymers, any two blocks can be hydrophilic or hydrophobic. Thus, depending on molecular characteristics/structure/ type of block copolymer and solution conditions, aggregates with different morphologies like spherical (S), cylindrical (C), gyroid (G) and lamellar (L) can be produced [10-13].

Fig.1.4 shows that the different morphologies of a typical linear diblock copolymer evolve from spherical to lamellar and can undergo disorder to order transitions, as a function of the composition of blocks (f) and the number of repeating units (N) in the bulk. In the figure, the S & S' = body-centered cubic spheres, C & C' = hexagonally packed cylinders, G & G' = bicontinuous gyroids, and L = lamellae in the shape.

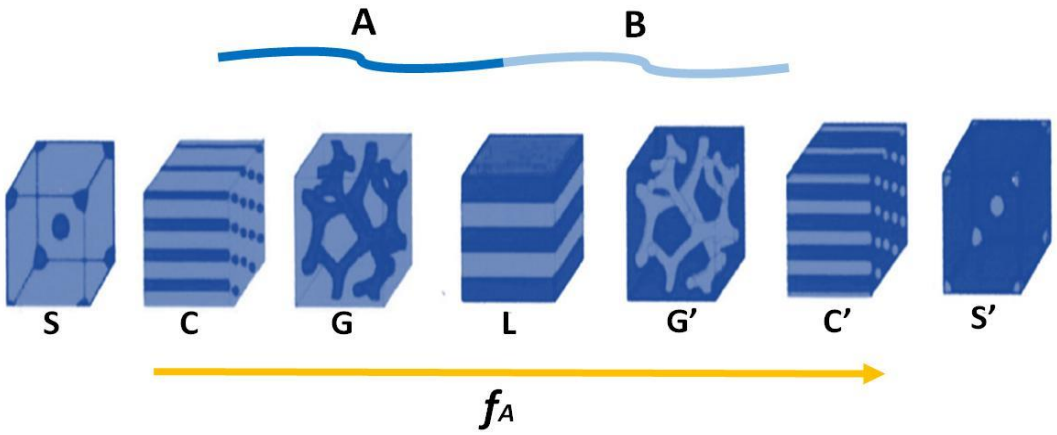

Fig.1.4: Morphologies of diblock copolymers in bulk.

The self-assembly of amphiphilic BCs has been a popular subject to research in the areas of nano-cargo delivery, biomedical/pharmaceutics, and nanotechnology [14-16]. Although the self-assembly of amphiphilic BCs is also driven by the minimization of free energy in the system. Self-assembly of BCs in dilute solution is quite complicated than self-assembly in bulk. The morphologies of self-assembled structures like micelles are determined by the chain packing parameter (CPP).

The formula of calculation for CPP is $\mathbf{P = V / a_0 l_c}$, where V is the volume of the hydrophobic part, a_0 is the optimal area of the hydrophilic part, and l_c is the length of the hydrophobic tail [7, 14].

Fig.1.5 represents the schematic presentation of nanostructures of BCs due to the inherent curvature of the polymer chain.

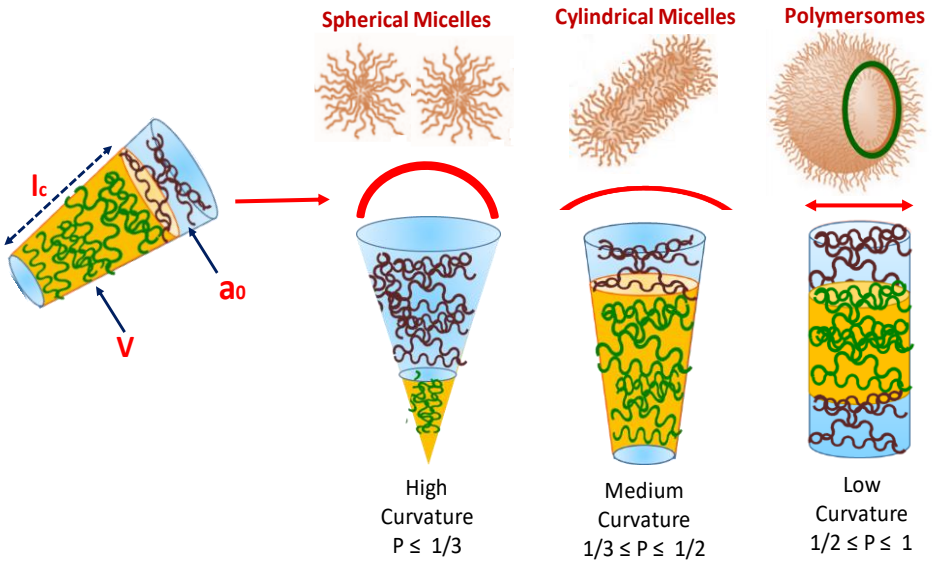

***Fig. 1.5: Types of Block copolymer micelles due to the inherent curvature of the polymer chains, as estimated by CPP* [7].**

When polymers aggregate with each other, they tend to form monolayers that have curvature allowing the most efficient packing of the molecules. To understsnd such packing of Polymer molecules,the CPP is calculated. The CPP is less than 1/3 when spherical micelles are formed, It lies in-between 1/3 and 1/2 than wormlike micelles and with CPP between 1/2 and 1 showing vesicles, and lamellar or bilayer structure at CPP is 1.

By controlling the factors responsible to change the CPP such as BC composition and concentration, water content, common solvent, and additives, a wide range of morphologies have been obtained [17, 18].

By definition, amphiphilic BCs consist of hydrophilic (water-loving) and hydrophobic (water-hating) polymer blocks. As the most common solvent, water is a selective solvent for hydrophilic block and above critical micelle concentration (cmc) the hydrophobic effect of hydrophobic blocks drives the self-assembled of BCs in an aqueous media, producing core-shell structure known as micelles. Block copolymeric micelle consists of two regions: an inside region of hydrophobic polymer chains (core region) and an outer region of well-hydrated hydrophilic polymer chains (corona/shell region), which imparts good colloidal stability in the medium (Fig.1.6).

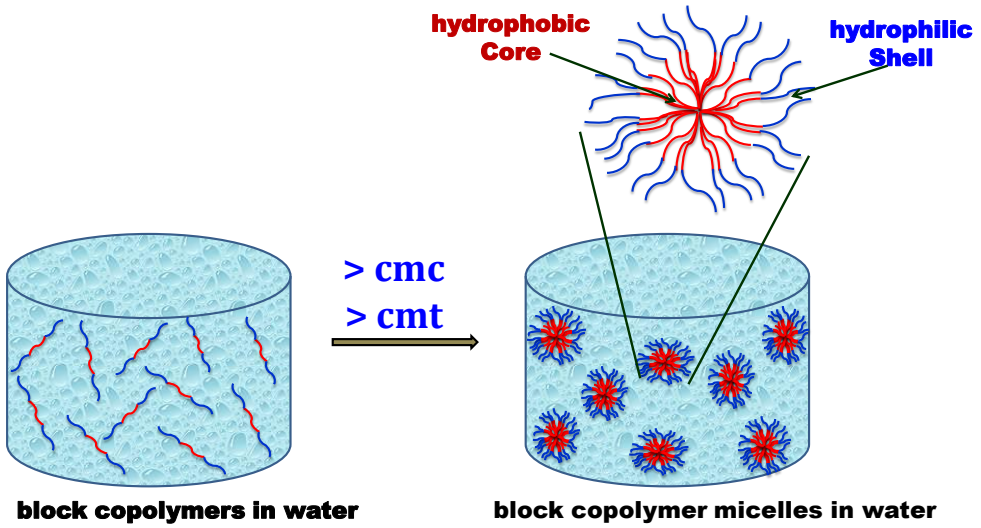

Fig. 1.6: Micellization of block copolymers in water

BCs can be designed to exhibit very low cmc in compared with low-molecular-weight surfactants. The cmc provides an indication of the thermodynamic stability of the micelles because it expresses the minimum concentration of polymers at which the micelles remain self-assembled (i.e., the stability). The cmc off BCs is affected by many factors, like nature of the hydrophobic blocks, such as hydrophobicity, the glass transition temperature (Tg), the degree of crystallinity, and the hydrophilic-hydrophobic blocks length ratio. Above the cmc, the polymeric micelles are in equilibrium with the unimers, in a situation qualitatively similar to conventional surfactants. However, polymeric micelles are assumed to have higher thermodynamic and kinetic stability (slower dissociation rate into unimers) than normal surfactant micelles due to the combined molecular effect and the entangling of the core-forming blocks. Generally, the size of polymeric micelles is of the order of tens to hundreds of nanometers which can be very useful in nanotechnology.

Micelles of BCs open scientists to construct nano-scale structures with molecular level accuracy. The advances in BC micelles offer effective control of morphology, surface chemistry, and environmental responsiveness.

1.3: Polyethylene oxide (PEO) - Polypropylene oxide (PPO) block copolymers

BCs consisting of polyethylene oxide (PEO) and polypropylene oxide (PPO) can exhibit surfactant properties in aqueous solutions, because PPO homopolymer phase-separates (macroscopically) from water at relatively low temperatures (at about -5°C for PPO homopolymer of molecular weight 1200Da), whereas PEO homopolymer (also known as PEG: polyethylene glycol, or POE: polyoxyethylene) is well soluble in water (at least up to 100°C) [19,20]. The presence in the same BC molecule of both PEO (hydrophilic) and PPO (hydrophobic) blocks leads to the self-assembly in solutions (microscopic phase separation occurs because of the tendency to minimize the contact between the hydrophobic PPO parts and the aqueous polar medium) and their adsorption at surfaces and interfaces. Fig.1.7 displays the molecular structure of various BCs based on hydrophilic PEO and hydrophobic PPO blocks.

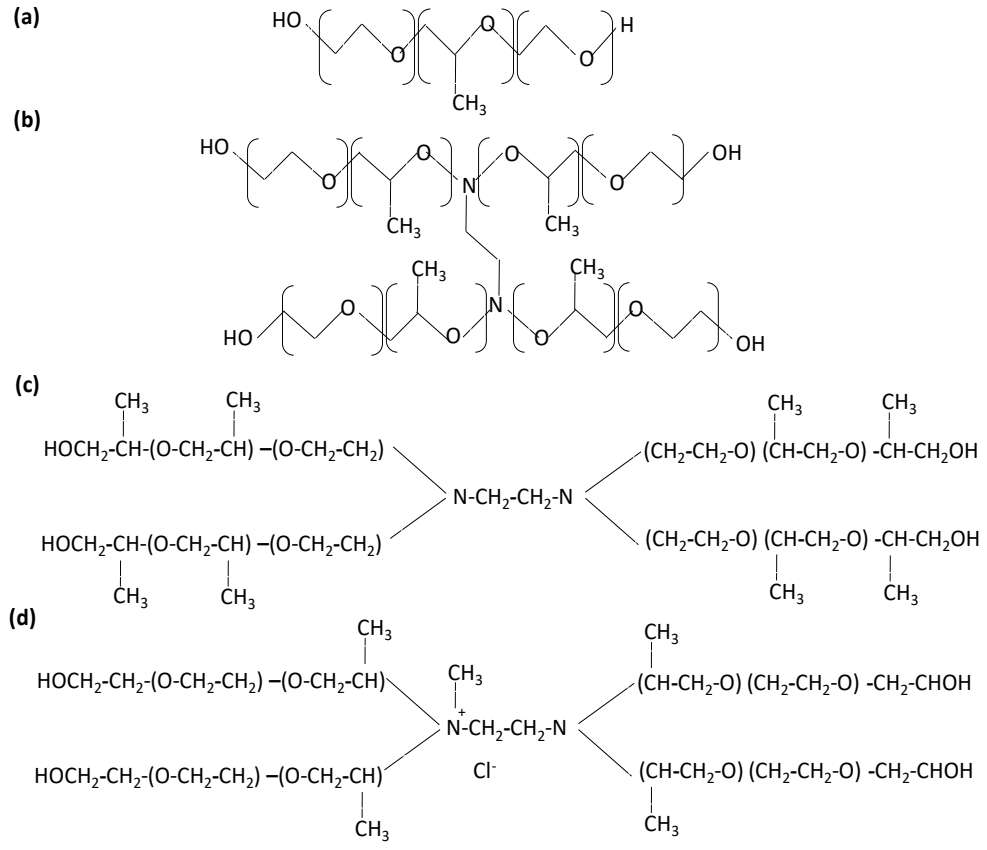

Fig.1.7: Various PEO-PPO block copolymers (a) Pluronic, (b) Tetronic, (c) Reverse sequential poloxamine, and (d) Methylated sequential poloxamine.

Poloxamers and Poloxamines are examples of biocompatible BCs that were first introduced by BASF USA in the 1950s during their requirement for applications in detergent development, agriculture, food, and paints formulations [21, 22].

Majority of researchers in the area of medical sciences have been studying for new treatments that are safer, faster, less invasive, and with high % efficacy using lower doses. But the delivery of effective therapeutic agents drugs to a target cell still concern and problem for researchers.

T investigate Poloxamers arise as a good alternative to surpass this problem, as BC polymer therapeutics', because of their micellization and stimuli-sensitive behavior [23]. These biocompatible BC can self-assemble to form polymeric micelles in an aqueous medium, allowing the possibility to encapsulate a drug or a nucleic acid molecule, being a potential and promising nanosystem to be applied in the treatment of diseases [23-25].

1.4: Polyethylene oxide(PEO)-Polypropylene oxide(PPO)-Polyethylene oxide (PEO) triblock copolymers (Poloxamers)

Over the past few years, Poloxamers also referred as Pluronic polymers have been gaining more attention in the research area of pharmaceutical, food, agrochemicals, detergency, oil-extraction, paints, cosmetics, etc. mainly due to their advantages as potential nano-assemblies in the systems.

Fig.1.8 shows the number of publications with the topic "*Pluronic*" over the past three decades which reflects the importance of these smart polymer materials in the recent and upcoming research.

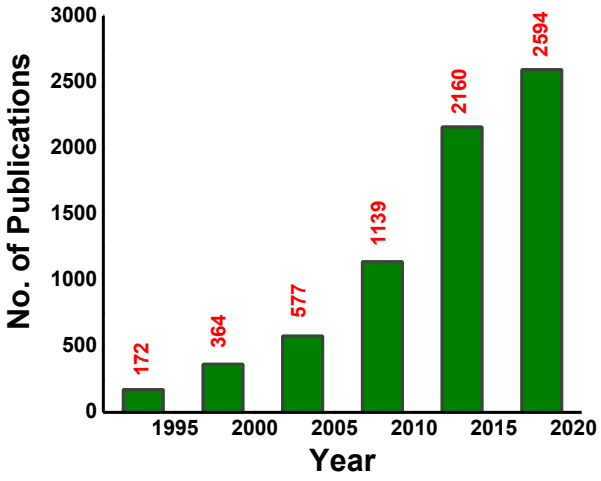

Fig. 1.8: The number of publications with a "Pluronic" as topic against year. The data were obtained from the Web of Science (2018 Clarivate Analytics).

Poloxamers are triblock copolymers of polyethylene oxide (PEO)-polypropylene oxide(PPO)-polyethylene oxide(PEO), available under the trade name of *Pluronic*®(BASF) *Lutrol*®(BASF), *Kolliphor*(BASF), *Synperonic*®(Croda) and *Antarox*®(Rhodia) [20–21]. They are formed by two hydrophilic PEO blocks, which are connected to a hydrophobic PPO block being arranged according to the chemical structure, $PEO_nPPO_mPEO_n$, in which n = number of PEO units and m = number of PPO units, respectively [21].

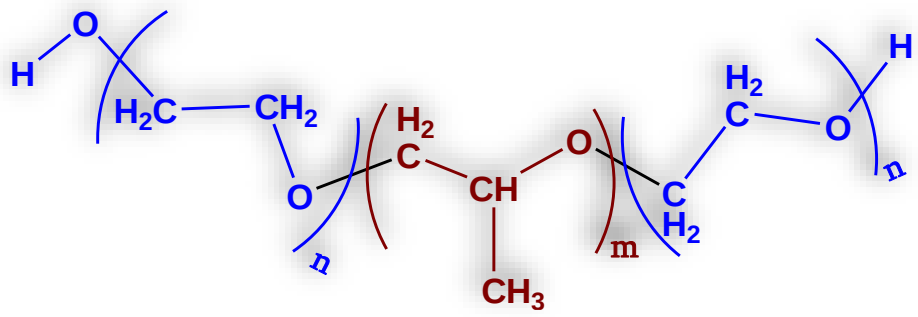

Fig. 1.9: Molecular structure of PEO-PPO-PEO triblock copolymers (Pluronic)

Pluronic polymers are synthesized through the sequential addition of PO and EO monomers in the presence of an alkaline catalyst, such as sodium or potassium hydroxide, producing various Pluronics with a different number of hydrophilic EO and hydrophobic PO

units, which are also characterized by their distinct hydrophilic-lipophilic balance (HLB) value [22, 23]. The synthesis of Pluronic consists of two-steps : In a 1st step, propylene oxide is reacted with a suitable starting material. Such as propylene glycol to form polypropylene oxide (PPO). In the 2nd step, PPO reacts with ethylene oxide to form PEO-PPO-PEO block copolymer. As these steps are performed in an alkaline catalyst with KOH, this then requires neutralization of the Pluronic product after synthesis [24, 25].

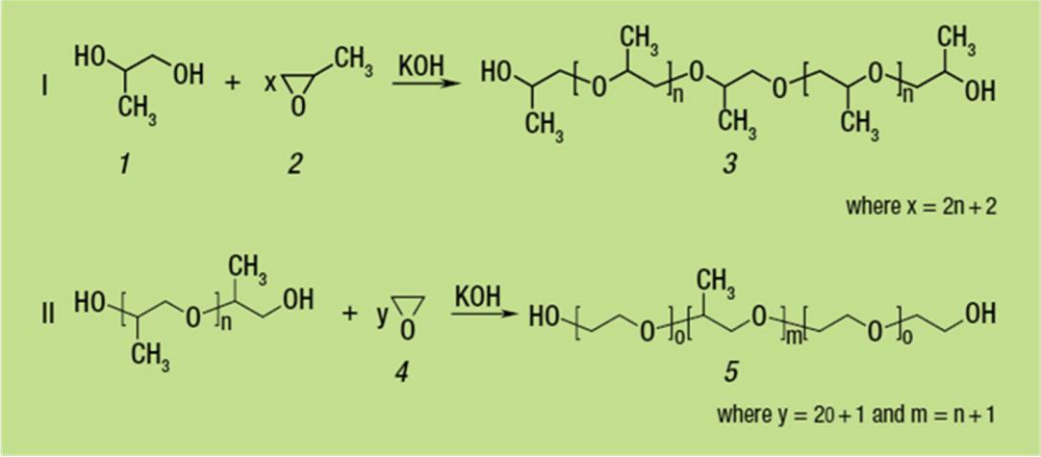

Fig. 1.10: Synthesis of PEO-PPO-PEO triblock copolymers(Pluronic) **[25]**

Commercial Pluronic triblock copolymers have been reported to have some impurities of PEO-PPO diblock copolymers and pure PPO polymers. It is still not much clarity regarding the effects these impurities on the solution behaviors of Pluronics [26].

PEO-PPO block copolymers also exists an inverted substructure with the composition of PPO–PEO–PPO sequence, called as reverse Pluronic (Pluronic® R) and they are commercially available and used as a wetting and defoaming agents in many industrial processes [27].

The hydrophobicity of PPO blocks at temperatures exceeding the cloud point(>15 °C) and the high hydrophilicity of PEO blocks in temperature range between the 0°–100°C prove that these BCs pluronic polymers have amphiphilic nature accompanied by surface-active properties [26]. Many Pluronic block copolymers are already approved by the Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) for several applications,

such as food additives, drug delivery carriers in cosmetics, pharmaceutical ingredients, and tissue engineering [28, 29].

Fig.1.11 presents the Pluronic grid which contains many polymers with their designated letters. The nomenclature of Pluronic polymer starts with the letters, **F**, **P**, or **L**, which is defined as the physical state of polymers, namely solid, paste and liquid at room temperature, respectively. This alphabet letter followed by two or three numeric code [30, 31]. These numeric codes are concerned to their structural parameters, this because the last digit shows the PEO content in tens of weight percent (e.g. 50% wt. if the digit is 5) [30, 31]. Meanwhile, the first one or two digits translate the molecular mass of the PPO, where it is to multiply the corresponding number by 300 (e.g. The PO block of F88 has an MW of 300*8 = 2400) [30, 31]. The use of the grid system is recommended for molecular weight estimation to ensure that all Pluronic grades conform.

The physical and chemical properties of Pluronics can be tuned through modifying the molar mass ratio between the PEO and PPO blocks PEO/PPO, which directly modifies the properties and interactions with biomaterials, and provides high potential for the design of innovative nanomedicines and new biomaterials

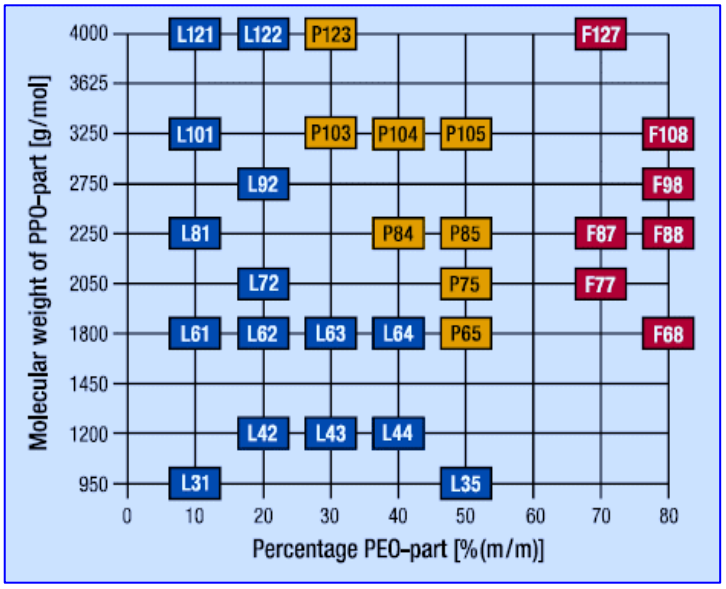

Fig. 1.11: Grid system displaying the nomenclature of Pluronic **[25].**

1.5: Self-assemblies/micelles of Pluronic block copolymers

Pluronics exist as unimeric form in the water below cmc and at higher concentration (above cmc) they aggregate to form spherical micelles which are in equilibrium with the unassociated unimers. Alexandridis et al [32-36] have been thoroughly investigated the micellization of Pluronics and thermodynamic parameters of the micellization process. It was observed that micellization of Pluronics in water is entropy driven process [33]. Pluronics form micelles at a much lower concentration in comparison to conventional surfactants. All Pluronic micelles have hydrophobic core formed by PPO chains and hydrophilic corona/shell formed by PEO chains. The core formed by PPO chains is water incompatible which is separated from the aqueous environment by hydrophilic chains of PEO corona, thereby forming a reservoir for the encapsulation of various hydrophobic therapeutic agents. Using mean-field lattice theory, Linse et al [37] have predicted theoretically about the structure of the micelles. According to this theory, the core of micelle was filled with hydrophobic block and the shell filled with hydrophilic block. The theory also concluded that the segmental densities are constant in different regions and no solvent penetration to the core was allowed. With minimizing the free energy and application of mean field theory, various micelle properties like micellar size, aggregation number, cmc, etc., were determined. After that, the other two models were also developed to study the structure of micelles. It is a hard sphere model and the cap-and-gown model [38, 39]. The hard sphere model was based on the core-shell structure and a hard sphere inter-micellar interaction while the cap-and-gown model shows a compact and diffused corona structure. The amount of polydispersity is considered in the hard-sphere model to fit the scattering intensity distribution, whereas no polydispersity is counted in a cap-and-gown model.

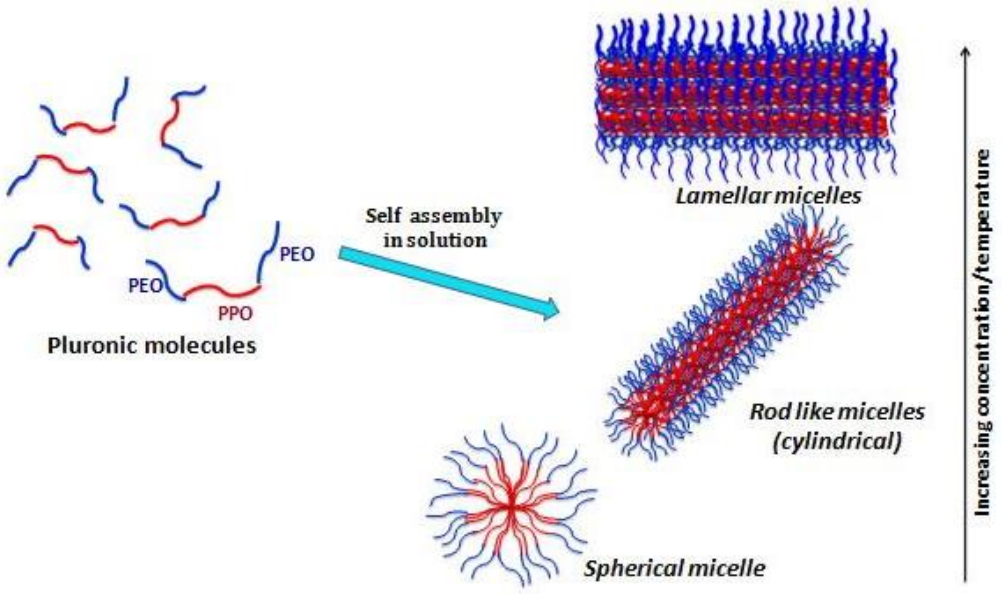

Fig. 1.12: Schematic illustration of morphologies of micellar phases formed by the Pluronics in the water at increasing concentration/temperature.

Pluronic micelles can be spherical, rod-like or lamellar depending upon the length of PPO and PEO chains, concentration, temperature, etc (Fig.1.12). Pluronic micelles are also very much temperature sensitive. As the temperature increases, the aspect ratio of the Pluronic micelles increases leading to an anisotropic growth of micelles and results in an *ellipsoid* or *worm-like* or *cylindrical structures* [40-42]. At higher temperatures, the association number increases which increase the Pluronic micelle core radius. Due to this, the core radius exceeds the stretched length of PEO block and micelles now transform to prolate ellipsoid. Due to this ellipsoidal structure of Pluronic micelles, the interaction between micelles is very much repulsive. The change from spherical to ellipsoidal structure leads to a minimization of the interaction energy at shorter distances by the alignment of the structures along the majority axis. At higher temperature and concentration, the micellar structure change from spherical to prolate ellipsoid and increased hydrophobicity of PEO blocks, leads to the formation of rod-like structures with hexagonal symmetry. Further increase in temperature finally leads to the formation of ordered lamellar structure. The change in the structure of micelles from spherical to cylindrical structures can also be induced in the

presence of various additives like inorganic salts, hydrotropes, etc. The presence of salts, hydrotropes, organic compound, and other additives very much influenced on micellar behavior of Pluronics [43,44].

1.6: Micelles of Pluronic block copolymers in drug delivery applications

The introduction of better and safer materials for drug solubility and targeting purposes which can also facilitate more efficient loading and controlled release of a large number of hydrophobic drugs, for which no delivery system is yet available. Pluronic micelles could represent a solution to the drying of pharma industries drug discovery pipeline with the nano-sized micellar system.

The rapid development of applications of Pluronic polymers in the pharmaceutical sciences is primarily due to the chemical flexibility of structure, which gives an opportunity for the design of versatile drug carriers. For instance, the size of both the hydrophilic PEO and the hydrophobic PPO parts can be varied to achieve desired hydrophilic-lipophilic balance (HLB).

Most advantageous about Pluronic micelles is that having polyethylene oxide (PEO) as corona-forming block. The PEO shell has a high flexible structure, a high degree of hydration, non-toxicity, and weak immunogenicity and therefore it has been approved by the FDA. Previous reports have mentioned that PEO has been the preferred choice as a hydrophilic block because it imparts colloidal stability for the Pluronic micelle. PEO chains as a shell of micelles are devoid of pendant sites that could be utilized to conjugate various functional groups for active targeting. Due to the presence of steric repulsion, the outer PEO shell of the Pluronic micelle resists the adsorption of proteins and other biological components in the blood-stream so that there is no recognition by the RES (Reticuloendothelial cells system). Hence, it was achieving higher circulation half-time in the body and having a protective effect during prolonged circulation.

Another good thing about Pluronic micelles is that having the polypropylene oxide (PPO) as core-forming blocks. The PPO has nontoxicity and biodegradable natures with defined degradation rates. As the hydrophobic nature of PPO blocks, it attracts the

hydrophobic drug and encapsulates in the core of the Pluronic micelle. High drug encapsulation with hydrophobicity the release rate of drug decreases in the micelle, and the thermodynamic stability of the system also enhanced [45]. Controlling the release of drugs from these PPO cores of micelles is one of the major challenges nowadays, and therefore vast research is being done to obtain controlled drug release.

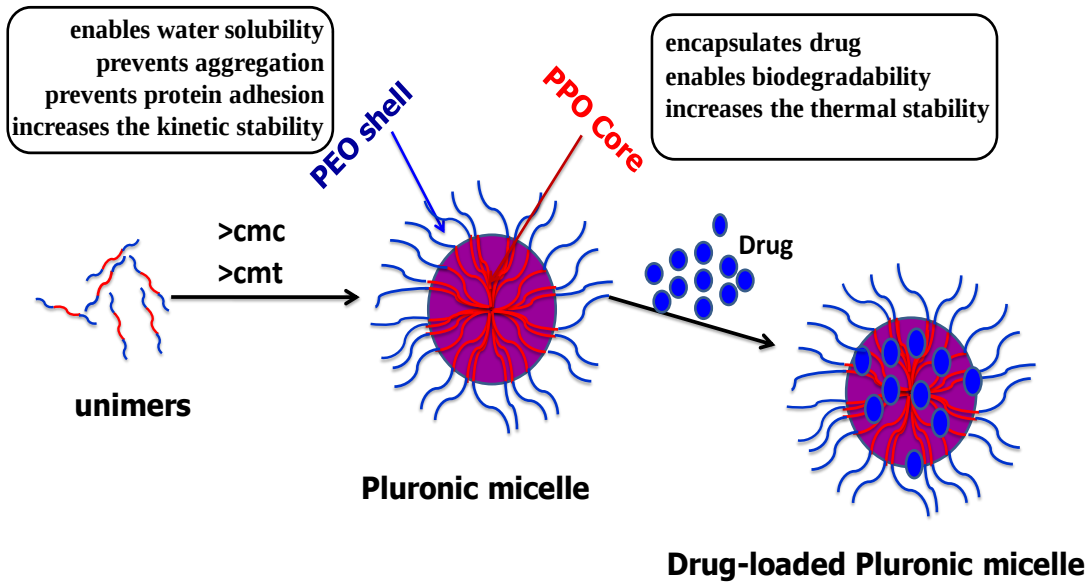

Fig. 1.13: Pluronic micelles as drug nanocarriers

Many researchers already reviewed the efficiency of Pluronic micelles as nanovehicles of drug delivery applications [22,46-52]. It is important to prepare drug-loaded Pluronic micelles that can carry higher amounts of drug and prevent against the burst release when enters in the bloodstream. Hence, it is a challenge to prepare drug-loaded Pluronic micelles that do not release drug quickly and are long-time stable in the blood.

Various methods have been developed to synthesize the drug-loaded Pluronic micelles. There are four commonly used methods for the synthesis of the drug-loaded Pluronic micelles: direct dissolution temperature-induced phase transition, thin film hydration, and solvent evaporation method. Fig.1.14 presents the schematic diagram of methods for the preparation of drug loaded Pluronic micelles.

The direct dissolution method may comprise the solubilization of the copolymer to get Pluronic micelles and the subsequent solubilization of the drug that initially remains in suspension and it is gradually loaded into the Pluronic micelles until its complete dissolution. The drug is added in the solutions of various Pluronics and equilibrated by continuous stirring for 24 to 48 h at a constant temperature. Then, the undissolved drug is removed by filtration and the drug payload quantified. Direct dissolution method is quit convenient because it prevents the use of solvents and easy in operations.

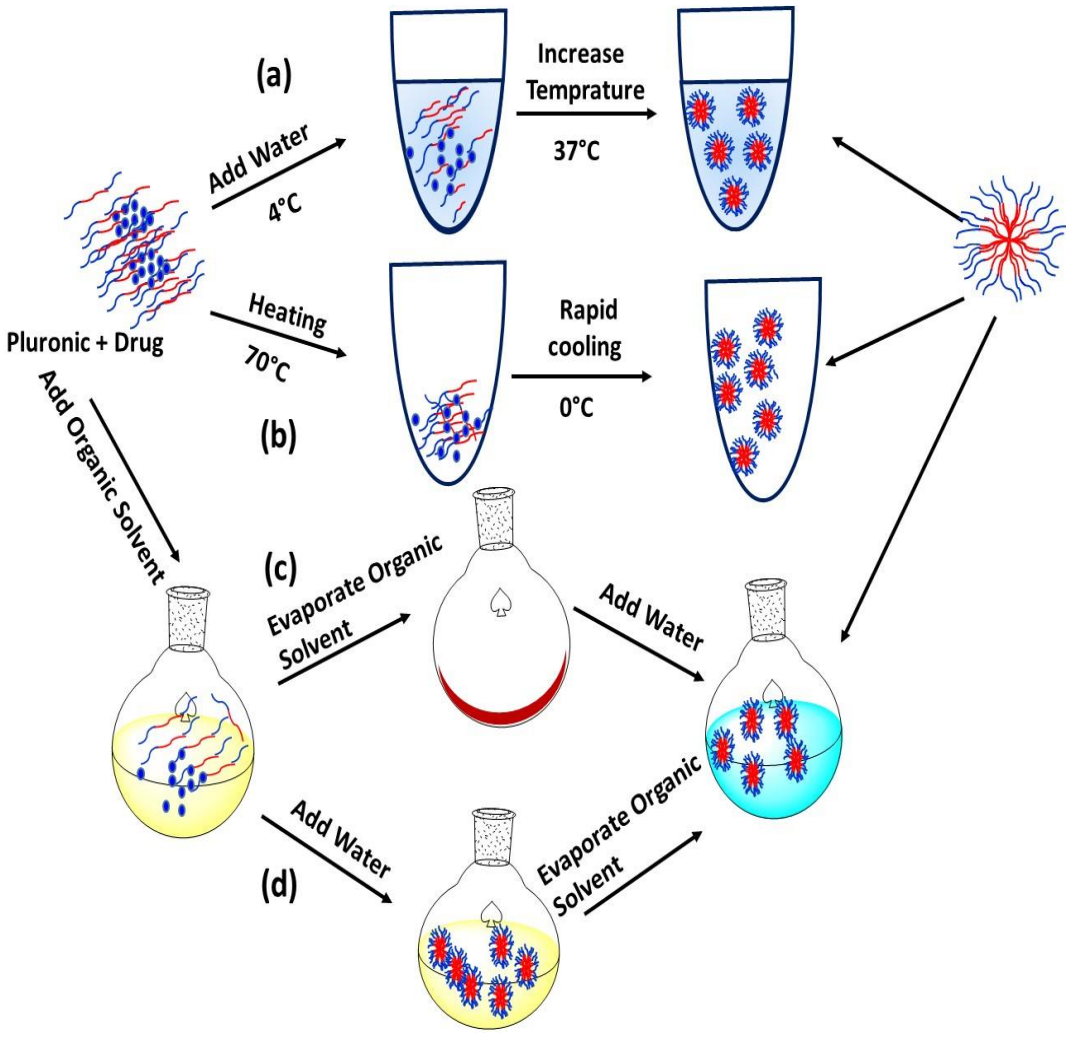

Fig.1.14: Methods for the preparation of drug-loaded Pluronic micelles: (a) direct dissolution, (b) temperature-induced phase transition, (c) thin film hydration, and (d) solvent evaporation/dialysis

In the temperature-induced phase transition method, the mixture of Pluronic and drug molecules is heated at 70°-80°C temperature to form the micelles with a good amount of drug loading. Then, the solutions is rapidly cooled to 0°C (freeze-drying) and obtain the drug-loaded Pluronic micelles. In other solvent evaporation or dialysis method, the Pluronic and drug are primarily solubilized in a water-miscible organic solvent (e.g. dimethylformamide, acetone, ethanol, etc.) and poured into water. Then, drug-loaded Pluronic micelles are formed upon the removal of the organic solvent by evaporation or dialysis. In the thin film hydration method, the Pluronic and the drug are dissolved in a volatile organic solvent. The solvent is evaporated and a polymeric film is obtained and hydrated with water by stirring or sonication, leading to a formation of drug-loaded Pluronic micelles [22]. It is obvious that changes in the preparation method may result in micellar systems with different drug payloads, size and size distribution, and physicochemical stability.

After the preparation of drug-loaded Pluronic micelles, it is important to take into consideration the structural and chemical characterization of these Pluronic micelles. In this sense, various techniques are employed to characterize the size and shape (morphology) of micelles, crystallinity, polydispersion index, zeta potential thermochemical behavior of micelles, etc. [41]. Table.1.1 shows the various characterization techniques used for Pluronic micelles with measuring parameters.

Table.1.1: Characterization techniques for drug-loaded Pluronic micelles.

Characterization techniques	Characteristics
Dynamic light scattering (DLS) and Static light scattering (SLS)	Size of micelles hydrodynamic diameter (D) and size distribution of micelles, polydispersity index, zeta potential, etc.
Small angle neutron Scattering (SANS)	Shapes/morphologies of micelles core radius (Rc), hard sphere radius, radius of gyration, aggregation number, volume index, etc.
Transmission electron microscopy (TEM) and Scanning electron microscopy (SEM)	Size and shape of micelles morphological arrangments, aggregation, dispersion, etc.
Differential scanning calorimetry (DSC),	Thermochemical properties of micelles Glass transition temperature(Tg), drug compatibility, stability, critical micelle temperature, phase-transition
Thermogravimetry analysis (TGA)	Thermochemical properties of micelles weight loss as a function of temperature, stability,

	polymorphic transitions, or solid-state chemical degradation pathways etc.
X-ray diffraction (XRD)	The physical form of micelles Crystallinity, stability,drug compatibility etc.
Nuclear magnetic resonance spectroscopy (NMR	Position of the drug in micelles chemical structure and the dynamic of drug molecules, compatibility, etc.
Raman spectroscopy and Fourier Transform InfraRed spectroscopy (FT-IR)	Compatibility of micelles with drug functional groups and provide quantitative information, drug compatibility, and encapsulation
UV-Visible Spectroscopy (UV-VIS) HPLC (High-pressure liquid chromatography)	Concentration, drug solubility in micelles calibration, solubility of the drug, encapsulation efficiency, drug loading, measuring cmc and cmt

Due to their good stability in water and ability to form micelles, Pluronic is suitable for use as solubilizers. Encapsulation of low molecular weight drugs into Pluronic micelles can increase drug solubility and stability and can improve drug pharmacokinetics and biodistribution. In the use at anticancer chemotherapy, drug encapsulation in Pluronic micelles can diminish drug extravasation into normal tissues and provide for a passive drug targeting to tumors through enhanced permeability and retention (EPR) effect.

Fig.1.15 represents the EPR effect of Pluronic micelles. The EPR is realized due to the abnormally high permeability of tumor blood vessels combined with prolonged circulation of the Pluronic micelles due to their decreased extravasation in normal vessels and lack of renal clearance. The first anticancer micellar formulation to reach clinical evaluation was actually a mixed micelle of Pluronics L61 and F127 contained the doxorubicin(Dox) drug. It is SP1049C currently developed by Supratek Pharma Inc. [53]. Analysis of pharmacokinetics and biodistribution of Dox-loaded Pluronic micelles (SP1049C) showed more efficient accumulation of the micellar drug in the tumors compared to the free drug. This study also indicated that the peak levels of Dox formulated with SP1049C in the tumor were delayed and the drug residence time was increased in comparison with the free Dox [54-56]. Therefore, the Pluronics not only induce the modulation of Dox pharmacokinetic properties but are also took part in the biological effect of the formulation.

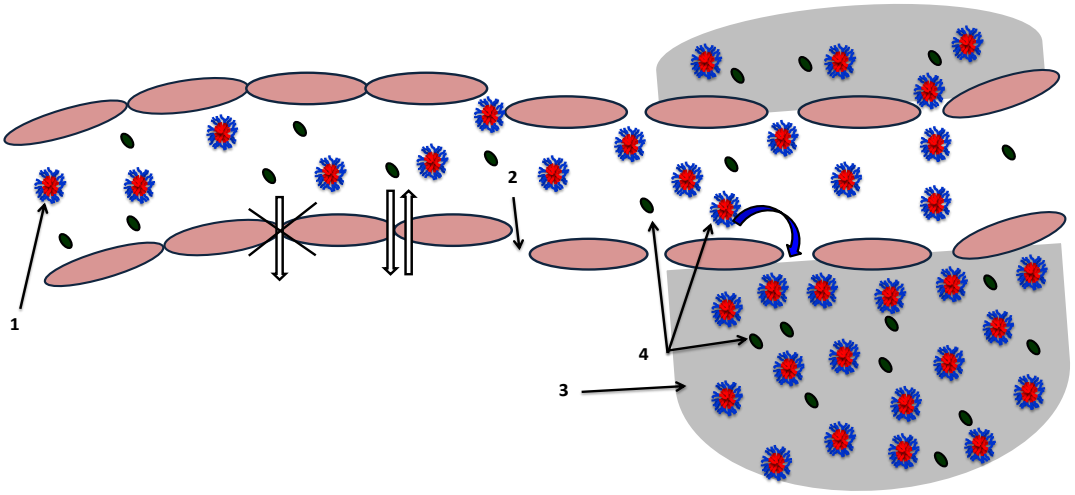

Fig.1.15. EPR effect. Long-circulating Pluronic micelles (1) penetrate through the leaky vasculature (2) into the tumor interstriatum (3) and degrade there, releasing free drug (4) and developing its high concentration.

Another important anticancer drug, docetaxel(DTX) is clinically used in a formulation with the non-ionic surfactant Tween 80. This formulation, named Taxotere®, was approved by the FDA in 2004. But Taxotere® found many side effects like hypersensitivity, nephrotoxicity, neurotoxicity, and incompatibility. In 2013, Fang et al [57] demonstrated that DTX-loaded in mixed micelles of Pluronic P105 and F127 shows higher cytotoxicity towards A549Taxol-resistant cells compared to Taxotere® such effective results motivate the uses of Pluronic micelles as therapeutic agents in cancer formulations.

The effective utilization of Pluronic micelles in gene delivery was also thoroughly reported by Kabanov et al [52]. Pluronics have the ability to increase expression of genes delivered into cells using non-viral vectors, to increase the transfection with adenovirus and lentivirus vectors, to conjugate with polycations, to condense DNA and to form polyplexes, and the regional increase of naked DNA expression in tumors counted much attention for gene delivery applications.

It is clear that the utilization of nanotechnology tools for the design of polymer nanoparticles, although being still an emergent concept, has already shown tangible promise in medicine. Pluronic block copolymers are particularly suitable for the exploration of bio-inspired, bioengineered and biomimetic NPs. In parallel with the design of new Pluronic-based drug delivery systems and Pluronic-containing formulations, the great effort has also been devoted to elucidating their role in the activity enhancement of the encapsulated drug,

their biological mode of action and metabolism. Hence, Pluronic has gained much attention and offers a promising way to use for bioavailability of many good numbers of drugs.

In the present thesis research work, we have tried to focus particularly on the self-assemblies/micelles of Pluronic block copolymers as nanovehicles for bioavailability of poorly water-soluble drugs like curcumin, quercetin, and lamotrigine.

In the foregoing chapters, a study of micellization of single and mixed Pluronic polymers and solubilization of some hydrophobic drugs have been carried out using the variety of multiple techniques like UV-Vis spectroscopy, DLS, SANS, FT-IR, TEM, XRD, DSC, TGA, CP, ST, etc. The biological analyses were also done for a better understanding these Pluronic systems for futuristic application in drug delivery.

1.7.References

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