Deanship of Graduate studies
Al- Quds University

PHASE BEHAVIOUR OF SOME PLURONICS WITH LIMONENE AND WATER

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M. Sc. Thesis

Jerusalem Palestine

1431/2010

THESIS TITLE:
"PHASE BEHAVIOUR OF SOME PLURONICS WITH LIMONENE AND WATER"

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A thesis submitted in partial fulfillment of requirement for the degree of Master of Applied and Industrial Technology. Department of Science and technology/ Program of Applied and Industrial Technology /Alquds University

1431/2010

Al-Quds University
Deanship of Graduate Studies
Applied and Industrial Technology
Department of Science and Technology

Thesis Approval

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Jerusalem – Palestine

1431/2010

DECLARATION

I certify that this thesis submitted for the degree of master, is the result of my own research, except where otherwise acknowledged, and this thesis has not been submitted for the higher degree to any other university or institution.

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Date: ..10th...April...2010

ACKNOWLEDGEMENTS

Firstly I would like to thank Dr. Ibrahim Kayali, who gave me the all his support and to perform this work at the laboratories of Al-Quds University. I am grateful for his support on the sometimes stony road. His knowledge and guidance have helped me achieve my goals and helped me to grow as an individual. I would also like to thank the other members of my graduate committee

My thanks to all members of Chemistry Department for giving me a helpful hand on the way to prepare this thesis.

I am very grateful towards my friends, old and new, who have believed in me and stood by my side, and for their help and encouragement during the writing of this thesis.

Special thanks to my wife and my family for their advice and continued support, trust, and love , they provided the needed love and patience during my work.

ABSTRACT

Pluronics are triblock copolymers of poly(ethylene oxide)- poly (propylene oxide) – poly (ethylene oxide) (PEO-PPO-PEO) with wide range of hydrophilic - lipophilic balance . In order to investigate the phase behaviour of pluronics as nonionic surfactants with water and Limonene , pluronics F127 ($PEO_{106}PPO_{70}PEO_{106}$) , F108 ($PEO_{141}PPO_{44}PEO_{141}$) , F98 ($PEO_{123}PPO_{47}PEO_{123}$) and P104 ($PEO_{18}PPO_{58}PEO_{18}$) were selected . Samples were prepared individually by weighing appropriate amounts of different pluronics F127 , F108 , F98 , and P104 separately and D.Water and R(+) Limonene into (8mm) and (10 mm) test tubes with different ratios beginning from (0.5:9.5) as pluronic : water to (9.5:0.5) weight ratio , The initial total weight is 1 gm. , and limonene of about 0.02% of total amount into each addition , all tubes are immediately flame sealed , followed by mixing on the vortex until good homogeneity and all samples were kept at 25˚ C ± 0.5˚ C . Following equilibrium , Samples were checked for phase separation and birefringence . In order to distinguish between the isotropic (nonbirefringent) micellar solution or cubic liquid crystal and the anisotropic (birefringent) lamellar and hexagonal liquid crystal , Cross polarizers and Polaroid microscopy were used to detect birefringence.

The pluronics F127 , F108, and F98 with larger molecular weights showed limited phase diagram composed only of normal micelles and cubic liquid crystal while P104 of smaller molecular weight and higher hydrophobicity showed wide spectra of different lyotropic liquid crystals in phase diagram composed of cubic liquid crystal , normal hexagonal , lamellar liquid crystal in addition to normal micelles. Percentage of limonene solubilized in each of these phases was high especially hexagonal with a percentage of limonene reaching about 12% while in lamellar liquid crystal the percentage of limonene reaching 32% , this was due to larger hydrophobicity which helped limonene to enter an apolar space of structured molecules. Tetrabutyl ammonium bromide (TBAB) was added as co-surfactant to each of the pluronics F127,F108 and F98 with (1:1) weight ratio . It increased the amount of limonene solubilized in the normal micelles and cubic liquid crystal regions. On the other hand effect of temperature on liquid crystals were investigated and showed converting one liquid crystal to another by increasing temperature and vice versa. This conversion was investigated by using cross polarizers and optical microscope.

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LIST OF ABBREVIATIONS

- ***n :number of blocks***
- ***e.g. : example***
- ***A : Monomer A***
- ***B : Monomer B***
- ***ATRP : Atom transfer free radical polymerization***
- ***RAFT: Reversible addition fragmentation chain transfer***
- ***ROMP: Ring opening metathesis polymerization***
- ***M : Monomer***
- ***k : reaction rate constant***
- ***r : molar ratio***
- ***PEO :Polyethylene Oxide***
- ***PPO: Polypropylene oxide***
- ***a: Ethylene oxide portion***
- ***b: propylene oxide portion***
- ***P: Poloxamer***
- ***xyz: Three digits***
- ***cde : Three digits***
- ***EO: ethylene Oxide***
- ***PO: propylene oxide***
- ***M.Wt. : Approximately molecular weight***
- ***g/mol : Gram per mole***
- ***No. : Number***
- ***°C : Unit of temperature***
- ***Fig. :Figure***
- ***CMC : Critical micellization concentration***
- ***CMT : Critical micellization Temperature***
- ***Lα: Lamellar liquid crystal***
- ***H1 : Hexagonal liquid crystal***

- ***I1: Cubic liquid crystal***
- ***L1 : Normal micelles***
- ***cgc : critical gel concentration***
- ***TBAB : Tetra butyl ammonium bromide***
- ***O/W : Oil in water***
- ***W/O : Water in oil***
- ***3Φ: Three phase region***
- ***LC : Liquid crystal***
- ***D. Water : Distilled water***
- ***mm. : Millimeter***
- ***gm. : Gram***
- ***NaCl : Sodium Chloride***
- ***PEO-PPO-PEO : Triblock copolymer of two ethylene oxide blocks and propylene oxide central block***
- ***Et al. : Others***
- ***p. : Page***
- ***pp.: Pages***
- ***Vol. : Volume***
- ***Pt. : Part***
- ***& : And***
- ***Chap. : Chapter***

TABLE OF FIGURES

CHAPTER ONE

INTRODUCTION

1. INTRODUCTION.

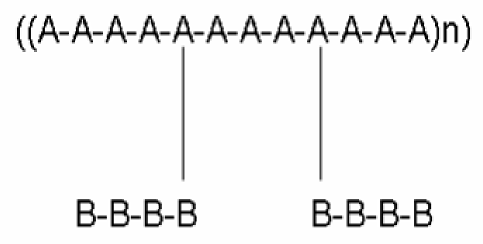
1.1.COPOLYMERS

1.1.1.Definition of copolymers:

Copolymers are polymers derived from two or more units of monomers and in other words composed of more than one homopolymer which are derived from only one monomer *(Odian,2004)*.[1]

1.1.2.Types of copolymers:

- Copolymers can be classified based on how the monomers units are arranged along the chain .These may also be described due to branching in the polymer structure. Linear copolymers consist of a single main chain but branched copolymers consist of a single main chain with one or more polymeric side chains, Classes of copolymers are summarized as following types *(IUPAC,1996)*:[2]
- **Alternating copolymers** (regular A and B units) as follows (A-B-A-B-A-B-)n
- **Periodic copolymers** (repeating sequence of A and B units) as follows $(A\text{-}B\text{-}A\text{-}B\text{-}B\text{-}A\text{-}B\text{-}B\text{-}B)_n$
- **Random copolymers** (random sequences of monomer A and B) (as follows (A-B-B-B-A-B-A-B-A-A)n)
- **Statistical copolymers** (the order of the monomers sequence obeys statistical rules)
- **Block copolymers** (two or more homopolymer linked by covalent bonds) (as follows (A-A-A-A-B-B-B-B-B)n).
- **Graft copolymer :** (branched copolymer in which side chains are different from the main chain) as follows .



There are also other types of branched copolymers as **star**, **brush** , and **comb copolymers** as shown in figure 1.1.

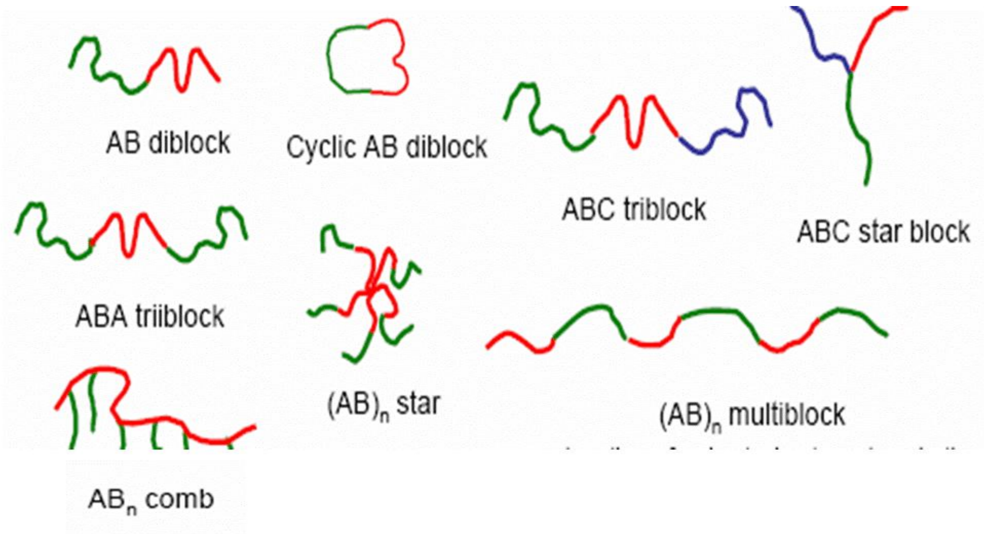


***Fig.1.1.:Types of copolymers* * .**

1.1.3.Block Copolymers:

Block copolymers are a special kind of copolymer made up of blocks of different polymerized monomers. These include the following types according to number and type of blocks as shown on figure 1.1. :

* *Adapted from Anthony J. Ryan OBE. , From University of Sheffield , From a presentation titled of coating "that create color "*

1. Diblock copolymer that contains two different chemical blocks.
2. Triblocks copolymer with three blocks.
3. Tetrablocks copolymer and
4. Multiblocks copolymer, etc.

Diblock copolymers are made using common polymerization techniques, such as:

1. Atom transfer free radical polymerization (ATRP)
2. Reversible addition fragmentation chain transfer (RAFT)
3. Ring opening metathesis polymerization (ROMP)
4. And cationic or anionic polymerization.

1.1.4.Copolymerization equation:

Copolymerization equation or (Mayo – Lewis equation) describes the distribution of monomers within the copolymer *(Mayo & Lewis,1944)*: [3]

$$\frac{d[M1]}{d[M2]} = \frac{[M1]\,(r_1[M1] + [M2])}{[M2]\,([M2] + r_2[M2])}$$

where $r_1 = k_{11}/k_{12}$ & $r_2 = k_{22}/k_{21}$, k is the reaction rate constant, M1 is monomer 1 and M2 is monomer 2 , r_1 & r_2 are reactivity ratios .

- When $r_1 = r_2 >> 1$ then homopolymer is released .
- When $r_1 = r_2 > 1$ then homopolymers lead to block copolymer.
- When $r_1 = r_2 =$ □ 1 then random copolymer will be released.
- When $r_1 = r_2 =$ □□ 0 then alternating copolymer will be released. And the molar ratio of the monomer in the polymer is close to one .

1.2.POLOXAMERS OR PLURONICS

1.2.1. Definition and properties of Poloxamers:

Poloxamers , known by the trade name Pluronics or synperionics , are nonionic triblock copolymers composed of a central hydrophobic chain of polyoxypropylene (poly(propylene oxide)) connected to two hydrophilic chains of polyoxyethylene (poly(ethylene oxide)) , each of them on one of the sides . The general structure for the poloxamer can be stated as figure (1.2.) *(Semenov & et al. ,1995),(Milner &Witten,1992)and (Goodman, 1982).*[4,5,6]

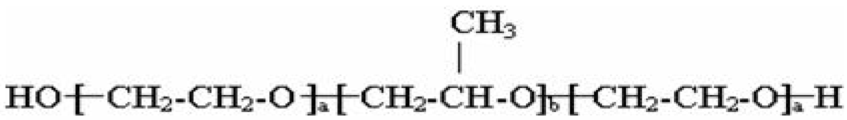


Fig. 1.2.: General Structure of Pluronic ,(a. represents EO and b. represents PO)

1.2.2. Coding of poloxamers :

Poloxamers are coded with the letter "P*xyz*" i.e. a letter (P) which means Poloxamer , followed by three digits (*xyz*) , the first two digits (*xy*) multiplied with 100 give the approximate molecular mass of the polyoxypropylene core, and the last digit (*z*) multiplied with 10 gives the percentage polyoxyethylene content (for example, P407 = Poloxamer with approximately polyoxypropylene molecular mass of 4,000 g/mol and a 70% polyoxyethylene content) .

For the Pluronics , coding of these copolymers starts with a letter that defines the physical form of the pluronic at room temperature (L = liquid, P = paste, F = flake (solid)) followed by two or three digits (*cde*), the first digit(s) (*cd*) multiplied with 330 refer to the approximately molecular mass of the polyoxypropylene core and the last digit (*e*) multiplied with 10 gives the percentage polyoxyethylene content (for example , F127 = Pluronic with approximately polyoxypropylene molecular mass of 4,000 g/mol and a 70% polyoxyethylene content). In the previous example given, poloxamer 407 (P407) = Pluronic F127. Table no.1.1. shows the percentage of polyoxyethylene content , the molecular mass and approximately molecular weight of the pluronics used in this research.

Table No. 1.1. : Pluronic grades and their chemical composition*.

Pluronic	*#of(ethylene oxide) EO (a)*	*# of (propylene oxide)PO(b)*	*% of EO*	*M.Wt.*
F108	*141*	*44*	*~85%*	*12700-16400*
F127	*106*	*70*	*~75%*	*10800-14600*
F98	*123*	*47*	*~83%*	*12000-14000*
P104	*18*	*58*	*~38%*	*4500-6500*

1.2.3. General properties of pluronics:

Pluronics are waxy, white granules and are odorless and tasteless. Pluronics are very stable in aqueous solutions of pluronic especially in presence of acids, alkalis, and metal ions. The poloxamers are readily soluble in aqueous, polar and non-polar organic solvents. The pluronics are inert and safe products *(USP,2002)*.[7] The typical properties of the pluronics used in this research are in table no. 1.2.

* *Adapted from Technical Brochure, BASF Corporation. Accessed November 26, 2007.*

Table No.1.2:Typical properties of Pluronics

Typical Properties	*F108*	*F127*	*F98*	*P104*
Form	Prill	Prill	Prill	Paste
Average M.wt.	~14600	~13400	~13000	~5900
Specific gravity	1.06	1.05	1.06	1.04
Viscosity cps at 77˚C	2800	3100	2700	390
Melting point ˚C	57	56	58	32
Cloud point	> 100	> 100	> 100	81
Surface tension 0.1% aqueous (dyne / cm)	41	41	43	33
HLB	>24	18-23	>24	12-18
Solubility in water at 25˚ C	>10%	>10%	>10%	>10%

1.2.4.Definition and properties of Limonene :

Limonene : "Methyl-4-isopropenyl cyclohexene" is a hydrocarbon composed of ten carbons as figure 1.3, classified as a cyclic terpene. It is a clear liquid at room temperatures with an extremely strong smell of oranges. It takes its name from the lemon. Limonene is a chiral molecule, biological sources produce one enantiomer: the principal industrial source, citrus fruit, contains D-limonene and R((+)-limonene), which is the (*R*)-enantiomer. Racemic limonene is known as dipentene *(Mann & et al.,1992).* [8]

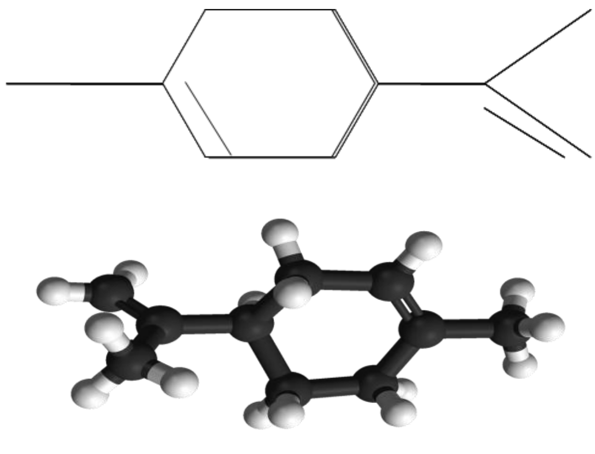


Fig. 1.3. :Structure of limonene

Here are some general properties of limonene :

Molecular formula : $C_{10}H_{16}$

Molar mass : 136.24 g/mol

Density: 0.8411 g/cm³

Optical rotation: 87° - 102°

Melting point: -74.35 °C, 199 K

Boiling point: 176 °C, 449 K

1.2.5. Definition and properties of TBAB.:

Tetrabutyl ammonium bromides (TBAB) are group of ammonium salts , they have a central nitrogen atom joint to four organic radicals or alkyl , aryl , or aralkyl groups , these show a variety of physical , chemical and biological properties , they are mostly soluble in water and strong electrolytes , they have a tendency of locating at the interface of two phases , their applications are wide and shown in application section. The structure of tetra butyl ammonium bromide is shown in figure 1.4

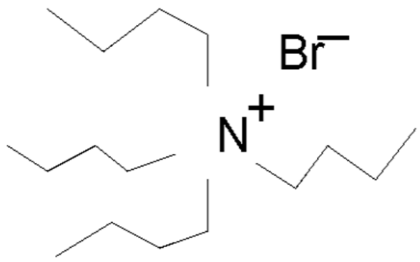


Figure 1.4 : Molecular structure of TBAB " Tetra butyl ammonium bromide".

1.3.PHASE BEHAVIOUR OF PLURONICS

1.3.1. General review in phase behavior of pluronics:

Some pluronics as defined above consist of a central polypropylene oxide –PPO- block, and with polyethylene oxide –PEO-blocks on either side) , these are a triblock copolymers . Polypropylene oxide (PPO) forms central hydrophobic core wherein methyl groups interact via Van der wa'al forces with solvent. However, the polyethylene oxide (PEO) block interact by hydrogen bonding interactions of ether oxygen with water molecules *(Schmolka & Tarch , 1991).* [9]

The hydrophobocity increases as temperature increases that can aggregate to form micellar structures similar to those formed by simple surfactant molecules .The self-association of the triblock copolymers into spherical micelles is above a critical micellization concentration (CMC) and a critical micellization temperature (CMT) . But when in solution, pluronics can exhibit very interesting and rich phase behavior and can aggregate to form structures as bicontinuous phases, micro emulsions, and micelles , otherwise poloxamers have amphiphilic character which is a case between hydrophilic and lipophilic as shown in figure (1.5).

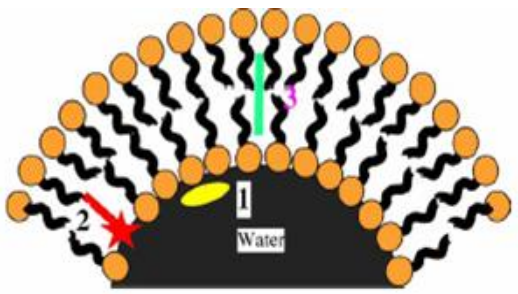


***Fig.1.5.: 1 is hydrophilic , 2 is amphiphilic , 3 is lipophilic* * .**

* *Adapted from L. Sagalowicz*, M.E. Leser, H.J. Watzke and M. Michel , Monoglyceride self assembly structures as delivery vehicles ,Food Science, Nestle´ Research Center, Vers-Chez-Les-Blanc, CH-1000 Lausanne 26, Switzerland ,2003.*

Phase behavior depends strongly on the followings: *(Rassing & Atwood ,1983) , (Wanka & et al. , 1990).*[10, 11, 12]

1. The combination of monomers constituting the block
2. Molecular weight
3. Solvent composition
4. Temperature
5. Block size
6. Increasing of alkyl chain length
7. Process of addition used.
8. And the interaction parameters between the different polymer units and the solvent .

The CMT and CMC vary depending on the block composition of the various pluronics which allows selection of the optimal surfactant for the desired application. On other hand pluronics can self - assemble to form structures with water and without water which also helps for wide range of applications. The self assembly is shown in figures 1.6.a and 1.6.b .

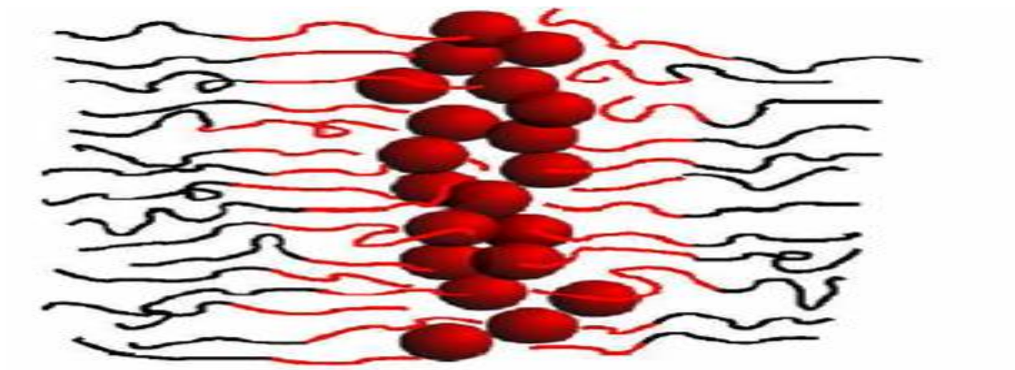


Fig.1.6.a: Self assembly of diblock copolymers surfactants * .

* *Adapted from* ***Self-Assembling Nanotechnology,*** *by Russell B. Thompson, Dept. of Physics, University of Waterloo, Phys 13 news,p4 / Winter 2005.*

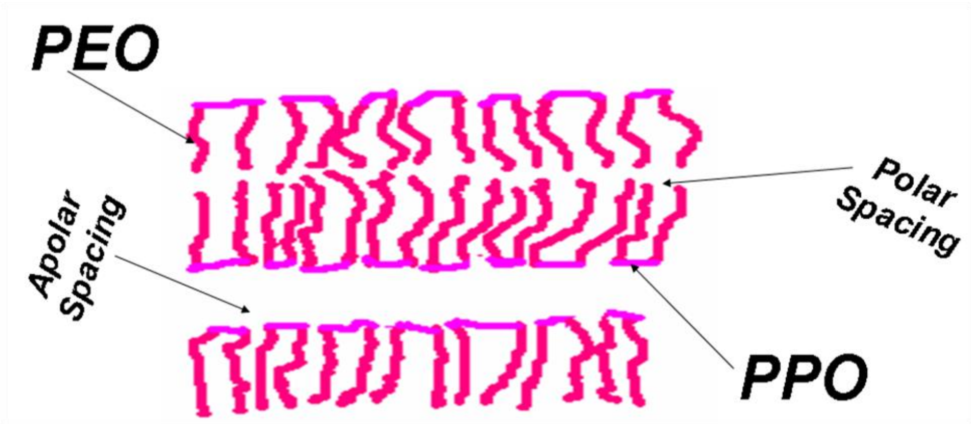


Fig.1.6.b: Self assembly of triblock copolymers surfactants.

1.3.2.Micellar Behavior Of Poloxamers:

At low concentration of Poloxamers, as any surfactant when dispersed in liquid form micelles. This leads to decrease in the surface tension and surface free energy *(Alxandridis & et al., 1994).*[13] Micelles are obtained as a result of dehydration of poly (propylene oxide) block *(Ivanova & et al.,2001).*[14]

But as the concentration of the pluronic in the system increases, leads to the formation of multimolecular aggregates. Micellar behavior of different block copolymers is found to be dependent upon solvent composition and temperature. Micelle structure consist of hydrophobic PPO block lying in the micelle core and the PEO block in the corona *(Rhee , 2006).*[15] That's shown in figure (1.7)

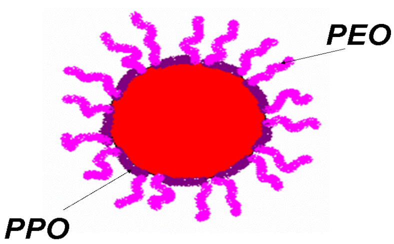


Fig. 1.7 : Micelle of pluronics

1.3.3.Microstructures Of Phase Behavior Of Poloxamers:

Modification of the structure and additional degree of freedom depends on type and addition of solvents . If water is the solvent, it swells PEO blocks and causes formation of structures of higher curvature. As concentration of water increases, the hexagonal structure reverts to micellar cubic structure and forms micellar water-rich solution ,but when temperature increases micelles are revert to cubic structure and more increasing of temperature then cubic reverts to hexagonal structure as figure (1.8) .

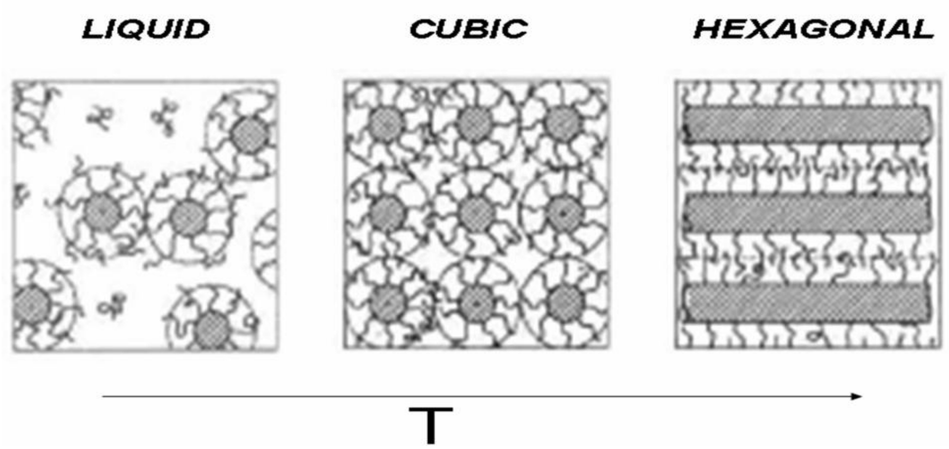


Fig.1.8.: Schematic illustration of micellar phases formed by the Pluronics with increasing temperature or decreasing water content ** .

Large varieties of lyotropic liquid crystalline structures are observed in partially water miscible solvents as cubic , hexagonal ,bicontinuous , lamellar, inverse cubic , inverse hexagonal , and inverse bicontinuous, as shown in figure (1.9.) , but non polar solvents show fewer structures *(Binks & Dong , 1998)* .[16]

** *Adapted from, J Pharm Pharmaceut Sci , 9 (3): 339-358, 2006*

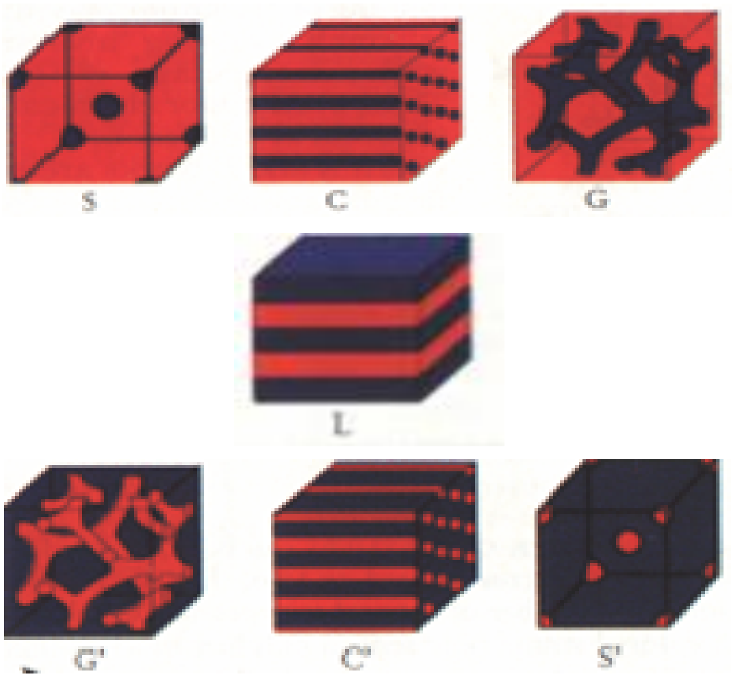


Fig.1.9.: Microstructures of Phase Behavior, S : Cubic , C : Cylindrical ,G : Bicontinuous , L : lamellar , G': Inverse bicontinuous , C' : Inverse cylindrical , S': Inverse cubic .

Copolymers can form other phases like sponge phase but these copolymers are different from pluronics as shown in figure 1.10.

Fig.1.10.: Transmission electron micrographs of (a) the L1 (micellar) phase, (b) the asymmetric L3 (vesicular) phase, and (c) coexisting LR (swollen lamellar) and symmetric L3 (sponge) phases in blends with copolymers possessing 20, 30 and 40 wt % styrene/isoprene midblock, respectively. Note that the morphology depends strongly on copolymer architecture in these blends of equal composition ** .

** *Adapted from Jonathan H. Laurer, Jennifer C. Fung, John W. Sedat, Steven D. Smith , Jon Samseth , Kell Mortensen, David A. Agard, and Richard J. Spontak, From Micelles to Randomly Connected, Bilayered Membranes in Dilute Block Copolymer Blends , Langmuir, Vol. 13, No. 8,p2179, 1997.*

1.3.4. Viscosity And Gelling Point Of Aqueous Poloxamers :

In general Increasing polymer concentration give an increase in solution viscosity and an increase in surface and interfacial activities , also all polymers exhibit smaller decrease in solution viscosity at high temperatures .

A poloxamer solution becomes pseudo plastic around the gelling point. During heating from a low temperature, the viscosity of the polymer solution initially decreases slightly and then, increased gradually. When the temperature approaches the gelling point, the viscosity of the poloxamer solution increases gradually. This change in viscosity in the poloxamer solution is caused by what called gels.

Micelle formation occurs at the critical micellization temperature as a result of dehydration of poly (propylene oxide) block .With increasing temperature, and at a certain point, the micelles obtained. In addition, the formation of highly ordered structures, such as a cubic crystalline phase, has been proposed as the driving force for gel formation with inorganic salts decreased the gelling point of an aqueous poloxamer solution and that effect could be reached due to a reduction in the water activity leading to an increase in the active concentration of the polymer in the system. Anionic surfactant is known to increase the gelling point due to micellar solubilization *(Rhee , 2006).*[15] Gelling behavior depends on the molecular weight and percentage of hydrophobic portion. The gel formation occurs only when concentration is above critical micellar concentration *(Schmolka , 1994).*[17]

1.3.5. Effect Of Additives On Micellar Behavior:

Triblock copolymer surfactants have been an active research topic due to their wide spread use in important industrial areas and as pluronics have a wide spread applications , the additives to these pluronics can be useful for optimizing their applications.

Various salts and additives, surfactants, polymers, co solvents added have marked effect on micellization, clouding, solubilization behavior of pluronic solutions. Addition of sodium chloride , lowers the CMC due to fact that it develops the hydrophobicity in PPO and hydrophilicity of PEO is reduced and lower the critical micellar temperature significantly *(Wanka & et al. , 1990)* .[11] The phase inversion temperature increases with increasing of number of oxyethylene groups and decreases with increasing alkyl chain length. The phase inversion temperature also decreases on adding NaCl but increases on adding tetra butyl ammonium bromide as electrolyte *(Alexandridis & et al., 1995)* .[18]

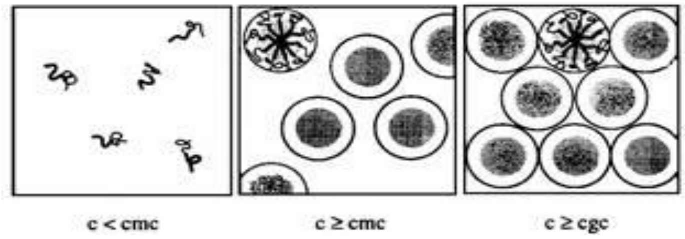


Fig.1.11. : Illustration of the critical micelle concentration (cmc) and critical gel concentration (cgc) in a block copolymer solution [*] **.**

Pluronics in their non aggregated state better interact with the anionic surfactant than with cationic and nonionic ones *(Ortona & et al. ,2006)*.[19] Salts with multivalent cations when added in specified concentrations, inhibit formation of gel in case of some pluronics .

Addition of tetrabutyl ammonium bromide "TBAB" structured in figure (1.4) increase solubility of nonionic surfactant and enhance cloud point as the additive concentration increased *(Roy & Moulik , 2003)*.[20]

1.3.6. Effect of co-solvents on phase behaviour of Poloxamers :

The effect of co-solvents or surfactants on the phase behaviour of poloxamers are quantified in terms of location of co-solvents / surfactant molecules in different domains of poloxamer self assembly, that's depending on the polarity of solvents which specified the location to be in PEO - rich or PPO – rich domains in microstructure *(Alexandridis , 1998)*.[21] Due to this idea Limonene is located inside apolar domain when solubilized in lamellar liquid crystal of poloxamers *(Kayali & et al. ,2006)*. [22] Some solvents act as co–

[*] *Adapted from Hamley, I. W., The physics of block copolymers, Oxford University Press; New York, USA, pp. 1-20, 1998.*

surfactants and behave due to amphiphilic character and located at the interface between PEO- rich and PPO – rich domains *(Huang & et al. , 2001)* .[23]

The effect of co-solvents on poloxamer phase behaviour depends on the highest co-solvent / water ratio able to stabilize liquid crystalline structures , and affect lyotropic liquid crystals due to the degree of relative swelling of co-solvent per poloxamer content *(Opsteen , 2004)* .[24]

1.3.7. Temperature Dependence And Behavior Of Poloxamer Micelle:

Critical micellar concentration (CMC) of solutions decreases with increasing temperature. However, the critical micellar concentration is strongly dependent on temperature. This has been led to the concept called critical micellization temperature which is the temperature at which micelles appear in PEO/PPO/PEO solution at certain concentration . When temperature approaches to critical micellization temperature, in aqueous solution, the antisymmetric C-H stretching vibration of methyl groups shifts towards lower wavenumber *(Su & et al. , 2000).*[25] This interaction of methyl groups with water molecules is weakened by heat, and dehydration of methyl groups increased making the polymer more hydrophobic *(Alexandridis & et al. , 1995).* [26]

1.3.8. Thermo reversible Behavior Of Poloxamers:

Poloxamers, as type of copolymers, show characteristic property of thermo reversible characteristic *(Chavez & et al. , 2006).*[27] They are liquid when refrigerated (4-5 ˚C) but turn into gel form when at room temperature. The gel thus formed is reversible on again cooling *(Wanka & et al. , 1990)*..[11] When the pluronic is placed into cold water, at low concentrations; hydration layer surrounds the poloxamer molecule and hydrophobic portions are separated due to hydrogen bonding , but increasing of temperature causes breakage of hydrogen bonds and release desolvation of the hydrophilic chains *(Miller & Drabik , 1984).*[28] The gel formed is micellar and the liquid micellar phase which is stable at low temperature undergoes conversion into cubic structure as the temperature increases

(Chen – Chow , 1980).[29] While the hexagonally packed cylinders are formed with more increasing of temperatures as shown in figure (1.8.) *(Schmolka , 1994).*[17] This gelling property is useful in the various drug delivery systems such as oral, ocular, nasal, topical, dental, and other biomedical fields *(Quadir & et al. ,2007).* [30]

1.4. Applications

1. 4.1.General Review:

These materials are used as **nonionic surfactants** in industrial and technical applications that because of the amphiphilic properties, they can be used **to increase the water solubility** of hydrophobic, oily substances or otherwise **increase the miscibility** of two substances with different hydrophobicities. In addition they are used **in cosmetics**, and **pharmaceuticals**. They have also been used as **model systems for drug delivery applications.**

Poloxamer block copolymers have a wide range of applications in **experimental medicine** and **pharmaceutical sciences**, their formulations, particularly gels, w/o and o/w emulsions, nanoparticles coated with block copolymer and solid polymer blends.

Pluronic micelles are used **in drug delivery**, for solubilization of water insoluble drugs, preparation of stable micellar formulations and specific **applications in cancer**, **gene therapy** and other areas.

Pharmaceutical excipients are inert as non-active formulation ingredients and these formulation components are referred to as **'functional excipients'**. Pluronic block copolymers fall into this functional excipient category.

It is used as **an emulsifying agent, solubilising agent, surfactant, and wetting agent for antibiotics**. Poloxamer is also used **in ointment and suppository bases and as a tablet binder or coater**.

Pluronics have wide range of applications in pharmaceutical industry as a featured excipient. Various grades of them were used as **emulsifier**, **suspension stabilizer in liquid orals, parenteral and topical dosage forms** and also **as solubilizer for hydrophobic**

drugs. In solid dosage forms, they act **as wetting agent, plasticizer, tablet lubricant** and has wide application **as gelling agent** due to thermoreversible gelatin behavior.

Pluronics are known to form **hydrogels**, but these polymers are nonbiodegradable, and thus limiting their biomedical applications *(Lee & et al. ,1995).* [31]

1.4.2. Pharmaceutical applications Of Poloxamers: [*]

Pluronics are efficient for the drug delivery as well as other biomedical applications summarized as follows:

1. Ophthalmic Applications:

2. Intranasal Applications:

3. Vaginal Delivery:

4. Rectal Applications:

5. Ear Applications:

6. Dental Applications:

7. Buccal Applications:

8. Transdermal and Topical Applications:

9. Injectable Routes:

10. Subcutaneous Route:

11. Intramuscular Route:

[*] *Adapted from J . J. Escobar-Chávez1, M. López-Cervantes1, A. Naïk2, Y. N. Kalia2, D. Quintanar-Guerrero1, A. Ganem-Quintanar1.* ***Applications Of Thermoreversible Pluronic F-127 Gels In Pharmaceutical Formulations*** **,** *J Pharm Pharmaceut Sci (www. cspsCanada.org) 9 (3): 339-358, 2006*

12. Intravenous route:

13. Biomedical and Other Applications:

1.4.3. Applications of limonene :

In general Limonene is common in cosmetics , in food manufacturing and some medicines as flavoring agent , it is added to cleaning products such as hand cleaners as fragrance , Limonene is increasingly being used as solvent for cleaning purposes such as removal of oil from machine parts *(Salonen & et al. , 2007).*[32]

Below are some of applications of limonene which was used as oil and fragrance at the same time in this research:

- ***Fragrances***
- ***Cleaners & Degreasers of (Automotive, Floor, Furniture, Household , Industrial , Outdoor, and Institutional)***
- ***Emulsifiers***
- ***Air Fresheners***
- ***Polishes***
- ***Herbicides***
- ***Insecticides***
- ***Laundry Products***
- ***Metal Products***
- ***Paint Thinners***
- ***Care Products***
- ***Pesticides***

1.4.4. Applications of TBAB.:

Here are some of the applications of tetra butyl ammonium bromide .

- ***Surface-active agents***
- ***Emulsifying agents***
- ***Solvents***
- ***Intermediates***
- ***Active ingredient for conditioners***
- ***Antistatic agent***
- ***Softener for textiles and paper products***
- ***Phase transfer catalyst***
- ***Antimicrobials***
- ***Sanitizers***
- ***Slimicidal agents***
- ***Algaecide***
- ***Pigment dispersers***

1.5. PROBLEM

This subject must take a special care to be searched and learned widely because of :

1. Wide range of applications of pluronics and also wide range of applications of limonene especially as fragrance and the realization that pluronics can self assemble with water and without water to form liquid crystals .especially when use the two components of pluronic and limonene with each other with water and without water .

2. The effect of cationic co-surfactant on the phase behavior when combined with pluronics which will help in the solubilisation and emulsification.

3. The effect of the temperature and salinity on phase behaviour of pluronics which will help in converting of liquid crystals one to another .

1.6. PURPOSE

1. To illustrate the phase behavior of different pluronics (F127 , F108 , F98 and P104) of different polarities and different molecular weights with R(+)limonene and water and search this subject about all conditions.

2. To investigate the effect of cationic surfactant (Tetra butyl Ammonium Bromide) and nonionic surfactants (Pluronics) on the phase behavior especially when combined together .

3. To show the effect of temperature and salinity on the phase behavior.

4. To show the effect of the short chain copolymer and long chain one on the phase behavior and also the effect of polarity of copolymer.

1.7. QUESTIONS TO BE ANSWERED

1. What is the effect of molecular weight of the block copolymer on the phase behaviour of that block copolymer?

2. What is the effect of polarity of the poloxamer on the phase behaviour ?

3. What is the effect of temperature on phase behaviour ?

4. What is the percentage of limonene that can be solubilised in the one phase regions of poloxamers ?

5. What is the identity of micro structure that can be obtained from phase diagram of poloxamers with limonene and water ?

6. What is the effect of cationic co-surfactant on phase behaviour?

7. Does the low molecular weight polymers behave as large molecular weight polymers?

8. What is the proposed mechanism by which limonene may enters the structure of poloxamer or vice versa?

CHAPTER TWO

EXPERIMENTAL

2.EXPIREMENTAL

2.1. MATERIALS AND EQUIPEMENTS

2.1.1. Materials:

- *Pluronic F-108* _ PEO141PPO44PEO141 of average molecular weight about 14600 / Prill / 0btained from BASF and used as received.

- ***Pluronic F-127* _** PEO106PPO70PEO106 of average molecular weight about 13400 / Prill / 0btained from BASF and used as received .

- ***Pluronic F-98* _** PEO123PPO47PEO123 of average molecular weight about 12000 / Prill / 0btained from BASF and used as received.

- ***Pluronic P-104*_** PEO18PPO58PEO18 of average molecular weight about 5000 / Paste / 0btained from BASF and used as received.

- ***R-(+) Limonene***, of purity = 97% / 0btained from Lancaster and used as received .

- *Tetra butyl Ammonium Bromide (TBAB)* , of purity = 99% and molecular weight of 322.38 g/mol. / Obtained from BASF and used as received **.**

- *Distilled water* / Alquds university and used as received.

2.1.2. Equipments:

300 test tube.

300 glass vials.

Shaker (Mixer) - Whirlmixer (Fisons).

(4) Digits analytical balance (Ramco).

Autoclave (Memmert).

Water bath (Selecta).

Polaroid microscope.

Cross polarizers .

Centrifuge.

Thermometer.

2.2. METHODOLOGY

2.2.1. Preparation of samples:

Samples were prepared individually by weighing appropriate amounts of different pluronics F127 , F108 , F98 , and P104 separately and D.Water and R(+) Limonene into (8mm) and (10 mm) test tubes with different ratios beginning from (0.5:9.5) as (pluronic : water) ratio "at the water corner of phase diagram" to (9.5:0.5) as (pluronic : water) ratio "at the pluronic corner of phase diagram" , The initial total weight without limonene is 1 gm. , and titrated with limonene of about 0.02% of total amount into each addition , all tubes are immediately flame sealed , followed by mixing on the vortex until good homogeneity .The samples can be centrifuged in different directions to facilitate mixing (when viscous) and then in one direction to speed up separation if not single phase and some times to remove air bubbles from the samples, all samples were kept at 25˚C ±0.5˚C .

Samples of the other part of research are prepared by the same way but with weight ratio (1:1) of cationic (Tetra butyl Ammonium Bromide) / nonionic (Pluronics)

2.2.2.Determination of Phase Boundaries and graphs :

Following an equilibration period , the samples were checked for phase separation (when the sample is clear and macroscopically homogeneous it is one phase sample ; but if sample is opaque or heterogeneous it is two or three – phase sample) and check if isotropic or anisotropic (miceller solutions or cubic lyotropic liquid crystals are isotropic / nonbirefringent , while lamellar or hexagonal lyotropic liquid crystals are anisotropic / birefringent) . All the notes are recorded and all the points are immediately reported and placed on the phase diagram graphs . Accurate points are taken at the round of the boundaries.

2.2.3. Effect of temperature on the liquid crystals:

Two or three samples of each micelles , hexagonal and cubic liquid crystals are prepared ,they are sealed well , placed in the water bath at different temperatures ranged from (25, 30, 40, 50, 60, and 70˚C), each of these temperatures the samples must be placed for one hour and tested microscopically at each temperature. The inversion from one to another can also be checked by the inversion from isotropic to anisotropic liquid crystal .

2.3. RESULTS

2.3.1.Ternary phase diagram of pluronics(F108, F127, F98)-water–limonene :

The isothermal phase diagram obtained at 25 ˚C ± 0.5˚C for ternary systems (EO)x (PO)y (EO)x –water- limonene for F98, F108 ,F127 are presented in figures 2.3.1 to figure 2.3.3 respectively , the three pluronics show the same phase diagram because they have approximately the same molecular weight , micelles (L1) as isotropic solution and cubic liquid crystal (I1) also as isotropic . As shown in figures 2.3.1. , 2.3.2. ,and 2.3.3. normal micelles were identified at the water rich corner till (22:78) (pluronic : water) at the binary system of (water : pluronic) then cubic liquid crystal which identified from (22:78) (pluronic : water) to about (42:58) (pluronic : water) at the binary system of water and pluronics , which is very viscous and isotropic and stiff , nonbirefringent , the percentage of limonene entering these phases ranged from 1-3 % limonene.

The phase boundaries of the one phase regions are drawn in figure 2.3.1, 2.3.2. and 2.3.3. , the samples whose compositions fall out side the one phase regions are more than one phase , the tie lines in the two phase regions and the triangles show the borders of three phase regions have been determined and shown in figures 2.3.2. and 2.3.3. , at this research the focus was on the rich one phase regions.

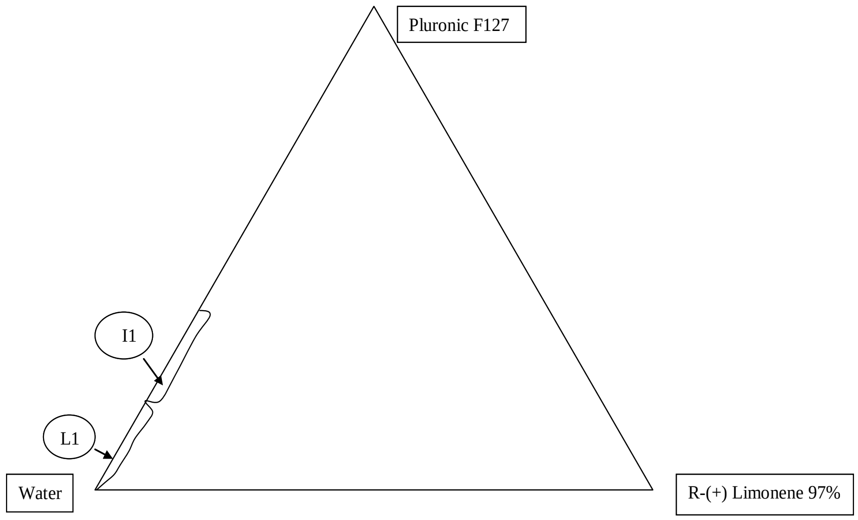


Figure 2.3.1. : Phase diagram of pluronic 127 , with water and limonene

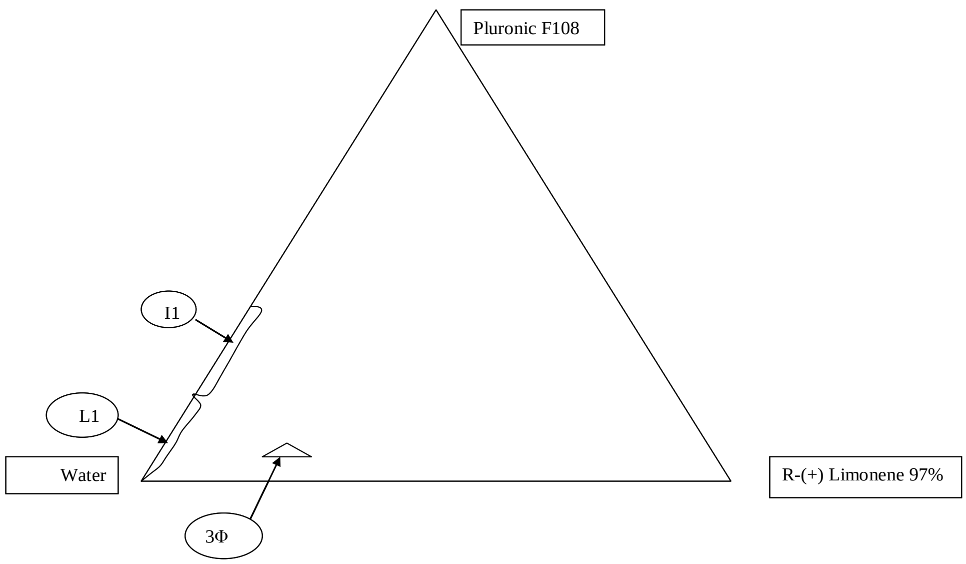


Figure 2.3.2. : Phase diagram of pluronic 108, with water and limonene

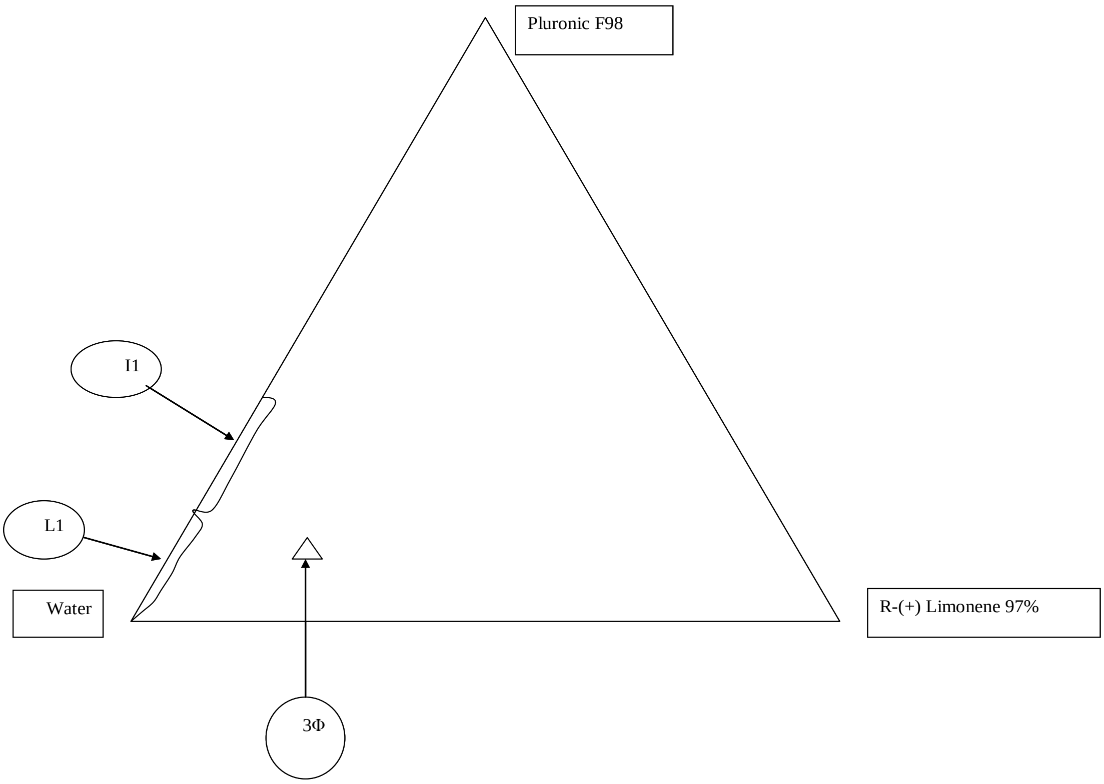


Figure 2.3.3. : Phase diagram of pluronic 98 , with water and limonene

2.3.2. Ternary phase diagram of pluronic (P104)-water – limonene :

The isothermal phase diagram obtained at 25 ˚C ± 0.5˚C for ternary systems (EO)x (PO)y (EO)x –water- limonene for P104 presented in figure 2.3.4. , a four different phases are obtained in the partial phase diagram , micelles (L1) as isotropic solution and cubic liquid crystal (I1) also as isotropic and nonbirefringent , hexagonal (H1) as anisotropic liquid crystal and birefringent ,and lamellar (Lα) as anisotropic and birefringent liquid crystal were obtained . Normal micelles was identified at the water rich corner till (30:70) (P104:water) at the binary system of P104 and water, but it is a very narrow region and a very small amount of limonene were solubilised in this region and not more than 1.5% as maximum percentage , this is shown in figure 2.3.4.

Cubic liquid crystal was observed at the range of (30:70) surfactant (P104) : water to about (45:55) surfactant P104 : water , which is very viscous and isotropic and stiff clear gel , nonbirefringent , the percentage of limonene entering this phase was not more than 5 % limonene as maximum percentage.

Hexagonal liquid crystal was observed at the range of (45:55) (surfactant : water) to about (70:30) (surfactant : water) , which is very viscous and anisotropic and stiff clear gel , birefringent , the percentage of limonene solubilised in this phase was not more than 12 % limonene as maximum percentage. Its birefringence is shown in figure (2.3.12.)

Lamellar liquid crystal was obtained at the range of (70:30) (surfactant P104 : water) to about (82:18) (surfactant :water) ,with a very large region , lamellar liquid crystal wasn't very viscous and anisotropic and clear gel , birefringent , the percentage of limonene solubilised in this phase was not more than 32 % limonene as maximum percentage. Its birefringence is shown in figure (2.3.13).

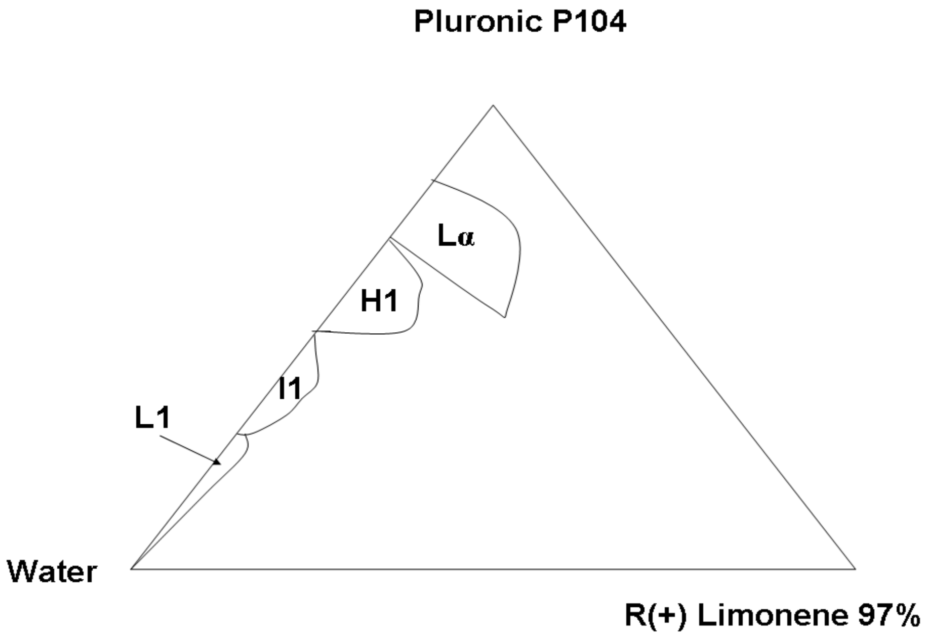


Figure 2.3.4.: Phase diagram of pluronic P104, with water and limonene

2.3.3. Ternary phase diagram of pluronics(F108, F127, F98)- TBAB(1:1)-water – limonene :

The isothermal phase diagram obtained at 25 ˚C ± 0.5˚C for ternary systems (EO)x (PO)y (EO)x-TBAB(1:1)–water- limonene for F98, F108 ,F127 are presented in figures 2.3.5. , 2.3.6. and 2.3.7. respectively , the three previous pluronics show the same sequence in phase diagram because they have approximately the same molecular weight but they shows a different amounts of limonene entering these phases , micelles (L1) as isotropic solution and cubic liquid crystal (I1) also as isotropic . Normal micelles was identified at the water rich corner till (40:60) (surfactant- co surfactant : water) then cubic liquid crystal which obtained from (40:60) (surfactant- co surfactant : water) to about (69:31) surfactant – co surfactant : water at the binary system of water and surfactant - co surfactant line as shown in each of figures 2.3.5., 2.3.6. , and 2.3.7. , were it was found at maximum percentage of limonene of 14% at the ternary system , cubic phase was reached at the percents of 17-18% water , 11-12% limonene and 60-62% surfactant-co surfactant (1:1) it is very viscous and isotropic and stiff , nonbirefringent

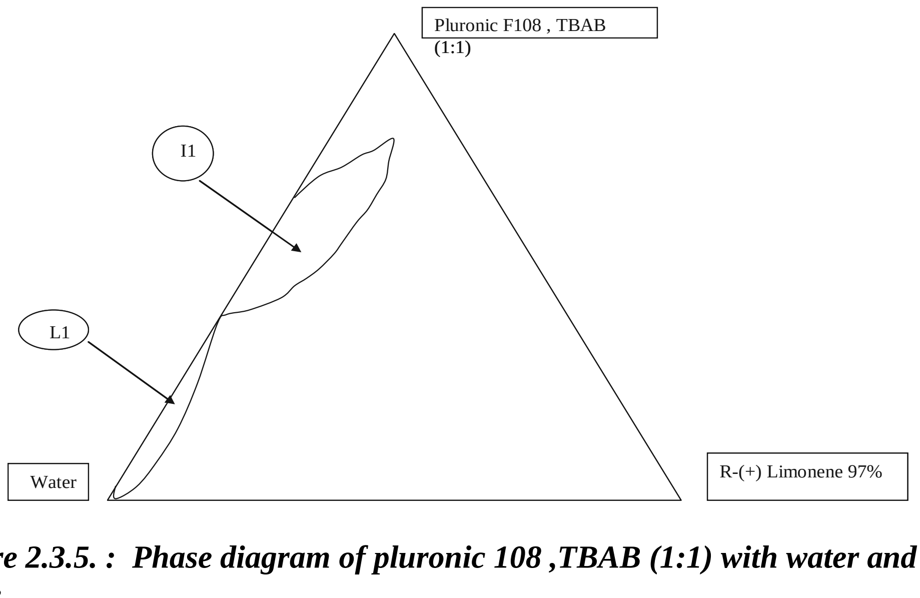


Figure 2.3.5. : Phase diagram of pluronic 108 ,TBAB (1:1) with water and limonene

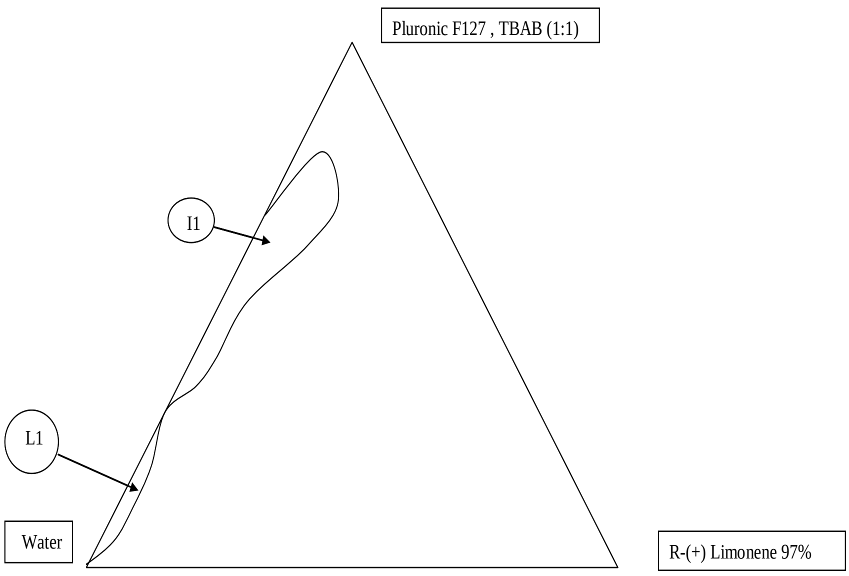


Figure 2.3.6. : Phase diagram of pluronic 127 ,TBAB (1:1) with water and limonene

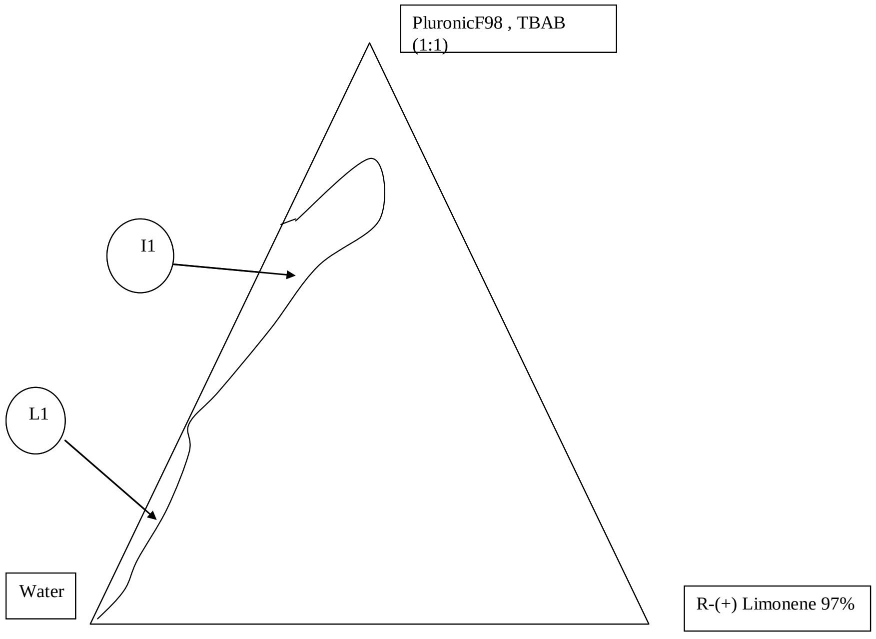


Figure 2.3.7. : Phase diagram of pluronic 98 ,TBAB (1:1) with water and limonene

2.3.4. Ternary phase diagram of pluronics(F108, F127, F98)-water–limonene :

As shown in figures 2.3.8., 2.3.9. ,2.3.10 and 2.3.11 , the pluronics used in this diagram were F108, F127, F98 which shows the regions of one phase , two phases and three phases and how the micelles inverted to two liquid layers as increasing of percentage of limonene more than 4% .

On the other side cubic liquid crystal is inverted to cloudy gel as increased amount of limonene more than 14% as maximum followed by creamy gel observed of one homogeneous cream and finally two layers of liquid and gel at the oil corner.

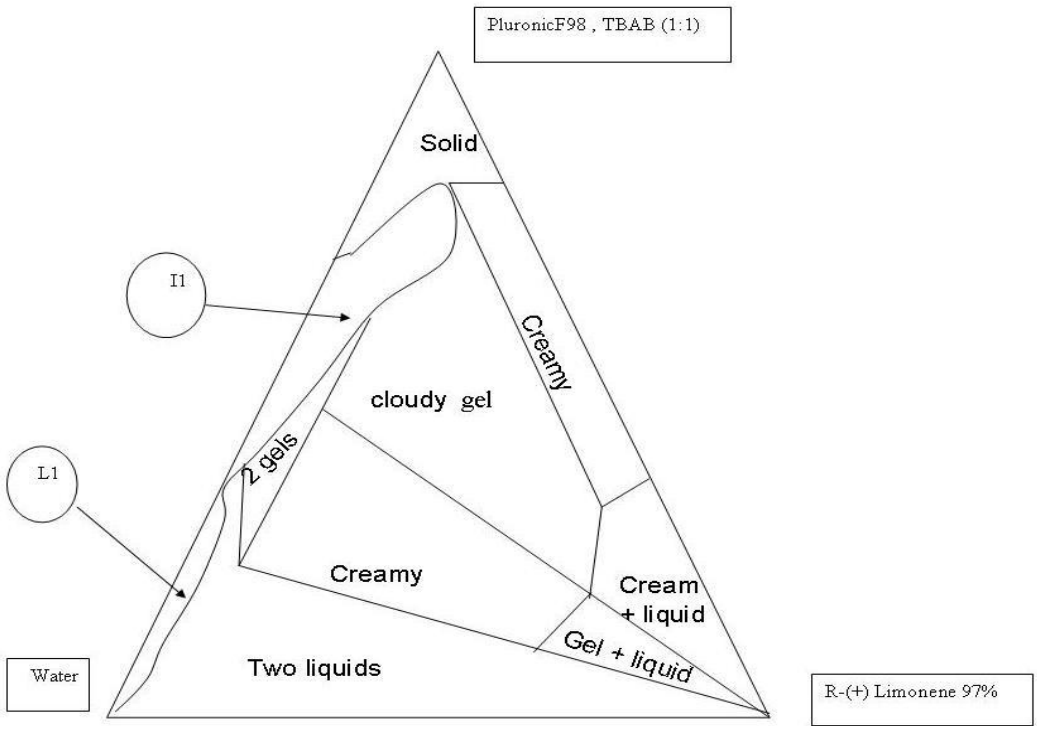


Figure 2.3.8. : Phase diagram of pluronic 98 ,TBAB (1:1) with water and limonene

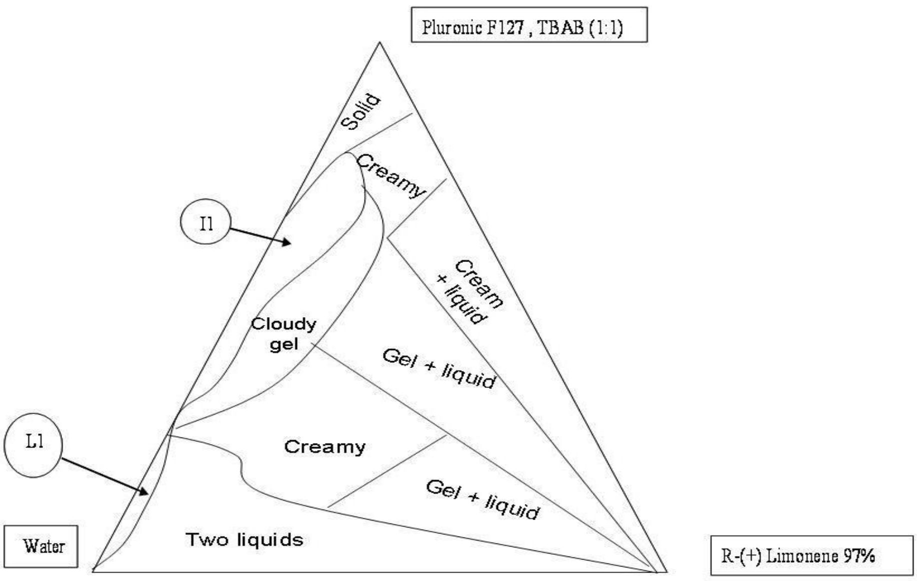


Figure 2.3.9. : Phase diagram of pluronic 127 ,TBAB (1:1) with water and limonene

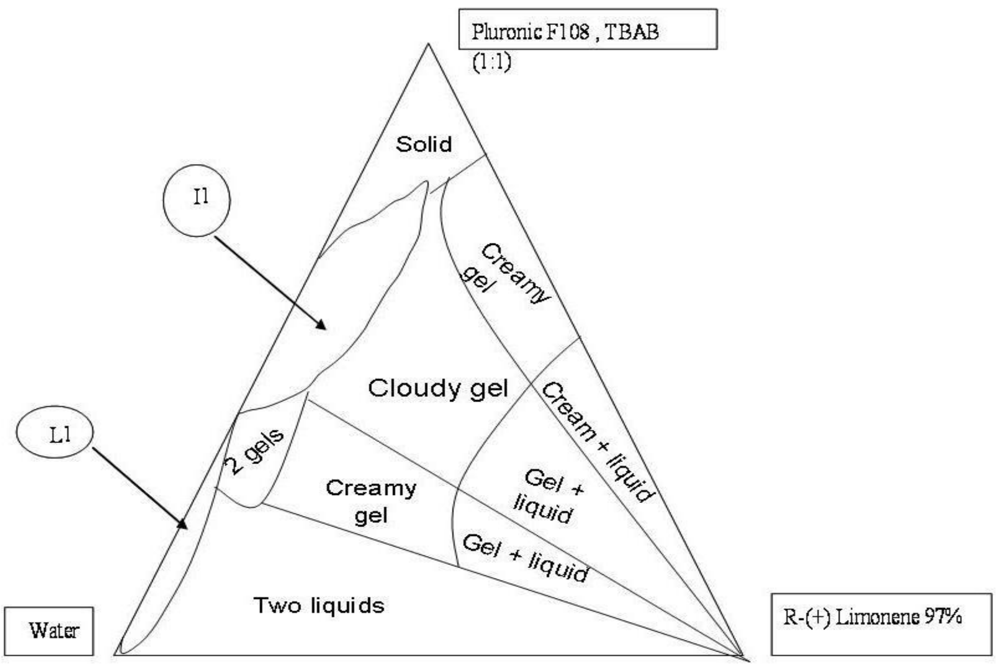


Figure 2.3.10. : Phase diagram of pluronic 108 ,TBAB (1:1) with water and limonene

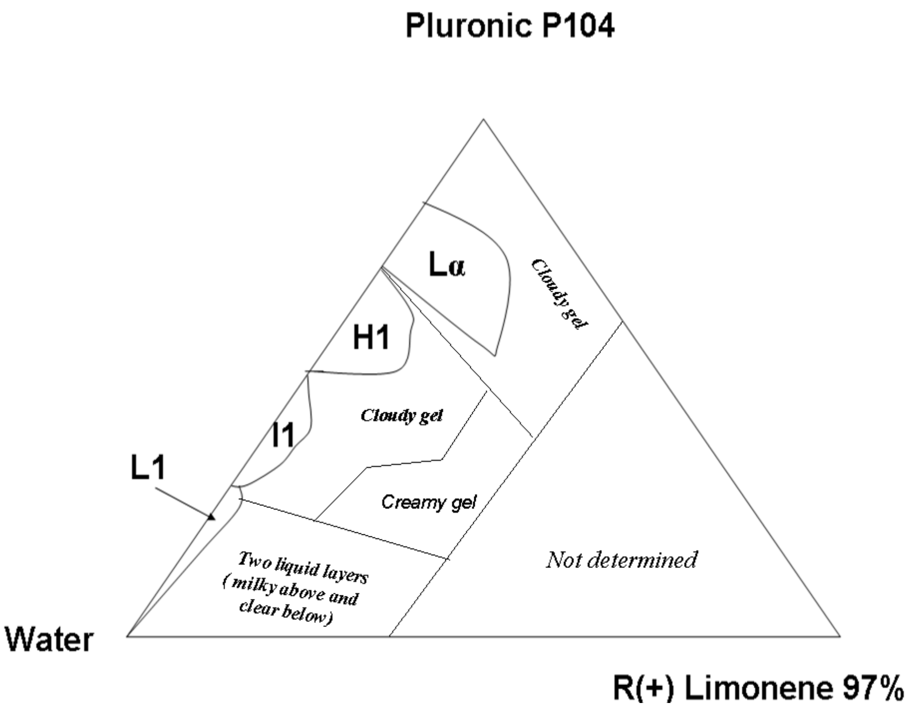


Figure 2.3.11. : Partial phase diagram of pluronic P104 , with water and limonene

2.3.5. Effect of temperature on phase behavior of liquid crystals:

The samples of each one of micelles , cubic , hexagonal were prepared , the ratios of cubic are 40% P104 and 60% water , but the concentration of micelles is 20%surfactant and 80% water the results are shown in table 2.1.

Table 2.1. : Effect of temperature and converting of liquid crystals from one to another.(H1 means Hexagonal liquid crystal , I1 means cubic liquid crystal)

Initial Liquid crystal	*%of P104*	*% of water*	*25˚C*	*30˚C*	*40˚C*	*50˚C*	*60˚C*	*70˚C*
Normal micelles	***20***	***80***	***No change***	***No change***	***No change***	***I1***	***I1***	***H1***
Cubic liquid crystal	***40***	***60***	***No change***	***No change***	***No change***	***H1***	***H1***	***H1***

The most surprising thing observed was inversion of micelles to cubic and cubic to hexagonal at 50˚C which is the same as theoretical review.

2.3.6. Determination Of Birefringence Of Anisotropic structures :

Birefringence of anisotropic liquid crystals of each of lamellar and hexagonal liquid crystals are determined by using either optical microscope with cross polarizers and polarized microscope by taking a hexagonal sample of concentration (60:40) P104 : water , which gives a very nice birefringence (the cloudy regions on the birefringence) as shown in figure 2.3.12 , otherwise birefringence of lamellar liquid crystal of concentration is (70:30) P104 : water. Which shows a narrow birefringence of lamellar liquid crystal (the multi crosses) as shown in figure 2.3.13

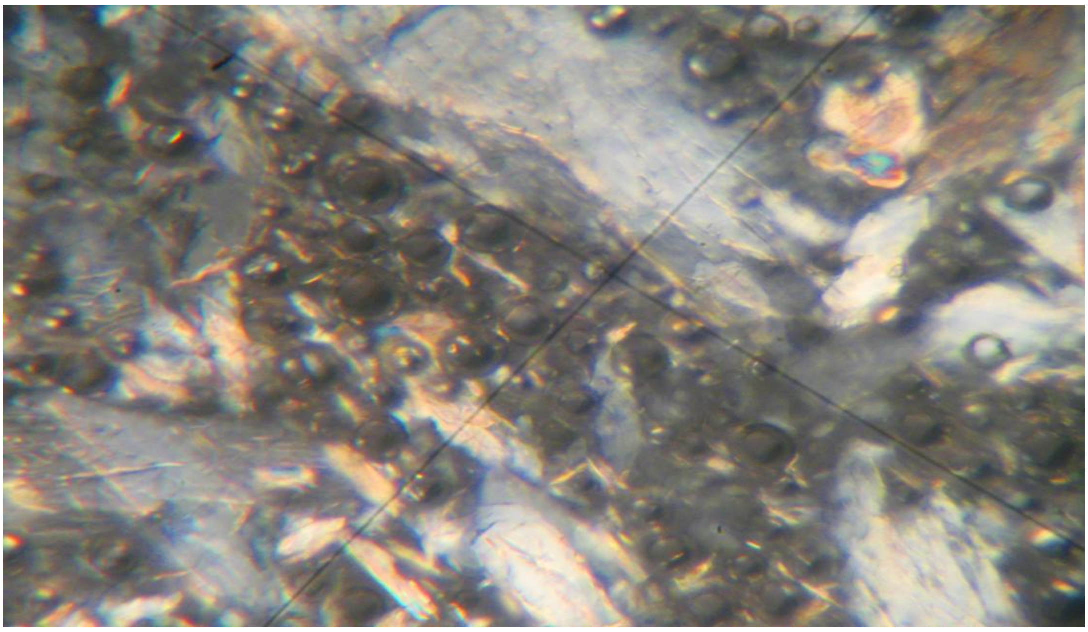


Fig:2.3.12: The birefringence of hexagonal liquid crystal of 60% P104 and 40%water at optical cross microscope .

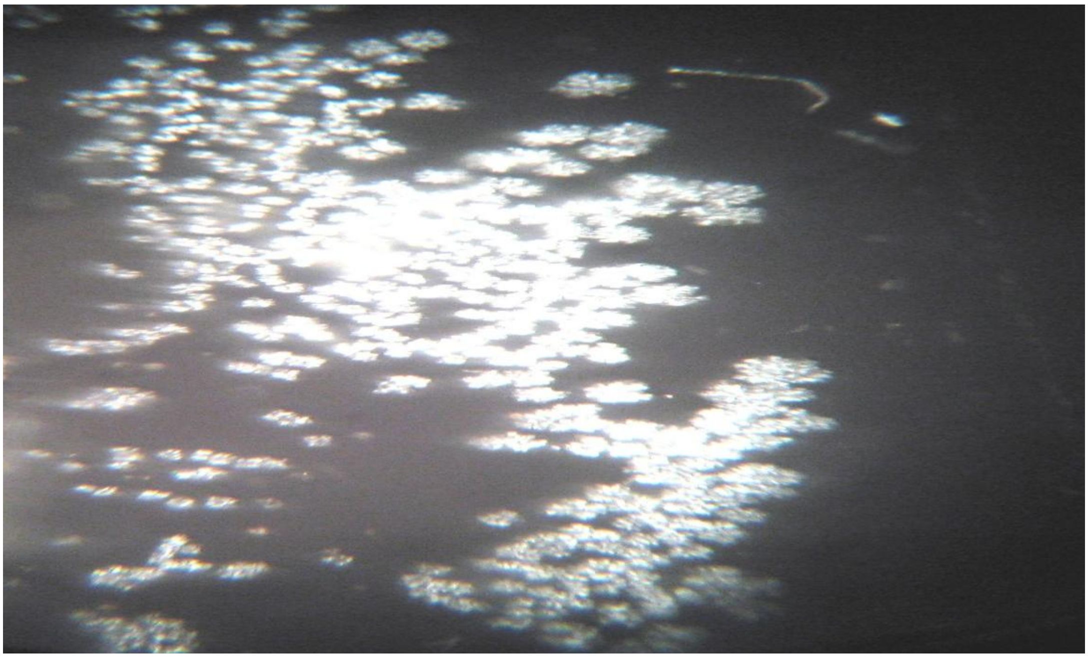


Fig.:2.3.13: The birefringence of Lamellar liquid crystal of 70% P104 and 30% water at optical cross microscope .

2.4. DISCUSSION

The three phase diagrams in figures (2.3.1.),(2.3.2.) and (2.3.3.) of F127, F108 and F98 respectively with water and limonene shows the same phase diagram and same regions of micelles and normal cubic , this is due to the approximately same average molecular weight of the three poloxamers , the average molecular weight of F108 is in the ranges of 12700-16400 , 11000-13000 for F198 and 11000-14600 gm./mol. for F127 , and also the polarity of the three poloxamers approximately the same , that is F108 has 44 monomers of PO , F127 has 56 monomers of PO , and finally F98 has 47 monomers of PO , this gives an indication that polarity of these three poloxamers is slightly different , this difference in polarity didn't affect the phase behaviour with water and limonene and without TBAB ,while when TBAB is used as cationic co-surfactant with a ratio of (1:1) with pluronic in figures (2.3.5.) , (2.3.6.) and (2.3.7.) , the phase diagrams are widely different and shows a large area of normal cubic and micelles , this point is so important , that is TBAB increases the solubility and emulsification of components but these three phase diagrams show the same ratios of poloxamers as those without TBAB , the phase diagrams without TBAB shows a ratio of poloxamer of (42:58) of pluronic and water at the binary system as maximum ratio to give cubic and shows a minimum ratio of (25:75) (pluronic : water) at the binary system , while with TBAB the maximum ratio to form cubic was (40:40:20) of Pluronic : TBAB : water at the binary system at the three phase diagrams with TBAB and this indicates that TBAB is the surfactant who enlarges the cubic region and not the poloxamer .The effect of slightly difference in polarity between the three pluronics appeared in micelles region in each of the three pluronics . The phase diagram of F108 with TBAB, the micelles region is longer than F98 and F127 which shows the shorter region , F108 forms micelles to (20:20:60) F108:TBAB:Water as maximum ratio while (17.5:17.5:65) F98:TBAB:water and (15:15:70) F127:TBAB:water at the binary systems which is the least polar one of the three .

The effect of TBAB was cleared when increases the amount of limonene solubilised in the cubic phase , and this is obtained for F127, F108, and F98 respectively as following percentages (13, 13, 15%) as maximum percentage of limonene , where amount of limonene solubilised in the micelles region reached only 4% as maximum percentage in the three phase diagrams with TBAB . These results are due to TBAB co-surfactant which increased solubility and emulsification of pluronics and limonene.

In figure (2.3.4.) which shows the phase diagram of P104 with water and limonene , In this phase diagram micelles , normal cubic , hexagonal , and lamellar liquid crystals are obtained , this is because P104 is shorter triblock copolymer than F127,F108, and F98 and has average molecular weight of about 4900. On other hand P104 is less polar than other three pluronics because it contains only 18 EO monomers in each side block and 58 PO monomers in central block .

The very narrow region of micelles in phase diagram of P104 with water and limonene is due to less of polarity of that poloxamer , The maximum ratio of P104 in cubic phase is (45:55) of P104: water at the binary system , this is approximately the same as the phase diagrams of other three pluronics used .

On other side Hexagonal and lamellar liquid crystals are observed with large regions , the hexagonal liquid crystal is obtained at the range of 40-70% P104 with water at the binary system and a maximum amount of limonene of 12% at the ternary phase diagram, while lamellar liquid crystal which obtained at the range of 70-82% of P104 at the binary system and a maximum ratio of limonene of 32% at the ternary phase diagram , and this is due to the large space of apolar region where limonene enters , and this fact is also proposed for hexagonal liquid crystal. This apolar space is wide because EO blocks are short when compared with PO region and so limonene solubilised in the non polar region easily , while in the long chain polymers limonene can't solubilised in the apolar space easily because of long EO chains . The lamellar liquid crystal is obtained near the corner of surfactant in the phase diagram and this improves the self assembly fact of P104 with water and without water.

The effect of temperature on phase behaviour of pluronics is an important subject to be discussed . The mesophases of the block copolymers show a thermotropic behaviour and reverse transition from one liquid crystal to another or from one mesophase to another and this can be brought at constant concentration by increasing temperature and then decreasing of that temperature , This effect is due to the fact that the compounds become much more lipophilic with increasing temperature.

The birefringence of block copolymers is much weaker than other surfactants because the interiour of micelles is probably much less ordered than that for single chain hydrocarbons surfactants , and the large scale domain structure is less well developed for polymers than for the normal surfactants . And so the birefringence of lamellar and hexagonal liquid crystals of P104 with water and limonene are very weak.

3. CONCLUSION

The microstructures formed by four pluronics as nonionic surfactants (F127, F108 , F98, and P104) with water and limonene , with TBAB and without TBAB have been investigated . the water is a selective solvent for PEO and Limonene is a selective solvent for PPO ,The first three pluronics with large molecular weight shows only micelles and normal micellar cubic while fourth on P104 shows a wide range of spectra that micelles , normal micellar cubic , normal hexagonal and lamellar liquid crystals are obtained , the four different phases are thermodynamically stable at room temperature . The rich structural polymorphism observed in ternary amphiphile containing mixtures are affected by molecular weight of poloxamer , polarity of poloxamer , temperature , amount of solvent , order of addition and finally addition of cationic surfactant as co-surfactant.

Addition of TBAB as cationic co-surfactant enlarges the regions of normal micelles and normal micellar cubic in phase diagram because it enhance the solubility and emulsification of the components used . The birefringence of anisotropic liquid crystals is investigated using optical microscopy and polarized microscopy.

The effect of temperature is also observed when normal micellar cubic converts to hexagonal liquid crystal when temperature was raised to 50 ˚C or more , and this proved the fact of effect of temperature and thermo reversible effect.

This research will release a wide range of applications due to use of limonene with pluronics , while each of the two components has previously a large amount of applications because pluronics are safe products and limonene as fragrance . and now the two important components with each others will release a surprising number of applications , why not ? , limonene is solubilised in lamellar liquid crystal in P104 phase diagram with a large percentage reaches 32% limonene and is solubilised in hexagonal liquid crystal with a maximum percentage of 12% limonene .

4.REFERENCES

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العنـــــوان: "تشـكل بعـض المبلمرات التي تسـمى بلورونكس مع الماء والليمونين"

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ملخص:

البلورونكس (Pluronics) هي مبلمرات ثلاثية مكونه من ثلاثة أجزاء، كل جزء منها مبلمر وتتكون من مبلمر أكسيد الايثيلين (PEO) – مبلمر أكسيد البروبيلين (PPO) - مبلمر أكسيد الايثيلين (PEO) وتعرف بهذا الشكل (PEO-PPO-PEO)، هذه المواد لها خاصية التوازن بين قابلية الذوبان في المذيبات القطبية والمذيبات غير القطبية في آن واحد فمثلا مبلمر أكسيد الايثيلين له خاصية الارتباط مع المذيبات القطبية أما مبلمر أكسيد البروبيلين فيرتبط مع المذيبات غير القطبية، كما أن لهذه المواد خاصية التشكل الذاتي بوجود الماء أو بعدمه بالإضافة إلى أنها آمنه للإنسان وغير مضره بالصحة، وقد تسبب هذا الأمر بفتح مجالات تطبيقية واسعة جدا فيما يتعلق بهذه المواد وخصائصها.

ومن أجل دراسة قدرة هذه المواد على التشكل من خلال معايرة (المبلمر والماء معا) بالليمونين (Limonene) وحيث أن هذه المبلمرات تعتبر مساعدات غير أيونيه (Nonionic Surfactants) على الذوبان وخصوصا عند استخدامها مع الماء والليمونين، فقد تم اختيار أربعة من هذه المبلمرات وهي: F127(PEO106PPO70PEO106)، F98(PEO123PPO47PEO123) F108(PEO141PPO44PEO141)، وأخيرا P104 (PEO18PPO58PEO18)

لقد تم الرسم بالأبعاد الثلاثة عن طريق توزين كميات كافية ومحددة من المبلمرات بنسب من (9.5-0.5) ومن الماء (0.5-9.5) وكان الوزن الأولي لكلاهما معا 1 جرام ، وتم معايرة الناتج بالليمونين بمقياس 0.02% لكل اضافه. حيث تم إغلاق الأنابيب جيدا وتمت عملية التذويب جيدا، وقد تم حفظ العينات على درجة حرارة 25 مئوي. وتم انتظار الاتزان لهذه العينات ، وبعدها تم تفقد العينات من أن يكون هناك فصل بين المذيبات وكذلك تم فحص البصمه بين السوائل البلورية المشع مثل (السائل البلوري اللاميلر والسائل البلوري الاسطواني) والتي يكون لها بصمه أو السوائل البلورية غير المشعة مثل (السائل البلوري المكعبي والمايسلر) بحيث تم استخدام قطع طي استقطاب متعاكسات (cross polarizers) والميكروسكوب البولارويد (Polaroid microscope) لتحديد ماهية البصمه .

الثلاثة الأولى من هذه المواد والتي لها وزن جزيئي عالي أظهرت أشكال محدودة خلال الرسم ثلاثي الأبعاد (Phase Diagram)والخاص بعملية إذابة كل من هذه المواد بالإضافة للماء ومعايرتها مع الليمونين و قد انحصرت هذه الأشكال في المايسلز (Micelles) والشكل المكعبي للسائل البلوري (Cubic) بينما في المبلمر الرابع الذي سبق ذكره وهو الأقل في الوزن الجزيئي والأقل في القطبية فقد أظهر أشكالا متعددة من هذه الأشكال حيث نتج عندنا من خلال عملية المعايرة بالليمونين أشكال مثل المايسلز (Micelles) و المكعبي للسائل البلوري (Cubic) والاسطواني للسائل البلوري (Hexagonal) واللاميلر للسائل البلوري (Lamellar) وقد كانت نسبة الليمونين المذاب في هذه الأشكال عالية جدا خصوصا الشكل الاسطواني حيث وصلت نسبة الليمونين المذاب فيه 12% أما اللاميلر فقد وصلت نسبة الليمونين المذاب فيه إلى 32% وهذا يعود إلى عدم قطبية مذيب الليمونين والقطبية القليلة جدا للمبلمر الرابع والتي سمحت لهذا المذيب لان يعبر المجال غير القطبي في هذه الأشكال.

تم إضافة مساعد آخر على الذوبان يسمى (TBAB)(Tetra butyl Ammonium Bromide) تترا بيوتيل أمونيوم برومايد لكل من المبلمرات الثلاثة الأولى أنفة الذكر وهو عبارة عن مساعد إضافي (Co surfactant) على الذوبان وقد أضيف بنسبة (1:1) مع المبلمر وتم إضافته مع الماء ومعايرته بالليمونين وقد كان لهذه المادة الأثر الأكبر في زيادة الذائبية للمبلمرات والليمونين في الماء ونتج عن ذلك اتساع للمناطق (One-Phase)أحادية التشكل وهي المايسلز والمكعبي وكذلك زادت نسبة الليمونين المذاب في هذه الأشكال. من ناحية أخرى تم دراسة أثر الحرارة على هذه الأشكال المتكونة وظهرت لدينا نتائج رائعة وخصوصا عند تحوله ا من شكل إلى آخر مع ازدياد درجة الحرارة والعكس بالعكس.