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Phase diagram of tyloxapol and water – I

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Summary

Tyloxapol, a nonionic liquid polymer of the alkyl aryl polyether alcohol type, described as freely soluble in water, is widely used in pharmacy. At room temperature and above, tyloxapol does not dissolve immediately in water but forms liquid crystalline structures in the contact zone with water resulting among others in the slow formation of aqueous one-phase systems. Macroscopically isotropic aqueous systems with a concentration-dependent viscosity are formed below 35 wt% tyloxapol. Around 35 wt% there is a narrow two-phase coexistence region. From 37.5 to 65 wt% textures of lyotropic liquid crystalline hexagonal phases are observed in the polarizing microscope. Solubilization tests indicate a hexagonal phase. This phase exists in a broad concentration and temperature range as derived from hot-stage polarizing microscopy and differential scanning calorimetry. The hexagonal phase exhibits the highest transition temperature (59°C) and the highest transition heats (0.5 J/g) around 50 wt%. Transmission electron microscopy (TEM) observations indicate a supramolecular arrangement consisting of parallel cylinders of non-uniform length resulting in two-dimensional order. In a narrow concentration range around 70 wt% and below 30°C, there is a stiff lyotropic liquid crystalline cubic phase with a transition heat of 1.3 J/g. Between 74 and 80 wt% at room temperature there is a liquid crystalline lamellar phase with low viscosity exhibiting no measurable transition heats. TEM observations indicate a supramolecular arrangement consisting of extended stacked lamellae exhibiting only one-dimensional order. The retransformation of the cubic phase from the melt is highly retarded. In contrast, the liquid crystalline hexagonal phase and lamellar phase are immediately formed on cooling of the melts to room temperature. Above 80 wt% the systems represent crystal dispersions.

Introduction

Tyloxapol is described as a nonionic liquid polymer of the alkyl aryl polyether alcohol type in the official monographs of the US Pharmacopeia (USP XXII, 1990). Besides tyloxapol (Martindale, 1989; Merck Index, 1989; Pharm. Stoffliste, 1990; USAN, 1990; USP XXII, 1990), synonyms such as polymer of *p*-(1,1,3,3-tetramethylbutyl)phenol with ethylene glycol and formaldehyde (Pharm. Stoffliste, 1990 (WHO)), 4-isooctylpolyoxyethylenphenol formaldehyde polymer (Pharm. Stoffliste, 1990), phenol 4-(1,1,3,3,-tetramethylbutyl)-, polymer with formaldehyde and oxirane (USP XXII, 1990) and Triton WR-1339 (Merck Index, 1989) are often used. Triton A20 is an aqueous solution of the substance. Tyloxapol was first registered in the National Formulary (NF) of the USP (NF XIV, 1978) and later in the USP (USP

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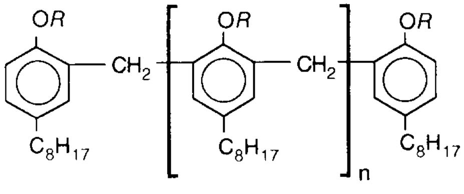

$R = CH_2CH_2O(CH_2CH_2O)_mCH_2CH_2OH$;

$m = 6 - 8$; $n \leq 5$.

Fig. 1. Structural formula of tyloxapol.

XX, 1980). In Martindale the substance first appeared in 1941 and in the Chemical Abstracts in 1948.

The structural formula of tyloxapol is given in Fig. 1. It is a nonionic surfactant with detergent properties (Lewis, 1981) and has been widely used in pharmacy as an additive but has also been introduced as a pharmacologically active substance (Lewis, 1981; Pharm. Stoffliste, 1990). According to the Merck Index (1989), it is a mucolytic and several tyloxapol containing mucolytic products are available. In addition, it is used in a cleaning, wetting and lubricating liquid for artificial eyes (Pharm. Stoffliste, 1990).

Although tyloxapol is described as being freely soluble in water (Merck Index, 1989), homogeneous mixtures of tyloxapol, which is a liquid, and water, cannot be obtained immediately at room temperature. Non-liquid intermediate structures are formed in the tyloxapol-water contact zone which dissolve only slowly at room temperature. This is what is described as 'slowly but freely miscible with water' by Martindale (1989). Although the surface activity of tyloxapol (technical bulletin of Sterling Organics on Tyloxapol N.F.) and its micelle forming properties have been described (Guttman et al., 1961), no information is available about the structure of the non-liquid binary systems. The aim of the present study was to fill this gap by investigating the phase behaviour of tyloxapol/water mixtures between 20 and 65°C. The structures were characterized by various techniques. Hot-stage polarized light microscopy, differential scanning calorimetry (DSC) and transmission electron microscopy (TEM) of replicas of freeze-fractured samples were used to obtain information concerning the phase behaviour of the binary mixtures and to obtain an optical impression of the supramolecular structures of the phases. A subsequent publication will deal with viscosity measurements and synchrotron radiation X-ray scattering experiments performed to obtain information on the dimensions of the supramolecular structures and of the underlying molecular arrangements.

Materials and Methods

Materials

Tyloxapol USP (Sterling Organics), methylene blue (Merck), Sudan Red 7B for microscopy (Merck) and bidistilled water were used.

Preparation of binary tyloxapol / water systems

Tyloxapol was weighed into 8 ml glass vials and bidistilled water was added without shaking or stirring to a final sample weight of 5 g. The samples (w/w) were allowed to equilibrate at room temperature for 4–12 weeks. The following tyloxapol concentrations (w/w) were prepared: 0.1–1.5 in steps of 0.1%, 1.75–3.25 in steps of 0.25%, 4, 5, 6.5, 8, 10–30 in steps of 1%, 32.4, 35, 37.5, 40, 42.4, 45, 47.5, 50, 60, 62.5, 64.8, 67.4, 70, 72.5, 74.8, 77.3, 80, 82.6, 85.1, 87.5, 90, 92.4, 94.2, 97.2%. Unless otherwise stated all concentrations below are given in wt% tyloxapol.

Dye-solubilization test

The test was performed with fine crystals of the water-soluble dye methylene blue and the lipophilic dye Sudan Red 7B. 10 min after carefully strewing a few small dye crystals on the samples (about 150–200 mg) the amount of dissolved and solubilized dye in the lyotropic liquid crystalline phase was visually examined.

Polarized light microscopy

Polarized light microscopy studies were performed at room temperature to identify the phases and during temperature scans (1°C/min) to study the thermotropic mesomorphism. The binary systems were viewed in a Zeiss microscope III (Zeiss, Oberkochen, Germany) equipped with crossed polarizers and λ-sheet. Above room temperature a Mettler FP52 hot-stage holder connected with a Mettler FP5 control unit (Mettler, Gießen, Germany) was used. The temperature was scanned at 1°C/min. The temperature values for the transition from an optically anisotropic to isotropic system (heating runs) correspond to the temperatures of the first appearance of complete isotropy and, for the transitions of optically isotropic to anisotropic systems (cooling runs) to the temperatures of the first appearance of anisotropy.

TEM

Freeze-fracturing and freeze-etching of samples were performed with a BAF 400 freeze-fracture unit (Balzers AG, Liechtenstein, Switzerland) using samples sandwiched between two flat holders.

Fast freezing was achieved either by the slush method in melting nitrogen or propane (golden holders) or by jet freezing with liquid propane (copper holders). The fracturing temperature was 173 K. The fractured frozen samples were shadowed under 45° with platinum/carbon (layer thickness: 2 nm) and under 90° with pure carbon for replica production. Replicas were cleaned with chloroform-ethanol (1:1, v/v), picked up on uncoated microscope grids and viewed with an electron microscope (Model EM 300, Philips, Kassel, Germany).

DCS

Calorimetric measurements were performed on a Perkin Elmer DSC-2C with a thermal analysis data station (Perkin Elmer, Überlingen, Germany) using a scan rate of 5 K/min. Samples were prepared at room temperature by accurately weighing 10–17 mg into standard volatile sample aluminium pans (Perkin Elmer). An empty pan was used as reference. Each sample was run four times. Samples were subjected to a five-step temperature program: (1) 293 to 349 K, 3 min at 349 K; (2) 343 to 283 K, 15 min at 283 K; (3) 283 to 343 K; (4) stored at room temperature for at least 5 days and (5) 293 to 343 K.

Results

Macroscopic observations

In the present study, the optical properties and dye-solubilization characteristics of the binary systems were observed macroscopically. The addition of water to tyloxapol at room temperature results in the spontaneous formation of an intermediate gel-like system in the contact zone. Depending on the weight ratio of the components, equilibration of the systems takes up to 8 weeks. After equilibration systems containing less than 35 wt% tyloxapol are macroscopically isotropic liquids with a tyloxapol concentration-dependent viscosity. The water-insoluble dye Sudan Red 7B can be solubilized in all aqueous systems within 10 min demonstrating the existence of micelles. In a narrow concentration range around 35 wt%, a liquid (aqueous) phase is observed in equilibrium with a semi-solid phase. At 37.5 wt%, however, a semi-solid opaque system that does not exhibit macroscopic phase boundaries is found. From 37.5 to 65 wt% there are opaque semi-solid one-phase systems. The increase in tyloxapol concentration from 37.5 to 65 wt% results in an increase in the viscosity. Systems containing more than 40 wt% do not start to flow under their own weight within several minutes and systems containing more than 42.5 wt% exhibit a yield value. All systems dissolve or solubilize, respectively, crystalline methylene blue within 10 min, but not crystalline Sudan Red 7B. At a tyloxapol concentration of 67.5 wt% two phases, a slightly opaque and an optically clear one, become visible. The system containing 70 wt% is an optically clear one-phase system that is extremely stiff compared with the semi-solid opaque ones found between 37.5 and 65 wt%. Again the system does not dissolve crystalline Sudan Red 7B but slowly dissolves crystalline methylene blue within 10 min. At 72.5 wt% there are two phases, a clear and an opaque one. Systems containing 75 wt% and more tyloxapol are opaque one-phase systems and exhibit lower viscosities than the opaque semi-solid systems found between 37.5 and 65 wt%. Even the system containing 75 wt% does not exhibit a yield value despite its vicinity to the stiff 70% system. All systems containing 75 wt% and more

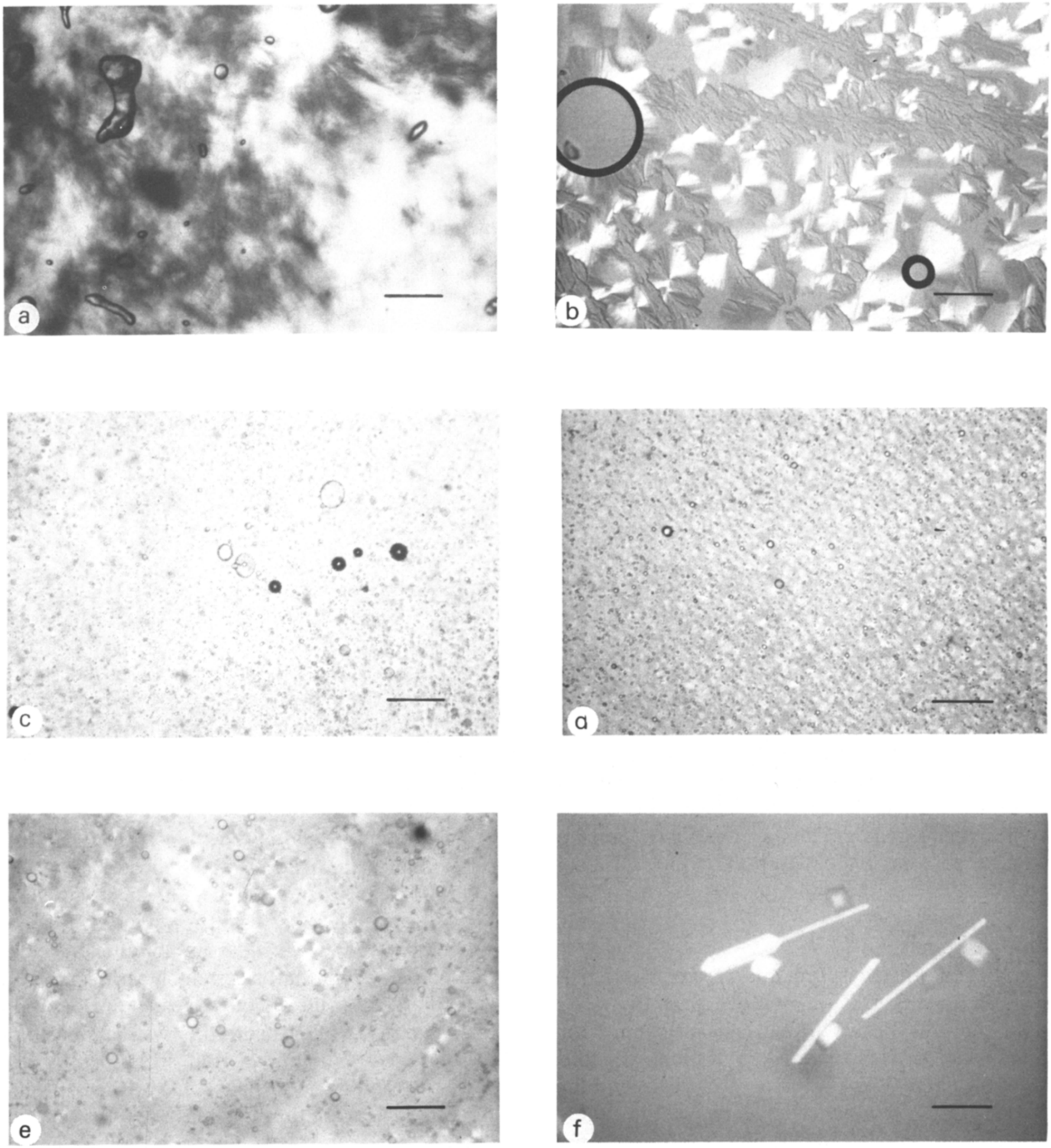

Fig. 2. Polarized light microscopy picture (scale bar: 125 μm) of (a) the hexagonal phase containing 50 wt% at room temperature, (b) the fan-like texture of the hexagonal phase on cooling from its melt, (c) the lamellar phase containing 75 wt% at room temperature, (d) the lamellar phase containing 75 wt% at room temperature after the heating/cooling cycle, (e) the lamellar phase stored at room temperature for 60 min after its coverage by the cover slide, (f) the isotropic liquid system containing 87.5 wt%, (g) system containing 80 wt% of the polymer about 14 h after the heating/cooling cycle, (h) the contact zone between tyloxapol and water (microscope penetration technique): (w) water-rich site, (h) hexagonal phase, (c) cubic phase, (l) lamellar liquid crystalline structures, (t) tyloxapol-rich site.

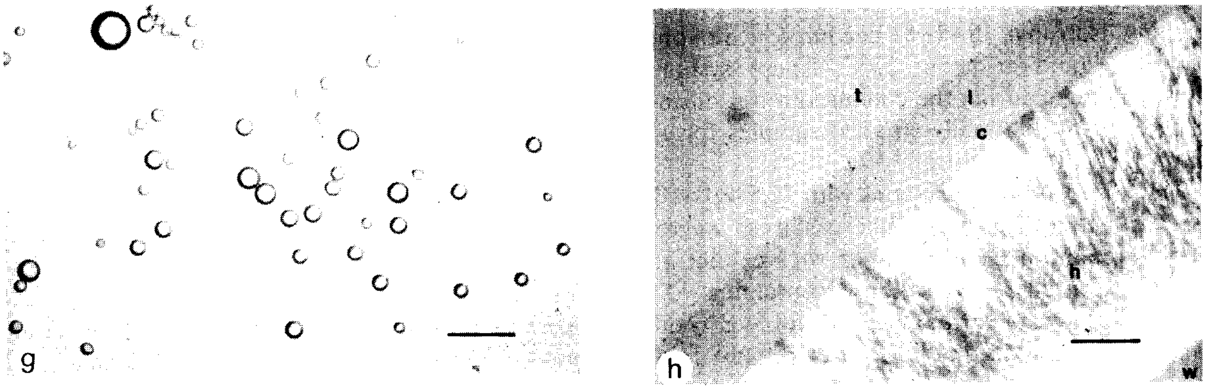

Fig. 2 (continued).

tyloxapol flow under their own weight. The viscosity of these systems decreases with increasing tyloxapol concentrations. In contrast to the semi-solid systems found between 37.5 and 65 wt%, the systems containing more than 70 wt% dissolve both methylene blue and Sudan Red 7B crystals, but slowly compared to the dissolution of methylene blue in the semi-solid systems. Systems containing 80 wt% tyloxapol and more are optically clear viscous liquids and do not dissolve visible amounts of methylene blue. The dissolution of Sudan Red 7B is slow.

The variability in the macroscopic properties of the binary systems such as dye-dissolution and solubilization characteristics, viscosity and optical appearance suggest the existence of micellar and different lyotropic liquid crystalline phases at room temperature. The viscosities and dye solubilization properties of the various lyotropic liquid crystalline phases indicate the existence of a lyotropic liquid crystalline hexagonal phase, a cubic phase and a lamellar phase in the phase diagram.

Polarized light microscopy

At room temperature all liquid systems with tyloxapol concentrations below 35 wt% are optically isotropic in the polarizing microscope whereas those with concentrations ranging from 37.5 to 65 wt% are optically anisotropic as illustrated in Fig. 2a. The appearance of these systems in the polarizing microscope indicates the existence of lyotropic liquid crystalline hexagonal phases over the whole concentration range (Rosevear, 1954). During a 1°C/min temperature scan the systems do not change their optical appearance until they start floating and finally become floating isotropic liquids. The textures in the direct vicinity of the optically anisotropic/isotropic transition are, however, difficult to interpret. At the present stage it cannot be excluded that an additional anisotropic/anisotropic phase transition exists close to the melting temperature. The temperature of the anisotropic/isotropic transition is concentration dependent. It increases from about 46°C at 37.5 wt% to approx. 62°C at 50 wt% and then decreases to about 45°C at 65 wt%. Cooling (1°C/min) of the isotropic liquids to room temperature results in a retransformation into optically anisotropic structures. In most cases the formation of non-geometric and fan-like textures is observed on cooling of the melts (Fig. 2b). The retransformation temperatures are 1–5°C lower than the corresponding transition temperatures. Although all samples retransform into optically anisotropic structures, some thermally stressed systems display residual isotropic areas. Especially systems containing tyloxapol concentrations close to the phase boundaries do not retransform completely into anisotropic systems at the end of the temperature cycles and the system is stored at room temperature for about 15 min.

In contrast, the macroscopically clear, stiff system containing 70 wt% is isotropic in the polarizing microscope at room temperature and corresponds to a lyotropic liquid crystalline cubic phase. During the temperature scan the system remains isotropic until it becomes a floating isotropic liquid at about 33°C. These systems solidify neither during the cooling run nor during storage of the thermally stressed samples for 15 min at room temperature.

The observations on systems with 72.5–80 wt% are difficult to interpret. Whereas fresh microscopic preparations with 37.5–65 wt% exhibit intensely coloured textures, those containing 72.5 and more wt% appear optically isotropic at room temperature or display a few extremely faint coloured fine lines on an isotropic background as illustrated in Fig. 2c. These systems exhibit huge numbers of optically isotropic droplets and during the temperature scans these systems remain isotropic or weakly coloured until they become isotropic liquids still containing isotropic droplets which start floating on liquefaction. On rapid cooling to room temperature, however, they display intensely coloured Maltese crosses or a mosaic texture (Rosevear, 1954) beside isotropic droplets as illustrated in Fig. 2d. Similar observations were made on samples which were stored protected against shear forces on the microscope object slide covered by a microscope cover glass for more than 30 min (Fig. 2e). Anisotropic structures and Maltese crosses form spontaneously but disappear on shearing of the specimen which becomes nearly optically isotropic again. Between 72.5 and 80 wt% lyotropic liquid cystalline lamellar phases were observed. Their birefringence vanishes upon shearing and they contain isotropic droplets pointing to the coexistence of phases. In addition, crystals which melt around 45°C are observed in the 77.5 wt% sample. These crystals are similar to those found in the more concentrated systems.

Above 80 wt% the samples contain large numbers of fine crystals dispersed in an isotropic fluid medium (Fig. 2f). In contrast, pure tyloxapol is completely isotropic in the polarizing microscope. The occurrence of crystals in the water-containing samples but not in the pure polymer probably results from the formation of a crystalline hydrate. The crystals start to melt around 45°C and become isotropic droplets dispersed in the isotropic liquid phase around 55°C. The molten and dispersed phase does not dissolve in the continuous phase within 15 min and does not recrystallize upon cooling to room temperature. Even after storage of the thermally stressed samples for 14 h at room temperature the droplet dispersion existed, indicating a dispersed supercooled melt (Fig. 2g).

The rapid formation of the three liquid crystalline phases after contact of tyloxapol with water was additionally checked with the microscope penetration technique (Tiddy et al., 1982). Along the tyloxapol/water concentration gradient the formation of three liquid crystalline phases was observed within a few minutes (Fig. 2h).

TEM

Replicas of freeze-fractured specimens were viewed by TEM in order to gain a direct insight into the supramolecular arrangement of the various lyotropic liquid crystalline phases using artefact-free specimens. None of the other techniques give a direct impression of the internal structure of the different compositions and liquid crystalline phases.

The TEM images of the system containing 47.5 wt% (Fig. 3) and the system containing 75 wt% (Fig. 4) exhibit clear differences in the

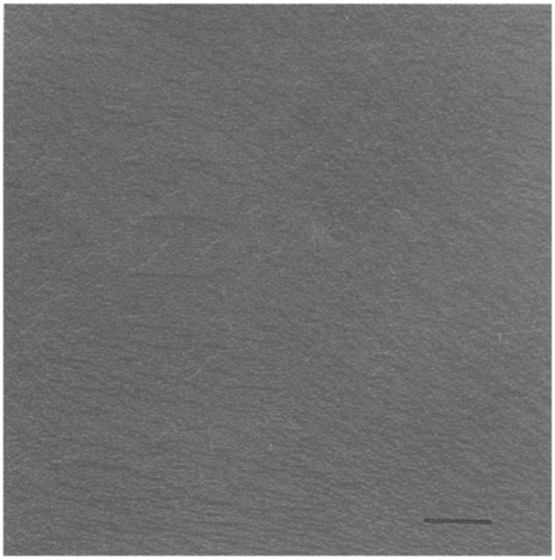

Fig. 3. TEM micrograph of the 47.5 wt% system (scale bar: 152 nm).

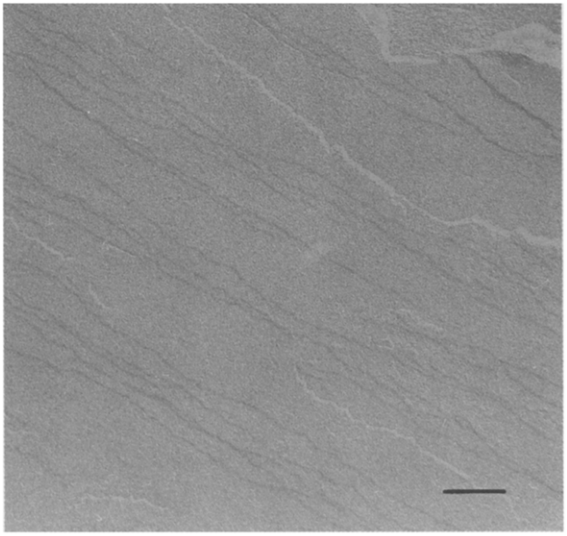

Fig. 4. TEM micrograph of the 75 wt% system (scale bar: 152 nm).

supramolecular structures of the two phases. The optical appearance of the 75 wt% system indicates that the system consists of extended stacked lamellae. Within each layer no order was observed indicating the existence of a liquid crystalline lamellar structure (neat phase or G phase (Fontell, 1974)). The 47.5 wt% system also exhibits a layered structure but each layer seems to consist of extremely fine parallel aggregates. Since these rod-like aggregates do not have a uniform length, only two-dimensional order exists. Such a parallel arrangement of cylindrical aggregates of indefinite length is characteristic of the hexagonal phase (middle phase or M_1 phase (Fontell, 1974)).

The micrographs give an estimate of the dimensions of the supramolecular structures but do not allow one to derive their exact value. The diameter of the cylinders as well as the thickness of the lamellae seems to be close to 5 nm (i.e., close to the limit of resolution of the replica technique).

The existence of isotropic spheres dispersed in the textures of the lamellar phase observed in the polarized light microscope suggests the coexistence of a lamellar liquid crystalline phase and of a dispersed isotropic phase. Globular structures dispersed in the lamellar phase were also observed in the TEM for systems containing around 75 wt%. These spheres exhibited fracturing characteristics of small vesicles and no fractures through the cores could be obtained. The outer parts of the spheres obviously consist of centrosymmetrical shells (Fig. 5) typical of liquid crystalline lamellar arrangements such as multilamellar liposomes.

DSC

A summary of the DSC results is given in Table 1. During heating runs endothermic transitions are observed exclusively. Thermal transitions during cooling are exclusively exothermic. No thermal events are detected for systems containing more than 72.5 wt%. In contrast, the stiff hexagonal liquid crystalline systems between 40 and 65 wt% as well as the cubic systems exhibit broad transition peaks. The transition temperatures given in Table 1 correspond to the peak maxima and in all cases are 2–7°C lower than the data derived from hot-stage polarized light microscopy which correspond to the first occurrence of complete optical isotropy. The most temperature-resistant hexagonal phases around 50 wt%

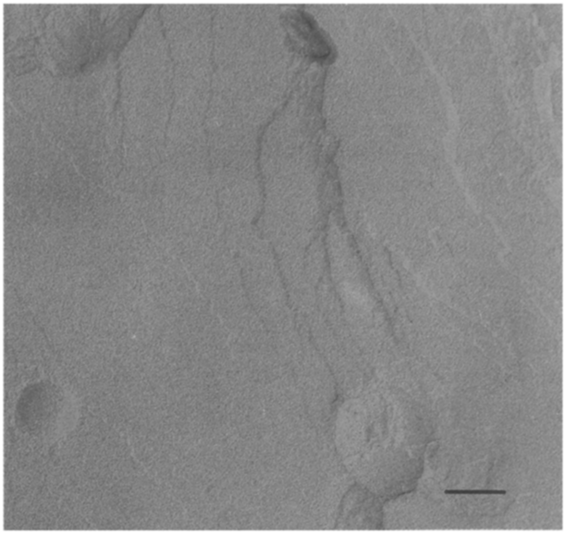

Fig. 5. TEM micrograph of the 75 wt% system exhibiting globular structures dispersed in a liquid crystalline lamellar phase. No plane fractures through the cores exist. The fractures follow the centro-symmetrical shell structures close to the surface of the globules (scale bar: 152 nm).

TABLE 1

Summary of DSC data

wt% [a]	Transition temperature (°C)			Transition type	ΔH (J/g)	
	a	b	c		a	b
37.5						
40	52	–	–	$H \rightarrow I$	0.33	–
42.5	54	–	54	$H \rightarrow I$	0.36	–
45	57	56	57	$H \rightarrow I$	0.51	0.35
	52 [ba]			$I \rightarrow H$	−0.12	
47.5	59	58	59	$H \rightarrow I$	0.50	0.23
	54 [ba]			$I \rightarrow H$	−0.29	
50	58	57	59	$H \rightarrow I$	0.53	0.43
	53 [ba]			$I \rightarrow H$	−0.36	
60	48	47	47	$H \rightarrow I$	0.26	0.24
	42 [ba]			$I \rightarrow H$	−0.22	
62.5	47	–	–	$H \rightarrow I$	0.45	
65	36	–	–	$H \rightarrow I$	0.31	
67.5	35		–	$C \rightarrow I$	0.19	
70	29	–	–	$C \rightarrow I$	1.28	
72.5	27	–	–	$C \rightarrow I$	0.21	
75	–					
77.5	–					

[a] First heating run, [b] second heating run, [ba] first cooling run, [c] third heating run after several days of storage at room temperature. H, hexagonal; I, optically isotropic solution; C, cubic.

exhibit the largest transition heats. Their corresponding optically isotropic liquids exhibit supercooling, pointing to first order transitions. The transition heats decrease from the first to the third heating run whereas the transition temperatures are reproducible. There are no exothermic transitions in the hexagonal and the cubic systems during the cooling run which are close to the concentration-dependent phase boundaries.

The stiff cubic phase of 70 wt% has the largest transition heat of all compositions during the first heating run but no further transitions could be observed during either cooling or the second heating run.

Discussion

The phase behaviour of tyloxapol/water mixtures was studied between 20 and 65°C. This temperature range was chosen because the properties of the mixtures at storage temperature (room temperature) and body temperature as well as the investigation of possible liquefaction processes were of special interest. Note that there may be other interesting phenomena outside this range such as a cloud point between 92 and 97°C (USP XXII, 1990).

The combination of the various techniques allows one to characterize the different phases and their relationships.

Macroscopically isotropic aqueous systems with a concentration-dependent viscosity are formed below 35 wt% tyloxapol. Solubilization experiments suggest the occurrence of micellar solutions. A narrow two-phase coexistence region around 35 wt% separates a homogeneous mesomorphic phase region from the isotropic solutions. From 37.5 to 65 wt% a semi-solid phase is found which exhibits the textures of lyotropic liquid crystalline hexagonal phases in the polarizing microscope. The position of the hexagonal phase in the concentration/temperature phase diagram and its ability to solubilize the hydrophilic dye methylene blue within 10 min but not the lipophilic dye Sudan Red 7B suggest that the hexagonal phase is a middle or M_1 type phase (Fontell, 1974). The hexagonal phase exists not only exist in a broad concentration range but also in a broad temperature range as derived from hot-stage polarizing microscopy and DSC. Hexagonal phases containing about 50 wt% of the polymer are the most temperature-resistant ones and exhibit the highest transition heats ($\cong 0.5$ J/g) when they transform to an isotropic melt at about 59°C. TEM indicates a supramolecular arrangement for the hexagonal phase consisting of parallel cylinders of non-uniform length resulting in a two-dimensional order. This corresponds to Fontell's middle phase (Fontell, 1974).

The narrow single phase around 70 wt% has been interpreted to represent a cubic phase. The cubic nature was derived from the optical isotropy and the extreme stiffness of the system. The range of water content of the cubic region and its temperature range (below 30°C) are very restricted compared with the hexagonal phase, suggesting that highly specific conditions are required for its formation. This conclusion is also in agreement with its relatively high transition heat (≅ 1.3 J/g) compared with the hexagonal systems during the first heating run and its extremely slow formation from the melt upon storage at room temperature.

Between 74 and 80 wt% at room temperature a liquid crystalline lamellar phase (neat phase or G phase (Fontell 1974)) with low viscosity is found which has no measurable transition heats. TEM observations indicate a supramolecular arrangement consisting of extended stacked lamellae exhibiting no order within the lamellae (i.e., one-dimensional order). No birefringent textures typical of lyotropic liquid crystalline lamellar phases could be observed for samples which were freshly placed on a slide and covered by a cover glass. The weak optical anisotropy of these systems directly after mild shearing, e.g., by covering the sample with a cover slide, and the recovery of the anisotropy upon storage at room temperature are indicative of weak supramolecular interactions. The long-range order of the systems is already highly disturbed by shearing during preparation of the microscopy sample. Storage of the sample at room temperature for more than 30 min as well as the run of a liquefaction/cooling cycle resulted in healing of the lamellar structures and Maltese crosses or mosaic textures occurred. The weakness of the interactions between the lamellae can also be deduced from the low viscosity of the lamellar phases. These phases have no macroscopically observable yield value despite the direct vicinity to the extremely stiff cubic phase region. A comparison of DSC runs on the hexagonal and the lamellar systems leads to the same conclusion. While the hexagonal systems delivered measurable transition heats on heating and on cooling, the thermograms of the lamellar systems were flat.

In the range of temperature which was studied the three lyotropic liquid crystalline phases (hexagonal, cubic and lamellar) do not exhibit thermotropic liquid crystalline transitions, but transform directly into structured liquids upon heating. The lyotropic liquid crystalline one-phase regions in the phase diagram (Fig. 6) are separated from each other by narrow two-phase regions. A narrow two-phase region was also observed between the micellar and the hexagonal phase. Polarizing microscopy indicated the occurrence of crystalline material in all systems containing more than 75 wt%.

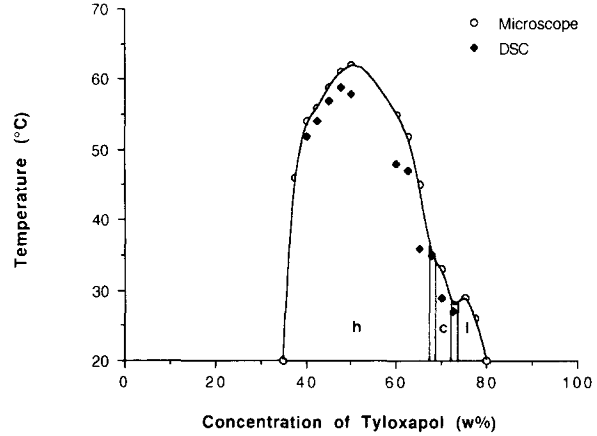

Fig. 6. Binary phase diagram of tyloxapol and water in the temperature range of 20–65°C: (h) hexagonal phase, (c) cubic phase and (l) dispersion of isotropic droplets in lamellar phase.

The results obtained from hot-stage polarizing microscopy, TEM of freeze-fractured specimen and DSC allow the construction of a phase diagram in the temperature range from 20 to 65°C (Fig. 6). The transition temperatures derived from hot-stage polarizing microscopy and DSC are in good agreement. The transition heats indicate an increase of order from the lamellar phase (one-dimensional order) via the hexagonal phase (two-dimensional order) to the cubic phase (three-dimensional order on the molecular level). This conclusion is in accordance with the observed viscosities, yield values and the dependence of the optical properties on shear forces.

Even though the methods applied so far allow the construction of a phase diagram, none of them provides reliable data about the dimensions of the supramolecular structures. Moreover, they do not give any information concerning the underlying molecular arrangements. Complementary viscosity and synchrotron radiation X-ray scattering experiments presented in a subsequent paper cover this aspect.

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