A new versatile Microemulsion Gel Technology with flexible Viscosity

Ulrich Kux, Jörg Schreiber, Khiet Hien Diec, Sabine Ripke, Klaus-Peter Wittern

R&D cosmed, Beiersdorf AG, Hamburg, D-20245, Germany

Phone: ++49-(0)40-49095967

Fax: ++49-(0)40-4909185967

E-Mail: Ulrich.Kux@Beiersdorf.com

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Synopsis

It has been shown that transparent microemulsion gels of flexibly adjustable viscosity containing less than 10% w/w surfactants can be obtained just by cooling down through a new 1-step preparation procedure (via 4 different in-situ colloidal systems) using PIT-technology with a range of emulsifiers, co-emulsifiers and lipids. They can be used for a wide scope of applications. Specific examples have been given with antiperspirant formulas that proof the stability of these thickened microemulsions even with high content of electrolytes and low pH. We propose that the structure of these microemulsion gels can be described by cross-linking of nano-fine oil droplets via an ABA-triblock copolymer. A new generation of transparent antiperspirant roll-ons with significantly improved skin tolerance can now be formulated as an attractive alternative to alcohol-based products.

Introduction

It is well known from market research that many consumers prefer transparent deo and antiperspirant products, as they convey freshness, pureness and cleanliness. Many women, however, complain about burning and itching in the arm pits after product application, especially after arm pit shaving. This often stems primarily from the alcohol (ethanol), which is incorporated in nearly all marketed transparent roll-ons and pump sprays. Its function is to boost freshness, to solubilize the fragrance and to reduce stickiness from antiperspirant ingredients like Aluminum or Aluminum Zirconium actives. Moreover, ethanol is a penetration enhancer and thus may facilitate quick absorption of fragrance ingredients into deeper skin layers. They have been identified as one of the causes for allergic contact dermatitis, a type of skin irritation becoming more and more spread amongst consumers according to dermatologists [1,2].

Therefore it is desirable to develop transparent deo and antiperspirant products without alcohol. One might think that the easiest way would be just omitting alcohol and to mix deodorant and antiperspirant ingredients together with fragrance and water. However, such simple mixtures are very tacky and lack cosmetic appeal. Our goal was therefore to find a formulation type that would

allow to incorporate antiperspirant actives in efficacious amounts, deliver transparent products of high skin tolerance, has low raw material costs and can be easily produced.

Microemulsions

We were looking for suitable technologies and found microemulsions to be interesting candidates. According to the classical textbook definition "microemulsions" can be described as thermodynamic stable, transparent, optically isotropic dispersions of two immiscible liquids (water and oil) containing appropriate amounts of surfactants and cosurfactants [3]. They are mostly being described as systems of water- or oil-thin viscosity. One can distinguish between O/W-, W/O- and bicontinuous microemulsions. The dispersed phase consists in the case of O/W-microemulsions with low oil content of small oil droplets with diameters ranging from 10 to 100 nm and ultra-low interfacial tensions.

Various definitions of systems containing dispersed particles of diameters from 10 to 100 nm can be found in literature. Tadros [4] explains nanoemulsions as systems that cover the size range of 50-200 nm and which are kinetically stable systems with long-term physical stability (against creaming or sedimentation, flocculation and coalescence). They are easily formulated using high-pressure homogenizers with proper choice of surfactants and/or polymers. Microemulsions, on the other hand, are thermodynamically stable systems usually in the size range of 5-50 nm that form spontaneously. Landfester [5] differentiates between miniemulsions and microemulsions. She defines miniemulsions as dispersions of critically stabilized oil droplets with interfacial tensions larger than zero and a size between 50 and 500 nm prepared by shearing a system with high energy input containing oil, water, a surfactant and a hydrophobe. Microemulsions are thermodynamically stable with an interfacial tension at the oil/water interface close to zero. The high amount of surfactant which is required for the preparation leads to complete coverage of the particles, and therefore the surface tension of the microemulsion reaches the minimum value. Nakajima [6] distinguishes swollen micellar solutions from microemulsions and ultra-fine emulsions. If surfactants self-assemble in aqueous solutions above the CMC, swollen micellar solutions form spontaneously. They are thermodynamically stable single-phase systems. O/W-Microemulsions are basically the same, but with higher amounts of solubilized oil. Ultra-fine emulsions might have the same appearance as microemulsions, but are thermodynamically unstable and two-phase dispersions.

Microemulsion Gels

Several publications mentioned the formation of "microemulsion gels" of higher viscosity [7,8]. Aqueous solutions of surfactants, liquid crystalline phases, coarse emulsions and surfactant-free delivery systems are not covered by the microemulsion terminology. Recently published delivery systems like lecithin microemulsion gels should also not be classified as microemulsions [9]. The formation of a gel comes in this case from an entangled network of worm-like reverse micelles that lecithin forms in polar solvents upon small addition of water.

The term "microemulsion gel" was often used in the past for delivery systems consisting of an oil phase, water and a very high surfactant/cosurfactant concentration. In these formulations 10-20%

w/w of an oil phase is solubilized with a high amount of a surfactant (15-20%)/cosurfactant (5-10%) combination. Probably a lot of such formulations should nowadays be better described as oil-containing liquid crystals of hexagonal, lamellar, inverted hexagonal or cubic type.

Thickening the external water phase of a low viscous O/W-microemulsion with polymers like polyethylene glycol, hydroxyethylcellulose or an acrylate is often not suitable for preparation of the corresponding microemulsion gel. There is a loss of transparency of the system due to a not controlled interaction process of the nano-fine droplets with the polymer backbone. Some of these polymers are not compatible with antiperspirant actives. For topical long-term applications a microemulsion gel should therefore contain a low surfactant/cosurfactant concentration (< 10% w/w).

We summarize that the main problems to formulate transparent, lipid-containing and water-based formulations of state of the art for our purposes are

- the high surfactant content that is usually necessary to solubilize the lipids and which may have a negative influence on skin tolerance

- the non-existence of a more general technological approach to formulations with broader flexibility concerning lipids and surfactants.

Experimental materials and methods

Manufacturing

Our microemulsion gels form spontaneously through phase inversion using the PIT-technology (Phase Inversion Temperature) in a one step process, without the need for high energy input through shear (figure 1, route A).

INSERT Figure 1

All batches have typically been prepared on a 1 kg scale using "Kitchen Aid" equipment. Some formulations have been successfully produced for commercial purpose even up to a scale of 5 tons. For more convenience of preparation both all hydrophobic and hydrophilic formula components should be heated separately to a temperature of at least 5° C above the PIT. It has to be ensured that all ingredients are in a dissolved, liquid state. After combining both phases (oil phase to water phase or vice versa) simple stirring during cooling down - without the need for homogenization - leads in a 1-step process directly to the desired O/W-microemulsion gel. Thus we avoid to obtain white, coarse O/W-macroemulsions, which inevitably would form if not heating the combined water and oil phase above the PIT (figure 1, route B).

All presented results have been obtained with a batch prepared close to formula F1, additionally containing an antiperspirant active and a fragrance.

Viscosity

Viscosity has been measured with a Viscotester VT-02 using Rotor Nr.3, Fa. Haake, at 25° C.

Electrical conductivity

Electrical conductivity has been monitored as function of temperature with an InoLab Cond Level 2, using Tetra con 325 detection cell, Fa. WTW, Weilheim. The cooling rate was approximately 1° C/min.

Transmittance

Transmittance has been determined at 420 nm wavelength on a HP 8453 diode array spectro-photometer in disposable cuvettes from Fa. Plastibrand (1 cm light path) and using UV Visible Chem Station software.

Particle size distribution

The droplet size distribution has been measured at 23°C by PCS (Photon Correlation Spectroscopy) with N4 Plus from Beckman Coulter. For this purpose the microemulsion gels were diluted with water to an appropriate concentration. The distribution function has been calculated by CONTIN-analysis from the PCS.

Rheological measurements

The ARES 8 from Rheometric Scientific was used to run a thixotropic loop test at a constant temperature of 28°C. The samples were measured in a Couette geometry with a bob diameter of 25 mm and a cup diameter of 26 mm (standard ARES cylinder). During recording the shear rate was increased from 0 to 1000 s^{-1} within 5 minutes (350 points per zone with logarithmic sampling mode) and vice versa.

Results and discussion

Manufacturing

During manufacturing interesting observations can be made via transmittance and measurement of electrical conductivity (figure 2).

INSERT Figure 2

After combining the separately heated oil and water phase at a temperature of at least 5° C above the PIT the conductivity of the white, highly viscous solution is close to zero, which is typical for a high internal phase W/O-emulsion (HIPE) with big dispersed water droplets (figure 3A). Upon cooling, just at the PIT (75° C in our example), the system turns suddenly thinner accompanied by a dramatic increase in conductivity (figure 3B). At this point, the W/O-emulsion inverts to an O/W-emulsion of still white, but more translucent appearance. It is interesting to mention that in many of our antiperspirant active-containing formulations the PIT is a clearly distinct temperature rather than a temperature range.

During further cooling the O/W-emulsion shows slightly decreasing conductivity and gains more and more transparency, which is reached in our example between 37° C (figure 3C) and 34° C (figure

3D). This clearly indicates the gradual formation of the microemulsion gel, as increasing transparency means decreasing size of the emulsified oil droplets.

Insert Figures 3A   3B   3C   3D

We propose from our data that formation of microemulsion gels occur via the following 4-step mechanism during cooling of the mixtures:
1) formation of a coarse W/O-emulsion (HIPE)
2) phase inversion at the PIT
3) formation of a coarse O/W-emulsion
4) formation of a transparent O/W-microemulsion gel by cross-linking of oil droplets

The exact PIT depends on the type and amount of used oils, emulsifiers and other formula components and can therefore vary. It is desirable for product development, however, to set the temperature range of product transparency well beyond the typical temperatures consumers would use the product at (e.g. -10 to 40° C).
In case of warming up the product above the temperature range of transparency (in our example T > 34° C) there is no need to worry: upon cooling down the emulsion turns transparent again. Moreover, even the complete formation of this microemulsion gel is fully reversible (figure 14).

Formulations
One can obtain transparent microemulsion gels (figure 4) with a broad variety of ingredients following our manufacturing procedure.

INSERT Figure 4

Various antiperspirant active-containing formulations with long-term stability (at least 6 months at ambient temperature or 3 months at 40° C) were prepared with the following ingredients.

Emulsifiers:	Isoceteth-20, Isoceteth-21, Isoceteth-22, Isosteareth-20, Ceteareth-15, Ceteareth-16, Ceteareth-17, Polysorbate-60, PEG-25 Stearate, Glyceryl Isostearate
Lipids:	Octyldodecanol, Caprylic/Capric Triglyceride, Dicaprylyl Ether, Dicaprylyl Carbonate, Ethylhexyl Cocoate, Ethylhexyl Isostearate, Tridecyl Isononanoate, Isotridecycl Isononanoate, Cetearyl Isononanoate, Cyclomethicone
Thickeners:	PEG-150 Distearate, PEG-250 Distearate, PEG-160 Sorbitan Triisostearate, PEG-200 Hydrogenated Glyceryl Palmitate/PEG-7 Glyceryl Cocoate

The model formulas F1-F6 are just to show typical examples and the influence of composition on mean particle size (table I). They have not been tested thoroughly on physical long-term stability. For product development, it has to be taken into account that incorporation of additional ingredients

(e.g. emollients, moisturizers, antiperspirant actives, fragrances) might have a strong influence on the PIT, transparency and formula stability. For each finished product the formulation (especially ratio of emulsifiers to lipids and their amounts) has therefore to be adjusted individually for the specific purpose.

INSERT Table I

Flexible viscosity

The viscosity can be easily adjusted over a wide range (100 to 20000 mPa s) by ABA-triblock copolymers, e.g. PEG-150 Distearate. Figure 5 shows the influence of ABA-triblock copolymer concentration on microemulsion gel viscosity.

INSERT Figure 5

Structure determination

The emulsified nano-fine oil droplets can be easily detected by determination of particle size distribution (PCS) and typically have a mean particle size of 20-65 nm (figure 6), which is mandatory for transparency.

INSERT Figure 6

As to be expected, microemulsion gel samples show a strong Tyndall effect due to the incorporated oil which makes them easily distinguishable from simple molecular solutions of antiperspirant actives in hydro-alcoholic gels (figure 7).

INSERT Figures 7A   7B

Yet the reason for the thickening ability of the polymers leaves to be clarified. We run 2 experiments for this purpose as follows:

1) Polymer solubility

An ABA-triblock copolymer (PEG-150 Distearate) dissolved in water, without presence of any other components, heated to about 80° C and subsequently cooled down to ambient temperature shows the typical behaviour for associative thickeners. It does not increase viscosity in small amounts noticeably and forms a turbid solution/suspension of opalescent appearance.
Dissolving the same amount of this polymer into a high-viscous W/O-emulsion above the PIT, however, delivers after cooling down the transparent, high-viscous microemulsion gel described herein before. The incorporated oil/emulsifier system obviously interacts with the polymer and aids to dissolve it completely. One can even add the polymer at ambient temperature to the fluid O/W-

microemulsion just by stirring. It takes longer to dissolve the polymer into the system, but viscosity increase starts immediately and a microemulsion gel forms, too.

2) Gel dilution

The gel viscosity strongly correlates with decreasing oil concentration upon dilution with water (figure 8).

INSERT Figure 8

Dilution of the microemulsion gel leads to a bigger mean oil droplet/oil droplet distance and makes it therefore more difficult for the polymer to interact with two oil droplets simultaneously and thus to build up viscosity. Indeed, dilution of a sample with just 10% water affects already a loss of merely 60% viscosity. However, there is still some gel structure left in the system as long as the decline of viscosity at high shear rates indicates shear-thinning of the gel network (figure 8).

Dilution does not influence microemulsion stability as such at all, which can be nicely shown by following particle size distribution over time by PCS (figure 9). Monitoring the transmittance of the system proves that the dispersed oil droplets do not coalesce (figure 10), which would cause a loss of transparency.   As a comparison: the undiluted sample (= 100 / 0) has a transmittance of 76,2% measured 1 day after preparation.

INSERT Figures 9A   9B   9C

INSERT Figure 10

Based on these 2 experiments we suggest that the ABA-triblock copolymer thickens the formulation by cross-linking the emulsified nano-fine oil droplets (figure 11). This shows some similarities to a mechanism that has been discussed in literature for the interaction of associative thickener with latex particle surface [10].

INSERT Figure 11

Study of thermal stress on in-situ emulsion types and its influence on finished O/W-microemulsion gel stability

It has been reported that standard PIT-emulsions might separate when kept too long at their PIT during preparation. Therefore it is recommended to cool down rapidly through the PIT area [11]. We also investigated the behaviour of our formulation keeping it for up to 6 hours at its PIT during preparation (75 °C in the example). This stress had no negative influence on the formation and stability of the finished microemulsion gel, monitored again by particle size distribution (figure 12) and viscosity/rheology (figure 13). The rheological graph monitors the viscosity of the

microemulsion gel vs. the shear rate. It can be seen that all samples – independent from their preparation history – show the same rheological behaviour. Furthermore, it can be learnt that the microemulsion gel does not exhibit thixotropy but pseudo-Newtonian flow at medium and pseudo-plastic flow at high shear rate.

INSERT Figures 12A   *12B*   *12C*

INSERT Figure 13

Study of multiple heating/cooling stress cycles and their influence on finished O/W-microemulsion gel stability

Starting from ambient temperature with a finished sample, being previously manufactured according to the proposed preparation (figure 1, route A), and then repeatedly heating it up above the PIT and subsequently cooling down to ambient temperature (10x) always leads to the same finished microemulsion gel, without any indications for instability during long-term storage as monitored by PCS (figure 14). This demonstrates that all involved in-situ steps are fully reversible.

INSERT Figures 14A   *14B*   *14C*

Summary of the experiments

Based on experiments studying

- Tyndall effect
- polymer solubility
- gel dilution
- thermal stress on in-situ emulsion types and its influence on finished O/W-microemulsion gel stability
- multiple heating/cooling stress cycles and their influence on finished O/W-microemulsion gel stability

we conclude that our O/W-microemulsion gels can be described as systems being built of two components:

1) a underlying low-viscous O/W-microemulsion whose physical stability is independent from the presence of the polymer plus

2) a polymer gel network which interacts with system a) and does not form without the presence of dispersed oil droplets.

Stability of the underlying low-viscous microemulsion can be easily tracked by particle size distribution, stability of the additionally incorporated gel network by measurement of viscosity/rheological behaviour.

This demonstrates the wide flexibility of these microemulsion gels. Taking into consideration the model formulas and the influence of formula composition on mean particle size (Table I), it is now

possible to develop tailor-made formulations wherein one can

1) alter the optical appearance (from transparent via translucent to opaque) by fine-tuning the composition of the underlying low-viscous microemulsion while keeping viscosity built up by polymer constant

2) vary the viscosity by amount of polymer while keeping the optical appearance unchanged

3) adjust 1) and 2) simultaneously

Skin tolerance

The improved skin tolerance of these new microemulsion gels - compared to current hydro-alcoholic formulations - was demonstrated by market research data. One consumer study has been run with 150 female roll-on users (age 20-55) for each test product (figure 15). The test has been performed as a monadic in-home use test for a period of 2 weeks with subsequent filling out a questionnaire. Almost all panelists used the product at least once a day, 1/3 even several times a day. About 2/3 of women did shave their armpits during the test at least once. Both test products contained the same fragrance and antiperspirant ingredients in equal amounts. Concerning skin tolerance the microemulsion gel was statistically significant better in all presented categories. The scale of the evaluation score goes from 1 (does not comply at all) to 7 (complies fully).

INSERT Figure 15

A second market research test run with another panel under similar circumstances confirmed previous convincing results.

Conclusions

It was the aim of this work to develop alcohol-free transparent antiperspirant formulations with improved skin tolerance compared to currently marketed hydro-alcoholic antiperspirant roll-ons. We made new versatile O/W-microemulsion gels of high viscosity through a new 1-step preparation procedure (via 4 different in-situ colloidal systems) from the crude, hot mixture using PIT-technology (Phase Inversion Temperature). This leads just by cooling spontaneously to transparent O/W-formulations, even without the need for high energy input through shear. The viscosity of these formulations can be easily adjusted over a wide range (100 to 20000 mPa s) by ABA-triblock copolymers, e.g. PEG-150 Distearate, which we suggest thickens the formulations by cross-linking the emulsified nano-fine oil droplets (20-65 nm). The formulations contain less than 10% w/w surfactants and can be made with a range of emulsifiers, co-emulsifiers and lipids. Specific examples with antiperspirant formulas proof the excellent physical stability, even with high content of electrolytes and low pH. Thus a new generation of transparent antiperspirant roll-ons with significantly improved skin tolerance can now be formulated as an attractive alternative to currently marketed alcohol-based products. Stability, rheological and optical data were discussed and the manufacturing method explained in detail.

Acknowledgements

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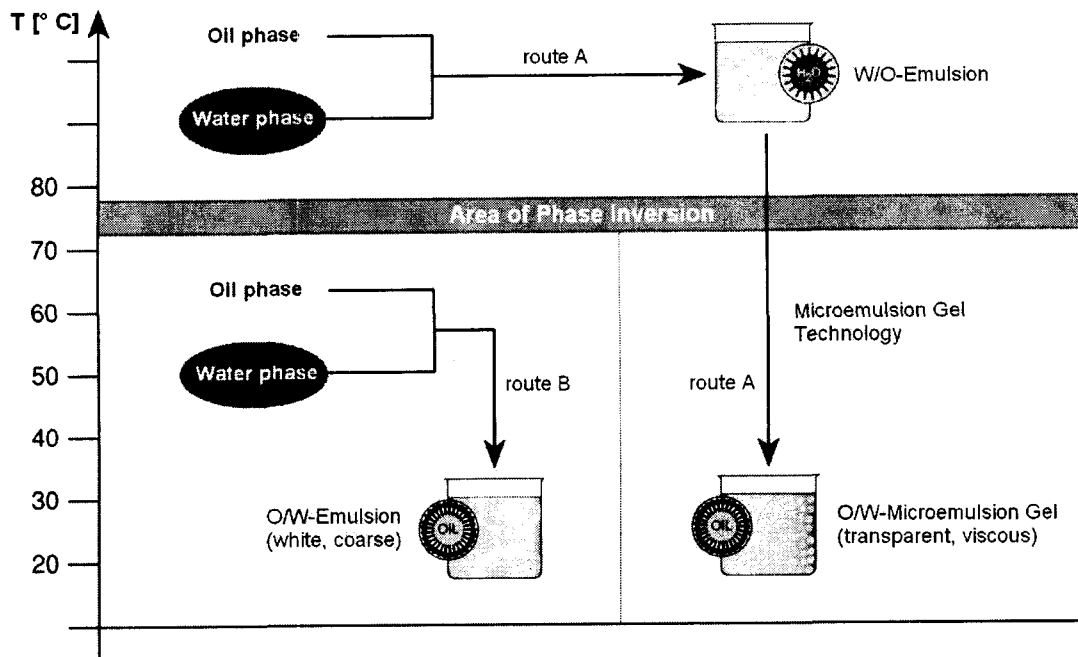
Figure 1: Emulsification according to Microemulsion Gel Technology (route A). Route B does <u>not</u> lead to microemulsion gel formation
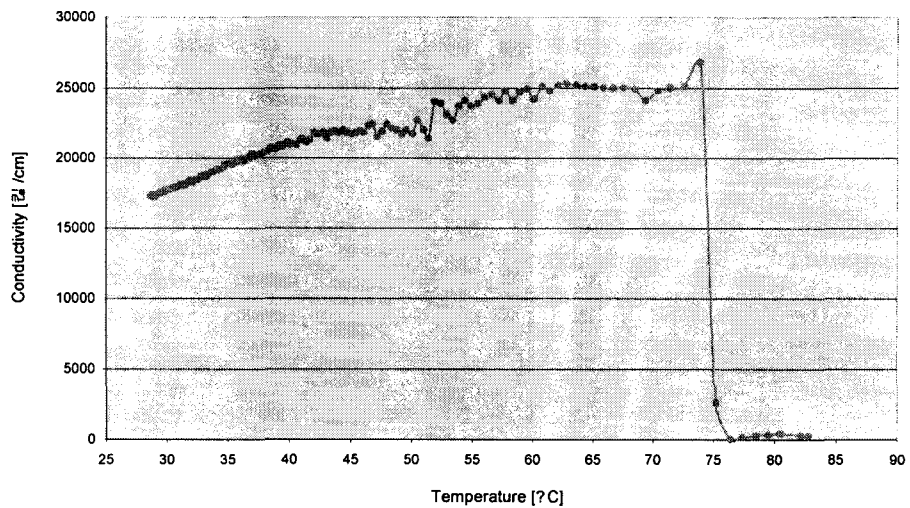
Figure 2: Graph of electrical conductivity during manufacturing of a microemulsion gel
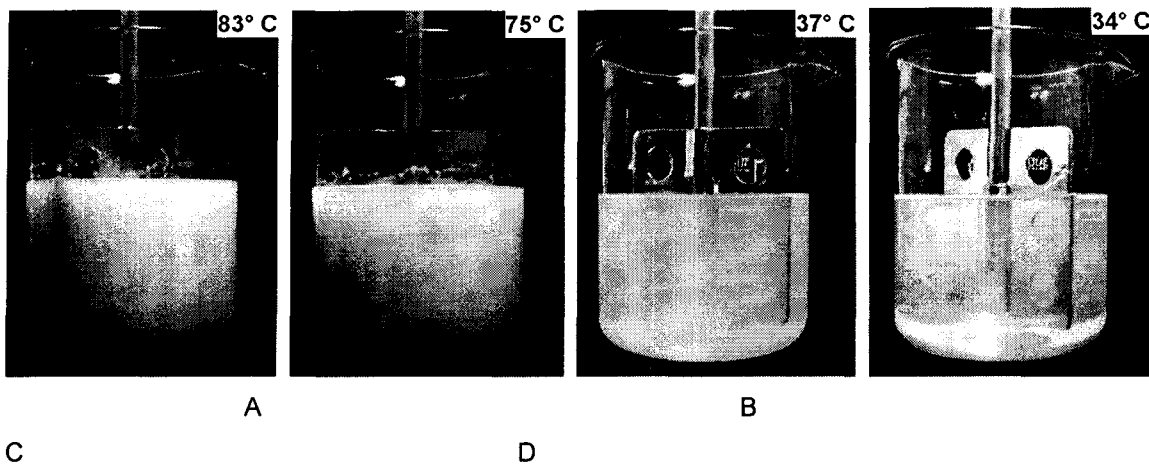
Figure 3: Pictures of microemulsion gel (D) formation from a hot W/O-emulsion above its PIT (A) through phase inversion at different temperatures (B, C) during cooling down
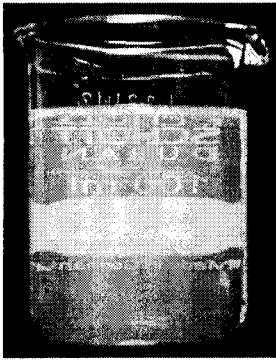
Figure 4: Transparency of a microemulsion gel with 12% w/w content of lipids and emulsifiers

Ingredient / Formula	F1	F2	F3	F4	F5	F6
Oil phase						
Isoceteth-20	5.0	5.0	5.0	5.0		
PEG-25 Stearate					5.0	
PEG-20 Sorbitan Isostearate						5.0
Glyceryl Isostearate	2.5	2.5	2.5	2.5	2.5	
Sorbitan Isostearate						2.5
Dicaprylyl Ether					5.0	5.0
Diethylhexylcyclohexane	5.0					
Caprylic/Capric Triglyceride		5.0		5.0		
Coco-Caprylate/Caprate			5.0	5.0		
PEG-150 Distearate	1.0	1.0	1.0	1.0	1.0	1.0
Water phase						
Glycerol	3.0	3.0	3.0	3.0	3.0	3.0
Water	83,5	83,5	83,5	78,5	83,5	83,5
Mean particle size [nm]	32	42	47	116	54	37

Table I: Model formulas
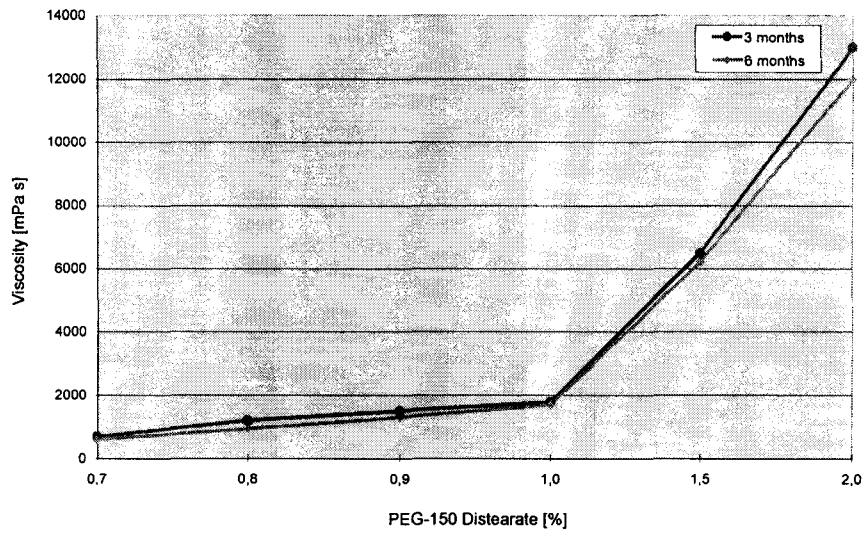
Figure 5: Influence of ABA-triblock copolymer amount on microemulsion gel viscosity. Sample stored for up to 6 months at ambient temperature
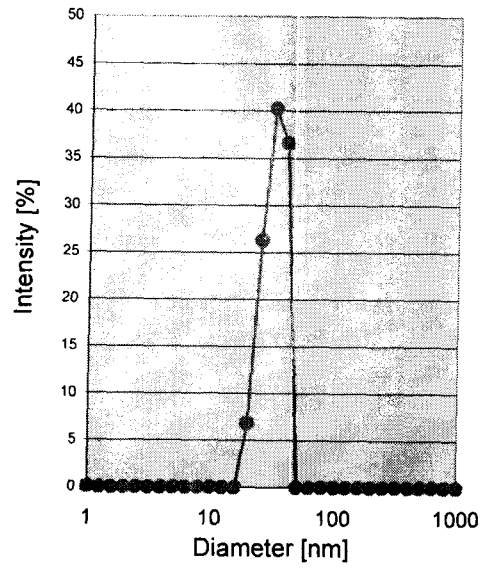
Figure 6: Particle size distribution of a microemulsion gel (PCS)
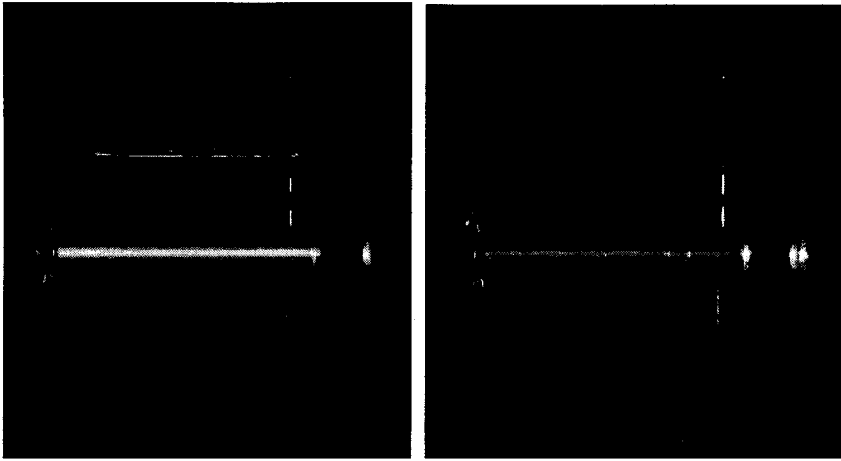
A   B

Figure 7: Strong Tyndall effect in a microemulsion gel (A), demonstrated by laser beam (λ = 650 nm). A hydro-alcoholic gel (B) as comparison shows no Tyndall effect.
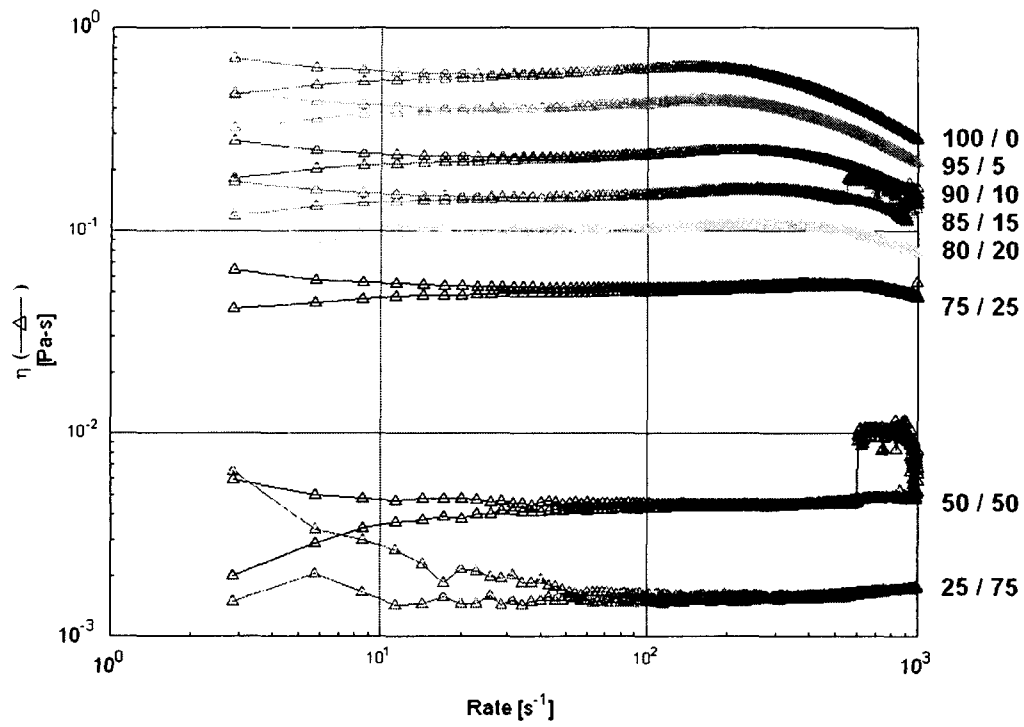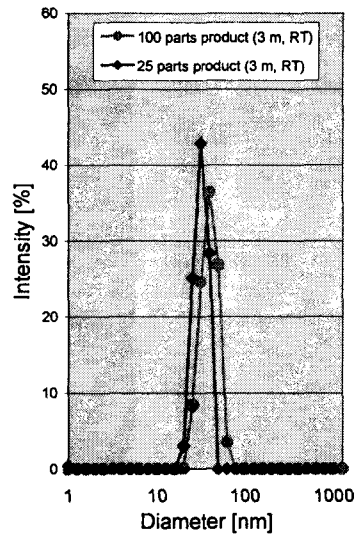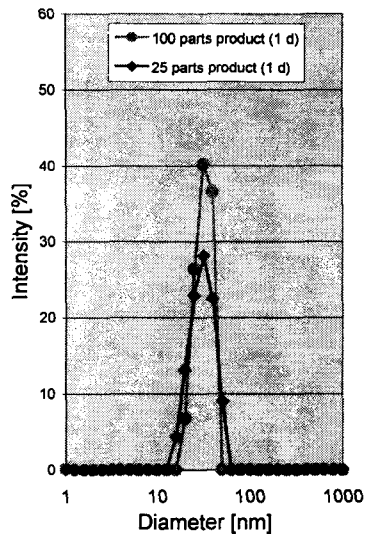
Figure 8: Dilution of a microemulsion gel sample with water and its influence on gel network viscosity (thixotropic loop test). Right beside diagram: left number shows v/v % of microemulsion gel / right number of water in mixture
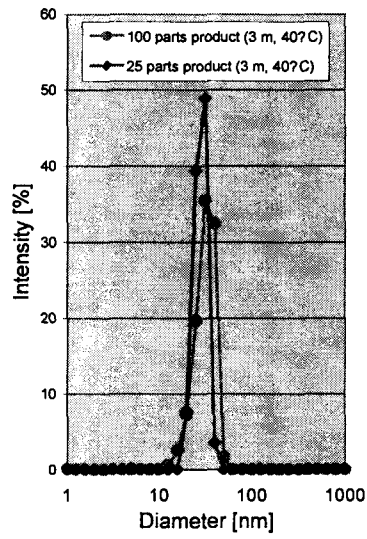
A

B

C

Figure 9: Stability of a diluted sample (mixture of 25% finished microemulsion gel + 75% water) vs. an undiluted microemulsion gel sample over time (PCS). Freshly diluted (A), stored 3 months at ambient temperature (B), stored 3 months at 40° C (C)
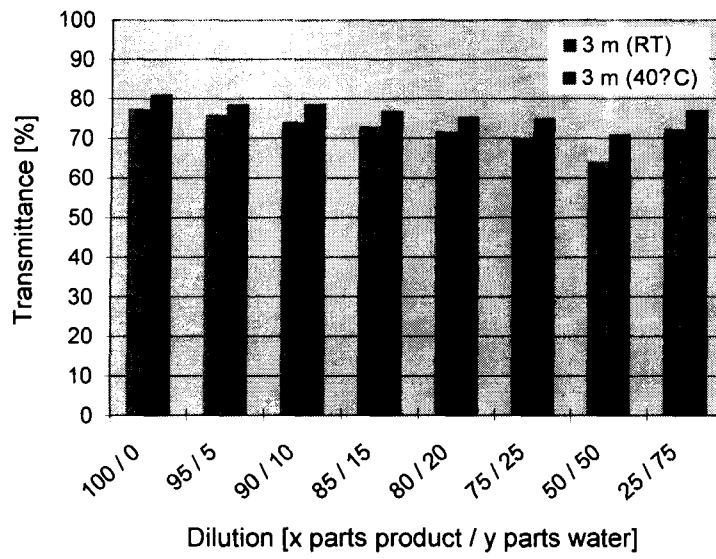
Figure 10: Transmittance of various diluted microemulsion gel samples. Left number shows v/v % of microemulsion gel / right of water in mixture
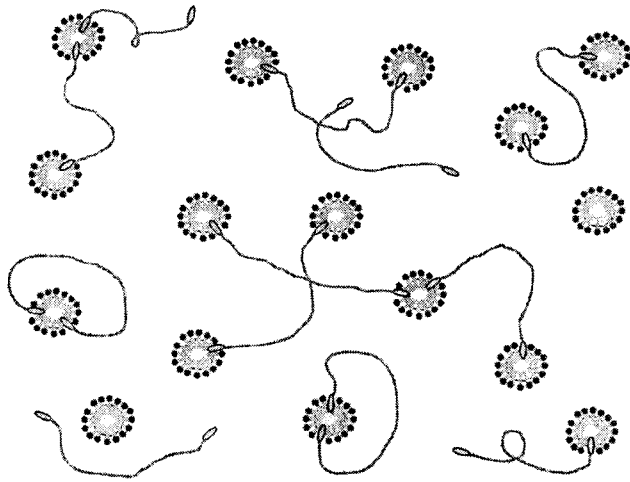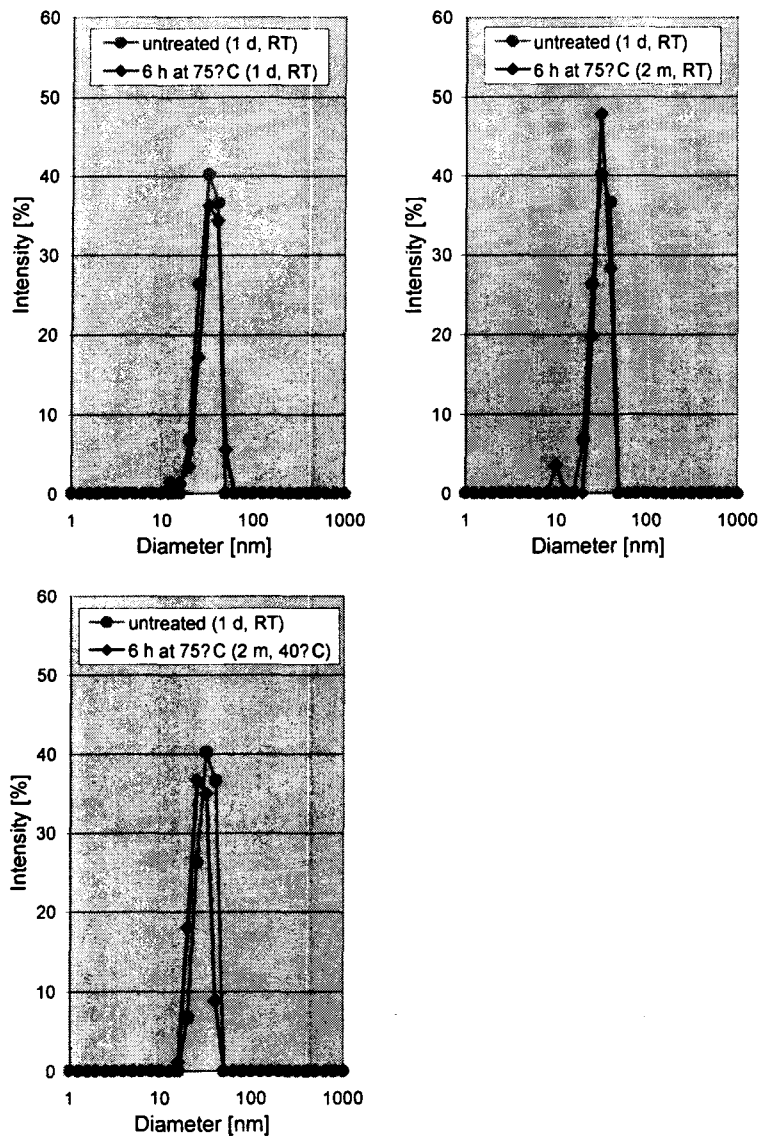
Figure 11: Illustration of suggested thickening mechanism in an O/W-microemulsion gel by cross-linking of nano-fine oil droplets by an ABA-triblock copolymer

A

B

C

Figure 12: Stability proof of a finished microemulsion gel sample kept 6 hours at the PIT during preparation vs. an immediately cooled down sample (= untreated) (PCS)
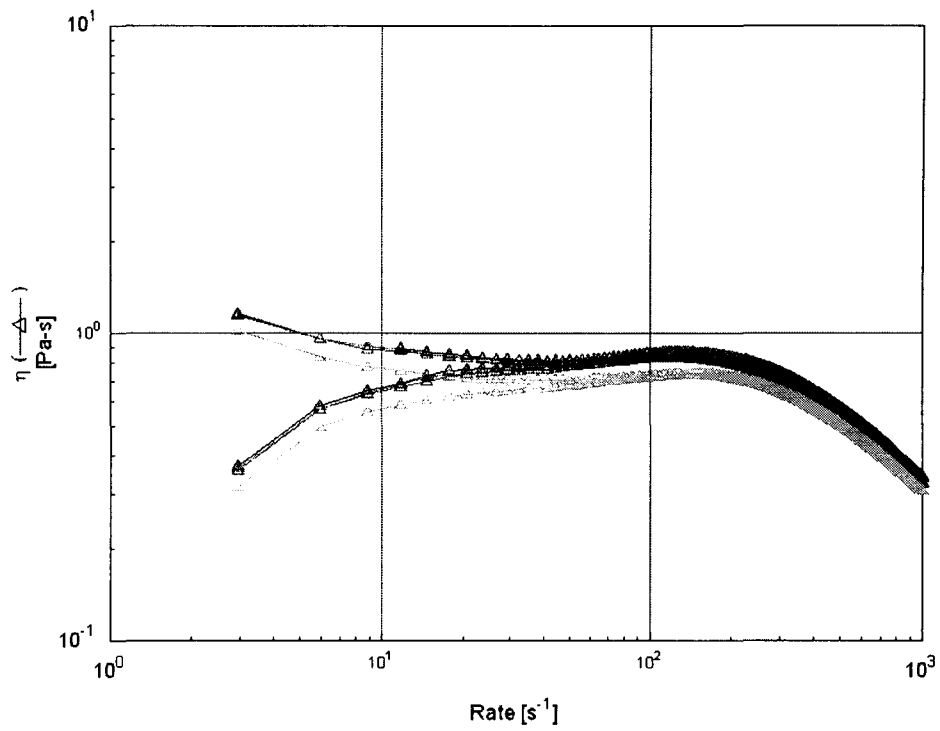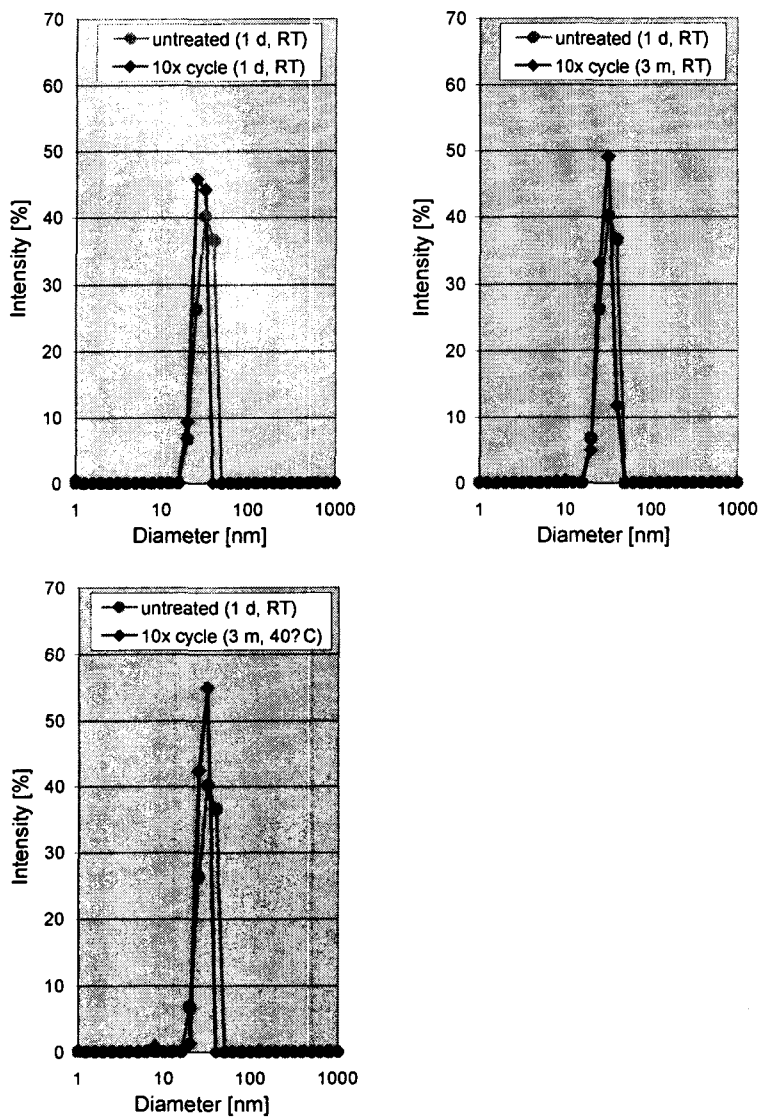
Figure 13: Rheological graph of microemulsion gel samples which were kept for 2/4/6 hours at the PIT during preparation and then stored for 1 month at ambient temperature vs. an immediately cooled down sample (= untreated) (thixotropic loop test)

A

B

C

Figure 14: Stability of a microemulsion gel sample upon 10x heating/cooling cycles vs. an untreated sample over time (PCS). Freshly 10x cycled (A), stored 3 months at ambient temperature (B), stored 3 months at 40° C (C)
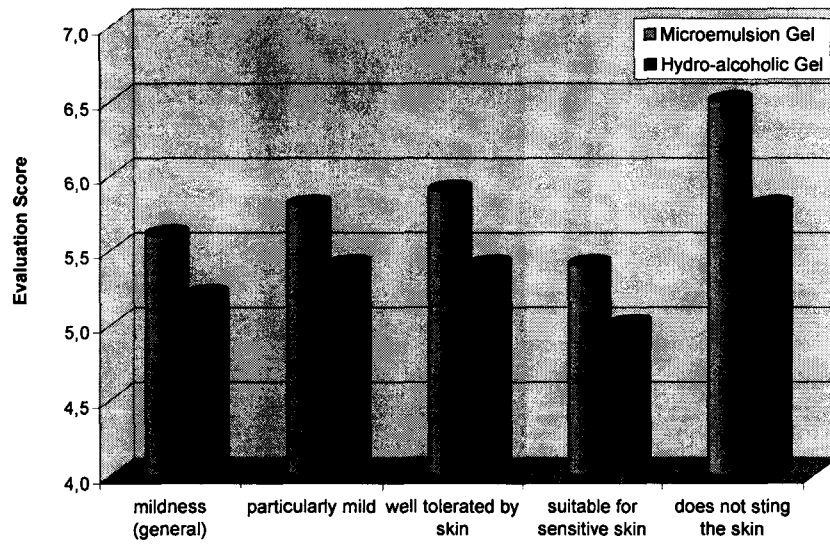
Figure 15: Market research test data showing improved skin tolerance of an O/W-microemulsion gel compared to a hydro-alcoholic gel roll-on