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Thermo-sensitive poly(methyl vinyl ether) micro-gel formed by high energy radiation

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Abstract

A thermo-sensitive hydrogel was synthesized by irradiation of an aqueous solution of poly(methyl vinyl ether) (PMVE) with electrons. At high polymer concentration a bulk gel was formed. Irradiation of diluted polymer solution at a temperature above the phase transition temperature conserves the structure of the polymer in the phase-separated state. The micro-particles formed under irradiation conditions possess also typical thermo-sensitive properties. Their diameter roughly amounts to 300–500 nm in the swollen state depending on the temperature of the solution. Static and dynamic light scattering were used to determine the dimension of the formed particles. The dry, swollen, and shrunk state were structurally characterized by field emission scanning electron microscopy (FESEM). © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

An aqueous solution of poly(methyl vinyl ether) (PMVE) has a lower critical solution temperature (lcst) at about 37°C. At higher temperature the hydrogen bonds are decomposed by the thermal motion of water molecules and the dehydrated PMVE molecules aggregate together. When an aqueous solution of PMVE is irradiated with electrons or γ-rays the solution is transformed into a hydrogel. The cross-linking process is caused by the formation of radicals from water molecules, which attack PMVE molecules. This hydrogel possesses thermo-sensitive properties similar to those of the PMVE solution. It swells at temperatures below the lcst and shrinks above this temperature.

Stimuli-responsive hydrogels that undergo abrupt changes in volume in response to external stimuli such as temperature, have potential applications in the creation of 'smart' material systems. Hydrogels made of hydrophobic polymers that undergo transitions near 37°C (temperature of human body) have been considered as drug delivery systems, and materials for tissue reconstruction.

The kinetics of volume change is controlled by diffusion processes, in particular by the cooperative diffusion coefficient of the polymer chains ($D_{\mathrm{coop}} \approx 10^{-7}\ \mathrm{cm^2/s}$). Since diffusion times scale with the square of dimension, decreasing the characteristic dimension of the network will increase the swelling/shrinking rates dramatically. In former works [1] we investigated thin layers (thickness in the μm-range) of photo cross-linked T- and pH-sensitive hydrogels. A gel body with porous microstructure is expected to give rise to faster volume change, since the effective diffusion distance can be controlled by the average distance between neighboring pores. Suzuki and Hirasa [2] synthesized bulky PMVE gels with a fine porous structure to obtain quick response gels. The swelling or shrinking of sponge-like gels is orders of magnitude faster than any other responsive gels of comparable dimension. The higher the temperature of the aqueous PMVE solution, the higher the mean cross-sectional area of the pores formed by the phase separation. The pore sizes decreased with increasing PMVE concentration and typically amount to several μm.

Spherical particles with diameter in the μm- or nm-range are predestinated for fast response too. Therefore it seems obvious that micro- and nano-gels could find applications in different fields.

According to Ref. [3], a micro-gel is an intramolecularly cross-linked macromolecule which is dispersed in normal or colloidal solutions. Depending on its degree of cross-linking and on the nature of the solvent, the micro-gel is more or less swollen. Micro-gels are distinguished from linear and

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branched macromolecules by their fixed shape, which limits the number of conformation of their network chains like in cross-linked polymers of macroscopic dimensions. Intramolecular cross-linking by electron irradiation of an aqueous solution of poly(vinyl pyrrolidone) was already described some years ago [4]. Intramolecular cross-linking in that context means unchanged molecular mass M_w but a reduced radius of gyration R_g. Intra- and intermolecular cross-linking by γ-irradiation was used to obtain poly(vinyl alcohol) micro-gels of larger size [5]. However, sometimes the term micro-gel is also used in the literature for micrometer-sized gels obtained by intermolecular cross-linking like in this paper.

Several papers dealing with the synthesis and potential applications of thermo-sensitive *N*-isopropylacrylamide-based micro-gels were published recently (see e.g. Ref. [6]). Spherical hydrogel particles of NIPAAM can be formed by inverse suspension polymerization [7]. Another method for the preparation of hydrogel beads in the submicron region (0.2–1 μm) is the inverse emulsion polymerization [8].

Thermo-sensitive micro-gel particles are preferentially used for applications in two different fields:

(i) wastewater treatment, for what, e.g. poly(*N*-isopropylacrylamide) is used to eliminate heavy metal ions [9],
(ii) adsorption or desorption of biomolecules, for what, e.g. the thermo-sensitive behavior of the micro-gels can be used [10].

Further novel applications of micro-gels, however, could be for example the temperature-dependent adsorption/desorption-controlled uptake and release of substances for oil cleaning [11]), the thermo-sensitive Bragg-refraction [12], and the use as catalysts [13].

All the published synthetic routes are rather time-consuming. Another disadvantage is the need of additives to prepare the dispersion or emulsion (like surfactants) as well as to initiate the polymerization and the cross-linking.

The aim of our work was the development of a method to synthesize in a more simple way spherical particles of a thermo-sensitive polymer without any additives.

One method to achieve this goal is the cross-linking of PMVE by electron irradiation. As described in Ref. [14] a disadvantage of the electron irradiation is the radiation-induced heating. The increase of temperature depends clearly on the applied radiation dose. We found about 2.5°C per 10 kGy for our experimental conditions. Because of radiation-induced heating a diluted polymer solution can be warmed up above the volume phase transition temperature at higher irradiation doses and phase separation may occur. Another possibility is the irradiation of a phase-separated polymer solution (phase separation by heating or mixing with non-solvents). Irradiation of this solution could conserve the structure of the phase-separated polymer. Due to the short time of irradiation and the radiation-induced heating the phase separation is stable during the radiation process. In principle, there is a possibility that micro-gel with a size in the order of magnitude of 100 nm is formed.

2. Experimental

2.1. Characterization of PMVE

PMVE was obtained as a 50 wt% aqueous solution from Aldrich. The molecular weight was determined by static light scattering in butanone to $M_w = 46{,}000$ g/mol. The glass transition temperature of the polymer was found to $T_g = 242$ K by Differential Scanning Calorimetry. The measured intrinsic viscosity in butanone was smaller than the calculated value ($[\eta] = 9.2 \times 10^{-4} M^{0.58}$, $[\eta]$ in dl/g, see Ref. [15]). The comparison of both values allows to conclude that the PMVE-molecules are branched. The number of branches per molecule was estimated to 4–5 from the ratio of viscosity. M_w in water was always higher (up to 20 times) than M_w in organic solvent, even for aqueous PMVE solutions of low concentration and at temperatures lower than the lcst. The measured molecular weight in water depends on the condition of preparation of the solution. From these results follows that PMVE-molecules were not mono-molecularly dissolved in water, even in the dilute state. Consequently, the structure of the formed micro-networks must be influenced by two effects: the aggregation structure and, if phase separation occurs, the structure determined by the phase separation.

Static light scattering measurements were performed on a modified static light scattering apparatus FICA 50 (SLS Systemtechnik G. Baur, Freiburg, Germany) using a laser light source (633 nm) at scattering angles $15° \leq \theta \leq 145°$ in steps of 5°. The solutions were filtered directly into the optical cells through 0.2 μm PTFE (butanone) membrane filter or 0.45 μm CME (water) membrane filter, respectively. The optical cells were brought to the right temperature in the light scattering equipment for 30 min before starting the measurements. The refractive index increment was measured by a DLS 1 (SLS Systemtechnik G. Baur, Freiburg, Germany) and amounts at 25°C to 0.0895 cm^3/g for butanone and to 0.1438 cm^3/g for water, respectively.

The dynamic light scattering measurements were performed with a DLS 700 (Otsuka, Japan) at $\theta = 90°$ and a concentration $c_B = 4.9$ g/l. An apparent (no extrapolation to $\theta \rightarrow 0$ and $c_B \rightarrow 0$) value of the hydrodynamic radius $R_{h,app}$ was calculated by using the Stokes-equation.

2.2. Preparation of micro-gel

For irradiation, a solution of 4.0 g PMVE/l was prepared by dilution of the high concentrated PMVE solution with bi-distilled water. Oxygen can interfere with a free radical reaction. Therefore, it was necessary to remove as much of it by degassing the homogenized polymer solution before starting the irradiation. For this purpose argon was blowing

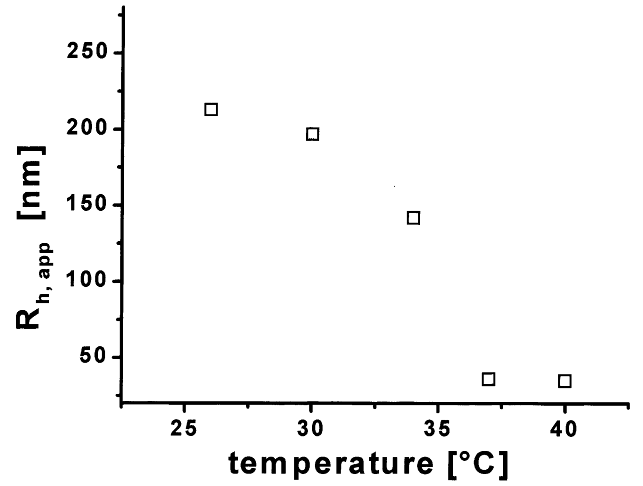

Fig. 1. Dynamic light scattering (DLS) of diluted PMVE-solution, apparent hydrodynamic radius ($R_{h,app}$) vs. the temperature.

(for 5 h) through the solution under stirring. After degassing, the prepared solutions were poured in Petri dishes and subsequently irradiated. Purging the solution with argon and sealing with PARAFILM® helps to reduce the rate of oxygen uptake in the non cross-linked polymer solution.

The irradiation conditions were as follows: linear accelerator ELV-2 (Budker Institute for Nuclear Physics Novosibirsk, Russian Federation); electron energy: 1.0 MeV; doses: 20 and 80 kGy; solution temperature: 60°C.

After irradiation the uncross-linked polymer was not extracted. For further experimental details see Ref. [16].

2.3. Field emission scanning electron microscopy of micro-gel

A valuable novel methodical approach for the structural characterization of thermo-sensitive hydrogels is the field emission scanning electron microscopy (FESEM) combined with cryo preparation techniques [17]. Three different states of the intermolecularly cross-linked micro-gel related to the temperature of the solution were investigated: the swollen state (at 25°C), the shrunk state (at 40°C), and the dry state (samples in the shrunk state were co-prepared with latex beads having approximately a diameter of 0.5 μm were air-dried at 50°C). The preparation of the cross-linked micro-gel in the swollen and shrunk state was done as follows: a small droplet of solution at 25 and 40°C, respectively, was dropped onto a small fragment of silicon (Si)-wafer having a corresponding temperature. The micro-gels were adsorbed (physisorption) for approximately 90 s to the Si-wafer, before the excess solution was removed with filter paper. Immediately following, the samples were rapidly frozen by plunging into liquid ethane (cooled to approximately -196°C) to avoid ice crystal formation (vitreous ice embedding) [18]. Freeze drying was performed within 6 h at approximately -80°C and a pressure of 5×10^{-6} Torr using a BAF 300 (Balzers, Principality Liechtenstein) equipped with a turbo molecular pump. After warming up to room temperature (RT) the freeze-dried samples were subsequently rotary shadowed with 1.5 nm platinum/carbon (Pt/C) at an elevation angle of 65°.

The air-dried samples were also rotary shadowed at RT with 1.5 nm Pt/C at an elevation angle of 65°. Additionally, an unidirectional shadowing at an elevation angle of 30° with 2.5 nm Pt/C was applied to monitor elevated structures by their shadow. The height H of a particular structure is simply related to the length L of its shadow, given by $H = L \tan \alpha$ and can be estimated if the local elevation angle α is known (this local elevation angle is given by the relation $\sin \alpha = 2RL/(L^2 + R^2)$, where $2R$ represents the diameter of the latex sphere). This trick in preparation allows a rough estimation of drying artifacts due to the surface tension (e.g. flattening) which can occur with soft samples when air-drying is used [19].

The coated samples were examined in a high resolution field emission scanning electron microscope ('in-lens' type, model S-5000, Hitachi Ltd, Tokyo, Japan) in high vacuum ($p = 4 \times 10^{-7}$ Torr) at room temperature. Micrographs were recorded at 8 kV acceleration voltage using secondary electrons (SE) (for further methodical details of the FESEM see Refs. [20,21]). For photography the SE micrographs were recorded using Agfapan APX100 film.

3. Results and discussion

The dimension of the PMVE molecules solved in water depends on the temperature. Dynamic light scattering measurement of aqueous PMVE solution in dependence on the temperature suggests the formation of particles in the 100 nm range and clearly monitors that their apparent hydrodynamic radius $R_{h,app}$ is temperature-dependent (Fig. 1). Because of the formation of aggregates the values represent not the dimension of single macromolecules. The molecule dimension changes significantly between 32 and 36°C.

Frequently in the literature authors tried to extract information on the particle shape from a comparison of experimental scattering functions with $P(q)$ calculated for different particle shapes assumed. The comparison is performed graphically, often in co-ordinates $P(q)u^2$ vs. u, the so-called Kratky plot, where $u = \mathbf{q}\langle r^2 \rangle_z^{1/2}$ ($\mathbf{q}$ is the scattering vector, $\langle r^2 \rangle_z^{1/2}$ is the radius of gyration). The particle shape is estimated by the optimum fit of the experimental curve with the theoretical curves. The experimental scattering function is given by Eq. (1)

$$P(q) = \frac{1}{M_w (Kc/R_\theta)_{c=0}}, \tag{1}$$

where K is the optical constant, c the polymer concentration and R_θ is the reduced intensity of the scattered light at scattering angle θ.

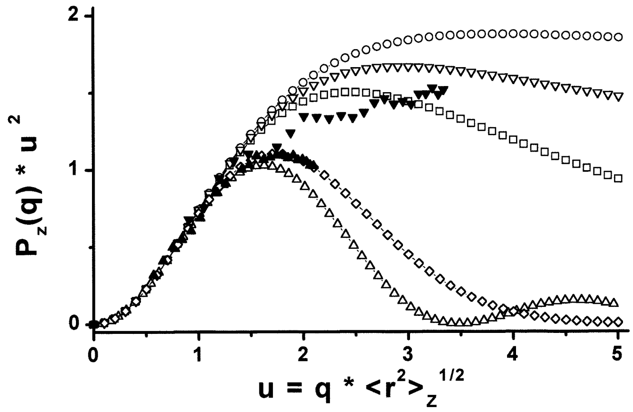

Fig. 2. Kratky plot of calculated and measured scattering functions $P(\theta)$. $\langle r^2 \rangle z^{1/2}$ was determined from the initial slope of the scattering function obtained by static light scattering. Calculated: 5-arm star (○); 10-arm star (▽); homogeneous branched (□); soft sphere (◇); and hard sphere (△). Measured: PMVE/water at 25°C (▼) and at 40°C (▲).

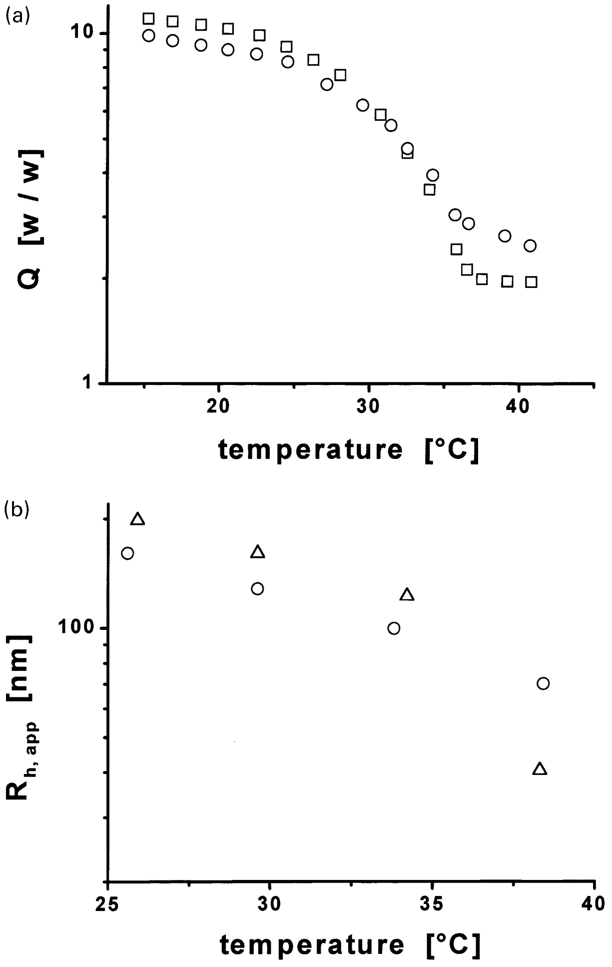

Fig. 3. (a) Temperature dependence of the degree of swelling of radiation cross-linked PMVE bulk gel. γ-radiation: dose = 80 kGy; concentration: 0.20 w/w; temperature at irradiation: 25°C (○) electron beam: dose = 80 kGy; concentration: 0.20 w/w; starting at 25°C (□). (b) Apparent hydrodynamic radius ($R_{h,app}$) of radiation cross-linked PMVE microgel vs. temperatures, radiation dose: 20 kGy (△); 80 kGy (○).

Fig. 2 shows calculated particle scattering functions for different shapes of macromolecules. We compare the measured $P(q)$ with the particle scattering function of homogeneous and star-branched macromolecules, hard spheres (mono-disperse) and soft spheres (for mathematically formulation and details of the different types of $P(q)$ see Ref. [22]). The differences between the calculated particle scattering functions are significant at high values of u ($u > 2$). They show typical asymptotic behaviour, which can be used to distinguish between different shapes of the scattered particles.

The PMVE aggregates changes their shape at the phase transition temperature. At temperatures above lcst they show a scattering function like 'soft spheres'. The soft sphere consists of a centrosymmetric unit of three branches, each of which terminates in another trifunctional branch point (first shell) and so on to successive shells. The polymer density decreases with increasing distance to the centre. At temperatures lower than lcst the particles show a scattering function like star-branched molecules.

As expected, the degree of swelling (Q) of PMVE-gel depends on the temperature (Fig. 3a). In comparison with other thermo-sensitive hydrogels, the degree of swelling at temperatures above the volume phase transition temperature is rather high (about 2). This indicates the sponge-like structure of the hydrogel. The graph of temperature dependence of dimension of non-cross-linked particles and of Q is comparable.

Comparing the temperature dependence of $Q$and of $R_{h,app}$ of micro-gel (Fig. 3b) indicates, that the volume phase transition is not as sharp as for the bulk gel and occurred at a higher temperature. This agrees with experimental findings described in the literature. According to Tanaka et al. [23] the volume phase transition temperature of a bulk gel is lower than that of a micro-gel. The degree of swelling changes continuously even if the bulk changes the volume stepwise. A reason for this behavior could be the inhomogeneous cross-linking density [24,25] of the micro-gel.

FESEM micrographs of the micro-gel after irradiation with a dose of 20 kGy in the swollen, shrunk, and dry state are shown in Fig. 4. In the swollen state we found almost globular particles with a sponge-like structure having a mean diameter in the range of 250–600 nm (Fig. 4a and b), however, most frequently particles with a mean diameter of approximately 350 nm occurred. Interestingly, the outer membrane of many of these particles has small holes with a diameter as small as 5–20 nm (Fig. 4b) which provide a corresponding membrane permeability. The globular particles were found as isolated and as into a polymeric net incorporated particles, respectively (Fig. 4a). Up to now, we are unsure about this polymeric net. It could be formed by uncross-linked polymer molecules (sol content). The shrunk state of the micro-gel showed also almost globular particles with a sponge-like structure having a mean diameter in the range of 250–400 nm (Fig. 4c and d). Like in the swollen state the outer membrane of many of

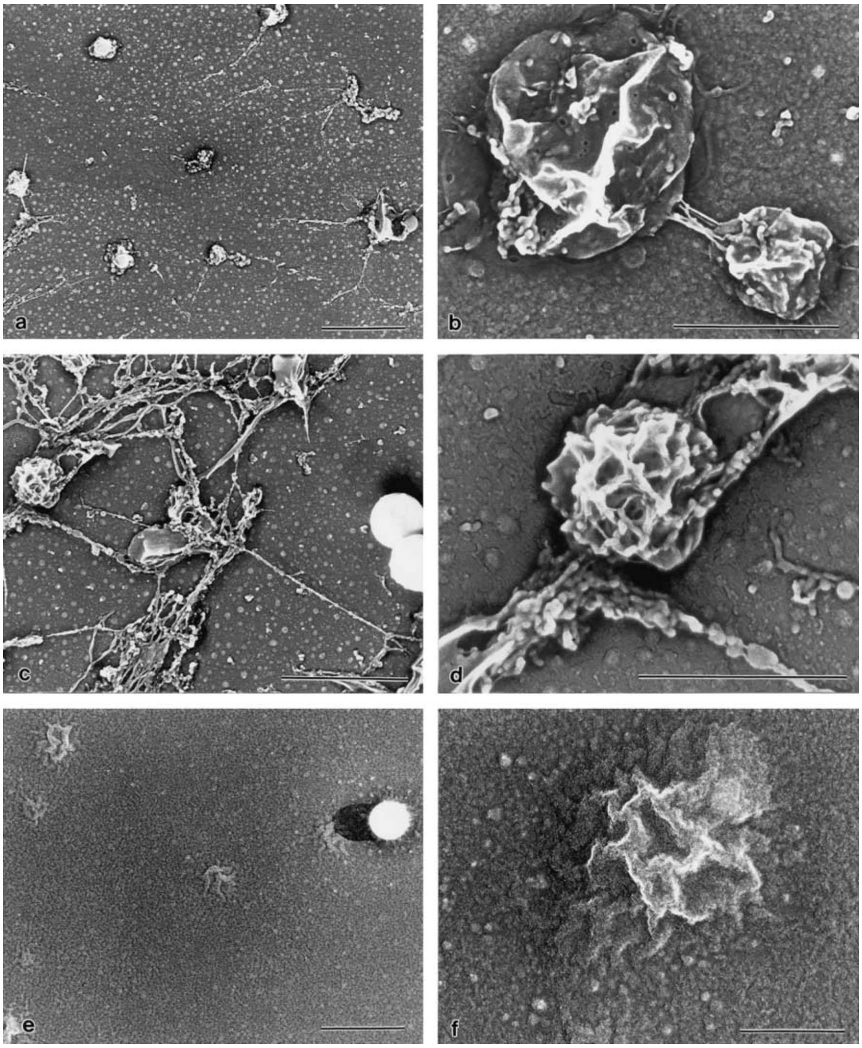

Fig. 4. SE micrographs of the micro-gel after irradiation with a dose of 20 kGy in the swollen (a,b), shrunk (c,d), and dry state (e,f) at different magnifications. (a) Globular particles isolated or bound to the polymeric net showed different shapes and sizes. (b) Individual sponge-like particle at high magnification. (c) Polymeric net with incorporated globular particles; the particle at the left is shown at high magnification in (d). (e) Particles in the dry state were flattened due to the effect of surface tension. Unidirectionally shadowed latex beads co-prepared with the air-dried micro-gel were used for the evaluation of the local elevation angle α ($\alpha = 26.5°$). (f) Individual flattened particle at high magnification. Bars correspond to 1 μm (a,c,e) and 0.5 μm (b,d,f), respectively.

these particles possessed small holes with a diameter of 5–20 nm. We also found a polymeric net, which incorporates many of the globular particles. Finally, in the dry state we found rather flat structures (as indicated by a very small length of their shadow in contrast to the shadow of a latex sphere) with diameters in the range of 250–800 nm (Fig. 4e and f). Most probably these structures correspond to the globular particles, which were strongly deformed due to flattening during the process of air-drying. It is known that flattening can form artificial structures with a significantly enlarged diameter. Thus, the microscopic data of the dry state of the micro-gel must be considered with great caution. We did not find a polymeric 'net' in the dry state like the one we observed in the swollen (Fig. 4a) and shrunk state (Fig. 4c), respectively.

The micro-gel after irradiation with a dose of 80 kGy in the swollen, shrunk, and dry state is shown in Fig. 5. In the swollen state we also found almost globular particles with a sponge-like structure having a mean diameter in the range of 250–450 nm (Fig. 5a and b), however, mostly the particles occur more dense than at 20 kGy. The outer membrane of these particles hardly possessed small holes in the range of 10 nm. The globular particles were either isolated or incorporated into a polymeric net (Fig. 5a). In the shrunk state the micro-gel revealed also globular particles but with a rather compact structure. Their mean diameter was in the range of 250–450 nm (Fig. 5c and d). Like in the swollen state the outer membrane of a few particles possessed small in the range of 10 nm. The particles were found to be either isolated or incorporated into a fine-meshed polymeric net (Fig. 5c). Interestingly, in the dry state we found globular structures with a mean diameter in the range of 200–600 nm (Fig. 5e and f). Most probably these structures are identical with the globular particles observed in the swollen and

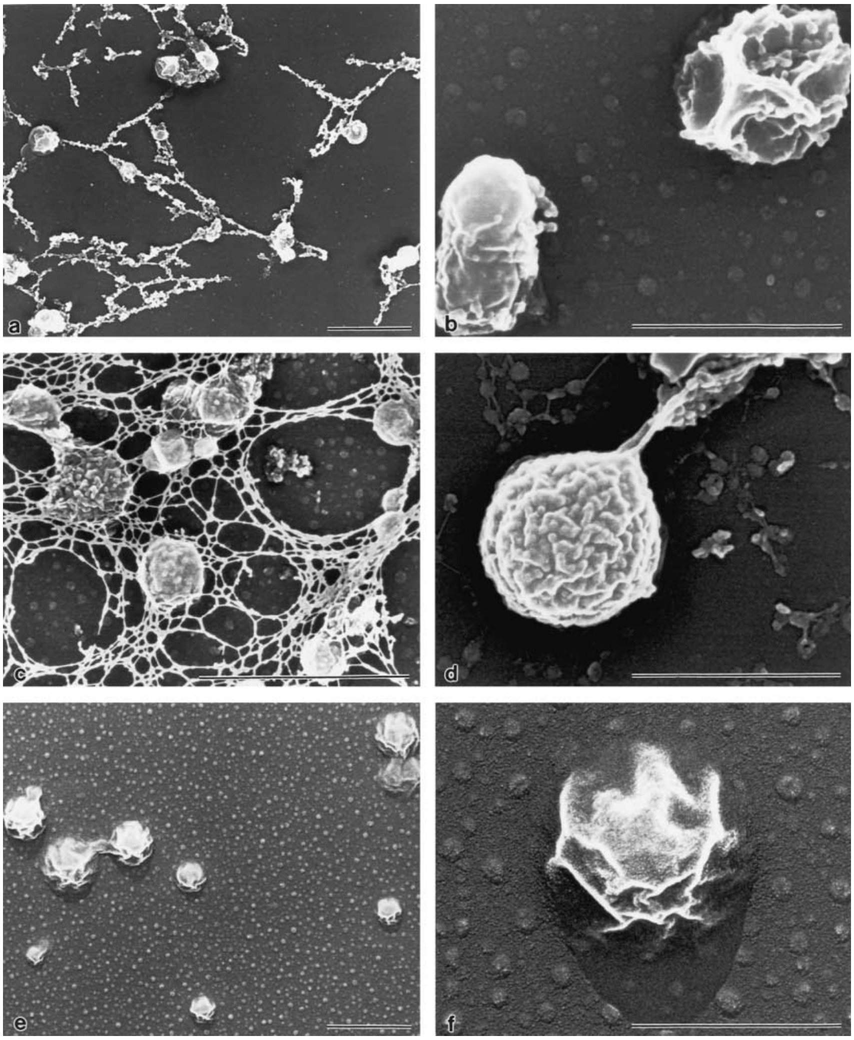

Fig. 5. SE micrographs of the micro-gel after irradiation with a dose of 80 kGy in the swollen (a,b), shrunk (c,d), and dry state (e,f) at different magnifications. (a) Globular particles bound to the polymeric net showed different shapes and sizes. (b) Individual sponge-like particles at high magnification. (c) Polymeric net with incorporated globular particles. (d) High magnification micrograph of a net-bound particle. (e) Particles in the dry state were flattened due to the effect of surface tension. (f) Individual flattened particle at high magnification. The local elevation angle α was 26.9° in (e,f). Bars correspond to 1 μm (a,c,e) and 0.5 μm (b,d,f), respectively.

shrunk state. As indicated by small length of their shadow the particle were deformed to a certain extent due to flattening during the process of air-drying. Although the flattening formed artificial structures it seems worth to mention that the degree of flattening obviously is significantly smaller than for the dry micro-gel at 20 kGy. This clearly indicates more stiff particles at 80 kGy. As already noticed at 20 and 80 kGy no polymeric net was found in the dry state.

4. Conclusions

The application of static and dynamic light scattering, cryopreparation, and state of the art high resolution field emission scanning microscopy proved to be a powerful combination of a scattering and an imaging method to characterize micro-gel in different states at the nanometer scale. A diluted aqueous solution of PMVE has a lower critical solution temperature and undergoes phase transition at temperatures above lcst. The dimension of the polymer aggregates formed under the condition of phase separation depends on the temperature. From the measured particle scattering function follows, that their shape can be best described by the model of a soft sphere. The macromolecules of these aggregates can be cross-linked by irradiation without any additives. The synthesized micro-gels are thermo-sensitive. In contrast to a bulk gel cross-linked by electron irradiation of concentrated PMVE solution, the volume phase transition is not sharp and the transition temperature is higher.

From the observation by FESEM, it was confirmed that particles having a spherical shape with a sponge-like structure and a mean diameter in the range of 250–600 nm are formed. Many of them have an outer membrane with holes with as small as 5–20 nm. Even the shrunk state of the micro-gel showed also almost particles with a sponge-like structure and an outer membrane with small holes. The micro-gel cross-linked at higher radiation dose occur more dense.

The knowledge of properties of micro-gel opens new avenues for their tailor-made designs and their technological applications as well.

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