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ORIGINAL ARTICLE

The electrostatic advantages of cross-linked polystyrene organogels swollen with limonene for selective adsorption and storage of hydrophobic drugs

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Abstract

The organogels poly(styrene-*co*-divinylbenzene), PS gel (**1**); poly(styrene-*co*-divinylbenzene-*co*-vinylpyridine), PS-VP gel (**2**); poly(styrene-*co*-divinylbenzene-*co*-vinylbenzoic acid), PS-VBA gel (**3**); and poly(styrene-*co*-divinylbenzene-*co*-styrenesulfonate), PS-SS gel (**4**) were prepared with limonene by varying the concentration of cross-linker and comonomer to control the properties of the gels. Limonene was used as the swelling solvent due to its low toxicity and environmental friendliness. Additionally, 4-vinylpyridine (VP), 4-vinylbenzoic acid, and 4-styrenesulfonate were introduced as cationic and anionic moieties to act as interaction units. An increase in the divinylbenzene ratio improved the mechanical strength, as evidenced by an increase in the G' value; for example, the G' of gel **3** improved from 15,000 Pa with 5% cross-linking to 93,000 Pa with 10% cross-linking. However, the increased cross-linking reduced the solubility in limonene, resulting in a decrease in the swelling ratio from 1.5 to 0.7. Cationic gel **2** can adsorb anionic compounds, while anionic gel **4** can adsorb cationic compounds. Gel **2** with 5 mol% VP was able to adsorb approximately 4.4 mg/g of an anionic dye, while gel **4** with 5 mol% SS was able to adsorb approximately 6.6 mg/g of a cationic dye. The limonene organogels were used for lipophilic drug storage and the controlled release of testosterone due to their dense polymer network.

Introduction

Organogels, which are semi-solid systems of three-dimensional network polymers, are immobilized in the organic liquid phase. Due to their hydrophobic structure, such gels have been widely used in various applications, such as vehicles for drug delivery [1–3], pollutant recovery materials [4], and sensor materials [5]. Their properties can be controlled by varying the components and their interactions in the gel network. In general, such gels can be classified into two categories, physical and chemical gels, depending on the type of interaction in the network structure. The framework of chemical gels consists of cross-linked subunits formed by covalent bonds, while physical gels are held together by noncovalent bonds, such as hydrogen bonds, π–π interactions, and van der Waals interactions [6, 7]. Numerous physical gels made from oils have been extensively studied, probably due to the effective hydrogen bonding network in oils, but most of the resulting gels lack the mechanical properties that would enable them revert to a sol solution [8, 9]. Thus, chemical gels made from oil are sought to improve the mechanical properties and thermal stability. For this, we examined natural oils to avoid the toxicity of organic solvents, which is still a limitation in the application of oil gels.

D-Limonene (4-isopropenyl-1-methylcyclohexene) is an environmentally friendly, biodegradable solvent [10]. It can be used safely and effectively in a wide range of products. D-Limonene is listed in the Code of Federal Regulations as generally recognized as a safe [11]. It has possible applications for environmental and medical materials because of

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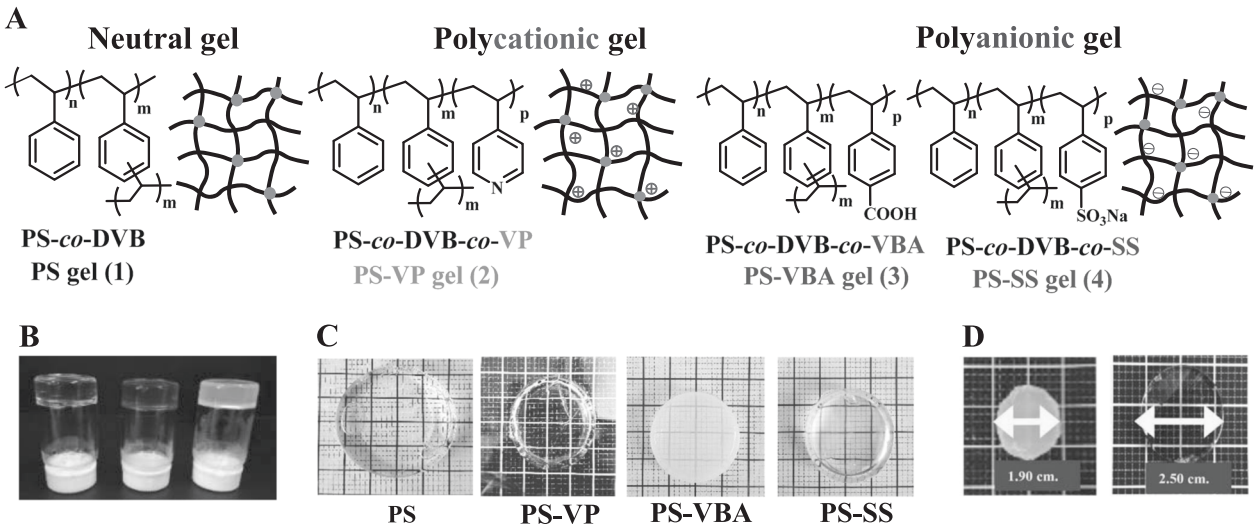

Fig. 1 **a** Chemical structures and polymer models of PS gel **1** (neutral gel), PS-VP gel **2** (cationic gel), PS-VBA gel **3**, and PS-SS gel **4** (anionic gel). **b** Inversion of vials of gels **1**, **2**, and **3**. **c** Photograph of gels **1**, **2**, **3**, and **4** (5% cross-linker) and **d** photographs of gel **1** in the dry state and swollen in limonene

its pharmacological and biological properties [12–15]. Due to its properties, D-limonene is a good candidate solvent for environmentally friendly materials. In particular, network structures consisting of polystyrene are well solubilized in D-limonene [16–18]. Since polystyrene is a hydrophobic material as well as a biocompatible material [19], it can be widely used in a variety of applications, such as the adsorbent material in pollutant recovery [20–22] and drug storage to control the release of lipophilic compounds [23]. A large number of different styrene copolymers have been produced [24, 25], but most are in the solid phase, such as the porous polymeric adsorbents of poly(styrene-*co*-divinylbenzene) (PS gel) [26]. If PS derivatives could be used as an organogels, drug diffusion into the gel would make it possible to utilize the volume effectively.

In our previous work, we prepared chemical oil gels using a cross-linked copolymer composed of a trimethylene carbonate derivative and L-lactide for drug storage of testosterone [27]. This gel can be used as a delivery vehicle for androgen in bone fractures instead of costly bone morphogenetic proteins. The gel used dimethyl sulfoxide (DMSO) and dimethylcarbonate (DMC) as immobilized solvents, but the time for release was quite fast, occurring in the first 3 h, because of the good miscibility of the organic solvent in water [28, 29]. Thus, we directed our attention to limonene gel, which is insoluble in water and could prolong release from the dense polymer network.

In this study, the preparation of chemically cross-linked polystyrene organogels including electrostatic interaction moieties with limonene as the solvent is presented for the first time, with the aim to control release and adsorption on the surface of aqueous media. The gel was designed to incorporate with poorly water-soluble compounds by using a hydrophobic core. Furthermore, we increased the recognition of organogels by introducing styrene derivatives as electrostatic interaction moieties, that is, by introducing 4-vinylpyridine (VP), 4-vinylbenzoic acid (VBA), and 4-styrenesulfonate (SS) as comonomers with styrene. PS gel (**1**), poly(styrene-*co*-divinylbenzene-*co*-vinylpyridine) (PS-VP gel: **2**), poly(styrene-*co*-divinylbenzene-*co*-vinylbenzoic acid) (PS-VBA gel: **3**), and poly(styrene-*co*-divinylbenzene-*co*-styrenesulfonate) (PS-SS gel: **4**), shown in Fig. 1 (Supporting Information, Table S1), were prepared and swollen in limonene. The mechanical strength of these gels was investigated by the swelling ratio, fracture stress, and rheological behavior upon increasing the amount of cross-linking units from 5 to 10 mol%. Finally, dye adsorption tests were also performed to confirm the electrostatic interactions within these designed oil gels by varying the amount and comonomer.

Materials and methods

Materials

Styrene (99.0%), azobisisobutyronitrile (AIBN) (98.0%), and phosphate-buffered saline (PBS) (×10) were purchased from Wako Pure Chemical Industry Ltd., Japan. Super dehydrated toluene (99.5%), divinylbenzene (50.0%), VBA (97.0%), VP (95.0%), sodium SS (93.0%), and testosterone (98.0%) were purchased from Tokyo Chemical Industry Co., Ltd., Japan (TCI). D-Limonene (90.0%), tetrahydrofuran (98.0%), dimethyl sulfoxide (99.0%), and bromocresol

purple (BCP) were supplied from Nacalai Tesque Inc., Japan. Rhodamine B was purchased from Sigma Aldrich.

Preparation of organogels

The cross-linked polystyrene gels were prepared via radical polymerization using AIBN as an initiator. All monomers were purified by distillation or recrystallization to remove inhibitor before polymerization. To prepare the organogels, styrene, divinylbenzene as a cross-linker and a styrene derivative (SD; VP, VBA, or SS) as an interaction unit were dissolve in toluene (4 M), followed by the addition of 2.5 mol% AIBN and sonication. The mixture was then deoxygenated by nitrogen bubbling. The mixture was heated at 60 °C for 24 h. The polymer network was polymerized randomly, providing PS_n-DVB_m-SD_p, where n, m and p refer to the feeding ratio of styrene, divinylbenzene, and the styrene derivative, respectively. Unreacted monomer, oligomer, and linear polymer chains that were not incorporated in the cross-linked network are denoted the soluble fraction. To determine this fraction, the reacted organogel samples were soaked in tetrahydrofuran (THF) for 72 h to wash away the soluble fraction. The solvent was renewed every 24 h for a total of three times. The THF gels were finally immersed in limonene (50 mL every 24 h × 3 times) to replace THF with limonene in the gel network.

Characterization

The organogels were measured via Fourier-transform infrared spectroscopy (FT-IR) to investigate the additional functional groups (i.e., pyridine, carboxylic, and sulfonic groups). The swelling ratio (Q) was evaluated in limonene solution at room temperature following the equation:

$$\text{Swelling ratio}(Q) = \frac{(W_s - W_d)}{W_d}.$$

The THF gel was dried under vacuum overnight and weighed (W_d). The dried gels were immersed in limonene for 48 h. Before drying, the gel swollen with limonene was weighed (W_s). The fracture stress was measured in compressive mode via EZ tests (EZ-SX, Shimadzu, Japan). The organogels were cut into squares with dimensions of $8 \times 8 \times 2\ mm^3$ and compressed at 1 mm/min until break. The rheological properties of the polystyrene organogels were measured using a rheometer (KNS2100, Kinexus, Japan). The organogel samples were cut into circles with a diameter of 20 mm and thickness of 4 mm and placed between two plates, where the lower plate was fixed and the circular upper plate (diameter 20 mm) was connected to the measuring system. The storage modulus (G') and loss modulus (G'') of the swollen limonene organogels were measured at 25 °C.

Dye adsorption

The amount of dye adsorbed was determined by ultraviolet–visible (UV–Vis) spectroscopy. All limonene gels ($8 \times 8 \times 4\ mm^3$, 180–200 mg) were immersed in 3.5 mL of a 0.2 mM aqueous dye solution (BCP as the anionic dye and rhodamine B as the cationic dye) in a cuvette for UV–Vis measurement. The adsorption capability of the organogels was determined by following the decrease in the dye concentration with a UV–Vis spectrophotometer (UV-2600, Shimadzu, Japan). The concentration was fitted to a calibration curve with a concentration range of 0.2–0.025 mM.

Drug release experiment

The drugs were dissolved to saturation in limonene. Then, the limonene gel (30 mg) was soaked in the solution for 24 h. The loaded gels were wiped with tissue paper to remove limonene from the gel surface. Then, the loaded gels were released in PBS solution (pH 6.8, 10 mL, 37 °C). The amount of drug released was determined by withdrawing 1 mL of solution and adding 1 mL of fresh PBS solution to maintain the same conditions, followed by detection by high-performance liquid chromatography (HPLC). The cumulative drug release (%) was determined based on the following equation:

$$\text{Cumulative release} = \frac{M_n}{M_\alpha} \times 100\%,$$

where M_n denotes the amount of drug released (μg) at each sampling time and M_α denotes the maximum amount of drug released. The amount of drug released was calculated using the following equation:

$$\text{Cumulative amount(Mt)} = C_n \times V_0 + \sum_{i=1}^{n-1} C_i \times V_i,$$

where C_n denotes the drug concentration at each sampling time, C_i denotes the drug concentration in the ith sample, and V_0 and V_i denote the volume of the receiver solution and the samples, respectively.

Drug assay

The testosterone concentration was determined using reverse-phase HPLC (Shimadzu, Japan). The HPLC system used a Cosmosil Packed $5C_{18}$-MSII column (4.6 mm × 150 mm, 5 μm). The detection condition was 60% MeOH in H_2O with a flow rate of 0.3 mL/min and 244 nm UV detector at 40 °C, and 100 μL of the sample was loaded. The characteristic testosterone peak appeared at 40.4 min. The concentration was fit to a calibration curve with a range

of 5–25 μg/mL ($R^2 = 0.998$) for testosterone in PBS solution.

Ibuprofen (isobutylphenyl propionic acid) was detected with a UV detector at 223 nm at 40 °C using 60% PBS in acetonitrile as the mobile phase. The flow rate was set to 0.6 mL/min, and 100 μL of sample was loaded. Under these conditions, the resolution time of ibuprofen was 5.01 min. A calibration curve was constructed using an ibuprofen standard solution in PBS over a concentration range of 6.5–46 μg/mL ($R^2 = 1$).

Results and discussion

As shown in Fig. 1, a neural gel, polycationic gel, and polyanionic gel were prepared with the polystyrene-*co*-divinylbenzene-*co*-styrene derivative. The PS gel (**1**), as the neutral gel, was prepared with 5 and 10 mol% divinylbenzene (cross-linker) to vary the gel network, providing PS_{95}-*co*-DVB_5 and PS_{90}-*co*-DVB_{10}, to observe the effect on the mechanical strength. We also selected VP and VBA as electrostatic interaction moieties, providing PS_{95}-*co*-DVB_5-*co*-VP_5 and PS_{90}-*co*-DVB_{10}-*co*-VP_5 for 5 and 10% cross-linked PS-VP gel **2** and PS_{95}-*co*-DVB_5-*co*-VBA_5 and PS_{90}-*co*-DVB_{10}-*co*-VBA_5 for 5 and 10% cross-linked PS-VBA gel **3**. Gelation was confirmed when a homogeneous substance that exhibited no gravitational flow upon inversion of the vial was obtained (Fig. 1b). The reaction time was selected as 24 h in order to use the gel under quantitative reaction conditions. All of the gels with VP yielded transparent gels (**2**), whereas over 5 mol% introduction of VBA gel (**3**) resulted in an opaque gel, probably due to the low solubility of VBA in toluene. Examples of the prepared gels are shown in Fig. 1c. After the gels were prepared in toluene and washed in THF, the gels were dipped into an excess amount of limonene to obtain transparent gels swollen in limonene (Fig. 1d). Incorporation of the interaction unit as an electrostatic interaction moiety was confirmed by FT-IR (Fig. 2).

Peaks were observed at 1415 and 1556 cm^{-1} for **2**, which were attributed to C–N and C = N stretching of aromatic amines. The presence of a C = O peak at 1720 cm^{-1} was also confirmed for **3**, attributed to the carbonyl group of carboxylic acids. Gel **4** contains sulfonic acid, which is characterized by peaks at 1035 and 1217 cm^{-1} corresponding to S = O and S–O bonds.

To study the mechanical strength, styrene-derivative copolymer (VP and VBA) gels with 5 and 10% cross-linking and swollen with limonene were used to evaluate the effect of the interaction unit and the density of the polymer network, as determined by the level of cross-linking (Fig. 3). The swelling ratio in limonene was investigated by fracture stress and rheological measurements. The swelling property of an organogel is essential in

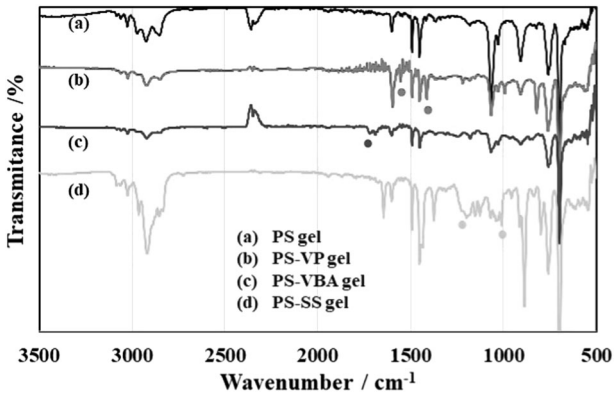

Fig. 2 FT-IR spectra of the 5% CL PS gel (**1**), PS-VP gel (**2**), PS-VBA gel (**3**), and PS-SS gel (**4**)

biomedical and pharmaceutical applications because the degree of swelling influences the diffusion of solute, the surface mobility, and the optical and mechanical properties.

When an organogel is to be used as a drug delivery system, its swelling ratio is directly related to its drug adsorption and release behavior. In general, low swelling ratios were observed as the amount of cross-linker increased. For example, PS gel (**1**), PS-VP gel (**2**), and PS-VBA gel (**3**) had swelling ratios of 3.4 (Fig. 3a(a)), 2.6 (Fig. 3a(c)), and 1.5 (Fig. 3a(e)) under 5% CL (PS_{95}-*co*-DVB_5, PS_{95}-*co*-DVB_5-*co*-VP_5, and PS_{95}-*co*-DVB_5-*co*-VBA_5), which reduced to 2.1 (Fig. 3a(b)), 1.4 (Fig. 3a(c)), and 0.7 (Fig. 3a(f)) under 10% CL (PS_{90}-*co*-DVB_{10}, PS_{90}-*co*-DVB_{10}-*co*-VP_5, and PS_{90}-*co*-DVB_{10}-*co*-VBA_5). The increase in the comonomer ratio when VP was the interaction unit resulted in low swelling ratios of 4.3, 2.6, and 1.1 for gel **2** with 2, 5, and 8 mol% VP (PS_{95}-*co*-DVB_5-*co*-VP_2, PS_{95}-*co*-DVB_5-*co*-VP_5, and PS_{95}-*co*-DVB_5-*co*-VP_8), respectively (Supporting Information, Figure S1). Similarly, gel **3** showed the lowest swelling ratios in limonene (Fig. 3a (e, f)) because of the lack of solubility of the comonomer in limonene, including the heterogeneous domains. This makes the gels strong, but the interaction units of the carboxylic acid moiety might not have the desired influence.

Furthermore, the fracture stress (Fig. 3b) confirms the stronger network structure of the 10% CL gels. The fracture stress of the 10% CL gels is approximately two times higher for gels **2** and **3** and six times higher for gel **1**. The mechanical strength of the limonene gels was thus influenced by both the degree of cross-linking and the solubility of the interaction unit. This makes the gels strong, but the interaction units of the carboxylic acid moiety might not have the desired influence.

To clarify the viscoelastic and rheological properties, the organogels swollen with limonene were characterized with 5 (Fig. 3c) and 10% CL (Fig. 3d). The oscillatory test was performed in the range of 0.1–10 Hz. In principle, the storage (elastic) modulus (G') represents the solid-like

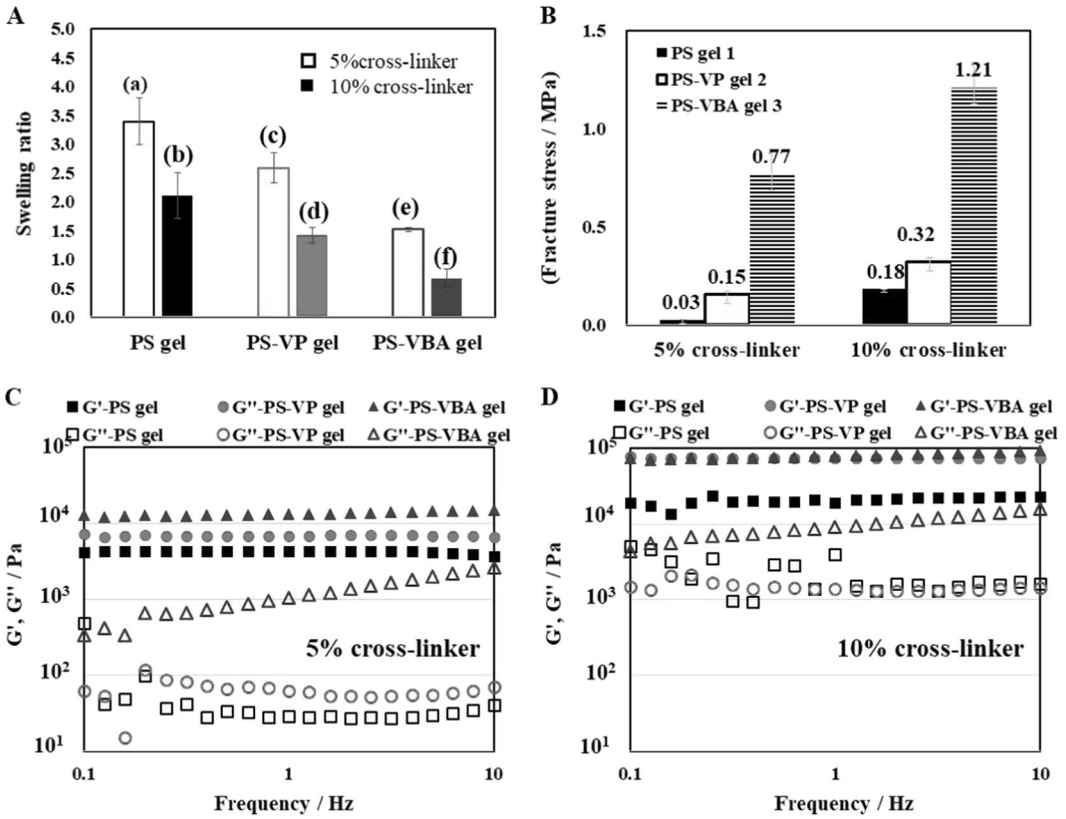

Fig. 3 Mechanical measurements of PS gel **1**, PS-VP gel **2**, and PS-VBA gel **3** with 5 and 10% cross-linker. **a** Swelling ratio, where the empty bars represent 5% cross-linker and the filled bars represent 10% cross-linker. **b** Fracture stress ($n = 3$). **c** Rheological measurement of the gel with 5 mol% cross-linker. **d** Rheological measurement of the gel with 10 mol% cross-linker ($n = 3$)

character and stored energy, while the loss (viscous) modulus (G'') reflects the liquid-like behavior and energy loss. For all samples, G' was higher than G'' at all frequencies, indicating gel-like behavior. The G' value of the 5% CL sample was about six times lower than the value of the 10% CL sample. For example, PS gel (**1**) changed from 3700 Pa with 5% CL to 23,000 Pa with 10% CL, while PS-VP gel (**2**) and PS-VBA gel (**3**) changed from 6700 and 15,000 Pa to 74,000 and 93,000 Pa, respectively. The highest elastic modulus G' of approximately 1400 Pa has been reported for organogels under similar conditions [32]. Furthermore, the value of G'' for the viscosity also remained constant, independent of the frequency, indicating the formation of a stable network via strong covalent bonds [30–32]. The G'' value of the 5% CL samples of gels **1**, **2**, and **3** are 30, 60, and 1000 Pa, respectively, which are much lower than that of the 10% CL gels of approximately 3900, 1400, and 9000 Pa for gels **1**, **2**, and **3**, respectively.

To study the adsorption with different interaction units, the polyionic gels were fixed with a 5% cross-link ratio and the ratio of styrene derivative (i.e., VP or SS) was varied to 2, 5, and 8 mol%, providing PS_{98}-*co*-DVB_5-*co*-VP_2, PS_{95}-*co*-DVB_5-*co*-VP_5, and PS_{92}-*co*-DVB_5-co-VP_8 for PS-VP gel (**2**) and PS_{98}-*co*-DVB_5-*co*-SS_2, PS_{95}-*co*-DVB_5-*co*-SS_5, and PS_{92}-*co*-DVB_5-co-SS_8 for PS-SS gel (**4**), as shown in Fig. 4. Color changes were observed (Fig. 4b), although it is difficult to evidence the electrostatic interaction. The swelling ratio of **4** is shown in Figure S2. By increasing the amount of the electrostatic moiety, the degree of swelling in limonene decreased from 1.05, 0.54, and 0.31 for 2, 5, and 8 mol% SS, respectively, because of its low solubility in limonene. Likewise, the mechanical properties of **2** and **4** (Supporting Information, Figures S3 and S4) were revealed in terms of the fracture stress and elastic stress. Furthermore, we studied the adsorption of organic compounds onto the organogels swollen with limonene, using BCP as an anionic hydrophobic drug and rhodamine B as a cationic hydrophobic drug, in aqueous solution. The VP and SS moieties were introduced in the organogels to provide cationic and anionic electrostatic interactions, respectively. The interaction units were evaluated at concentrations of 2, 5, and 8 mol%.

Only PS-VP gel (**2**) adsorbed anionic BCP molecules in aqueous solution, and PS-SS gel (**4**) and PS gel (**1**) did not show any adsorption (Fig. 4b). This evidence illustrates that the pyridine interaction unit shows cation-like electrostatic properties on the pyridine ring through the surface in aqueous media (Figure S5). Additionally, the color of PS-VP gel **2** gradually changed to green, while the color of the dye

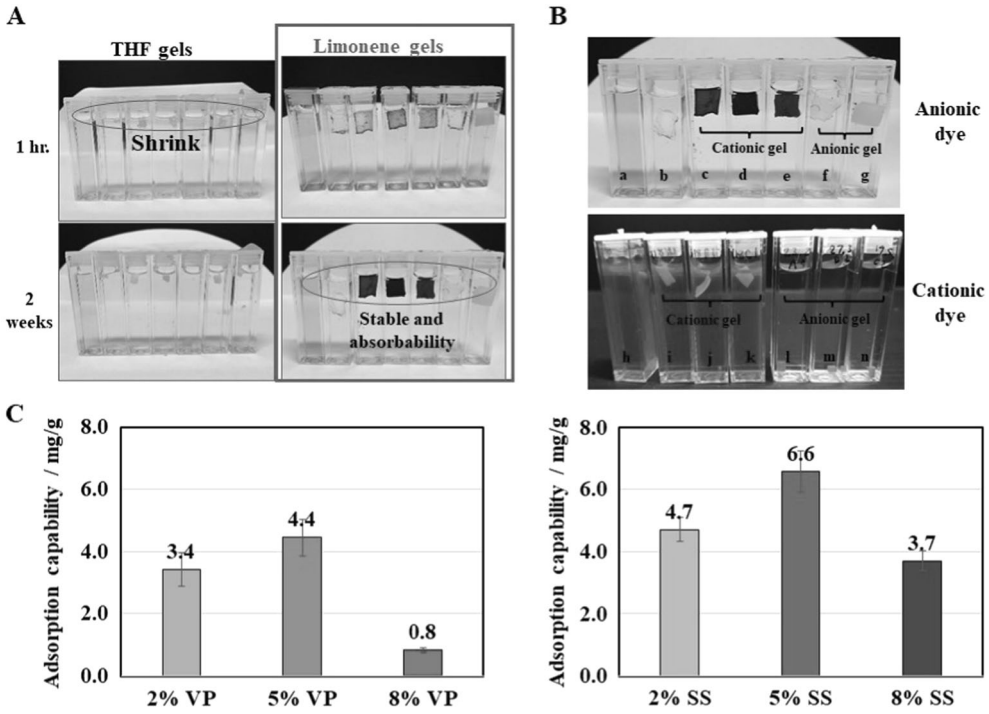

Fig. 4 Dye adsorption experiment. **a** Photographs of the THF gel (left) and limonene gel (right) submerged in an aqueous solution of bromocresol purple for 1 h and 2 weeks. **b** Photograph of the dye adsorption test: (a) bromocresol purple/anionic dye solution, (b) gel **1**, (c) gel **2** with 2 mol% VP, (d) gel **2** with 5 mol% VP, (e) gel **2** with 8 mol% VP, (f) gel **4** with 2 mol% SS, (g) gel **4** with 5 mol% SS, (h) rhodamine B/cationic dye solution, (i) gel **2** with 2 mol% VP, (j) gel **2** with 5 mol% VP, (k) gel **2** with 8 mol% VP, (l) gel **4** with 2 mol% SS, (m) gel **4** with 5 mol% SS, and (n) gel **4** with 8 mol% SS. **c** Adsorption of the dye compound (mg/g) by PS-VP gel **2** with 4-vinylpyridine concentrations of 2, 5, and 8 mol%. **d** Adsorption of the dye compound (mg/g) by PS-SS gel **4** with 4-styrenesulfonate concentrations of 2, 5, and 8 mol% ($n = 3$)

solution turned transparent, as observed by the naked eye (Figure S7), while the color of PS-SS gel **4** did not change. Gel **2** with 5 mol% VP showed a higher adsorption capacity of 4.4 mg/g than the gel with 2 mol% pyridine (3.4 mg/g) because of the large amount of cationic moieties (Fig. 4c and Figure S6). However, gel **2** with 8 mol% VP showed the lowest adsorption of approximately 0.8 mg/g, probably owing to the low swelling ratio (Figure S1) due to the low solubility of VP. The results indicate that the amount of comonomer introduced into the polystyrene gel greatly affects the limonene gel in terms of both solubility and electrostatic interaction with the target drug.

On the other hand, only the anionic PS-SS gel (**4**) was able to adsorb the cationic dye efficiently, as shown in Fig. 4b(l–n), whereby the adsorbed gel became pink in color. Cationic gel **2** did not adsorb the cationic dye rhodamine B, as recognized by the stable color, because of the electrostatic repulsion activity (Fig. 4b(i–k)). The adsorption depended on both the electrostatic moiety and the solubility of the interaction unit in limonene. The 5 mol% SS gel thus showed the highest adsorption of 6.6 mg/g (Fig. 4d). Moreover, the limonene organogels were immersed in aqueous solution for approximately 2 weeks and still retained their swollen size and adsorption ability. Because limonene is insoluble in water, the solvent is slowly released from the gels. This property is suitable for the prolonged release of a drug in aqueous solution (Fig. 4a). This was supported by the results of immersing gels swollen with THF in aqueous solution. THF is more easily dissolved in water, and the gels quickly shrank to half their size and turned opaque after being immersed in water for 1 h.

To study the controlled release of testosterone by the limonene gel, 5 mol% cross-linked limonene gels were used as drug storage vehicles (Fig. 5). The release profile was investigated in PBS at 37 °C. After 3 h, 5% cross-linked PS gel (**1**), PS-VP gel (**2**), and PS-VBA gel (**3**) released approximately 36, 25, and 29% of the stored testosterone, respectively. These results showed improved long-term release compared with the previous study of organogels swollen with DMSO and DMC solvents [27]. PS-VBA gel (**3**) has a more prolonged release than PS-VP gel (**2**) and PS gel (**1**). Thus, the release profile was controlled by the dense polymer network of the limonene gel because PS-VBA gel (**3**) shows the highest mechanical strength, followed by PS-VP gel (**2**) and PS gel (**1**). Testosterone, which is a neutral molecule, has a weak interaction with the polymer chain (interaction unit moiety and polystyrene), and thus the controlled release was not significantly different for the

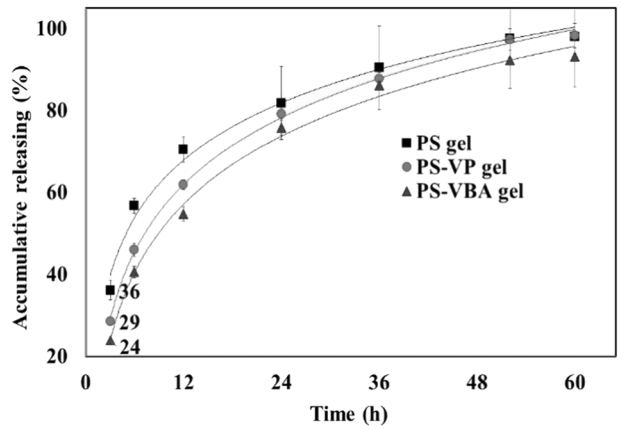

Fig. 5 Accumulative release of testosterone from the PS gel (**1**), PS-VP gel (**2**), and PS-VBA gel (**3**) with 5% cross-linker in PBS solution at 37 °C ($n = 3$)

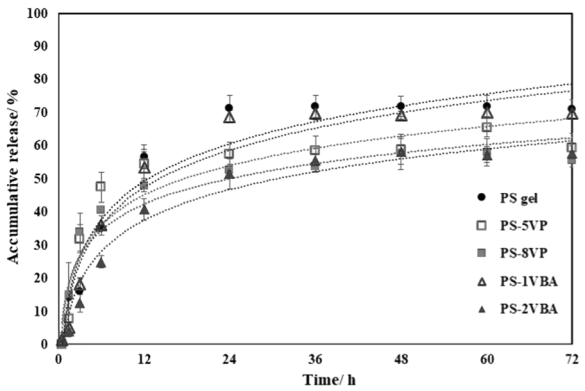

Fig. 6 Accumulative release of ibuprofen in PBS at 37 °C from the PS gel (**1**), the PS-VP gels (**2**) with 5 and 8 mol% VP, and the PS-VBA gels (**3**) with 1 and 2 mol% VBA ($n = 3$)

various electrostatic moieties. Therefore, the electrostatic activity of the limonene gels is effective for use with ionic drug molecules. Because of the strong interaction, the limonene gels could prolong the controlled release of drugs.

To clarify the controlled release by electrostatic interaction, ibuprofen release experiments were performed, as shown in Fig. 6. The drug contains a carboxylic group, which is supposed to bind with pyridine by dipole–dipole interactions or electrostatic interactions. The accumulative release was plotted against the release time, and the trend line was determined by logarithmic-plot theory. PS-VP gels (**2**) with 5 and 8 mol% VP and PS-VBA gels (**3**) with 1 and 2 mol% VBA were employed for observation of ibuprofen release. Interestingly, drug release from the gels with 8 mol % VP and 2 mol% VBA was more prolonged than that from the gels with 5 mol% VP and 1 mol% VBA, as well as the neutral PS gel. Therefore, the pyridine and carboxylic moieties in the gels swollen with limonene, which is an aprotic solvent, controlled the release of the ionic drug by interactions between the drug and the gel network.

Conclusions

In conclusion, novel cross-linked polystyrene organogels with electrostatic moieties swollen with limonene were prepared. The chemical organogels had improved mechanical strength, showing a G' of approximately 90,000 Pa and a fracture stress of 1.21 MPa for the PS-VBA gel (**3**), compared with physical organogels. The dense polymer network can be controlled by varying the concentration of the cross-linker (divinylbenzene) and the comonomers (VP, VBA, and SS). The selectivity due to electrostatic interactions was also used for drug adsorption. Only the PS-VP gel (**2**) had the ability to adsorb anionic dye, which occurred slowly through its surface. The gel with 5 mol% VP showed the highest adsorption of approximately 4.4 mg/g of the anionic dye (BCP). On the other hand, the PS-SS gel (**4**) could adsorb approximately 6.6 mg/g of the cationic dye (rhodamine B) because of the introduction of electrostatic interaction units. Moreover, the limonene gel served as a hydrophobic drug storage and controlled release vehicle. Gel **3** had a slower controlled release than gels **2** and **1**, which was influenced by the mechanical strength. Furthermore, the introduction of cat/anionic moieties could control the release of a charged drug via interactions with the drug molecule. The novel limonene chemical gels with incorporated interaction units are promising environmentally friendly materials that could serve as selective adsorbents and provide the controlled release of hydrophobic drugs.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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