CI&CEQ
Chemical Industry & Chemical Engineering Quarterly

Available on line at
Association of the Chemical Engineers of Serbia *AChE*
www.ache.org.rs/CICEQ

Chem. Ind. Chem. Eng. Q. 21 (1) 85–94 (2015) CI&CEQ

YOUNG HO KIM[1,2]
DONG WON LEE[1]
EUN JI JUNG[1]
JUN TAE BAE[1]
SANG GIL LEE[1]
HYEONG BAE PYO[1]
KUK HYOUN KANG[2]
DONG KYU LEE[2]

[1]R&D Center Hanbul Cosmetics Co. Ltd., Daesung-ro, Samsung-myon, Umsung-kun, Chungbuk, Republic of Korea
[2]Department of Engineering Chemistry, Chungbuk National University Cheongju, Republic of Korea

SCIENTIFIC PAPER

UDC 58:66:547.972

DOI 10.2298/CICEQ131002010K

PREPARATION AND CHARACTERIZATION OF QUERCETIN-LOADED SILICA MICROSPHERES STABILIZED BY COMBINED MULTIPLE EMULSION AND SOL-GEL PROCESSES

Article Highlights

- Silica microspheres loaded with quercetin were prepared using P/O/W emulsion/sol-gel method
- SEM/EDX analysis of silica microspheres showed the microcapsules filled with quercetin
- The encapsulation efficiencies of silica microspheres of quercetin ranged from 17.8±2.5 to 27.5±1.9%
- Residual content of quercetin encapsulated in silica microsphrere was still 82% at 42 °C

Abstract

Despite exhibiting a wide spectrum of cosmeceutical properties, flavonoids and related compounds have some limitations related to their stability and solubility in distilled water. In this project, we prepared silica microspheres using a novel method that uses polyol-in-oil-in-water (P/O/W) emulsion and sol-gel methods as techniques for stabilizing quercetin. A stable microsphere suspension was successfully prepared using a mixed solvent system comprising a polyol-phase medium for performing the sol-gel processing of tetraethyl orthosilicate (TEOS) as an inorganic precursor with outer water phase. The morphology of the microsphere was evaluated using a scanning electron microscope (SEM), which showed a characteristic spherical particle shape with a smooth surface. Furthermore, SEM/EDS analysis of a representative microsphere demonstrated that the inner structure of the silica microspheres was filled with quercetin. The mean diameter of the microsphere was in the range 20.6-35.0 μm, and the encapsulation efficiency ranged from 17.8 to 27.5%. The free and encapsulated quercetin samples were incubated in separate aqueous solutions at 25 and 42 °C for 28 days. The residual content of the quercetin encapsulated by silica microspheres was 82% at 42 °C. In contrast, that of the free quercetin stored at 42 °C decreased to ~24%.

Keywords: microsphere, silica, flavonoid, quercetin, multiple emulsion, sol-gel.

Flavonoids and related compounds, a class of phenolic compounds widely distributed in plants, can protect an organism against reactive oxygen species (ROS). Quercetin is one of the most abundant natural flavonoids found in various common vegetables and fruits. Quercetin, a topical antioxidant, is known to delay ultraviolet (UV) radiation-mediated oxidant injury and cell death by scavenging oxygen radicals, protecting lipids against peroxidation to terminate the chain-radical reaction, and chelating metal ions to form inert complexes that prevent the conversion of superoxide radicals and hydrogen peroxide into hydroxyl radicals [1,2]. However, the therapeutic usefulness of these potential benefits is limited by the unfa-

Correspondence: D.K. Lee, Department of Engineering Chemistry, Chungbuk National University Cheongju 361-763, Republic of Korea.
E-mail: dklee@cbnu.ac.kr
Paper received: 2 October, 2013
Paper revised: 16 April, 2014
Paper accepted: 24 April, 2014

vorable physicochemical properties of this compound; this includes its very poor water solubility and low stability [3]. Conventional formulations to improve solubility suffer from low bioavailability and poor pharmacokinetics [4]. Therefore, the double emulsion solvent evaporation method is insufficient to encapsulate some pharmaceutically useful drugs having poor solubility in water and selected organic solvents [5,6]. The design of custom polymer architectures (including amphiphilic block copolymers, comb-shaped polymers, dendrimers and hyperbranched polymers) has been extensively employed for the delivery of hydrophobic drugs by means of encapsulation in micelles, nanoparticles, microspheres, or capsules [7-10].

Microcapsules exhibit a number of interesting characteristics. The primary reasons for microencapsulation include the ability to control the release of encapsulated drugs, protect the encapsulated materials against oxidation or deactivation due to reaction in the environment, mask the odor and/or taste of encapsulated materials, and isolate the encapsulated materials from undesirable phenomena [11]. To date, most studies on this subject focus on encapsulation by the liposomal method, molecular encapsulation by cyclodextrin and nanostructured lipid carrier method [12-14].

Multiple emulsions are complex and thermodynamically unstable systems, which combine either o/w or w/o emulsions in one system [15]. Multiple emulsions have been used as a means of delivering drugs to specified targets in the body while preventing possible deleterious effects of these drugs on other organs and prolonging the release of the drugs that have a short biological half-life [16]. In addition, multiple emulsions have recently been used as reaction media to synthesize polymer microspheres encapsulating drugs, peptides or proteins by a solvent evaporation method [17,18].

Microencapsulation using inorganic materials such as silica can be performed by the sol-gel method. The sol-gel/emulsion approach is well suited to the control of shape, density, amount, and surface properties of hollow spheres, and it is a simple and economical method [19]. Stőber *et al.* [20] reported the synthesis of monodisperse silica particles in an aqueous alcohol solution from silica alkoxide using a sol-gel method that has been successfully utilized for the synthesis of inorganic particles.

This study suggests that the combination of a novel polyol-in-oil in water (P/O/W) emulsion with a sol-gel process can be applied to the encapsulation of flavonoids to produce capsules with high encapsulation efficiency and good properties. In addition, a newly developed quercetin-loaded silica microsphere system was devised to improve the quercetin stability and its properties as a cosmetic raw material, thus creating potential for its use in future applications. The formation of silica microspheres containing quercetin was confirmed by performing scanning electron microscopy(SEM)/energy-dispersive X-ray spectroscopy (EDS) analysis.

EXPERIMENTAL

Materials

The following chemicals were obtained from commercial sources and used as received: quercetin dihydrate were obtained from Sigma-Aldrich Cheme GmbH (Steinheim, Germany). Acrylates/C10-30 alkyl acrylate crosspolymers (Pemulen® TR-2), a co-surfactant, were obtained from BF Goodrich Company (OH, USA). PEG-10 Dimethicone (KF® 6017), a lipophilic surfactant, was purchased from Shinetsu Chemical Co. (Tokyo, Japan). Polyoxyethylene sorbitan monolaurate (Tween® #20), a hydrophilic surfactant, was purchased from Sigma-Aldrich Cheme GmbH (Steinheim, Germany). Hydroxyethylcellulose (Natrosol® 250), a stabilizer of emulsion structure, were obtained from Aqualon (Wilmington, NC, USA). Tetraethyl orthosilicate (TEOS, 98%), a silica source, was purchased from Sigma-Aldrich Cheme GmbH (Steinheim, Germany). Nitric acid (HNO_3, 60%), an acidic catalyst, was purchased from Samchun Pure Chemicals Co. Ltd (Seoul, Korea). 1,3-Butylene glycol was purchased from Kyowa Hakko Chemical Co. (Tokyo, Japan) and glycerin solvent was obtained from P&G (Selangor Darul Ehsan, Malaysia). The water used in this study was deionized and doubly distilled using a Milli-Q Plus system (Millipore, France).

Preparation of silica microspheres

Silica microspheres were prepared in three stages using a polyol/TEOS/water multiple emulsion and a sol-gel process (Table 1).

Stage 1: Preparation of polyol-in-oil-in-water emulsion and sol-gel transition

Quercetin was dissolved in a mixture of 1,3-butylene glycol and glycerin (50:50) containing 1.0 wt.% Pemulen® TR-2. The suspensions containing 5 mL of 2.0 wt.% quercetin was emulsified into 25 mL of TEOS containing a lipophilic surfactant (PEG-10 dimethicone) to obtain a primary polyol-in-oil (P/O) emulsion by homogenization at a rate of 7000 rpm using a homogenizer (T.K. ROBOMICS®, Tokushu, Kika Kogyo Co., Ltd., Tokyo, Japan) for 15 min. After homogenization, the primary P/O emulsion was emul-

Table 1. Processing conditions used throughout the study

Parameter	Processing conditions
Polyol phase	20.0 wt.% of polyol mixture (1,3-butylene glycol, glycerin, 50:50) containing quercetin 2.0 mass%
Oil phase	10.5–62.0 mL of TEOS 10.0–60.0 mass% and KF® 6017 0.5–2.0 mass%
Water phase	95.0 mL of Glycerin 40.0 mass% solution containing 2.0% Natrosol® 250, 0.10 M nitric acid and Tween® #20
Conditions used to prepare primary emulsion (P/O)	7000 rpm, 10 min, room temperature
Conditions used to prepare secondary emulsion (P/O/W)	2000 rpm, 10 min, room temperature

sified into a water phase containing 40.0% (*w*/*w*) glycerin, 2.0% (*w*/*w*) hydroxyethylcellulose, 0.1 M nitric acid, and 1.0% (*w*/*w*) polyoxyethylene sorbitan monolaurate at a rate of 2000 rpm using a homogenizer to prepare the P/O/W emulsion.

Stage 2: Gel maturation

After emulsification for 10 min, the P/O/W emulsion was agitated with a magnetic stirring bar at a rate of 600 rpm at 40 °C for 24 h.

Stage 3: Washing

After gel maturation, samples were centrifuged at 3000 rpm for 3 min to collect the particles. Obtained particles were washed repeatedly to remove oil, unreacted precursors, and surfactants. Then, the precipitate was filtered, washed with deionized water, and dried at 45 °C for 2 h.

Characterization

The external and internal morphologies of the microspheres were analyzed using SEM (Carl Zeiss, LEO-1530, Tokyo, Japan). The microspheres were fixed on a brass stub using double-sided adhesive tape, and, subsequently, were rendered electrically conductive by coating them with a thin layer of platinum (~3–5 nm) in a vacuum for 100 s at 30 W. The particle size distribution was analyzed using a particle size analyzer (Malvern Mastersizer 2000, Malvern Instruments, Worcestershire, UK) by dispersing the microspheres in an aqueous solution. Particle size was expressed as the mean equivalent volume diameter. Three replicates were analyzed for each batch of microspheres. Energy-dispersive X-ray spectrometer (EDS) analysis was conducted using an Iridium Ultra™ energy-dispersive X-ray spectrometer (IXRF Systems, USA) to characterize the atomic percents in the particles on carbon coated copper grid with FE-SEM (VEGA3 LMU, TESCAN, Czech Republic).

Encapsulation efficiency

100 mg of dried microspheres were suspended in 10 mL of MeOH. The microsphere aggregates and quercetin were dispersed by sonication. After dilution, the samples were assayed for quercetin content using high-performance liquid chromatography (HPLC). The encapsulation efficiencies were calculated using the following equation:

$$\text{Encapsulation efficiency}\,(\%) = \\ = \frac{\text{Entrapped drug}}{\text{Initial added drug}} \times 100 \quad (1)$$

Determination of quercetin concentration (HPLC analysis)

The quantification of quercetin was performed using a Waters 2695 Alliance HPLC system (MA, USA) and a Waters 996 PDA detector (MA, USA). The samples were separated on a Waters 120 ODS-BP column (4.6 mm×250 mm, 5 μm, Daiso Watchers, Osaka, Japan). Mobile phases comprising 100% methanol were used. The quercetin in the samples was identified and quantified using standards by comparing the retention time and UV detection at 370 nm.

Determination of quercetin stability

To determine the effect of encapsulation on the quercetin stability in aqueous solution, free quercetin and encapsulated quercetin were incubated at 25 and 42 °C, respectively, for 28 days. Microspheres equivalent to 10 mg of quercetin were suspended in 20 mL of isotonic phosphate buffer solution (PBS, pH 7.4±0.2) containing 1.0% polysorbate 80. The samples were collected at predetermined times for evaluating their residual quercetin concentrations, as described above. All the samples were analyzed using HPLC immediately after their preparation.

Data analysis

The experimental results are expressed by the mean ± standard deviation (*SD*). The mean and *SD* of

the results from at least three independent experiments were calculated using Microsoft Excel (WA, USA) software. All data were subjected to statistical analysis using the one-way analysis of variance (ANOVA) to examine for them any significant difference. *P* values of < 0.05 were considered to be significant. The paired t-test was used for estimating of the difference between the means of the two groups. The paired t-test assumes that the variances of two populations are equal. The determination of whether the assumption of equal variances is valid requires the use of a one-way ANOVA.

RESULTS AND DISCUSSIONS

Preparation of silica microspheres using combined P/O/W emulsion/sol-gel process

Silica microspheres were prepared by a novel P/O/W emulsion/sol-gel process using quercetin as a model flavonoid drug. According to a report by Lee *et al.* [5], when selecting a polyol as an inner polyol phase medium, it is imperative that the polyol should be able to solubilize quercetin. 1,3-Butylene glycol is a good solvent for quercetin. However, the use of 1,3--butylene glycol alone as an inner polyol-phase medium did not ensure the formation of a stable emulsion; therefore, glycerin was included to increase the stability of the primary P/O emulsion. Finally, Lee *et al.* [5] produced quercetin-loaded poly (methyl methacrylate) microcapsules using a polyol-in-oil-in--polyol (P/O/P) emulsion and a solvent evaporation method.

In this study, microspheres were used to study the respective effects of TEOS concentration, lipophilic surfactant concentration in the oil phase, hydrophilic surfactant concentration, and nitric acid concentration as acidic catalyst in the water phase on the mean size of microspheres, as well as on the quercetin-encapsulation efficiency. The results are given in Table 2.

Several investigators have reported that the molar ratio of H_2O to TEOS (R_w) significantly affects the synthesis of particles by the sol-gel technique [21,22]. Lindberg *et al.* reported that an additional parameter affecting the original emulsion is the amount of ethanol released during the hydrolysis step of TEOS [23].

Morphology

The SEM images of quercetin-loaded silica microspheres are presented in Figure 1. The microspheres produced by the combined P/O/W emulsion/sol-gel method were spherical and not aggregated.

Furthermore, no significant differences were observed between the outer surface morphology of microspheres within the same batch (Figure 1a). Figure 1b shows a cross section image of quercetin-loaded silica microsphere which form highly branched silica network.

Effect of R_w (molar ratio of H_2O to TEOS) on microspheres

According a study by Lee *et al.* [21], the increase in R_w causes a stronger nucleophilic reaction between H_2O and alkoxide molecules. Thus, the hydrolysis is fast and more alkoxides are converted to the corresponding metal hydrates. Then, the monomers of metal hydrates react with each other to form particle-like polymers and many nuclei of constant surface area are formed in the solution.

Thus, particles have larger sizes with higher density after the growth step. However, a low R_w value leads to the formation of wide distributed nuclei, after the growth process, the obtained particles have small spherical and homogeneous particles (Figure 1c-f). These results, indicative of more complete hyd-

*Table 2. Synthesis of silica microsphere loaded quercetin by sol-gel method; *p < 0.05, **p < 0.01*

Sample	H_2O/TEOS molar ratio (R_w)	Surfactant in oil phase mass%	Nitric acid in water phase (M)	Particle size μm	Encapsulation efficiency %
A	40	1.0	0.10	20.6±3.2 **	17.8±2.5 *
B	50	1.0	0.10	25.0±2.0 **	20.4±2.8
C	60	1.0	0.10	25.8±2.5 **	23.4±2.1 *
D	70	1.0	0.10	35.0±2.3	26.5±2.3
E	60	0.5	0.10	30.2±2.5	22.8±2.7
F	60	1.5	0.10	24.3±3.0 *	24.1±2.5 **
G	60	2.0	0.10	20.6±3.1 **	27.5±1.9
H	60	1.0	0.05	34.7±2.3	18.8±3.9
I	60	1.0	0.15	25.3±3.0 **	23.1±3.0 **
J	60	1.0	0.20	30.4±4.0	20.8±2.4

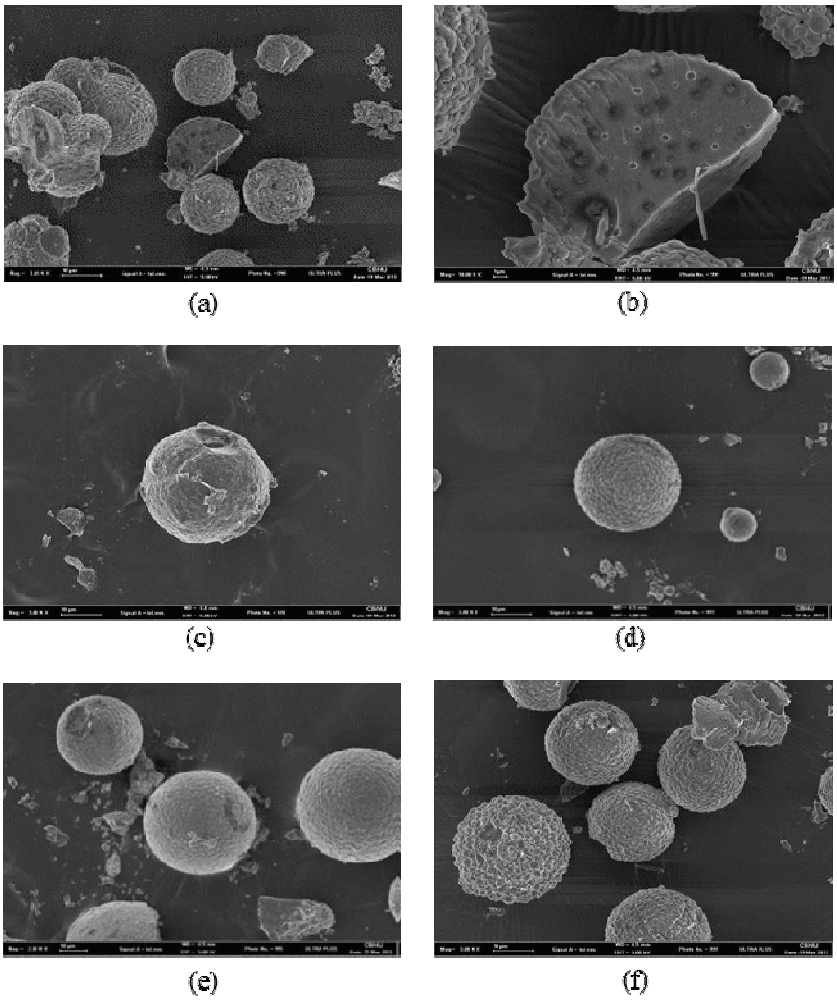

Figure 1. Scanning electron microscopy images of quercetin-loaded silica microspheres prepared using P/O/W emulsion and sol-gel method: a) surface morphology, b) cross-sectioned image of microcapsule; R_w: 40 (c), 50 (d), 60 (e) and 70 (f), with morphologies of silica particles formed by changing TEOS concentration.

rolysis and greater density with increasing R_w, are in agreement with those of other workers [22]. The mean particle size of the microspheres ranged from 20.6±3.2 to 35.0±2.3 μm. The increase of R_w resulted in a slightly increased mean particle size (Figure 2a). Analysis of the significance of R_w effect on the mean particle size showed that statistically significant differences existed ($p < 0.05$).

Effect of surfactant concentration on microspheres

The influence of the lipophilic surfactant concentration in the oil phase on the particle size (Figure 2b) was also evaluated, and it was observed that increased lipophilic surfactant concentration decreased the mean diameter of the microspheres, which reached a minimum at a surfactant concentration of 2.0%.

The size of the microspheres expressed as the mean geometric diameter (±*SD*, $n = 3$) ranged from 20.6±3.1 to 30.2±2.5 μm. The increase in the surfactant concentration slightly decreased the mean droplet size and increased the uniformity of the primary emulsion, and thus, led to a decreased mean microsphere size. An analysis of the significance of lipophilic surfactant concentration effect on the mean particle size showed statistically significant differences ($p < 0.05$).

Effect of nitric acid as catalyst on microspheres

Changes in the solution pH alter the relative rates of hydrolysis and condensation, yielding products ranging from slightly branched silicate polymers to compact particulate silica sols [24].

At low pH, acid catalysis promotes hydrolysis but hinders both condensation and dissolution reactions. At high pH, acid catalysis impedes hydrolysis but promotes both condensation and dissolution reactions [25]. Consequently, for the P/O/W emulsion

synthesis of silica particles using acid catalysis, silica growth is observed and homogeneous particles are formed (Figure 3a-d).

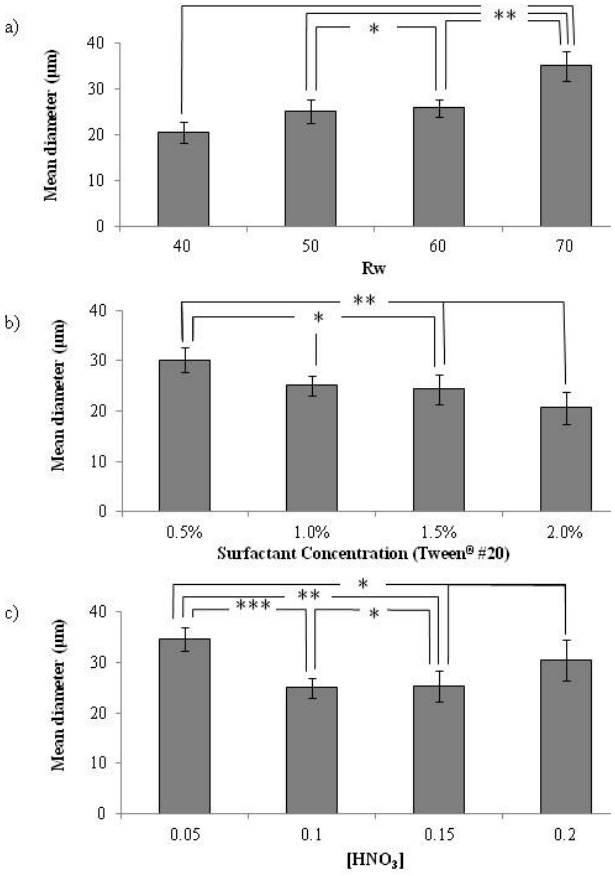

*Figure 2. Mean diameter of microsphers: a) formed at different R_w; b) different surfactant concentrations in oil phase; c) different contents of nitric acid: size of microsphers is expressed as the mean geometric diameter. Error bars represent s.d. of the mean (n = 3). Statistical differences were assessed by one-way ANOVA followed by paired T- test, *p < 0.05, **p < 0.01, ***p < 0.001.*

The influence of nitric acid as catalyst on the particle size was also evaluated, and it was observed that increased nitric acid concentration decreased the mean diameter of the microspheres, which reached a minimum value at 0.15 M (Figure 2c). An analysis of the significance of the nitric acid concentration effect on the mean particle size showed statistically significant differences ($p < 0.05$). However, at high concentration (0.20 M of nitric acid concentration), an unstable and rough spherical microsphere morphology resulted.

EDS Analysis of quercetin-loaded silica microsphere

In Figure 4, it can be clearly seen that the encapsulated silica materials show obviously the elemental compounds (carbon and oxygen) of quercetin in silica microsphere. Figure 4A shows the FE-SEM (Figure 4A (a)), EDS spectrum (Figure 4A (b)) and EDX mapping (Figure 4A (c)) of the silica microsphere whole area. It can be observed that C, O and Si were present on the surface with a composition of 73.27% C, 25.34% O and 3.39% Si. Figure 4B shows

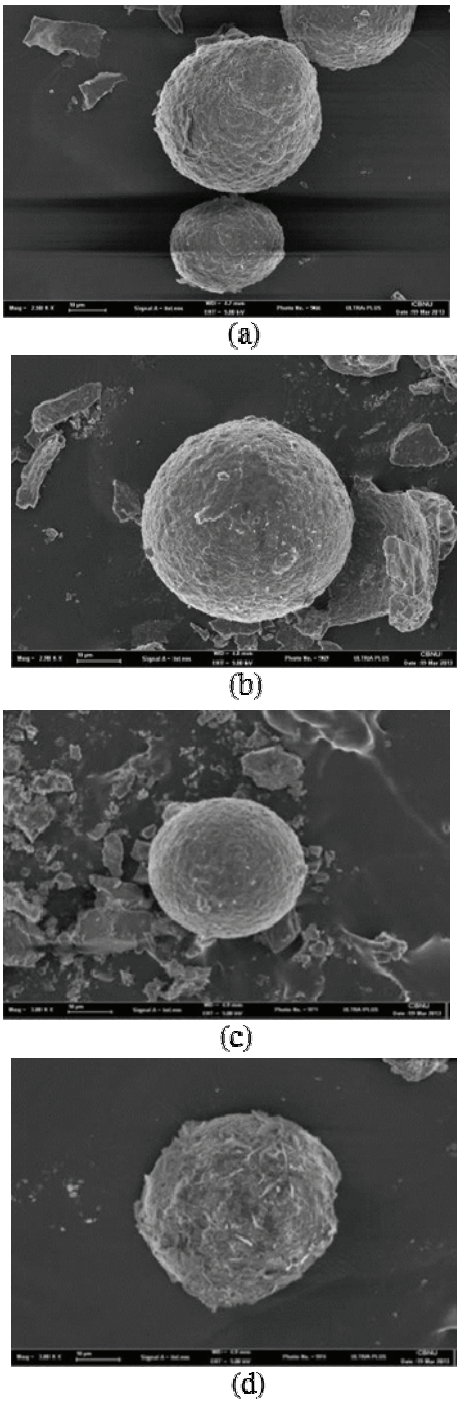

Figure 3. Scanning electron images of quercetin-loaded silica microspheres under four different molar content of nitric acid: a) 0.05, b) 0.10, c) 0.15 and d) 0.20 M.

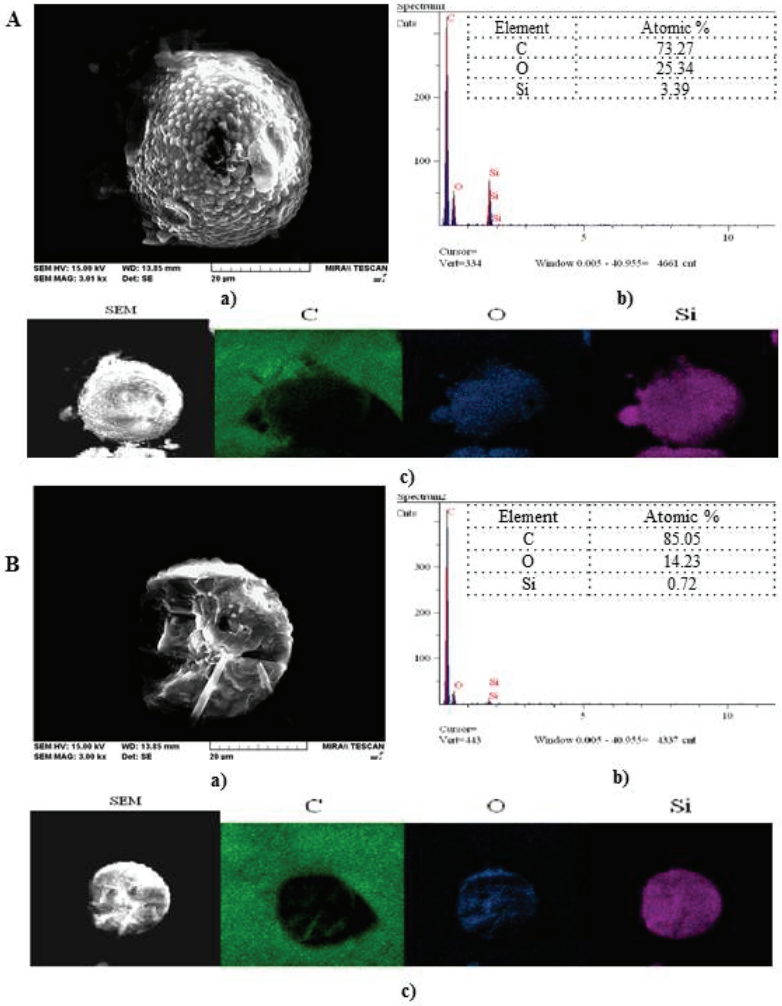

Figure 4. SEM Image (a), EDS spectrum (b) and EDX mapping (c) of carbon, oxygen and silicon content of quercetin-loaded silica microsphere; A) silica microsphere whole area, B) inside silica microsphere.

the FE-SEM (Figure 4B (a)), EDS spectrum (Figure 4B (b)) and EDX mapping (Figure 4B (c)) taken inside silica microsphere. It can be observed that C, O and Si were present inside silica microsphere with a composition of 85.05% C, 14.23% O and 0.72% Si.

According to SEM/EDX analysis, the encapsulated materials contain mainly silicon and oxygen atoms which form the highly branched silica network. The peak attributed to carbon atoms increased in the microsphere interior, similarly to what reported for flavonoid encapsulated in silica networks by Lacatusu *et al.* [26].

Encapsulation efficiency

An increase of R_w resulted in slightly increased encapsulation efficiencies (Figure 5a). The encapsulation efficiencies ranged from 17.8±2.5% to 26.5± ±2.3%. The encapsulation efficiency of the drug depended on the quantity of microspheres that encapsulated the drug in the continuous phase. An analysis of the significance of R_w effect on the mean particle size showed statistically significant differences ($p < 0.05$).

The effect of the lipophilic surfactant concentration in the oil phase on the encapsulation efficiency (Figure 5b) was also evaluated, and it was shown that increasing the lipophilic surfactant concentration increased the encapsulation efficiencies of the microspheres.

The encapsulation efficiencies of the microspheres (Table 2) ranged from 22.8±2.7 to 27.5±1.9%. Increase in the surfactant concentration significantly decreased the droplet size and increased the uniformity of the primary emulsion; this led to a decreased probability of effluence of the inner polyol phase into the water phase, thus increasing the encapsulation efficiency. An analysis of the significance of the lipophilic-surfactant-concentration effect on the mean particle size showed statistically significant differences ($p < 0.05$).

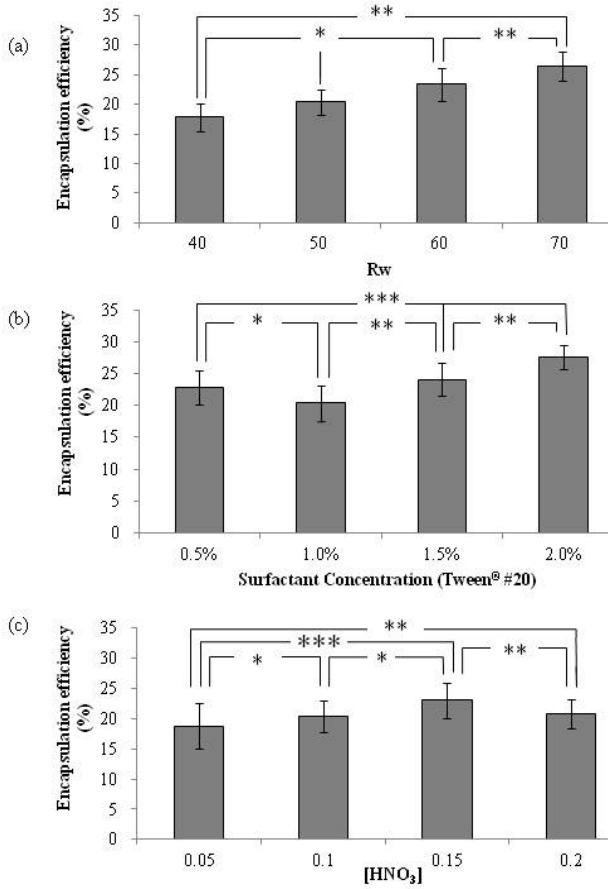

*Figure 5. Encapsulation efficiencies of microsphere: a) formed at different R_w; b) different surfactant concentrations in oil phase; c) different contents of nitric acid. Error bars represent the s.d. of the mean (n = 3). Statistical differences were assessed by one-way ANOVA followed by paired T- test, *p < 0.05, **p < 0.01, ***p < 0.001.*

Nitric acid was used as the acid catalyst and the effect of the nitric acid concentration on the encapsulation efficiency (Figure 5c) of the silica microspheres was also evaluated.

At low molar concentration ([HNO_3] = 0.05), the encapsulation efficiency was low, though at higher molar concentration, the encapsulation efficiency had higher value. An analysis of the significance of the nitric-acid-concentration effect on the mean particle size showed statistically significant differences (p < < 0.05). However, at the highest molar concentration, the encapsulation efficiency assumed the lowest value.

Effect of encapsulation on quercetin stability in aqueous solution

To determine the effect of encapsulation on quercetin stability in aqueous solution, both free quercetin and encapsulated quercetin were incubated separately at 25 and 42 °C, respectively, for 28 days. Then, the samples were collected at predetermined times for evaluating the residual quercetin concentration, as described previously.

As shown in Figure 6a, the free quercetin and the quercetin encapsulated in silica microcapsules in aqueous solution showed similar stabilities of quercetin at 25 °C at 28 days.

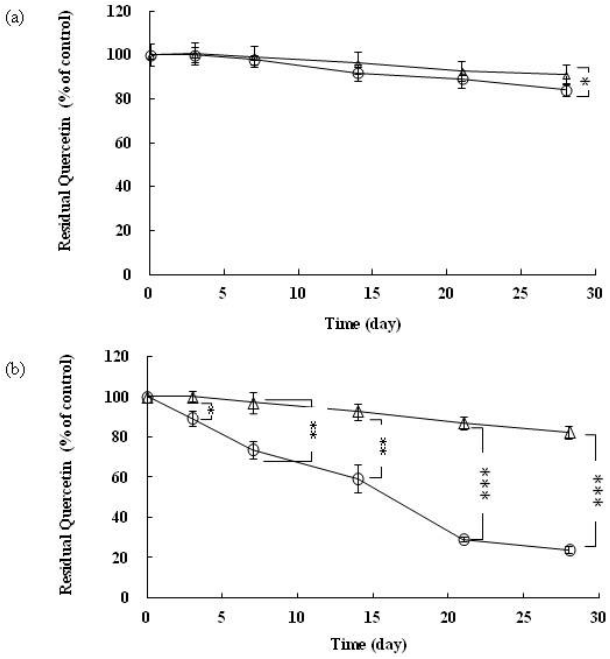

*Figure 6. Effect of encapsulation on quercetin stability in aqueous solution: stored at a) 25 and b) 42 °C; free quercetin (○), encapsulated quercetin (△). Error bars represent s.d. of the mean (n = 3). Statistical differences were assessed by one-way ANOVA followed by paired T- test, *p < 0.05, **p < 0.01, ***p < 0.001.*

However, the samples stored at a high temperature showed a significant difference. The quercetin contents of free quercetin and quercetin encapsulated in silica microspheres were reduced by ~80 and 20%, respectively, at 42 °C and 28 days (Figure 6b). This result agrees with the conclusions of Makris *et al.*, who reported that the sensitivity of flavonoids toward auto-oxidation and heating resulted in their poor stability in aqueous aerobic environments [27].

CONCLUSIONS

Silica microspheres were prepared by a novel polyol-in-oil in water (P/O/W) emulsion/sol-gel method, in which quercetin was tested as a model flavonoid drug. The microspheres were spherical with a smooth surface. EDS/SEM analysis of selected silica microspheres showed that individual microspheres were filled with quercetin. The mean dia-

meter was between 20.6±3.2 and 35.0±2.3 μm, and the encapsulation efficiencies ranged from 17.8±2.5 to 27.5±1.9%.

On storing the free quercetin at 42 °C for 28 days, the residual content of the quercetin gradually decreased by 76%, whereas that of the quercetin that was encapsulated in silica microspheres decreased by only 18%.

These diverse results suggest that the novel polyol-in-oil-in water (P/O/W) emulsion and sol-gel method can be successfully be applied to the encapsulation of flavonoids. Furthermore, a newly developed silica microsphere system was devised to improve the quercetin stability as well as its properties as a cosmetic raw material; this would make it potentially useful in future applications.

REFERENCES

[1] Q. Tan, W. Liu, C. Guo, G. Zhai, Int. J. Nanomed. **6** (2011) 1621-1630

[2] W. Bors, W. Heller, C. Michel, M. Saran, Methods Enzymol. **186** (1990) 343-355

[3] G. Berlier, L.Gastaldi, E. Ugazio, I. Miletto, P. Iliade, S. Sapino, J. Colloid Interface Sci. **393** (2013) 109-118

[4] H. Chen, C. Khemtong, X. Yang, X. Chang, J. Gao, Drug Discov. Today **16** (2011) 354-360

[5] D.H. Lee, G. S. Sim, J.H. Kim, G.S. Lee, H.B. Pyo, B.C. Lee, J. Pharm. Pharmacol. **59** (2007) 1611-1620

[6] A.D. Roberts, H. Zhang, Int. J. Pharm. **447** (2013) 241--250

[7] L.Y. Qiu, Y.H. Bae, Pharm. Res. **23** (2006) 1-30

[8] M.L. Adams, A. Lavasanifar, G.S. Kwon, J. Pharm. Sci. **92** (2003) 1343-1355

[9] C. Hoskins, P.K. Thoo-Lin, W.P. Cheng, Ther. Delivery **3** (2012) 59-79

[10] S. Svenson, Eur. J. Pharm. Biopharm. **71** (2009) 445-462

[11] H. Yoshizawa, KONA **22** (2004) 23-31

[12] G. Wang, J.J. Wang, L.P. Zhang, S.M. Du, J.Y. Liu, L. Wang, F. Ye, Expert Opin. Drug Delivery **9** (2012) 599--613

[13] C.U. Guo, C.F. Yang, Q.L. Li, Q. Tan, Y.W. Xi, W.N. Liu, G.X. Zai, Int J Pharm. **430** (2012) 292-298

[14] M.E. Carlotti, S. Sapino, E. Ugazio, G. Caron, J. Inc. Phenom. Macrocycl. Chem. **70** (2011) 81-90

[15] H. Wangqi, D. P. Kyriakos, Colloids Surfaces, A **125** (1997) 181-187

[16] J.H. Lee, T.G. Park, H.K. Choi, Int. J. Pharm. **196** (2000) 75-83

[17] Y.A. Bhatt, D.A. Shah, Int. J. Pharm. Pharm. Sci. **3** (2011) 234-239

[18] Y. Yeo, N.J. Baek, K.N. Park, Biotechnol. Bioproc. Eng. **6** (2001) 213-230

[19] R.K. Singh, A. Garg, R. Bandyopadhyaya, B.K. Mishra, Colloids Surfaces, A **310** (2007) 39-45

[20] W. Stőber, A. Fink, E. Bohn, J. Colloid Interface Sci. **26** (1968) 62-69

[21] M.H. Lee, S.G. Oh, S.K. Moon, S.Y. Bae, J. Colloid Interface Sci. **240** (2001) 83-89

[22] R.F.S. Lenza, W.L. Vasconcelos, J. Non-Cryst. Solids **273** (2000) 164-169

[23] R. Lindberg, J. Sjoblom, G. Sundholm, Colloids Surfaces, A **99** (1995) 79-88

[24] D.L. Meixner, P.N. Dyner, J. Sol-Gel Sci. Technol. **14** (1999) 223-231

[25] R. Ciriminna, M. Sciortino, G. Alonzo, D.A. Schrijver, M. Pagliaro, Chem. Rev. **111** (2011) 765-789

[26] I. Lacatusu, N. Badea, R. Nita, A. Murariu, F. Miculescu, I. Iosub, A. Meghea, Opt. Mater. **32** (2010) 711-718

[27] J.T. Chien, D.J. Hsu, B.S. Inbaraj, B.H. Chen, Int. J. Mol. Sci. **11** (2010) 2805-2820.

YOUNG HO KIM[1,2]
DONG WON LEE[1]
EUN JI JUNG[1]
JUN TAE BAE[1]
SANG GIL LEE[1]
HYEONG BAE PYO[1]
KUK HYOUN KANG[2]
DONG KYU LEE[2]

[1]R&D Center Hanbul Cosmetics Co. Ltd., Daesung-ro, Samsung-myon, Umsung-kun, Chungbuk, Republic of Korea
[2]Department of Engineering Chemistry, Chungbuk National University Cheongju, Republic of Korea

NAUČNI RAD

PRIPREMA I KARAKTERIZACIJA SILIKA MIKROSFERA SA KVERCETINOM STABILIZOVANIH SLOŽENIM EMULZIONIM I SOL-GEL PROCESIMA

Uprkos različitoj kozmetičkoj primeni, flvonoidi i slična jedinjenja imaju i odgovarajuća ograničenja vezana za njihovu stabilnosti i rastvorljivost u destilovanoj vodi. U ovom radu, novom metodom su pripremljene silika mikrosfere novom metodom koja koristi emulziju poliola, ulja i vode (P/O/V) i sol-gel metodom kojima se stabilizuje kvercetin. Stabilna suspenzija mikrosfera je uspešno pripremljena korišćenjem mešovitog sistema rastvarača koji sadrži poliolnu fazu u sol-gel obradi tetraetil ortosilikata (TEOS) kao neorganskog prekursora sa spoljnom vodenom fazom. Morfologija mikrosfera je određena korišćenjem SEM metode, koja je pokazala karakterističan sferni oblik čestica sa glatkom površinom. Takođe, SEM/EDS analiza reprezentativne mikrosfere je pokazala da je unutrašnja struktura silika mikrosfere ispunjena kvercetinom. Srednji prečnik mikrosfere je u opsegu 20,6--35,0 μm, a efikasnost enkapsulacije je u opsegu od 17,8 do 27,5%. Uzorci slobodnog i inkapsuliranog kvercetina su inkubirani 28 dana u odvojenim vodenim rastvorima na 25 i 42 °C. Zaostali sadržaj kvercetina inkapsuliranog u silika mikrosferi je 82% na 42 °C. Nasuprot tome, slobodni kvercetin skladišten na 42 °C smanjen je na oko 24%.

Ključne reči: mikrosfera, silika, flavonoid, kvercetin, složena emulzija, sol-gel.