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Membrane Emulsification – a Versatile Tool for the Synthesis of Polymeric Microspheres

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SUMMARY: A new emulsification technique by using a particular glass membrane was introduced. The membrane, having a narrow pore size distribution, produced fairly monodisperse oil droplets by carefully pushing the oil phase through the pore to an aqueous solution of stabilizers. Subsequent suspension polymerization of the monomer droplets or evaporation of solvent from the polymer solution yielded uniform polymer particles. Magnetite microcapsules and hybrid polymer particles including inert substances for polymerization were also prepared by this unique emulsification.

Introduction

Membrane emulsification is an attractive technique as a low energy, low shear process for treating shear-sensitive ingredients or surfactants. Shirasu porous glass (SPG) membrane, which possesses a uniform pore size distribution with a free choice of the nominal pore size ranging from 0.1 to 18 μm(1), has been fabricated by Nakashima et al(2). After moulding of the base glass, spinodal decomposition induced by the second heat treatment yields a bicontinuous structure composed of $CaO\text{-}B_2O_3$ and $SiO_2\text{-}Al_2O_3$, the former phase is washed away by an acid treatment, and the skeleton of the latter remains. For preparing an oil-in-water (O/W) emulsion, the oil phase is allowed to permeate through the pores of SPG under an adequate pressure. Fairly uniform oil droplets with the coefficient of variation (CV) around 10% are obtained due to the uniformity of the pore size. Annual meetings related to this particular membrane have been held in Japan since 1983, where research interests are focused not only on emulsification but also on ultra-filtration, micro-aeration, micro-carriers, sensors, and so forth. In Europe, two papers were recently presented in the Second World Congress on Emulsion (1997). The first one converted micro- or ultra-filtration discs with the pore size of 0.2 μm or less into the membrane emulsification(3), and the other employed

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ceramic membrane cylinders made of a-Al2O3 with pore sizes of 0.1 and 0.8 μm$^{4)}$. Their interests were on the formation of droplets with a narrow size distribution, and claimed a minor role of the shear force during the emulsification.

Preparation of uniform polymer particles

We noticed a potential availability of the SPG membrane for the preparation of uniform polymeric microspheres by suspension polymerization after the emulsification. The size of the particles covers a range from several μm to (desirably) 100 μm, an ultimate goal accomplished by Ugelstad et al. using seeded emulsion polymerization with the two-step swelling technique$^{5)}$, and also by Vanderhoff et al. with the repeated growth of the seed polymer particles under zero gravity, and its continuation on the ground level$^{6)}$. A narrow size distribution of the droplets will be retained if the break-up or coalescence is suppressed during the polymerization. Higuchi and Misra $^{7)}$ demonstrated that the addition of a small amount of water-insoluble substance in the oil phase prevented deterioration of the emulsion induced by the degradative diffusion process, which predicts that the smaller droplets will be eventually absorbed in the larger ones because of the higher solubility in water. This also implies that a uniform size distribution provides a further stability. Fairly uniform polystyrene (PS) and porous poly(styrene-co-divinyl benzene, PS-DVB) spheres were obtained by adding lauryl alcohol to the uniform monomer droplets $^{8)}$. The porous structure was easily introduced by adding inert solvents such as toluene, hexane, and heptane, the pore size shifting from micro to macro range by decreasing the solvency to PS-DVB. The relation between the average particle size and the pore was linear with a slope of 6.6. A major disadvantage of the SPG membrane is a wettability to hydrophilic substances. SiO_2-Al_2O_3 surface is easily wetted by hydrophilic methyl methacrylate (MMA) and hydroxyethyl methacrylate (HEMA). In order to clear this obstacle, the theory by Higuchi and Misra again provided a solution. If smaller, hydrophilic droplets are mixed with the larger, hydrophobic droplets of uniform size, then the former will be rapidly absorbed in the latter without affecting the uniformity of the latter. PMMA and porous poly(MMA-co-ethyleneglycol dimethacrylate, PMMA-EGDMA) spheres were successfully obtained according to the principle above $^{9)}$. Benzene-hexadecane cosolvent was converted to the uniform seed droplets. We refer to this principle, essentially the same as Ugelstad's two-step swelling technique$^{10)}$, as the droplet swelling. More hydrophilic PMMA-HEMA spheres, smooth and porous, were obtained later$^{11)}$. Successful droplet swelling technique tempted us to challenge the preparation of 100 μm uniform spheres. A maximum of 102 μm porous PDVB spheres were obtained from the DVB seed droplets swollen with the mixture of dichlorobenzene (DCB), isoamyl acetate (IA) and an extra DVB in smaller droplets to be absorbed; DCB was added to adjust the density of the droplets, while IA was added topromote the diffusion of the hydrophobic DCB and DVB during the swelling process[12]. Meanwhile, applications of these polymer particles were investigated, such as packing materials of GPC[13], and carriers of enzyme immobilization (glucoamylase)[14]. Also, the water-absorbing capacity of PMMA-HEMA proposed possible applications as a biomedical material[11]. Hollow polymer particles are now under investigation for light scattering materials.

Incorporation of functional substances, soluble in the monomer droplets and inert for polymerization, are also another advantage of the membrane emulsification. Polyimide prepolymer (diphenylmethane-4,4'-*bis*-allylnagiimide), which is not reactive with radical species and forms crosslinking networks when cured over 200 °C, was incorporated in uniform acrylate spheres with a maximum 28%[15]. Solvent evaporation, one of the most popular microencapsulation procedure, can be also employed to prepare polymer particleswhich are difficult to synthesize by emulsion or suspension polymerization. Polylactide microparticles were successfully obtained from the solution of dichloromethane, and the particle shape and morphology were investigated with respect to the polymer concentration and the ratio of polylactide and lauryl alcohol added as a hydrophobic additive[16]. Polyurethane-urea (PUU) spheres required chain-extension period after the droplet formation of urethane prepolymer dissolved in xylene. A cyclic diamine, piperazine, was added to the aqueous phase with a small amount of ethyl acetate to promote the diffusion of the diamine into the droplets. Magnetite microcapsules are also obtained with a slight modification of this technique. In principle, fine magnetite (Fe_3O_4) powders pre-treated with surfactants is suspended in polymer solution, and the solvent is removed by evaporation. The polymer wall should possess some hydrophilic moiety to overcome the hydrophobically treated magnetite. Our preparation route of polymeric microspheres is summarized in Fig. 1.The large size of polymer particles is

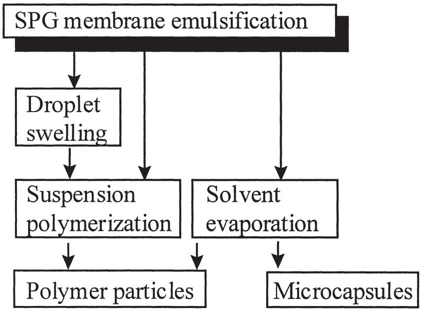


Fig. 1 : Preparation route of polymeric microspheres

favored for the visual observation of particle morphology which has been extensively investigated in the seeded emulsion polymerizations. Either thermodynamically or kinetically controlled morphologies, core-shell, hemisphere, salami, and raspberry, were reproducible by the suspension polymerizations from the droplets composed of monomer, dissolving polymer and solvent, and by the solvent evaporation from the droplets dissolving two kinds of immiscible polymers[17)].

We had two opportunities to review our research progress with respect to the SPG membrane emulsification and the synthesis of functional polymer particles[18,19)]. In this article, relatively new results, preparation of hollow spheres, PUU spheres, and magnetite microcapsules will be briefly introduced together with some particle morphology studies, in order to demonstrate the versatility of SPG membrane.

Experimental section

All the reagents were purchased from Kishida Chemical Co. unless otherwise stated.

Monomers All the monomers are commercial grade except acrylic acid (reagent grade,AA), and inhibitors were removed before use. Styrene and MMA are distilled under reduced pressure, whereas 2-ethylhexyl acrylate (2EHA) and EGDMA were washed with 3% sodium carbonate solution three times, washed with distilled and deionized water 5 times, and dried with 4A molecular sieve. AA was used after removing the polymer by filtration. All the treated monomers were stored in a refrigerator prior to use.

Solvents Benzene, xylene, toluene, heptane, hexanol, chloroform, and dichloromethane are all reagent grade, and were used as received. Commercial grade methanol was used for washing and precipitating polymers or polymer particles. Ethyl acetate was distilled prior to use.

Hydrophobic reagents Hexadecane (HD) and lauryl alcohol (LA) are reagent grade, and were

used as received.

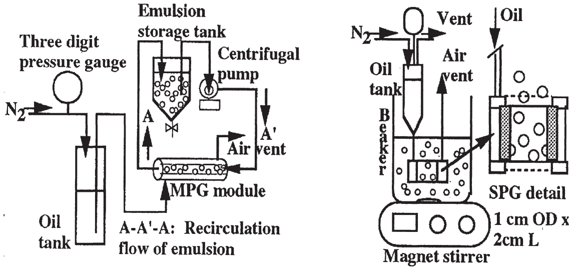
Initiators Benzoyl peroxide (with 25% moisture, BPO) and Azobisdivaleronitrile (ADVN) are reagent grade, and were used as received.

Stabilizer and emulsifier Polyvinyl alcohol (PVA-217, degree of polymerization = 1700, 88.5% saponified, Kuraray Chemical Co.) was used as a stabilizing agent together with a small amount of sodium dodecyl sulfate (biochemistry grade, Merck, SDS). MST-1 (an adduct of trilene diisocyanate and Pluronics, Nippon NSC Co. Ltd.) was used as a stabilizer for polyurethane emulsions.

Other reagents All are reagent grade. Sodium nitrite was used to suppress the secondary nucleation ofpolymer particles in the aqueous phase during suspension polymerization. Sodium sulfate anhydride was used as an electrolyte. Ferrous and ferric chloride, and sodium hydroxide were used for the preparation of fine magnetite powders. Piperazine was used as a chain extender of polyurethane prepolymer (hard segment= norbornane isocyanatomethyl, soft segments = 1,6-hexane diol and adipic acid oligomer, PU prepolymer, Nippon NSC Co. Ltd.).

Procedures

Emulsification Two emulsification apparatuses, with different capacities, are shown in Fig. 2. The principle of the emulsification is the same. SPG membranes, 1 cm outer diameter (OD) x 17 cm length (L) for Fig. 2a), and 1 cm OD x 2cm L for Fig. 2b), were installed in each pressure-tight stainlesssteel module. The annular cylinders of the membrane were 1 mm thick, and are rather fragile. The continuous phase dissolving stabilizers and other electrolytes was gently recirculating through the inner space of the module. A low shear, centrifuge pump was employed in Fig. 2a).



a) for SPG membrane b) MPG kit

Fig 2 : SPG (Shirasu Porous Glass) emulsification system

The pressure carefully monitored by a three-digit pressure gauge was applied to the oil storage tank, and the dispersion phase gradually filled up the annular space of the module, releasing the air through the vent valve. After the dispersion phase thoroughly replaced the air remaining in the annular space, the pressure was set to a desired level, and the droplets were released from the pores of the membrane to the recirculating stream of the continuous phase. When a sufficient amount of the dispersion phase was emulsified, the emulsion was subjected to the next treatment, suspension polymerization or solvent evaporation.

In the case in which the droplet swelling followed the emulsification, the components to be absorbed into the seed droplets were homogenized with a low concentration SDS solution, and then added to the original emulsion[9,12)]. The swelling period was regarded to be overwhen no smaller droplets were observed by an optical microscope.

Polymerization

The emulsion was transferred to a glass separator flask, where a gentle bubbling of nitrogen continued for 1 hr to remove the dissolved air. The nitrogen nozzle was then lifted up from the emulsion and the temperature was raised to 70°C. Polymerization was carried out under the nitrogen atmosphere for 24 hr.

Solvent evaporation

When dichloromethane was used as a solvent, the emulsion was allowed to stand in the atmosphere, and the solvent evaporated under a gentle stirring of the emulsion. In the case of toluene or chloroform, the emulsion was transferred to the same separator flask mentioned above, and the evaporation was processed under reduced pressure and gentle heating with a steady enhancement of the evacuation.

Analysis

The resulting polymer particles and microcapsules suspended in the serum were subjected to observation by an optical microscope, a simple but reliable method to identify particle shape and morphologies, for example those induced by the phase separation between polymer and solvent. The serum was removed by centrifuge, and the particles were washed with methanol several times, and dried in vacuum. The dried particles were observed with a SEM (JSM 5300, JEOL) to examine general features of the surface. In case the inside morphology was to be examined, the particles were embedded in epoxy resin, michrotomed, stained with RuO_4 vapor, and observed with a TEM (Hitachi, H-7000). The average diameter of the emulsion droplets were measured from photographs of the optical microscope. SEM photographs were normally used to count the average diameter of polymer particles.

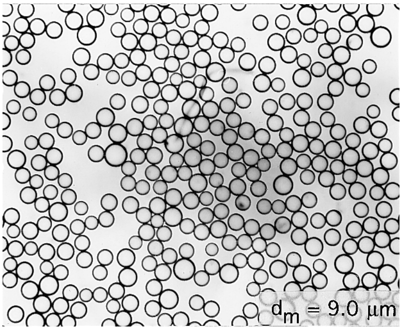


Fig. 3: Styrene monomer droplets

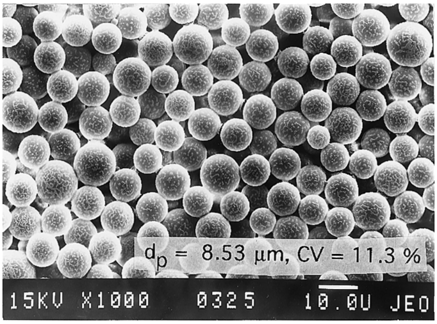


Fig. 4: Polystyrene particles

Results and discussion

Uniform droplets and polymer particles

A typical photograph of uniform styrene droplets is shown in Fig. 3[8)] An SEM photograph of PS particles is shown in Fig. 4. The pore size was 1.36 µm for each experiment.

Tiny white spots can be seen on the surface of the particles in Fig. 4, indicating the nucleation of secondary particles. PVA-120 (Kuraray Co., 98.5-99.4% saponified) was used in the earlier experiments. Even though hydroquinone was added in the aqueous phase, the nucleation was not suppressed. Switching to the less saponified PVA-217 (88.5%) was effective combined with the addition of water-soluble inhibitors, hydroquinone[8)], sodium nitrite[9)], and 2,5-dihydroxybenzene disulfonic acid, dipotassium salt (Aldrich)[12)].

Hollow PMMA particles

Submicron-scale hollow polymer particles have been prepared by using multi-stage (seeded) emulsion polymerizations. Hollows are created by the alkaline swelling of carboxyl group localized in core of the particles[20)], the stepwise alkali/acid treatment of carboxyl containing particles[21)], and the enhancement of the volume contraction during the polymerization[22)]. These latexes are used in coating, pigments, paper coating, and as a light-weight reinforcement material. The SPG process provides a larger hollow spheres in one step polymerization, which are, in particular, prospective as a light scattering material. The droplets were designed to include hydrophobic solvents, hydrophilic monomers, crosslinker, and a low Tg monomer. As the polymerization progresses, it is expected that the hydrophilic polymer will precipitate in the droplets, migrate to the interface because of its hydrophilicity, and eventually envelope the inert, hydrophobic solvents. The crosslinking and low Tg monomer were added to reinforce the polymer wall and provide elasticity. Hollow poly(MMA-co-EGDMA-co-2-EHA) particles are shown in Fig. 5[23]. The hydrophilic components, MMA and EGDMA, were impregnated in the hydrophobic droplets by the swelling method. Notice that the polymer wall is actually an aggregate of microglobules, and the skin is smooth with a few dents. Tiny holes were observed between the globules when the low Tg monomer was absent. Flexibility of the recipe was rather limited; MMA/EGDMA/2EHA = 7-7.5/2.5-2/2.0-3.0, and heptane/benzene = 4/1. If the good solvent (benzene) was added in excess, porous structure prevailed.

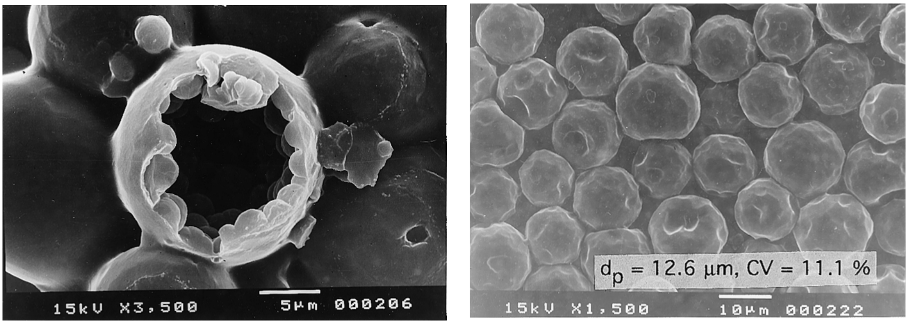
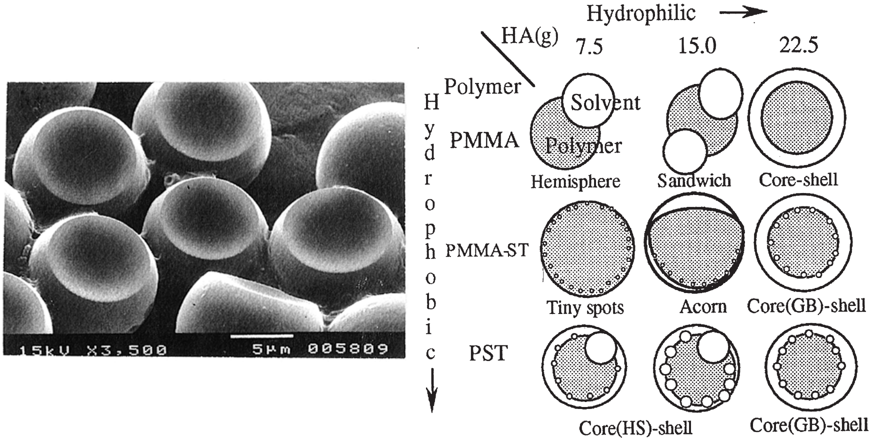


Fig. 5: PMMA hollow particles, a) A cross section, b) Surface feature

Modeling of particle morphology

Sundberg et al. prepared two-component[24)] and three-component[25)] polymeric microparticles from mechanical dispersion of the polymer solutions, and compared the developed morphologies with those predicted from the thermodynamic equilibrium yielding to a minimum free energy change. Real advantages of the SPG emulsification are not only the uniformity of the droplets but also in the fact that they are polymerizable, and reproduce kinetically controlled morphologies. Droplets of monomer plus inert solvents or monomer dissolving a particular polymer yield various morphologies after polymerization, depending upon the thermodynamic properties of the components. Figure 6a) shows a clear hemisphere morphology between PMMA and apparently more hydrophilic mixed solvent. The results obtained by changing the hydrophilicity of polymer and mixed solvent are summarized in

Figure 6b). The full detail will be published soon[26]. In case of PMMA, each morphology was retained after a few months elapsed, however, those of PS and poly(MMA-co-ST) were converted to the thermodynamically stable core(polymer) - shell(solvents) structure from the corresponding initial morphology illustrated in Figure 6b). Figure 7 shows PMMA/PS composite spheres prepared by the solvent evaporation technique[17]. 10%(w/v) dichloromethane solution of PMMA/PS (1:1) including 0.5 mL of lauryl alcohol was allowed to stand at the room temperature for the evaporation of the solvent. When no LA was added, and the polymer concentration was low (2%), the morphology development was rather slow, yielding a PS-PMMA core-shell. LA in Figure 7 is presumed to have played a dual role. One is a role of cosurfactant, a fraction of LA present at the surface of the particle allowed the formation of small PS domains protruding to the surface. The other fraction of LA partitioned in the particle may have played as a solubilizing agent, which decreased the interfacial tension between the domains, allowing PS dispersion in PMMA matrix. Fig. 7b) implies that the SPG emulsification and solvent evaporation are capable to design composite polymer particles with a particular morphology depending on the application purpose.

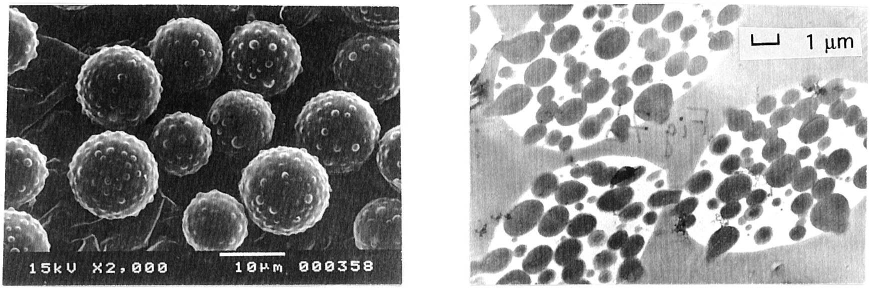


GB = golf ball, HS = hemisphere

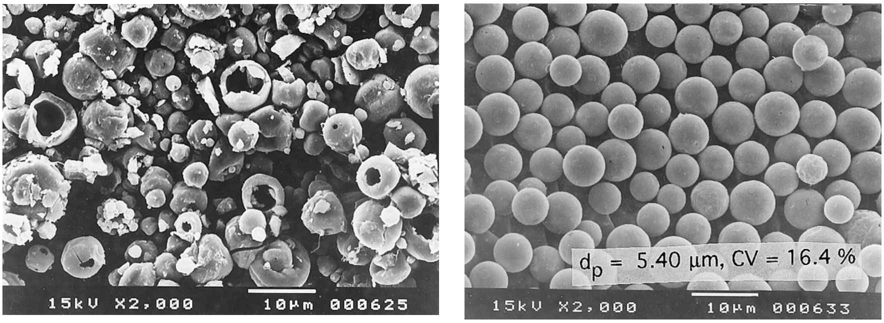
a) PMMA particles with 7.5g HA
Other solvents were fixed
Benzene 19.5 g, HD 4 g

b) morphology sketch

Fig 6 Morphology development – Effect of hydrophilicity of polymer and solvent.



a) SEM photograph (surface feature) b) PST domain stained with RuO_4.
Fig. 7: PST/PMMA (50:50) composite particles obtained from the evaporation of dichloromethane.



a) Emulsified with a homogenizer b) Emulsified with 1.42 µm SPG membrane
Fig. 8: Magnetite microcapsules with P(St-co-AA) 96:4 wall.

Magnetite microcapsules

Uniform, composite magnetite spheres were prepared by Ugelstad et al.$^{5)}$ with a series of the sophisticated procedures, synthesis of uniform porous spheres by the two-step swelling technique, incorporation of nitrile group, precipitation of ferrous and ferric hydroxide, and aerooxidation. Magnetite microcapsules can be prepared by a straightforward process of the SPG emulsification provided that the fine, nanosized magnetite particles permeate through the micropores of the membrane. Figure 8 shows a comparison of magnetite microcapsules prepared with a) a high shear homogenizer and b) the SPG membrane with the pore size of 1.42 µm$^{27)}$. Poly(styrene-co-acrylic acid, 96:4) was directly dissolved in a commercial magnetite fluid (Ferrotech Co., toluene solvent, 25wt% magnetite) diluted with an equal amount of toluene, the ratio of magnetite/polymer being 1.2:1. After the emulsification, toluene was removed under reduced pressure and heating. As shown in Fig.8a), a high shear process yielded a wide size distribution, and quite a few broken capsules, whereas in Fig.8b), uniform, smooth microcapsules were obtained. The average size was 5.4 μm with 16.4% CV.

Polyurethaneurea (PUU) microparticles

Quite uniform PUU spheres can be obtained with a similar emulsification process discussed above$^{28)}$. A xylene solution containing 20-40wt% PU prepolymer was emulsified. Reaction of isocyanate group with water during the emulsification period caused no serious failure for the permeation process and the resulting size distribution. After the emulsification, piperazine was added to the aqueous phase as a chain extender of PU, eventually yielding PUU particles. The reaction time for chain extension was greatly reduced by the addition of a small amount of ethyl acetate to promote the diffusion of piperazine into the droplets. Xylene was removed by freeze-drying.

Conclusion

Our recent developments concerned with the SPG membrane emulsification and the preparation of uniform, functional polymer particles were briefly introduced. The details of each topic will be published soon. In this review, principle and advantage of the low shear, low energy membrane emulsification process were stressed together with the related techniques such as the droplet swelling and the solvent evaporation. For commercial applications, a simple scale-up policy or a new development of more robust droplet formation system should be selected depending on the capacity of the market and sophistication of the products.

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