

Preparation of monodispersed emulsions by premix membrane emulsification without repetitive permeation: Influence of membrane permeation rate (flux) and emulsion viscosity

Jophous Mugabi^{a,*}, Jae-Ho Jeong^{a,*}, Noriyuki Igura^b, Mitsuya Shimoda^b

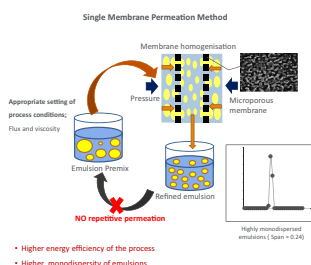
^a Thermal-Fluid Energy Machine Lab., Department of Mechanical Engineering, Gachon University, 1342, Seongnam-daero, Sujeong-gu, Seongnam-si, Gyeonggi-do, Republic of Korea

^b Lab. of Food Process Engineering, Graduate School of Bioresource and Bioenvironmental Science, Kyushu University, 744 Motooka, Nishi-Ku, Fukuoka City, Fukuoka, Japan

HIGHLIGHTS

- A new method of Premix membrane emulsification without repetitive membrane permeation was proposed.
- The energy efficiency of the PME method can greatly be improved by single permeation methods.
- Monodispersed emulsions prepared by adjusting the membrane permeation rate (MPR) and the viscosity ratio.
- Monodispersed emulsions prepared at low MPR (i.e., low energy input) by increasing the mean emulsion viscosity.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:

Emulsions
Premix emulsification
Repetitive permeation
Monodispersed
Membrane permeation rate (flux)
Viscosity ratio

ABSTRACT

A method for preparing emulsions with a narrow droplet size distribution (span) without repetitive membrane permeation, by controlling the premix emulsion viscosity and membrane permeation rate (MPR), flux, was provided. The mean emulsion viscosity and the MPR are some of the main factors that control the wall shear stresses responsible for droplet break up in premix membrane emulsification (PME). Hence, striking a balance between these two factors is important for preparing monodispersed emulsions.

When the emulsion viscosity and the viscosity ratio of the phase were low, the emulsion droplet size and polydispersity decreased linearly with PMR until MPR of $60 \text{ m}^3/\text{m}^2\text{h}$ at which the most monodispersed emulsions ($d_{50} = 5.80$, span = 0.24) were prepared. Beyond this the droplet size decreased further while polydispersity became higher, due to the uncontrolled wall shear stresses at higher MPR. Increasing the disperse phase viscosity (i.e., high viscosity ratio) lowered the shear stresses in the pores that the emulsion droplet size polydispersity became higher. Whereas, increasing the mean emulsion viscosity enabled us achieve the most monodispersed emulsions ($d_{50} = 5.80$, span = 0.24) at lower MPR of $10 \text{ m}^3/\text{m}^2\text{h}$. At low MPR the wall shear force could be increased by increasing the mean emulsion viscosity and emulsions with a small span could be prepared. Therefore, in this study it was proved possible to prepare highly monodispersed emulsions by adjusting the mean emulsion viscosity and MPR, without repetitive permeation, in PME.

* Corresponding authors.

E-mail addresses: mugajoph@gachon.ac.kr (J. Mugabi), jaeho.jeong@gachon.ac.kr (J.-H. Jeong), igura@agr.kyushu-u.ac.jp (N. Igura), mshimoda@gaea.ocn.ne.jp (M. Shimoda).

<https://doi.org/10.1016/j.colsurfa.2021.127560>

Received 23 June 2021; Received in revised form 10 September 2021; Accepted 14 September 2021

Available online 17 September 2021

0927-7757/© 2021 Elsevier B.V. All rights reserved.

1. Introduction

Emulsions are disperse systems of two or more immiscible liquids, such as oil and water, in which the dispersed phase fluid is finely distributed in the continuous phase liquid in form of droplets [1]. Monodispersed emulsions having a narrow droplet size distribution (span) are highly desired for formulation of functional products in many industries such as the food, cosmetic, chemical, pharmaceutical industries, etc. [2,3]. The control of droplet size and span during emulsification is of great interest as it greatly influences the emulsion products characteristics, functionality, application, and stability during usage [1,4].

Premix membrane emulsification (PME) is a suitable method for preparing emulsions with controlled droplet size and span, at high dispersed phase content (up to 90 vol%) and at high production rates (above $1 \text{ m}^3/\text{m}^2 \text{ h}$) [5, 6]. In this method, a coarse pre-emulsion (pre-mix) is permeated through a porous membrane [7] or through a packed bed of particles [8,9] in order to refine the emulsion droplet size and span. The emulsion droplets are broken into smaller and more uniform droplets by the internal shear stresses within the membrane pores without application of any external shear stresses. Further droplet size reduction and narrowing of droplet size distribution can be achieved by repetitive permeation of the emulsion through the membrane pores or packed bed of particles [6,8,10]. Selection of an appropriate membrane is essential in PME. The Shirasu porous glass (SPG) membrane is the most preferred membrane, due to its unique characteristics and superiority for preparing emulsions with controlled droplets size and uniformity [11,12]. Other kinds of membranes such as polytetrafluoroethylene (PTFE), ceramic aluminium oxide, silica glass and micro-fabricated metal membranes have also been successfully used to prepare emulsions [3,4].

The PME method has an advantage of preparing emulsions with droplet sizes smaller than the membrane pore size and at higher membrane permeation rates (flux) typically above $1 \text{ m}^3/\text{m}^2 \text{ h}$. The process is easier to control and operate, since the driving pressure, production rate or emulsifier properties are not so critical for the successful operation of the process [3,7]. However, some of the disadvantages of PME are high susceptibility to membrane fouling and higher polydispersity of emulsions usually with span values above 0.45. Emulsification using membranes with relatively short and straight-through pores such as nickel sieves [13] or replacing the microporous SPG membrane with a dynamic membrane made of a packed bed of particles [8], has proved capable of overcoming the challenge of membrane fouling. While the challenge of higher polydispersity has been solved by repetitive permeation of the emulsion through the membrane for about 5–10 times or more to further refine the final emulsion [10]. However, this approach renders PME a less energy-efficient method of emulsification [4]. Reducing the cycles of permeation through the membrane while guaranteeing low emulsion polydispersity would be an innovative way of improving the energy efficiency and productivity of PME method. Therefore, the aim of this study was to find a method for preparing monodispersed emulsions with span values of less than 0.45, in a single passage, without repetitive membrane permeation.

In our previous study, we observed that, the emulsion droplet size could be reduced to less than half the membrane pore size with a single pass through the membrane without the need of repetitive permeation, by controlling the membrane permeation rates [14]. However, the emulsions showed higher polydispersity, with span values in the range of 0.4–0.6. we also found out that adjusting the emulsion viscosity could improve the emulsion droplet size and polydispersity. Therefore, in this study we investigate the relationship between the phase viscosities and the membrane permeation rates, MPR under which emulsions with the smallest span values of less than 0.4 can be prepared, without repetitive membrane permeation.

1.1. THEORY

When a premix emulsion is permeated through the porous membrane above the critical pressure, droplet disruption occurs inside the membrane pores [15]. Large oil droplets are deformed into cylindrical oil segments of varying length and diameter as they pass through the pore channels. And a lubrication layer of continuous phase separates the oil segments from the hydrophilic pore walls. Due to the parabolic velocity distribution of the laminar flow in the pores, the oil segments move faster than the continuous phase liquid near the pore walls [16]. This flow gradient produces shear between dispersed phase and continuous phase layers, causing break-up as the dispersed oil segments stretch and elongate. The oil segments of length, L and diameter, d_o , become unstable and break up into smaller droplets when the ratio $L/d_o > \pi$ [15,17,18]. The critical length, L beyond which the droplet breaks down is known as the Rayleigh-Plateau length, λ . The tendency of the oil segments to break-up is affected by the thickness, h of the lubrication layer between the oil segments and the pore wall. The thickness, h is function of the mean velocity, V of the oil segments in the membrane pore channels as expressed in Eq. (1).

$$h = C_L d_p \left(\frac{\eta_c V}{\gamma} \right)^{2/3} \quad (1)$$

where, η_c is the continuous phase viscosity, γ the interfacial tension and C_L is a constant. The mean velocity, V is also related to the wall shear stresses ($\sigma_{w,p}$) inside the membrane pores (Eq. 2), which are responsible for the actual break-up of the oil segments in the pores [4,10].

$$\sigma_{w,p} = \frac{8\eta_e V}{d_p} \quad (2)$$

Where, η_e is the mean emulsion viscosity, d_p the mean pore size. At low disperse phase content, η_e is equivalent to the continuous phase viscosity, η_c . The mean velocity, V can be determined from Eq. 3.

$$V = \frac{J\xi_p}{\varepsilon} \quad (3)$$

where J is the MPR, ε the mean membrane porosity and ξ the mean tortuosity factor of the pores. Hence,

$$\sigma_{w,p} = \frac{8\eta_e J\xi}{\varepsilon d_p} \quad (4)$$

It can be observed that the wall shear stresses in pores are proportional to the product of the mean viscosity and the membrane permeation rate, $\eta_e J$. The tendency of droplets to break up may either be higher or lower, depending on the relative variations of J and η_e [15,19]. It is in our interest to study the relationship between J and η_e , under which emulsions with the smallest span can be prepared, without repetitive membrane permeation.

2. Experimental

2.1. Materials and apparatus set up

The apparatus consisted of a stainless-steel membrane module inside which a microporous membrane was inserted and sealed on both ends by rubber O-rings as shown in Fig. 1. The microporous membrane was a cylindrically shaped hydrophilic SPG membrane (SPG Techno Co. Ltd, Miyazaki, Japan) of mean pore size $5 \mu\text{m}$, outer diameter 10 mm and effective membrane length of 10 mm . Oil-in-water (O/W) emulsions were prepared using aqueous solutions of 1.0 wt% non-ionic Tween 20; Polyoxyethylene sorbitan monolaurate surfactant (Nacalai Tesque, Inc., Kyoto, Japan), as the continuous phase liquids. The viscosity of the continuous phase ($1.1 \text{ mPa}\cdot\text{s}$) was adjusted by dissolving sodium alginate (Nacalai Tesque, Inc., Kyoto, Japan). Kerosene, $0.9 \text{ mPa}\cdot\text{s}$ was used

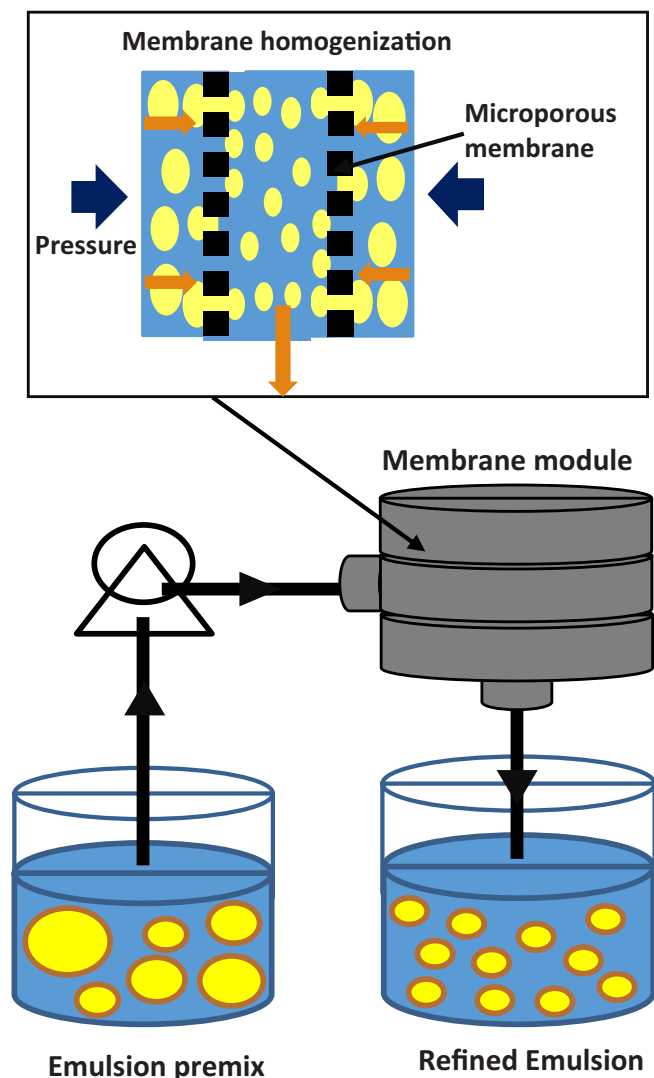


Fig. 1. Diagram showing the device and setup used for preparing emulsions.

as the low viscosity dispersed phase liquid while Liquid paraffin, 17 mPa·s (MORESCO Corporation, Kobe, Japan) and Liquid paraffin, 250 mPa·s (Wako Junyaku Co., Ltd, Hokkaido, Japan) were appropriately mixed to increase the viscosity of the dispersed phase liquids. The phase viscosities were measured at 25 °C using Viscomate Model VM-10A viscometer (Sekonic Corporation, Tokyo, Japan).

2.2. Preparation of oil-in-water (O/W) emulsion

O/W emulsions were prepared in two steps. In the first step, the emulsion premixes were prepared by stirring 80 vol% continuous phase and 20 vol% dispersed phase liquids at 5000 rpm for 45 s, using AHG-160D homogenizer (AS ONE Corporation, Osaka Japan). The pre-mix emulsions were prepared at a wide range of continuous phase to the dispersed phase viscosity ratios (1:0.2–1:18). The viscosity ratio was defined as η_d/η_c , where η_d is the dispersed phase viscosity and η_c the continuous phase viscosity.

In the second step, the premix emulsions were permeated through an SPG membrane with an effective membrane area of 3 cm² at various flowrates in the range of 10–1000 mL/min using a high pressure non-pulsating flow type plunger pump, NPGXL 1000 (NS Nihon Seimitsu Kagaku Co., Ltd, Tokyo, Japan) to prepare the refined O/W emulsions. The MPR at these flow rates was in the range of 2–200 m³/m² h, as calculated from Eq. (5). The MPR of above 200 m³/m²h were obtained

by reducing the effective membrane area to 0.125 cm² by attaching an adhesive tape to the SPG membrane tube. The membrane permeation rate (MPR), J of the premix emulsion through the membrane pores was defined as:

$$J = Q/A \quad (5)$$

where Q is the volumetric flow rate, and A is the cross-sectional area of the membrane. After use, the membranes were cleaned in place using ethanol and water, disassembled, then followed by sonicating in ethanol and water for 30 min each. In case of fouling detection, it was heated at about 500 °C for about 6 h in an electric muffle furnace, Advantec model KM-420 (Advantech Toyo Co., Ltd, Tokyo Japan), to restore its inherent properties.

2.3. The droplet size measurement

The droplet size distributions of the refined emulsions were measured using a laser diffraction particle size distribution analyser, (SALD2100, Shimadzu Co. Ltd., Kyoto, Japan). The droplet cumulative distribution at 50% was taken as the average droplet diameter (d_{50}). The droplet size distribution coefficient (Span) was defined by Eq. (6). Emulsions with span of less than 0.45 are generally referred to as monodispersed.

$$Span = (d_{90} - d_{10})/d_{50} \quad (6)$$

Where d_x is the diameter corresponding to x vol% on a relative cumulative droplet diameter distribution curve.

3. Results and discussions

3.1. Influence of MPR on the droplet size and span at lower and higher viscosity ratio

The relationship of membrane permeation rate (MPR) with the droplet size and span was analysed at lower and at higher viscosity ratios (η_d/η_c) of 1:1 and 1:18. At lower η_d/η_c , the viscosity of both phases was adjusted to 20 mPa·s, while higher η_d/η_c , the viscosity of the continuous phase was reduced to 1.1 mPa·s. All premixes were refined by a 5 μ m SPG membrane at permeation rates of 2–200 m³/m²h, without repetitive permeation. Fig. 2 shows a plot of the dimensionless droplet size (d_{50}/d_p) of the refined emulsion and its span against the MPR of the premix emulsion. The emulsion droplet size gradually decreased with increase in MPR at all viscosity ratios, due to increase in the wall shear stress in the pores and there was no significant difference in droplet size between emulsions prepared at lower and higher η_d/η_c . At higher wall shear stresses, the dispersed oil segments/droplets were more rigorously disrupted inside the pores, that the emulsions with mean droplet sizes (d_{50}) smaller than the mean pore size (d_p) could be prepared. The mean velocity, V of the dispersed oil segments flowing through the pores is proportional to the MPR (Eq. 3). Increasing the mean velocity, causes the thickness, h of the lubrication layer to increase and the diameter, d_o of oil segments to decrease until when they break up into smaller droplets when $L/d_o > \pi$. Conversely, emulsions prepared at lower η_d/η_c showed higher monodispersity with span values in the range of 0.24–0.45 as compared to 0.35–0.5 at higher η_d/η_c . Therefore, raising the viscosity ratio, by increasing η_d relative to η_c , did not improve the emulsification results but resulted in increased emulsion droplet size polydispersity. As the thickness, h of the lubricating continuous phase, is proportional to the continuous phase viscosity, η_c Eq. (1). Hence, increasing η_d/η_c by reducing η_c from 20 to 1.1 mPa·s, reduced the shear stresses in the pores. For this reason, we sought to increase the shear stresses in the system by raising further the MPR beyond 200 m³/m²h, while keeping the viscosity ratio of 1:18.

From Fig. 3, it can be observed that the emulsion droplet size was greatly reduced at higher MPR due to the high shear stresses generated

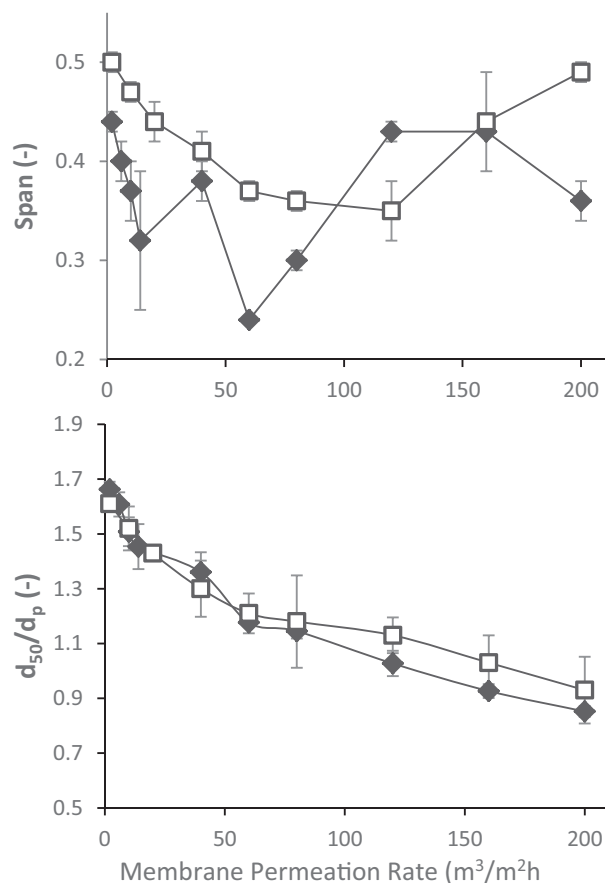


Fig. 2. Relationship between refined emulsion droplet size and span with MPR at viscosity ratio of 1:1 (◆) and 1:18 (□).

in the pores. However, the emulsion droplet size polydispersity did not improve as was expected. The span values increased greatly, in the range of 0.37–0.68. Although Suzuki et al. noted that the monodispersity of emulsions improves with the MPR of the premix emulsion in PME [7], in this study, it was observed to be true only for emulsification at low MPR, at higher MPR the emulsion polydispersity was increased greatly (Fig. 3). At very high shear stresses the emulsion droplets vigorously collided with the membrane pore walls resulting into a more intensive and uncontrolled mode droplet disruption, which give rise to higher polydispersity [20]. The uncontrolled droplet disruption was amplified more by large velocity difference between the continuous and dispersed phase liquids, generated as a result of their large viscosity ratio of 1:18 [21]. Therefore, for better control of the emulsion polydispersity, premix ME should be carried out at moderate MPR.

3.2. Influence of MPR on the droplet size and span at higher mean emulsion viscosity (η_e)

In this section, the shear stress in the membrane pores were increased by emulsifying at a higher η_e , while keeping the MPR, J low. Premix emulsions of 80 vol% continuous phase (68 mPa s) and 20 vol% liquid paraffin (70 mPa s) were prepared and refined by a 5 μ m SPG membrane at permeation rates of 2–200 m³/m²h. From Fig. 4, it can be observed that raising η_e considerably increased the shear stress in the pores. The emulsion droplet size at higher η_e was significantly smaller than emulsions obtained at lower η_e . The ratio d_{50}/d_p lowered from 0.85–1.7 to 0.57–1.32. The minimum possible span value in this study of 0.24 was obtained at a much lower MPR of 10 m³/m²h, although beyond that the polydispersity became higher (span = 0.4–0.52). It was observed that, when the η_e was low, the minimum span of 0.24 was obtained at MPR of

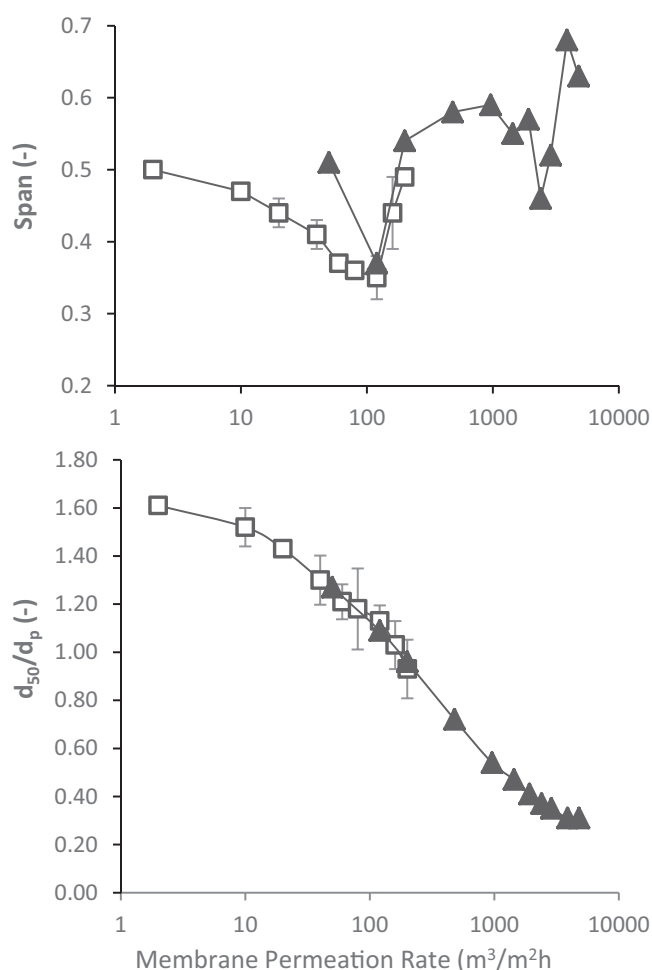


Fig. 3. Relationship between the final emulsion droplet size and span with MPR at viscosity ratio of 1:18; □ low MPR and ▲ higher MPR.

60 m³/m²h, whereas when the η_e was higher, it was obtained at MPR of 10 m³/m²h. This showed that at higher η_e , the shear forces acting on the oil segments were sufficiently high even at lower MPR. It was observed that when both η_c and η_d were high (low viscosity ratio), the shear forces were more stable, resulting into controlled breakup of the oil segments and high monodispersity (low span) of the emulsion. Whereas, when η_c was considerably low, that is, when η_d was considerably higher than η_c , enough shear force could only be generated at high MPR. The polydispersity of the emulsions tended to increase because the development of unstable shear stresses at higher MPR [22] and it was more pronounced when the viscosity ratio between the phases was high.

3.3. Method for preparing monodispersed emulsions without repetitive membrane permeation

The process of preparing monodispersed emulsions with spans of less than 0.4, without repetitive membrane permeation can be summarized in 3 steps.

In the first step, the emulsion premixes in which the continuous phase and a dispersed phase have a viscosity ratio (η_d/η_c) of 1:0.2–1:15 are prepared, as described in Section 2.2. It is preferable that the viscosity difference between the continuous phase liquid and the dispersed phase fluid is small. This helps keep the relative speed difference at the interface between the dispersed phase fluid and the continuous phase liquid to a minimum as the emulsion premix flows through the membrane pores. The η_d/η_c was preferably 1:0.5–1:2. The viscosity difference

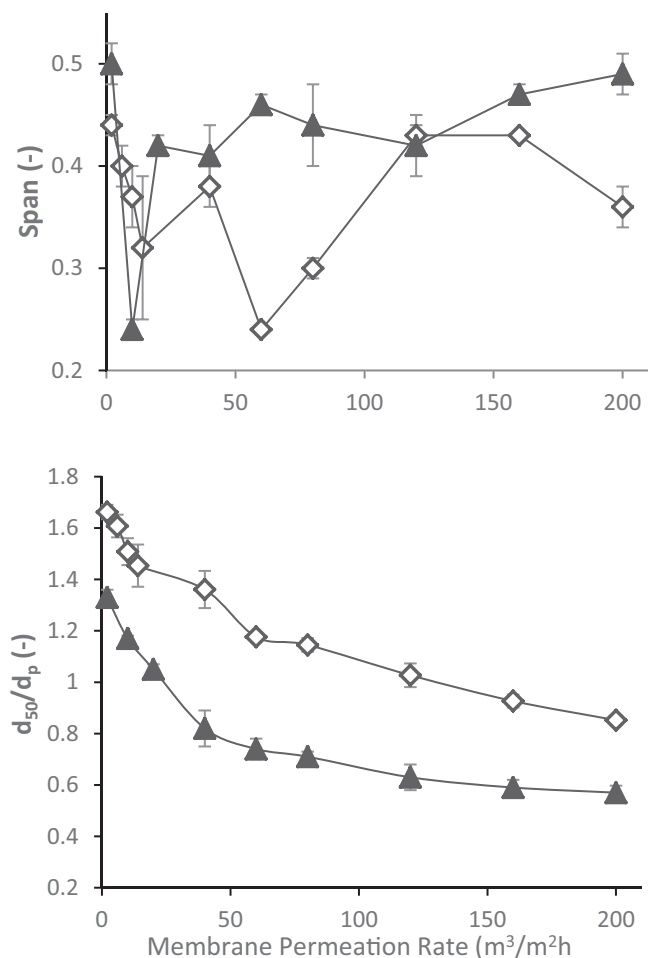


Fig. 4. Relationship between final emulsion droplet and span with MPR at viscosity ratio of 1:1;◇; lower η_e and ▲; higher η_e .

preferably less than 55 mPa s, more preferably less than 25 mPa s. And the η_c preferably 5 mPa s and less than 60 mPa s.

In the second step, the emulsion premixes are refined by permeating through the microporous membrane. The premixes are permeated through the porous membrane at various MPR and the droplet size of the final emulsions are measured. The relationship between the MPR and droplet size and span are determined and plotted, as in Fig. 2. From the plot, the values of MPR and the η_d/η_c at which the emulsions with smallest span can be prepared are specified. It is preferable to carry out the second step at a minimum MPR $10 \text{ m}^3/\text{m}^2 \text{ h}$ or more and at a maximum MPR of $200 \text{ m}^3/\text{m}^2 \text{ h}$ or less. When the MPR is $200 \text{ m}^3/\text{m}^2 \text{ h}$ or more, the mean droplet size of the prepared emulsions becomes smaller than the mean pore size of the porous membrane, but the span value tends to be higher. However, the MPR should not be too low as it will lower the process productivity.

In third step, the MPR and η_d/η_c specified in the second step can then be used to prepare emulsions with span values of less than 0.4. In this study, we obtained a minimum span of 0.24, however the minimum obtainable span may vary depending on the kind and the mean pore size of the microporous membrane used, and the formulation of the emulsion premixes. It was more susceptible to obtain highly monodispersed emulsions using the 5 and $10 \mu\text{m}$ pore size SPG membranes.

4. Conclusion

When a premix emulsion is permeated through the porous membrane above the critical pressure, the wall shear stresses responsible for

droplet disruption are proportional to the product of the mean emulsion viscosity, η_e and the MPR, J . However, its known that increase in the emulsion viscosity inversely affects the transmembrane flux through the pores, hence striking a balance between these two factors is important for preparing monodispersed emulsions.

We observed that when the viscosity of the phases and their viscosity ratio was low, the emulsion droplet size and polydispersity decreased linearly with PMR until the most monodispersed emulsions ($d_{50} = 5.80$ and span = 0.24) were prepared. However, beyond this the droplet size decreased further while polydispersity became higher.

Increasing the disperse phase viscosity (i.e., high viscosity ratio) lowered the shear stresses in the pores that the emulsion droplet size polydispersity became higher. Whereas, increasing the mean emulsion viscosity enabled preparation of the most monodispersed emulsions ($d_{50} = 5.80$, span = 0.24) at lower MPR of $10 \text{ m}^3/\text{m}^2 \text{ h}$. When the mean emulsion viscosity was high, the wall shear force could be increased even at a low MPR and emulsions with a small span could be prepared. Therefore, in this study it was proved possible to prepare highly monodispersed emulsions by adjusting the mean emulsion viscosity and MPR, without repetitive permeation, in PME. This revelation will be important for lowering the energy input involved Premix ME method and facilitate formulation of innovative emulsion products.

CRediT authorship contribution statement

Jophous Mugabi: Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Jae-Ho Jeong:** Supervision, Visualization, Writing – review & editing, Funding acquisition. **Noriyuki Igura:** Conceptualization, Methodology, Data curation, Project administration. **Mitsuya Shimoda:** Conceptualization, Methodology, Validation, Resources, Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The present research was partially supported by the Ministry of Trade, Industry and Energy (MOTIE, Korea) (No.2021202080023B) and the Korea Institute of Energy Technology Evaluation and Planning (KETEP) grant funded by the Korean government (No. 20203020020030).

References

- [1] R.C. Santana, F.A. Perrechil, R.L. Cunha, High- and low-energy emulsifications for food applications: a focus on process parameters, *Food Eng. Rev.* 5 (2013) 107–122, <https://doi.org/10.1007/s12393-013-9065-4>.
- [2] E. Piacentini, M. Dragosavac, L. Giorno, Pharmaceutical particles design by membrane emulsification: preparation methods and applications in drug delivery, *Curr. Pharm. Des.* 23 (2017) 302–318, <https://doi.org/10.2174/138161282366616117160940>.
- [3] G.T. Vladislavjević, R.A. Williams, Recent developments in manufacturing emulsions and particulate products using membranes, *Adv. Colloid Interface Sci.* 113 (2005) 1–20, <https://doi.org/10.1016/j.cis.2004.10.002>.
- [4] A. Nazir, K. Schroën, R. Boom, Premix emulsification: a review, *J. Memb. Sci.* 362 (2010) 1–11, <https://doi.org/10.1016/j.memsci.2010.06.044>.
- [5] K. Suzuki, I. Shuto, Y. Hagura, Characteristics of the membrane emulsification method combined with preliminary emulsification for preparing corn oil-in-water emulsions, *Food Sci. Technol. Int. Tokyo*. 2 (1996) 43–47, <https://doi.org/10.3136/fsti9596t9798.2.43>.
- [6] K. Suzuki, K. Hayakawa, Y. Hagura, Preparation of high concentration O/W and W/O emulsions by the membrane phase inversion emulsification using PTFE membranes, *Food Sci. Technol. Res.* 5 (1999) 234–238, <https://doi.org/10.3136/fstr.5.234>.
- [7] K. Suzuki, I. Fujiki, Y. Hagura, Preparation of corn oil/water and water/corn oil emulsions using PTFE, *Food Sci. Technol.* 4 (1998) 164–167, <https://doi.org/10.3136/fsti9596t9798.4.164>.

- [8] E.A. van der Zwan, C.G.P.H. Schroën, R.M. Boom, Premix membrane emulsification by using a packed layer of glass beads, *AIChE J.* 54 (2008) 2190–2197, <https://doi.org/10.1002/aic>.
- [9] A. Nazir, R.M. Boom, K. Schroën, Droplet break-up mechanism in premix emulsification using packed beds, *Chem. Eng. Sci.* 92 (2013) 190–197, <https://doi.org/10.1016/j.ces.2013.01.021>.
- [10] G.T. Vladislavljević, M. Shimizu, T. Nakashima, Preparation of monodisperse multiple emulsions at high production rates by multi-stage premix membrane emulsification, *J. Memb. Sci.* 244 (2004) 97–106, <https://doi.org/10.1016/j.memsci.2004.07.008>.
- [11] C. Charcosset, I. Limayem, H. Fessi, The membrane emulsification process—a review, *J. Chem. Technol. Biotechnol.* 79 (2004) 209–218, <https://doi.org/10.1002/jctb.969>.
- [12] G.T. Vladislavljević, U. Lambrich, M. Nakajima, H. Schubert, Production of O/W emulsions using SPG membranes, ceramic α -aluminium oxide membranes, microfluidizer and a silicon microchannel plate—a comparative study, *Colloids Surf. A Physicochem. Eng. Asp.* 232 (2004) 199–207, <https://doi.org/10.1016/j.colsurfa.2003.10.026>.
- [13] A. Nazir, K. Schroën, R. Boom, High-throughput premix membrane emulsification using nickel sieves having straight-through pores, *J. Memb. Sci.* 383 (2011) 116–123, <https://doi.org/10.1016/j.memsci.2011.08.051>.
- [14] J. Mugabi, K. Naohiro, Y. Hiroki, M. Miki, N. Igura, M. Shimoda, Preparation of small droplet size monodispersed emulsions at high production rate by continuous intramembrane premix emulsification method, *J. Chem. Eng. Jpn.* 52 (2019) 259–266, <https://doi.org/10.1252/jcej.18we074>.
- [15] G.T. Vladislavljević, M. Shimizu, T. Nakashima, Production of multiple emulsions for drug delivery systems by repeated SPG membrane homogenization: Influence of mean pore size, interfacial tension and continuous phase viscosity, *J. Memb. Sci.* 284 (2006) 373–383, <https://doi.org/10.1016/j.memsci.2006.08.003>.
- [16] S.G. Clerc, T.E. Thompson, A possible mechanism for vesicle formation by extrusion, *Biophys. J.* 67 (1994) 475–476, [https://doi.org/10.1016/S0006-3495\(94\)80503-X](https://doi.org/10.1016/S0006-3495(94)80503-X).
- [17] M. Kukizaki, Preparation of solid lipid microcapsules via solid-in-oil-in-water dispersions by premix membrane emulsification, *Chem. Eng. J.* 151 (2009) 387–396, <https://doi.org/10.1016/j.cej.2009.03.061>.
- [18] D.G. Hunter, B.J. Frisken, Effect of extrusion pressure and lipid properties on the size and polydispersity of lipid vesicles, *Biophys. J.* 74 (1998) 2996–3002, [https://doi.org/10.1016/S0006-3495\(98\)78006-3](https://doi.org/10.1016/S0006-3495(98)78006-3).
- [19] Q.Z. Zhou, L.Y. Wang, G.H. Ma, Z.G. Su, Multi-stage premix membrane emulsification for preparation of agarose microbeads with uniform size, *J. Memb. Sci.* 322 (2008) 98–104, <https://doi.org/10.1016/j.memsci.2008.05.025>.
- [20] S. Joseph, H. Bunjes, Preparation of nanoemulsions and solid lipid nanoparticles by premix membrane emulsification, *J. Pharm. Sci.* 101 (2012) 2479–2489, <https://doi.org/10.1002/jps.23163>.
- [21] M.E. Kurdzinski, B. Gol, A.C. Hee, P. Thurgood, J.Y. Zhu, P. Petersen, A. Mitchell, K. Khoshmanesh, Dynamics of high viscosity contrast confluent microfluidic flows, *Sci. Rep.* 7 (2017) 5945, <https://doi.org/10.1038/s41598-017-06260-6>.
- [22] A. Nazir, R.M. Boom, K. Schroën, Influence of the emulsion formulation in premix emulsification using packed beds, *Chem. Eng. Sci.* 116 (2014) 547–557, <https://doi.org/10.1016/j.ces.2014.05.009>.