**ABSTRACT**

MODELING THE FORMATION OF POLYLACTIDE MICROSPHERES. Biodegradable polylactide microspheres have been developed from a dispersion solution of polylactide in chloroform with polyvinyl alcohol in water. The present paper focuses on developing an understanding of microspheres formation through simple dimensional analysis and principle of system similarity for microstructure observation of microsphere diameter formed. Theoretical correlation between microspheres diameter and agitation rate was derived with the concept of similarity. While the empirical correlation between Weber (We) number and microspheres diameter was derived from dimensional analysis of variables that is useful for prediction of microspheres diameter to support Holmium powder. The empiric equation of the microspheres diameter forming as a function of essential process parameters is: \( \ln \left( \frac{d_m}{d_p} \right) = -4.81 + 0.593 \ln \text{We} \).

**Key words**: dimensional analysis, principle of similarity, microspheres

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**INTRODUCTION**

Microspheres are spherical particles made of ceramic materials, polymer or glass and sized from 10 nm to about 200 \( \mu \)m to support any materials, such as: gas, condensed matter or solids in form of inorganic as well as organic compound. Polymer microspheres can be made by forming dispersion by mixing two-polymer solutions, which do not dissolve each other. Based on material types to be carried, microspheres have a wide range of application area like radiopharmacy [1,2], catalyst and catalyst supporter, additives for food or cosmetics [3].

A study about microspheres synthesis based on polymethyl metacrylic (PMMA) and of microspheres based on polymer of biodegradable polylactide (PLA), which covers process parameters, like polymer concentration and time squealer of emulsion system, has been conducted [4-6]. The present paper focuses on developing an understanding of microspheres formation through simple dimensional analysis of various process variables that could be reduced to the essential parameter and the principle of similarity.

Dimensional analysis is a mathematical tool often used in physics, chemistry and engineering to simplify a problem by reducing the number of variables to the smallest number of essential parameters [7]. The principle of similarity is concerned with the relations between physical system of different size, and it is thus fundamental to the scaling up or down of physical and chemical processes. The principle of similarity is usually coupled with the method of dimensional analysis. The principle of similarity is more particularly concerned with the general concept of shape as applied to complex systems and with the implication of the fact that shape is independent of size and composition [7].

A mechanism of microspheres formation through dispersion is passing mixer rotation to make micro bubble at dispersed phase to rotate, so that system equilibrium is reached [7]. Forming of microspheres is assumed to happen at the step of emulsification and shall be no longer influenced by squealer time. According to that assumption, the microspheres diameter being
formed will be attributed to process variables, namely: tank cylinder diameter, churn diameter, baffles width, churn height position from the tank base, solution level in the tank, agitation speed of churn, viscosities, densities, and surface tension between phases. The diameter of microspheres as function of synthesis process parameter is written down mathematically as:

\[ d_m = f(d_p, d_s, d_b, Z, H, N, \mu, \rho, \sigma) \] ................................. (1)

**symbol:**
- \( d_m \) = diameter of microspheres, cm
- \( d_p \) = churn diameter, cm
- \( d_s \) = beaker glass diameter (tank cylinder diameter), cm
- \( d_b \) = baffle width, cm
- \( Z \) = churn height position from tank base, cm
- \( H \) = solution level in tank, cm
- \( N \) = agitation speed of mixer (rpm)
- \( \mu \) = viscosity, g cm\(^{-1}\) s\(^{-1}\)
- \( \rho \) = density, g cm\(^{-3}\)
- \( \sigma \) = surface tension between solution phase 1 and phase 2

Provided equation (1) is dimensionally homogeneous, the dimensional formulas of the variables must conform to power relation:

\[ d_m = k d_p^a d_s^b Z^c H^d N^e \mu^f \rho^g \sigma^h \] ............................... (2)

Primary quantities of mass [M], length [L] and time [T] are chosen and substituting the dimensional formulas:

\[ L = L^1 L^1 L^1 L^1 (T^1)^i (M L^1 T^1)^j (M L^3 T^2)^i \] ............................... (3)

From equation (3) the following relation is obtained:

**Condition on \( M \):**
\[ 0 = g + h - i \] .................................. (4a)

**Condition on \( L \):**
\[ 1 = a + b + c + d + e + g - 3h \] ........................................ (4b)

**Condition on \( t \):**
\[ 0 = f - g - 2i \] ........................................ (4c)

These equations can be solved for any three of unknown giving a set of solutions in term of the other three. Solving in term of \( a, f, h \)

\[ a = 1-b-c-d+e+g-3i \]
\[ f = g-2i \]
\[ h = -g-i \]

whence

\[ d_m = k d_p^{(1-b-c-d+2e-3i)} d_s^b Z^c H^d N^e \mu^f \rho^g \sigma^h \] ............................... (5)

or

\[ d_m = k d_p^{(1-b-c-d+2e-3i)} d_s^b Z^c H^d N^e \mu^f \rho^g \sigma^h \] ............................... (6)

Provided the viscosities of the liquids are relatively low and their densities are nearly equal, hence influence of viscosity represented by dimensionless group of \( \left( \frac{d_p^2 \mu}{N d_p} \right) \) which is known as Reynolds number upon flow pattern can be neglected [7]. Amount of size and dispersion of droplet is then only depending on system geometry, speed of agitation, and interface tension of both solutions represented by dimensionless group of \( \left( \frac{d_p^2 \mu}{N d_p} \right) \) or known as Weber number. If other dimensionless group of \( \left( \frac{d_p^2 \mu}{N d_p} \right) \) and \( \left( \frac{d_p^2 \mu}{N d_p} \right) \) are made constant during the experiment, thus equation of microsphere diameter formation is only influenced by essential parameter of Weber number:

\[ \left( \frac{d_m}{d_p} \right) = k (We)^i \] with \( k, i = \text{constants} \)

\[ Re = \left( \frac{\rho N d_p^2}{\mu} \right) \] ............................... (8)

\[ We = \left( \frac{\rho N^2 d_m^2}{\sigma} \right) \]

For dynamic similarity, the criterion is a constant ratio of centrifugal to surface tension force, whence:

\[ \frac{\rho N^2 d_m^2}{\sigma} = \text{const} \] ............................... (9)

For the mass density of \( \rho \), surface tension of \( \sigma \), and churn diameter of \( d_p \) are constants, hence equation of similarities above is:

\[ \left[ d_m N^2 \right] = \left[ d_p N^2 \right] \] ............................... (10)

\[ d_m = d_p \left( \frac{N^2_m}{N^2_p} \right) \] ............................... (11)

Equation (11) is the scale equation for predicted microsphere diameter at different stirrer speed namely \( N_m \) and \( N_p \).

This paper reports on developing an understanding of microspheres formation through simple dimensional analysis and principle of system similarity for microstructure observation on diameter of microsphere based on polylactide formed. The result that is expected from this research is to obtain quantitative relation of the influence of Weber number to microspheres diameter formed, and to apply the principle of similarities, which is useful to conduct scale up of process being studied.
EXPERIMENTAL METHOD

Materials

Polylactide (PLA, MW=39000) in form of palette is obtained from Wako (Japan); Polyvinyl Alcohol (PVA, MW=72000) is obtained from Merck (Germany). The solute used is chloroform (CHCl₃) degree of p.a. of Merck and aquadest.

Method

Mix each 50 mL of PLA 2% solution in chloroform and 50 mL of PVA 1% solution in water into 300 mL beaker glass whose diameter (dₑ) has been measured. The Polymer solutions is then swirled with a stirrer of type RW 10 R CE for 2 hours with stirrer speed with speed scale variation of 4 (2136 rpm), 5 (3004 rpm), 5.5 (3438 rpm), 6 (3872 rpm), 7 (4740 rpm) and 8 (4642 rpm) respectively and make other variables stated in equation (6) remain constant during the overall process. After 2 hours, squealer of emulsion is stopped; then the emulsion thinned into 500 mL of aquadest that has been prepared is swirled with the stirrer speed that is used to swirl polymer solution for 1 hour. Emulsion of two polymers is then left for 1 night so that precipitation occurs. The formed sediment is then decanted; the sediment of microspheres formed is collected into a cup, and dried in the oven at 60°C for 24 hours. The dimension of microspheres diameters can be identified using optical microscope.

RESULTS AND DISCUSSION

Polylactide microspheres containing Holmium is biocompatible for embolization of tumor and immobilization of ¹⁶⁶Ho which has favorable physical characteristic for image-guided radionuclide therapy [2]. The development steps of microspheres as carrier of radiopharmacy materials are: controlling the size and the shape of microspheres, admission filling of microspheres with nuclide, and activating nuclide loaded microspheres of nuclear reactor.

Equation (5) or (6) is the predicted equation to calculate microsphere diameter according all variables involved. To simplify the microsphere formation it is assumed that system equilibrium is reached, and forming of microspheres is occurred at the step of emulsification process and shall be no longer influenced by squealer time. Due to simplified mechanisms for microsphere formation, it is clear that foams are produced from the polylactide solution is occurred during emulsification steps. While the microsphere formation according to all variables involved have not been studied in detail, this paper reports the microspheres diameter formation is influenced by essential parameter called Weber number. To calculate the Weber number, all variables of agitation speed that is varied from experiment, density, diameter of microspheres obtained and surface tension between phases must be known. The density of solution was determined using pycnometer obtained by \( \rho = 1.2311 \text{ g/mL} \). The surface tension between phases is calculated by using equation of corresponding state [8], obtained by \( \sigma = 28.4745 \text{ g/s}^2 \).

Microspheres size as the function of agitation speed is shown in Table 1.

By making the graph of the last two columns in Table 1, the relation of ln \((d_m/d_p)\) to Weber number \((\ln \text{We})\) is obtain, seen in Figure 1. Linear regression of the graph produces equation:

\[
\ln \left( \frac{d_m}{d_p} \right) = -4.81 + 0.593 \ln \text{We} \quad \text{............... (12)}
\]

Equation (12) expresses that diameter of microspheres \(d_m\) is influenced by a constant, churn diameter of \(d_p\) and Weber number in a good position 0.593. Equation (12) is the equation of empiric microspheres forming for polymer based on polylactic. With the equation, the condition of the process to get the diameter of microspheres based on the wanted specification can be forecast.

Table 1 contains the relation of microspheres diameter influenced by speed of squealer (rpm). As agitation speed increased from 2136 rpm to 5609 rpm, the diameter of microsphere is seen to diminish from 87 microns to 35.3 microns, a reduction of approximately 60%. The third column of Table 1 contains diameter of microspheres that is calculated using the principle of similarities, where a dispersed globule of diameter \(d_m\) is spinning with maximum peripheral velocity \(v\), then the
total centrifugal force acting on the globule is proportional to $\rho d_m v^2$ and the total surface-tension force is proportional to $\sigma d_m$. For $\rho$, $\sigma$, $d_m$ are respectively the mass density of the dispersed phase, the interfacial tension, and churn diameter are constants equation (11) is satisfied to calculate the content of third column on Table 1. The data presented in second column of Table 1 are compared to the predictions following equation (11). The result of calculated $d_m$ are in reasonable agreement with the experimental values.

The assumption of Weber number as the only essential parameter affected the microspheres formation has been shown to be an approximation, and the need for more treatment of all variables involved of this process is evident.

CONCLUSION

The understanding of mechanism of microspheres forming process leads to the conclusion that Weber number gives influence to the process. The concept of dimensional analysis in microspheres synthesis based on polylactide produces the empiric equation of the microspheres diameter forming as a function of process parameters, namely:. Empirically, the equation that relates the formed microspheres diameter to the process variables has been derived, from which the size of microspheres diameter has linear ratio to the Weber number raised to the power of 0.593.

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