Product-Oriented Process Synthesis and Development: Creams and Pastes

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A systematic procedure is presented for the synthesis and development of manufacturing processes for creams and pastes. The procedure integrates the skills of a chemist and a chemical engineer to produce a product with specified properties. The desired functional and sensorial performance of the product is first identified in terms of quality factors. Then, the requisite ingredients are selected, and the process flowsheet, as well as the operating conditions, is synthesized. There are four steps in the procedure: identification of product quality factors, product formulation, flowsheet synthesis, and product and process evaluation. Design guidelines, as well as physical models describing relevant phenomena, are used to assist decision-making at each step of the procedure.

Introduction

Consumer and pharmaceutical products are a major component of the global chemical industry. Manufacturing and marketing of these products is the primary business of more than 75% of all chemical corporations in the U.S. (Lenz and Lafrance, 1996). Recent trends indicate an increasing demand for new products with improved performance and shorter product life cycle (Tanguy and Marchal, 1996; Pisano, 1997; Villadsen, 1997; Wintermantel, 1999). This places considerable pressure to accelerate product and process development.

Depending on the end use, such products are delivered in various physical forms. A significant portion, especially those applied to parts of the human body, is produced in the form of creams and pastes. These are basically a colloidal system containing immiscible liquid phases, as well as solid particles. Examples include cosmetic creams, suntan lotions, toothpastes, and antibacterial ointments. There are several reasons why they are often the preferred delivery vehicles. Various ingredients with very different physical and chemical properties can be brought together in the form of creams or pastes. Topical application is both easy and convenient. It is effective in delivering a small dosage of an active ingredient to the body.

Despite their wide usage and economic significance, the development of cream and paste products, as well as the corresponding manufacturing processes, is normally conducted on a case-by-case basis. The absence of systematic procedures is the primary cause for excessive development time and cost. In addition, a product successfully developed in the laboratory may fail to be produced commercially. For example, Ward et al. (1974) discussed a case history where equipment breakdown occurred when a very shear-thickening shampoo was processed in a filling machine.

Clearly, significant advantages can be gained by examining the synthesis and development of cream and paste manufacturing processes from the process systems engineering (PSE) perspective. Such an approach would integrate the skills of a colloid chemist and a chemical engineer to develop a product with the desired properties (Tadros, 1993). For example, cosmetic development involves both chemists and chemical engineers as an integrated team for product and process design (Mitsui, 1997). Similarly, Meusse et al. (2000) proposed the application of conceptual process design for making structured products such as mayonnaise and salad dressing.

This article presents a systematic procedure for synthesizing and developing manufacturing processes for creams and pastes. Issues in each development phase, from formulation to production, are considered. Because of the nature of these problems, the use of predictive models, experimental testing,

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Table 1. Procedure for the Synthesis and Development of Cream and Paste Manufacturing Processes

Step 1	Identification of product quality factors
Step 2	Product formulation • Selection of ingredients • Selection of emulsion type (if applicable) • Selection of emulsifier (if necessary) • Determination of product microstructure
Step 3	Design of manufacturing process • Synthesis of flowsheet alternatives • Selection of equipment units • Selection of feed addition policy • Selection of equipment operating conditions
Step 4	Product and process evaluation • Examination of the base case product • Determination of necessary modifications to meet the objectives • Evaluation of scale-up issues

and experiential heuristics in a complementary manner is essential. The procedure is expected to help minimize time and effort in developing a product with the desired performance.

Systematic Procedure

The procedure consists of four steps (Table 1). In the first step, a set of attributes that determines the product quality, referred to as the *quality factors*, are identified. In Step 2, necessary ingredients, as well as the desired product microstructure, are selected. This is important since they determine the product quality factors such as spreadability, tackiness, appearance, and shelf life. The process flowsheet is synthesized in Step 3. Equipment units and operating conditions are selected. Finally, the proposed product and process are evaluated with experimental tests. Scale-up considerations are also taken into account in this step.

Step 1: identification of product quality factors

The product attributes that the creams and pastes are expected to possess are determined first. While the primary concern is always functionality, quality factors such as the ease of application, stability, and appearance are often crucial in consumer satisfaction. For example, consumer perception when a moisturizing cream is applied to the skin, whether it is smooth, oily, cold, or tacky, is an important consideration, apart from protecting the skin from dryness. A cosmetic or pharmaceutical product should be stable for over a year, subject to the expected changes in external temperature, humidity, and the presence of direct sunlight. Table 2 lists some examples of typical product quality factors for creams and pastes.

The flow behavior is often a dominant attribute for two reasons. First, the flow behavior plays a major role in processing. The power consumption, as well as the blending time, depends on the viscosity of the product, which often varies with the shear level experienced during processing. Second, how the product flows upon application has a great impact on the consumer's perception. For example, the consumer expects a cosmetic cream to spread easily when rubbed to the skin, but does not flow by itself during normal handling. It is therefore important to translate the perception-related requirements into rheological requirements. For example, the cosmetic cream should have low viscosity at high shear, so that it flows readily when rubbed on the skin. On the other hand, its viscosity should increase significantly at low shear rates, so that it does not spill easily. In other words, it is desirable that the cream exhibits a pseudoplastic behavior.

Table 3 summarizes the key rheological properties of creams and pastes, along with appropriate mathematical models. A popular model is the power-law or Herschel-Bulkley model (Eq. 1). Another is the stretched exponential model (Eq. 2) (Barnes, 1997), which describes the change of viscosity with time after cessation of an applied shear. For many liquids, the relaxation time t_r is zero. However, it is common for emulsions to show thixotropic or rheopective behavior. Since an emulsion often contains a gel network structure, it may partially exhibit elastic behavior (Eq. 3). The storage modulus (G') describes the elastic component, while the loss modulus (G'') describes the viscous component. The ratio between the two moduli is equivalent to the Deborah number (N_{De}) (Reiner, 1964), which indicates whether a material behaves more fluid-like or solid-like.

We then need to quantify the relationship between flow properties and sensorial attributes described in qualitative terms such as "spreadable," "sticky," "creamy" and so on. Although psychophysical models relating rheological and sensorial attributes have been developed (Breuer, 1983), the use of experiential heuristics, such as those summarized in Table 4, is still the preferred means of specifying these attributes. For example, cosmetic emulsions assessed as good by a group of panelists have been found to have a low viscosity (about 0.025 Pa·s) when applied to the skin at a high shear rate (500 s^{-1} for lotions and 5,000 s^{-1} for creams). At very low shear rates the viscosity can be as high as 1,000 Pa·s (Brummer and Godersky, 1999). Products which are not supposed to flow readily or appear runny should have a yield point above 20 Pa, which is the shear stress contribution by gravity (Miner, 1993).

Table 2. Examples of Typical Quality Factors for Creams and Pastes

Functional Quality Factors Protects parts of the body Cleans parts of the body Provides a protective or decorative coating Causes adhesion to a surface Delivers an active pharmaceutical ingredient (API)
Rheological Quality Factors Can be poured easily Spreads easily when rubbed on the skin Does not flow readily under gravity but easy to stir Should give a uniform coating when applied to a surface Should not flow by itself, but can be squeezed out of the container
Physical Quality Factors Must be stable for a certain period of time Melts at a certain temperature Must release an ingredient at a controlled rate
Sensorial Quality Factors Feels smooth Does not feel oily Appears transparent, opaque, or pearlescent Does not cause irritation

Table 3. Rheological Properties of Creams and Pastes

Property and Models	*Term for Behavior*	*Description*	*Parameter Values*
Viscosity	Newtonian	Viscosity is constant irrespective of shear rate	$n=1,\ \tau_0=0,\ t_r=0$
$\mu_\infty = \frac{\tau_0}{\dot{\gamma}} + \mathrm{K}\dot{\gamma}^{n-1}$ (1)			
	Pseudoplastic (shear-thinning)	Viscosity decreases with increasing shear rate	$n<1$
$\mu = \mu_\infty + (\mu_0 - \mu_\infty)\left\{1 - \exp\left[-\left(\frac{t}{t_r}\right)^a\right]\right\}$ (2)	Dilatant (shear-thickening)	Vicosity increases with increasing shear rate	$n>1$
	Plastic	Exhibits a critical stress (yield value) below which flow does not occur	$\tau_0 > 0$
	Thixotropic	Viscosity decreases during shearing, and gradually increases to its original value after shearing stops	$n<1,\ t_r>0$
	Rheopective	Viscosity increases during shearing, and gradually decreases to its original value after shearing stops	$n>1,\ t_r>0$
Complex Modulus	Viscous	Energy is fully lost when the material is deformed under an external force	$G'=0,\ G''=\omega\mu$ $N_{De}=0$
$G^* = G' + iG''$ (3)			
	Elastic	Energy is fully stored when the material is deformed under an extranal force, and released when the force is relaxed	$G'=G,\ G''=0$ $N_{De}=\infty$
$N_{De} = \frac{G'}{G''}$ (4)	Viscoelastic	Combination of elastic and viscous properties	$G'\neq 0,\ G''\neq 0$ $0<N_{De}<\infty$

Step 2: product formulation

This step deals with ingredient selection and product microstructure determination. The formulation of consumer and pharmaceutical creams and pastes is often both an art and a science. There are no exact formulas as to what ingredients to select and in what proportion they should be mixed. Nonetheless, heuristics as listed in Table 5 are available to assist decision-making in this step. There are four key issues: selection of ingredients, selection of delivery vehicle (emulsion type), selection of a surfactant (if necessary), and determination of product microstructure.

Selection of Ingredients. With a product in mind, we first specify the active ingredients to meet the functionality requirements. Obviously, a drug should contain the active pharmaceutical ingredient (API) to be administered. A hand lotion for protecting the skin from dryness should contain an emollient to regulate the evaporation of moisture from the skin (Williams and Schmitt, 1992). The active ingredient may be a phytochemical or a synthetic chemical obtained through a series of chemical reactions.

Table 4. Heuristics for Specifying Sensorial Quality Factors

- Prefer a product with thixotropic behavior to deliver highly viscous product as a thinner material.
- Prefer a product showing shear-thinning behavior if the product should be thick at rest but spread easily upon shearing.
- Prefer a semi-solid or highly viscous product to avoid phase separation and to increase product stability.
- Aim for a yield value of above 20 Pa, if the product is not supposed to flow under gravity (Miner, 1993).
- Aim for a maximum viscosity of 120–500 Pa·s for lotions (liquid-like creams) and 1,350–3,500 Pa·s for solid-like creams to obtain the best acceptance (Brummer and Godersky, 1999).
- In making a product to be applied to the skin, aim for a viscosity of about 0.025 Pa·s at the application shear rate to obtain the best acceptance (Brummer and Godersky, 1999).

To meet the secondary requirements such as appearance and ease of application or administration, other ingredients are also needed in the product. Table 6 lists typical ingredients used to impart the desired product qualities. A multifunctional ingredient is preferred; for example, a fatty alcohol serves as both an emollient and a humectant in cosmetic creams. Care should be taken to make sure that the ingredients are compatible with each other. For example, the perfume oil used for a cosmetic lotion should not contain a reducing agent that can degrade the color of the product (Balsam and Sagarin, 1972). Information on raw materials and rheological additives for cosmetic and pharmaceutical creams and pastes is available in the literature (Clarke, 1993; Zetz et al., 1996; Mitsui, 1997; among others). The ingredients are then classified according to their compatibility (water-soluble, oil-soluble, or insoluble) and also to their sensitivity to processing conditions. For example, perfumes and flavors are usually grouped into a separate class since they are likely to be heat sensitive. Some ingredients, such as thickeners, may be insoluble but are readily dispersible in water.

Selection of Product Delivery Vehicle. Often, some ingredients are hydrophilic, while others are hydrophobic. In such a case, an emulsion is the appropriate product delivery vehicle. After selecting the ingredients, the appropriate type of emulsion has to be determined. An emulsion can either be an oil-in-water (O/W) type, a water-in-oil (W/O) type, or a double emulsion (W/O/W or O/W/O). The choice is mainly dictated by practical considerations such as ease of application

Table 5. Heuristics for Product Formulation

Selection of Ingredients

- Choose a multifunctional ingredient whenever possible.
- Favor the use of imperishable ingredients whenever possible.
- Avoid using oxidizing or reducing agents in products whose quality is affected by its color.
- Consider adding a hydrocolloid thickener with weak gel network structure (such as gum or carboxymethyl cellulose), if thixotropic behavior is desired for the emulsion product (Clarke, 1993).
- Consider adding rheological additives such as waxes or fatty alcohols to a W/O emulsion, if pseudoplastic behavior is desired (Sherman, 1970; Rogers, 1978; Klein, 1988).

Selection of Product Delivery System

- Use O/W (W/O) emulsion to obtain cool (warm) feeling upon application of the product on the skin.
- Use O/W emulsion if the product should not feel or taste greasy.
- Use W/O emulsion if the product should be resistant to washing and/or perspiration.
- Consider using a double emulsion, if the desired internal phase volume ratio does not give the specified rheological properties.
- Consider using a double emulsion for extended delivery of an active ingredient, such as a drug (De Luca et al., 1990).
- Consider using a W/O/W (O/W/O) emulsion to obtain a product containing incompatible materials which are both hydrophilic (hydrophobic).

Determination of Product Microstructure

- Aim for an emulsion with high dispersed-phase volume fraction, if it is desired to obtain a viscoelastic product and both the continuous and dispersed phases show Newtonian behavior.
- Aim for a small particle size (< 1 μm) of the dispersed solids or the continuous phase crystals, if it is desired to obtain a solid-like product with smooth texture.
- The viscosity of dilute (concentrated) emulsions and suspensions is mainly controlled by (does not depend on) the viscosity of the continuous phase, but does not significantly depend on (is controlled by) droplet size and phase volume fraction (Barnes, 1989; Otsubo and Prud'homme, 1994).
- Bimodal distribution leads to a product which is more prone to creaming (Sánchez et al., 1998).

and consumer perception. For example, a hand lotion is usually an O/W emulsion because this type of emulsion allows nonstickiness on application to the skin (Williams and Schmitt, 1992). Double emulsions are often used to create creams and lotions with desirable rheological properties of the external water phase, while allowing flexibility of the internal water/oil ratio (Friberg, 1979). It is also useful for slowly delivering an API, because the agent would have to pass through two interfaces (De Luca et al., 1990). When a considerable amount of insoluble solid ingredients is involved, as in most pastes, a suspension is the suitable product delivery system.

Selection of Emulsifier. If two or more immiscible phases are involved, the next key issue in the formulation step is the selection of a suitable surfactant or emulsifier. The surfactant assists the dispersion of a liquid phase into another liquid phase, or solid particles into a liquid phase. Depending on the relative amount of surfactant, oil, and water, mixtures of different characteristics may form. The thermodynamic phase behavior of the oil-water-surfactant system exhibits regions of liquid crystal phases, where surfactant molecules are packed in various arrangements (hexagonal, cubic, lamellar, and so on), as well as regions of immiscibility (Davis, 1994; Laughlin, 1994). Surely, the different phase behavior leads to different rheological properties and product stability characteristics. However, since the surfactant concentration in cream and paste products is usually low, we only consider the immiscible region, where liquid crystal phases are not likely to be present in a significant amount. In this region, the major role of the surfactant is providing kinetic stability instead of forming a thermodynamically stable mixture.

Often, a mixture of surfactants is used instead of a single one. The composition of the emulsifiers, as well as their distribution between the continuous and dispersed phases, can have a pronounced effect on the final emulsion, as will be discussed in Step 4. Many factors need to be considered in selecting emulsifiers (Table 7). Most important is the ability to form the desired emulsion type. The most widely used guideline for predicting emulsion type is that the continuous phase is the one in which the surfactant is more soluble (Bancroft, 1913). Thus, if an O/W emulsion is desired, a hydrophilic surfactant should be chosen. The purely empirical Bancroft's rule agrees with the so-called oriented wedge theory (Fox, 1974; Rosen, 1989). Consider a layer of surfactant at an oil-water interface. If the surfactant is more soluble in water, the hydrophilic portion is expected to be larger than the hydrophobic portion. These hydrophilic "heads" become hydrated and repel each other, causing the interface to curve in such a way that the water phase engulfs the oil phase.

A kinetic-based approach for determining emulsion type can also be used. Davies and Rideal (1961) argued that upon mixing oil and water phases, emulsions of both types (O/W and W/O) are formed. The relative coalescence rates between the droplets determine the final emulsion type. That is, if 1 represents oil droplets in water and 2 represents water droplets in oil, then an O/W emulsion is preferentially stable if

$$\frac{r_2}{r_1} \gg 1, \tag{5}$$

where r is the rate of coalescence. When the two rates are comparable, the phase that is present in excess is likely to be the continuous phase. They further related the coalescence rates with the chemical structure of the surfactant, and to the Hydrophilic-Lipophilic Balance (HLB) value

$$\frac{r_2}{r_1} = \frac{C_2}{C_1} \exp\left[2.2\,\theta(\text{HLB-7})\right] \tag{6}$$

where θ is the surface coverage by the surfactant. Assuming $C_1 = C_2$, $\theta = 1$, and $r_2 = 100\ r_1$, Eq. 6 would indicate that we should use a surfactant with an HLB of around 9 to make O/W emulsions. Since this value indicates a hydrophilic surfactant, it is in agreement with Bancroft's rule.

Considering the investment required in developing a new emulsifier, the selection is usually limited to time-tested, conventional materials using the HLB method (Lissant, 1991). The HLB value of an emulsifier quantifies its hydrophilic and hydrophobic tendencies. A low HLB value indicates a hydrophobic tendency, while a high HLB value indicates hydrophilic tendency. An HLB of between 6 to 17 is usually suitable for making O/W emulsions. The HLB value for a

Table 6. Examples of Typical Ingredients used in Creams and Pastes

Desired Function	*Ingredient*	*Typical Raw Materials*	*Typical Amount*
Control of product humidity	Humectant	Glycerol Propylene glycol Sorbitol	Up to 20%
Emulsion stabilization	Emulsifier	Sodium lauryl sulfate Parabens Formaldehyde	0.1–3%
Occlusivity/protection effect	Opacifier	Titanium dioxide Styrene/acrylate copolymers	Up to 10%
Film formation/ease of spread	Thickener	Beeswax Xanthan gum GMS (glycerol monostearate)	0.1–2%
Formation of cohesive structure	Binder	Precipitated silica Carboxymethyl cellulose Starch	Up to 15%
Dissolution of ingredients	Solvent	Purified water Mineral oil	20–85%
Regulation of pH	Buffer	Citric acid Sodium hydroxide Amino acids	q.s.
Stability against microorganisms	Preservative	Sorbic acid Methyl paraben Phenoxy ethanol	q.s.
Color	Pigment	Titanium dioxide (white) β-carotene (yellow) Iron oxides	q.s.
Odor	Perfume	Essential oils Synthetic aromatics	q.s.
Taste	Flavor	Salt Aspartame (sweetener) Cocoa powder	q.s.

mixture of emulsifiers can be calculated by adding up the individual component's HLB values, after weighting by the respective composition. To select the suitable emulsifier, we calculate the HLB value of the continuous phase, by first assigning HLB values to each ingredient in that phase. Then, we look for an emulsifier or a mixture of emulsifiers which has an HLB value matching this number (Fox, 1974).

Stability is a crucial issue since consumer products are often expected to remain usable for months or even years. Also, the emulsion needs to remain stable under the relatively harsh processing conditions such as high temperature during sterilization or high shear during filling. Typically, a more stable emulsion can be generated by reducing the interfacial tension, but very low interfacial tension has been found to cause instability (Madani and Friberg, 1978). Carefully selected surfactant type and concentration would give the desired interfacial tension. Solid particles can also be used for stabilizing an emulsion, because their presence at the interface between the two liquids creates a mechanical barrier against coalescence (Friberg and Jones, 1994).

Table 7. Criteria for Selecting Emulsifiers

- The emulsifier or combination of emulsifiers must favor the formation of an emulsion of the desired type.
- The resulting emulsion must be stable for a sufficiently long period of time, and, under various conditions that it may experience during processing, storage, and application.
- The emulsifier must be compatible with other components in the system, such that there would not be side reactions occurring in the mixture.
- The emulsifier must not be hazardous to the customer's health or to the environment.
- The cost of the emulsifier must be as low as possible.

The components should be compatible with each other. For example, an ester-type emulsifier is not suitable for a cream with high alkaline content, since hydrolysis of the ester would occur (Fox, 1974). Finally, health and safety issues should not be neglected. For example, cationic emulsifiers can be eye-irritant and are not suitable for products such as facial creams. For consumer product applications, the use of an emulsifier may be subject to government regulations, which makes the choice really limited (Lissant, 1991). Certainly, when there are several candidates meeting all the criteria, the cost becomes a factor to consider.

Surfactants can be used in a suspension to make the solid surface easier to wet, help cracking of clumps, and prevent reagglomeration of suspended particles by adsorbing on the particle surface (Nelson, 1988). A surfactant with an HLB of about 7 to 9 is suitable for use as a wetting agent (Davies and Rideal, 1961).

Determination of Product Microstructure. The rheological behavior of creams and pastes is determined by the microstructure, characterized by the phase volume fraction and droplet size distribution of the dispersed phase (Rogers, 1978). For suspensions and solid-like emulsions, where the continuous phase may be partially crystallized, the rheological behavior is mostly controlled by the fraction of solids and particle-size distribution (Narine and Marangoni, 1999).

To predict the dependence of emulsion rheological properties on microstructure, theoretical as well as semi-empirical

Table 8. Selected Models for the Prediction of Emulsion Rheological Properties

Emulsion Viscosity Dilute emulsions ($\phi < 0.62$)	$\mu_e = \mu_c \left(1 - \frac{\phi}{\phi_{\text{crit}}}\right)^{-k\phi_{\text{crit}}}$	(7)	Krieger and Dougherty (1959)
Dilute emulsions ($\phi < 0.7$)	$\mu_e = \mu_c \left[1 + \frac{(5\kappa+2)}{2(\kappa+1)}\phi + \frac{(5\kappa+2)^2}{10(\kappa+1)^2}\phi^2\right]\left[\frac{1+\lambda_1\lambda_2 N_{Ca}^2}{1+\lambda_1^2 N_{Ca}^2}\right]$	(8)	Oldroyd (1953); Pal (1995)
	$\lambda_1 = \frac{(19\kappa+16)(2\kappa+3)}{40(\kappa+1)}\left[1 + \frac{(19\kappa+16)}{5(\kappa+1)(2\kappa+3)}\phi\right]$	(9)	
	$\lambda_2 = \frac{(19\kappa+16)(2\kappa+3)}{40(\kappa+1)}\left[1 - \frac{3(19\kappa+16)}{10(\kappa+1)(2\kappa+3)}\phi\right]$	(10)	
Concentrated emulsions ($\phi > 0.74$)	$\mu_e = \frac{\tau_0}{\dot{\gamma}} + C(\phi)\mu_c N_{Ca}^{-0.5}$	(11)	Princen and Kiss (1989)
	$C(\phi) = 32(\phi - 0.73)$	(12a)	
	$N_{Ca} = \frac{\mu_c d_p \dot{\gamma}}{2\sigma}$	(12b)	
Yield Value Concentrated emulsions ($\phi > 0.83$)	$\tau_0 = \frac{2\sigma}{d_p}\phi^{1/3}Y(\phi)$	(13)	Princen and Kiss (1989)
	$Y(\phi) = -0.080 - 0.114 \log(1-\phi)$	(14)	
Complex and Shear Modulus Dilute emulsions ($\phi < 0.7$)			
	$G^* = G_c^* \left(\frac{1+3\phi H}{1-2\phi H}\right)$	(15)	Oldroyd (1953); Palierne (1990)
	$H = \frac{(8\sigma/d_p)(5G_d^* + 2G_c^*) + (G_d^* - G_c^*)(19G_d^* + 16G_c^*)}{(80\sigma/d_p)(G_d^* - G_c^*) + (2G_d^* + 3G_c^*)(19G_d^* + 16G_c^*)}$	(16)	
Concentrated emulsions ($\phi > 0.74$)	$G = 1.769\mu_c N_{Ca}^{-1}\phi^{1/3}(\phi - 0.712)$	(17)	Princen and Kiss (1986)
Crystallized continuous phase	$G = k_c \Phi^{1/(d-3)}$	(18)	Narine and Marangoni (1999)

models have been proposed. The most frequently used ones are summarized in Table 8. Droplet-size distribution is not taken into account in these models. Instead, an average droplet size such as the Sauter mean diameter (d_{32}) is typically used. It should be noted that dilute emulsions (low phase volume fraction) have a different rheological behavior compared to concentrated emulsions. The reason is that the flow behavior of dilute emulsions is controlled by the interaction between droplets, while that of concentrated emulsions is controlled by network structure of the continuous phase (Princen and Kiss, 1986). Therefore, the dilute emulsion viscosity is affected by the viscosity of the continuous phase, as well as of the dispersed phase, as reflected by the presence of viscosity ratio κ in the Oldroyd model (Eq. 8). On the other hand, the Princen-Kiss model can be written as

$$\mu_e = \mu_c \left[N_{Ca}\phi^{1/3}Y(\phi) + C(\phi)N_{Ca}^{-0.5} \right], \tag{19}$$

which is obtained by substituting Eq. 13 into Eq. 11. This equation indicates no dependence on dispersed-phase viscosity. For emulsions with the continuous phase partially crystallized, the shear modulus is given by Eq. 18. Here, d is the fractal dimension (around 2 for oils and fats) and k_c is an empirical constant depending on the size of the primary particles and the interactions among them (Narine and Marangoni, 1999).

Shear-thinning behavior in a dilute emulsion or suspension can be a result of droplet or particle flocculation at low shear (McClements, 1999). Due to the forces holding the particles together, the emulsion viscosity is relatively high. If the shear rate is increased, the flocs are disrupted and the viscosity decreases. In a dilute suspension of nonspherical particles, particles rotate freely in all directions at low shear rates, but become aligned at high shear rates (McClements, 1999). This can cause the suspension to exhibit shear-thinning behavior.

In general, the viscosity of a suspension decreases with increasing shear rate (Barnes, 1989). Beyond a critical shear rate $\dot{\gamma}_{\text{crit}}$, significant shear-thickening due to particle interactions is observed. An estimate for $\dot{\gamma}_{\text{crit}}$ can be obtained from a comparison of interparticle and hydrodynamic shear forces, as suggested by Boersma et al. (1990). Shear thickening occurs when the value of the dimensionless number

$$N_d = \frac{3\mu_c d_p^2 \dot{\gamma}}{4\epsilon_r \epsilon_0 \zeta^2} \tag{20}$$

Table 9. Typical Shear Rates in Processing and Application of Creams and Pastes

Action	*Shear rate, $\dot{\gamma}$ (s^{-1})*
Suspending pigment or active ingredients	$10^{-3} - 10^{-1}$
Pouring from a bottle	$5 \times 10^1 - 10^2$
Extrusion from a bottle or tube	$10^1 - 10^3$
Topical application of lotions/creams	$10^2 - 10^4$
Application of lipstick	$2 \times 10^3 - 10^4$
Application by brush	$5 \times 10^3 - 10^4$
Roller milling	$10^3 - 10^4$
Forcing through homogenizing valve	$10^3 - 10^5$
Colloid milling	$10^5 - 10^6$

is larger than unity. The internal phase (solid) volume fraction ϕ has a significant effect on $\dot{\gamma}_{\text{crit}}$. The prediction of $\dot{\gamma}_{\text{crit}}$ using Eq. 20 is limited to $\phi \approx 0.56$. For other values of ϕ, $\dot{\gamma}_{\text{crit}}$ is given by

$$\dot{\gamma}_{\text{crit}}(\phi_2) = \frac{f(\phi_2)}{f(\phi_1)} \cdot \dot{\gamma}_{\text{crit}}(\phi_1), \tag{21}$$

where 1 and 2 indicate the two volume fraction values and

$$f(\phi) = \left(\frac{8\pi}{3\phi\sqrt{3}} \right)^{1/3} - 2. \tag{22}$$

At very high shear rates, the suspension again behaves as shear-thinning, due to the formation of particle layers (Barnes, 1989).

When dealing with non-Newtonian fluids, it is crucial to estimate the viscosity at the actual experienced shear rate. The estimated shear rates of typical processing and application of creams and pastes are given in Table 9 (Ward et al., 1974; Laba, 1993). In an agitated vessel, the shear can be estimated as follows (Miner, 1993)

$$\dot{\gamma} = \frac{4\pi N}{1 - \left(\frac{D}{T} \right)^2} \tag{23}$$

where D and T are the impeller and vessel diameters, respectively. In a pipe, the shear rate is

$$\dot{\gamma} = \frac{4Q}{\pi R_p^3} \left(\frac{3n+1}{4n} \right) \tag{24}$$

where Q is the flow rate of fluid through the pipe and R_p is the pipe radius.

Microstructure also has an effect on other performance indices such as smoothness, opacity, and stability. An emulsion containing very small droplets (about 1–20 μm for cosmetic and pharmaceutical applications) is smoother, more stable, and may be transparent (Chappat, 1994). Using the rheological models and taking into account the desirable quality factors, we target the required droplet size and phase volume fraction.

Another important issue in emulsion processing is phase inversion. There can be a range of dispersed-phase volume fraction where an emulsion can either be of type O/W or W/O, depending on the method of preparation (Smith and Wang, 1994; Norato et al., 1998). For example, an O/W emulsion formed by slow addition of the oil phase to the water phase can achieve a maximum oil phase volume fraction of ϕ_{hi} before phase inversion occurs. However, when the order of addition is reversed, the oil-phase volume fraction in the thus-formed W/O emulsion can be as low as ϕ_{lo} before phase inversion occurs. Therefore, there is a region between ϕ_{lo} and ϕ_{hi} where either type of emulsion can be formed, depending on the order of addition. This region is referred to as the ambivalence region. To produce an emulsion with a high dispersed phase volume fraction, it is desirable that the ambivalence region be wide, so that ϕ_{hi} is higher. This region can be widened by decreasing interfacial tension or in-

Table 10. Heuristics for Synthesis and Development of Cream and Paste Manufacturing Processes

Synthesis of Flowsheet Alternatives

- Use pre-mixing steps to combine compatible ingredients, if water-soluble and oil-soluble ingredients are involved.
- Use size reduction equipment to reduce the particle size of the insoluble ingredients to the desired size.
- Use a homogenization step to produce an emulsion with droplet size below 100 μm.
- Heat up the process mixture during processing in order to reduce viscosity and thus facilitate mixing.
- Consider changing the order of phase combination or the surfactant location, if phase inversion becomes a problem.
- Perform homogenization prior to cooling, if it is desired to reduce the droplet size as much as possible, but still have a viscous final product (Bornfriend, 1978).
- Perform homogenization after cooling, if it is desired to permanently reduce the viscosity of the final product (Bornfriend, 1978).
- Consider using the low energy emulsification technique (mixing the dispersed phase into a portion of the continuous phase (C_1), and adding the rest of the continuous phase (C_2) after emulsification), if the dispersed phase volume fraction is less than 30%.
- If a thickener is involved, it should be dispersed in phase C_2 (Lin, 1978).
- Place post-treatment units that are only applicable to liquid, such as a sterilization unit, before crystallization.

Selection of Equipment Units

- Select equipment in the order of increasing energy consumption.
- Use a static mixer or an agitated vessel to mix separate phases to form a pre-emulsion.
- Use a ribbon mixer or planetary mixer to form a suspension with a high solids volume fraction.
- Choose an equipment unit without dead or stagnant zones, such as an agitated vessel with scraper, if the emulsion is sensitive to heating or cooling.
- Do not use an emulsification unit in which breakup occurs in a shear flow, such as a colloid mill, if the viscosity ratio between the dispersed and continuous phase is greater than 4 (Stein, 1996).
- Do not use a colloid mill if the viscosity of the continuous phase is less than 0.02 Pa·s (Schubert and Armbruster, 1992).

Selection of Feed Addition Policy

- The dispersed phase should be added slowly to the continuous phase.
- Ingredients that may interfere with the mixing step or may be destroyed during processing should be added last.
- Consider using phase inversion if it is desired to produce an emulsion with low dispersed phase volume fraction (less than 0.26) and a small droplet size.
- If surfactant migration from one phase to another can produce an undesirable change in product viscosity, consider distributing the surfactants between phases according to their solubilities.

Selection of Equipment Operating Conditions

- Prefer a propeller with high impeller-to-vessel diameter ratio (D/T) to achieve a more uniform shear rate distribution within the vessel, if the emulsion is highly viscous and shear-thinning (Miner, 1993).
- Do not use prolonged stirring if it can cause an irreversible reduction in product viscosity.
- Avoid mixing operation in which the impellers are not completely submerged, to minimize incorporation of air into the product (Krishnaswamy and Parker, 1984).
- For crystallization of the continuous phase, use slow cooling to obtain large and uniform crystals.
- If contamination of the product should be avoided during a processing stage, the equipment should be pre-sterilized and the operation should be performed under aseptic condition.

creasing continuous phase viscosity, while density has been found to have little effect (Norato et al., 1998).

Step 3: design of manufacturing process

After deciding on the ingredients and product microstructure, we proceed to design the manufacturing process. This step involves three key issues. First, a process flowsheet that can produce a product with the desired microstructure is synthesized. Second, appropriate equipment units are chosen. Finally, the feed addition policy and equipment operating conditions are selected. Again, only a rough estimate can be obtained using simple models discussed here. Table 10 provides some heuristics to assist decision-making in this step.

Synthesis of Flowsheet Alternatives. The flowsheet for creams and pastes manufacturing processes usually consists of only a few unit operations. Note that for batch processes, the flowsheet should be interpreted as a series of sequential actions. Figure 1 shows a generic flowsheet for these processes. If incompatible ingredients are involved, they are mixed separately to form the oil and water phases in the pre-mixing units. Insoluble solid ingredients may need pretreatment such as size reduction or surface modification before being dispersed into the liquid. The separate phases are then mixed in the mixing unit where one phase is dispersed as droplets in the other phase to form a pre-emulsion with relatively large droplet sizes. A subsequent homogenization step is often necessary to reduce the droplet size so that the target is met. Normally, the process up to this stage is performed at an elevated temperature (70–80°C) in order to minimize viscosity and hence facilitate mixing. The mixture is cooled back to room temperature either before or after homogenization. Heat-sensitive ingredients are added after the temperature is dropped to about 40–50°C. An alternative is to use the low energy emulsification technique (Lin, 1978; Lin and Shen, 1984; Reng, 1986), where only a part of the continuous phase is heated to the emulsification temperature. The rest of the continuous phase is added after a concentrated emulsion is formed. Compared to the standard technique, considerable savings in mechanical energy (for agitation), as well as thermal energy (for heating and cooling), can be realized using this technique. However, the technique is not suitable for producing emulsions with high internal phase volume fraction due to difficulties in initial mixing and danger of phase inversion.

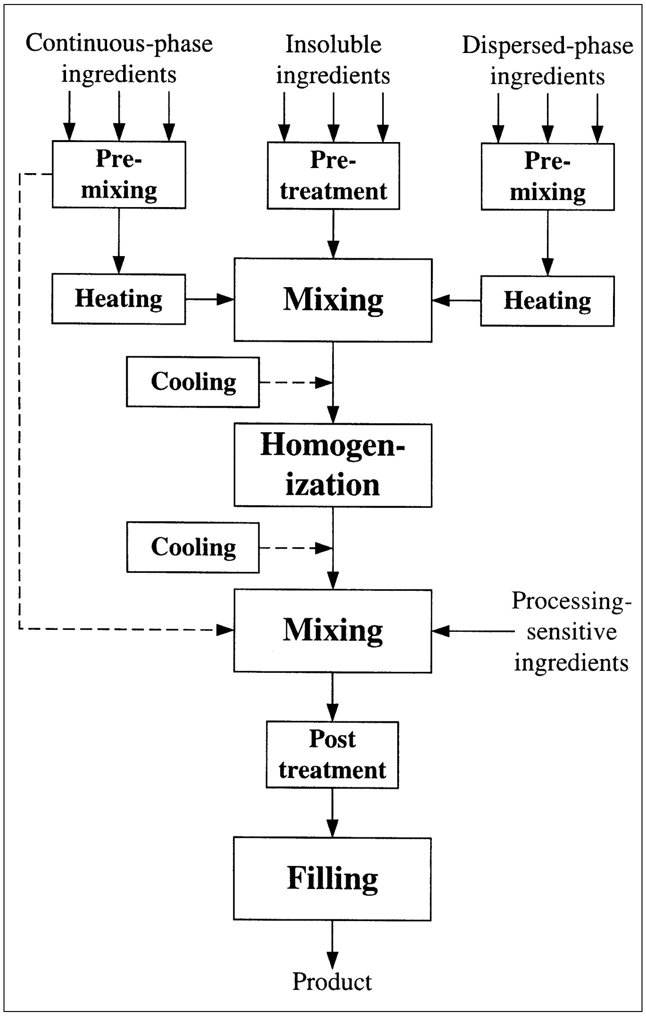


Figure 1. General structure of creams and pastes manufacturing process.

Table 11. Selected Equipment for Emulsification in Manufacturing Creams and Pastes

Equipment	*Breakup Mechanism*	*Batch/ Cont.*	*Design and Operating Variables*
Pre-emulsification			
Pipeline mixer	Turbulent shear	B, C	Pumping velocity
Agitated vessel	Turbulent shear	B	Agitation speed Vessel geometry
Ribbon mixer	Turbulent shear	C	Agitation speed Impeller geometry
Planetary mixer	Turbulent shear	C	Agitation speed Impeller geometry
Homogenization			
Colloid mill	Laminar/turbulent shear	B, C	Rotational speed Gap width
Tooth disc disperser	Turbulent shear	B, C	Rotational speed Gap width
Pressure homogenizer	Turbulent shear/cavitation	B, C	Homogenizing pressure
Ultrasonic homogenizer	Cavitation	C	Ultrasonic wave frequency and intensity

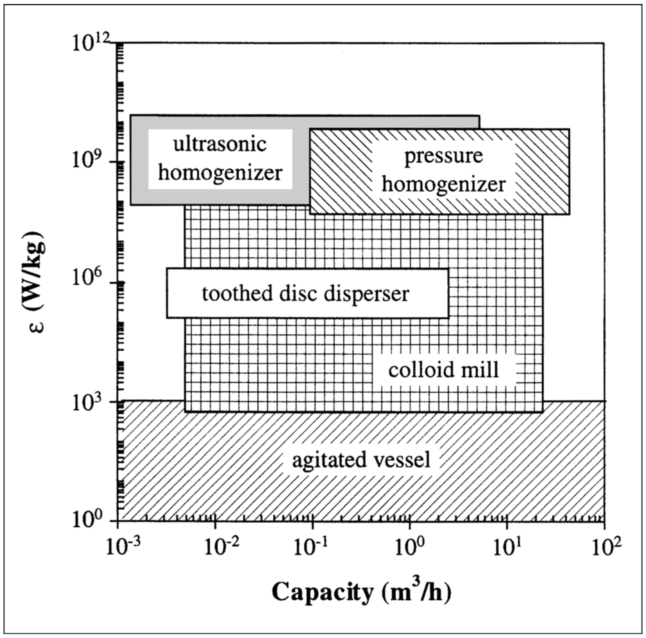


Figure 2. Typical capacity and energy consumption for selected emulsification units.

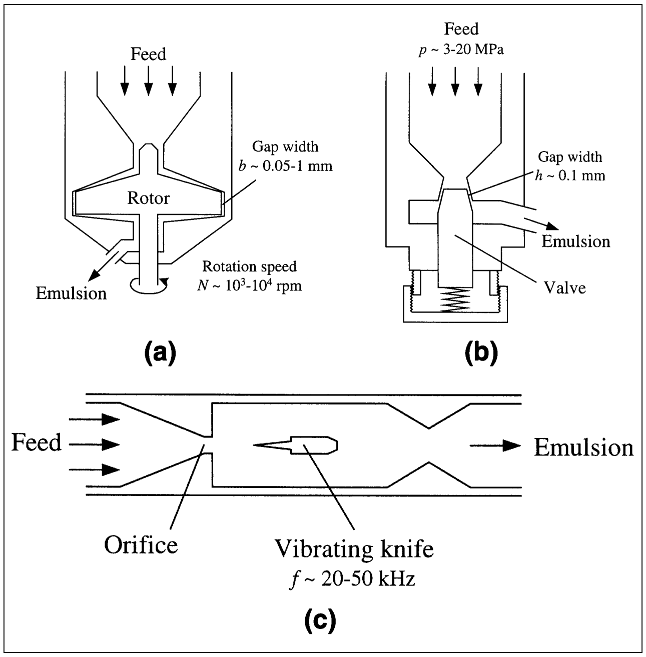


Figure 3. Selected equipment for homogenization in the manufacture of creams and pastes:

(a) Colloid mill; (b) pressure homogenizer; (c) ultrasonic homogenizer.

A post-treatment step may be necessary for some products. Sterilization is necessary in the production of pharmaceuticals prepared for oral administration. If the final product is a semi-solid, a chilling unit is added to perform crystallization or gel formation. The last step is filling the product to appropriate containers. Although this step seems trivial, it requires special attention because the final product is usually very viscous, thus imposing a high yield stress to the equipment.

Selection of Equipment Units. Selection of unit operations in the flowsheet should be accompanied by equipment selection. The typical equipment units used in consumer product manufacturing processes are summarized in Table 11 (Schubert and Armbruster, 1992; Ford et al., 1997; McClements, 1999; Myers et al., 1999). Typical capacity and energy consumption for selected units are depicted in Figure 2. The energy consumption per unit mass increases from top to bottom in Table 11. For premixing, preemulsification, and dispersion of solids into liquid, an agitated vessel is normally used. When the proportion of solids in the mixture is high, such as in a paste, a special mixer (for example, a planetary mixer or a ribbon mixer) may be necessary. Vacuum mixers may be needed if foaming or bubble inclusion in the product is to be avoided (Scott and Tabibi, 1996).

Figure 3 depicts three typical equipment units for homogenization. In a colloid mill (Figure 3a), droplet breakage is achieved by elongation and shear in laminar flow, such that the droplet burst into several child droplets. Colloid mill is not suitable if the viscosity ratio is too high, because the droplets would behave like rigid spheres and rotate instead of break. Another unit such as a homogenizer, which induces breakage by turbulence, must be used in this case. The energy dissipated by the high fluid velocity creates eddies and generates high shear. In the pressure homogenizer (Figure 3b), the feed is forced to pass through a narrow valve by the application of a high pressure. In an ultrasonic homogenizer (Figure 3c), the feed flows through an orifice and impinges on a sharp-edged knife. The impact causes the knife to rapidly vibrate and generate an intense ultrasonic field which breaks up the droplets (McClements, 1999). Compared to the colloid mill, homogenizers can produce smaller droplets, but are more energy-intensive. In practice, they are often used in combination with an agitated vessel (Myers et al., 1999).

Selection of Feed Addition Policy. In the preparation of emulsions, feed addition in the initial mixing stage is often an important factor in determining the type of pre-emulsion formed. The most common way is addition of dispersed phase to continuous phase. If the dispersed phase volume fraction is high, typically above 74%, it is the only way. For dispersed volume fractions of 30−70%, the order of addition has little effect on final emulsion viscosity (Mitsui et al., 1966). An alternative method to prepare an emulsion with low dispersed phase volume fraction (less than 26%) is phase inversion. The continuous phase is added to the dispersed phase, such that an emulsion of the reverse type will initially be formed. At high volume fraction, the continuous phase becomes a network of thin films, and finally bursts into small droplets. Emulsions prepared this way usually contain very small droplets.

The rate of addition can have an impact on emulsion type if the phase composition of the emulsion lies within the ambivalence region, and phase inversion is undesirable. Adding the dispersed phase slowly gives time for the undesirable emulsion droplets to coalesce, so that a particular emulsion type would be preferred (Weiser, 1949). In the preparation of suspensions, the rate of addition of solid particles must be

Table 12. Equations for Breakup and Coalescence in Emulsion and Suspension Formation

	Laminar Flow		*Turbulent Flow*	
Weber number (Walstra, 1983)	$N_{We} = \frac{\dot{\gamma}\mu_c d_p}{2\sigma}$	(27)	$N_{We} = \frac{C_3\,\rho_c\,\epsilon^{2/3} d_p^{5/3}}{4\sigma}$	(28)
Adsorption time (Walstra, 1983)	$\tau_{\text{adsorption}} = \frac{20\Gamma}{d_p m_s \dot{\gamma}}$	(29)	$\tau_{\text{adsorption}} = \frac{10\Gamma\mu^{1/2}}{d_p m_s\,\rho_c^{1/2}\epsilon^{1/2}}$	(30)
Collision time (Walstra, 1983)	$\tau_{\text{collision}} = \frac{\pi}{8\phi\dot{\gamma}}$	(31)	$\tau_{\text{collision}} = \frac{d_p^{2/3}}{15\phi\epsilon^{1/3}}$	(32)
Drainage time (Tsouris and Tavlarides, 1994)	—		$\tau_{\text{drainage}} = \frac{40.84\mu_c\,\xi}{\rho_c\,\epsilon^{2/3} d_p^{2/3}}$	(33)
			$\xi = 1.872\ \ln\,(0.2295\kappa + 1)$ $+ 0.127\ \ln\,(1.0136\kappa + 1)$	(34)
Fragmentation number (Hansen et al., 1998)	$N_{Fa} = \frac{3\pi\mu_c \dot{\gamma} d_p^3}{4A}$	(35)	$N_{\text{Fa}} = \frac{0.485\rho_c^{1/2}\mu_c^{1/2}\epsilon^{1/2} d_p^3}{A}$	(36)

such that sufficient time is available for wetting the particles, so that they would not form clumps with dry cores.

Product viscosity can be significantly affected by surfactant initial location. Placing all the surfactant in the aqueous phase would lead to the formation of an O/W emulsion with fine droplet size (Lin, 1968). On the other hand, if surfactant migration from one phase to another can produce an undesirable change in product viscosity, it is suggested to prevent such migration by distributing the surfactants between phases according to their solubilities. When two or more emulsifiers are used, it is a common practice of placing one emulsifier in the continuous phase and the other one in the dispersed phase. For example, by putting one emulsifier in the water phase and the other in the oil phase, an O/W emulsion with a very high volume fraction (up to 80%) of the oil phase can be produced without phase inversion taking place.

The effect of surfactant initial location on emulsion type can be explained using the argument that the ratio of coalescence rates (Eq. 5) depends on the distribution of surfactant between oil and water phases (Davies and Rideal, 1961)

$$\frac{r_2}{r_1} = \frac{C_2}{C_1}\left(\frac{c_w}{c_o}\right)^{0.75\theta}, \tag{25}$$

where c_o and c_w is the concentration of the emulsifier in the oil and water phases, respectively. Equation 25 can be combined with Eq. 6 to obtain

$$\text{HLB} = 7 + 0.36\ln\left(\frac{c_w}{c_o}\right). \tag{26}$$

If the rate of surfactant migration is relatively slow, the values of c_o and c_w in the final product are close to the initial surfactant concentration in the oil and water phases (before they are mixed). Therefore, for such a situation, the HLB of a surfactant can take different values depending on the initial distribution of the surfactant.

Selection of Equipment Operating Conditions. To relate the product microstructure with equipment operating conditions, we should examine the physical processes governing the dispersion formation. Table 12 summarizes the proposed models for linking various quantities relevant to emulsion or suspension formation with operating conditions and physical properties.

For emulsions, we need to consider two opposing phenomena: droplet breakup and coalescence (Walstra, 1983, 1993; McClements, 1999). In pre-emulsification, the bulk oil and water phases break and intermingle so that relatively large droplets are formed. In homogenization, larger droplets are disrupted into smaller ones. Nevertheless, both phenomena can be approached in the same way. The occurrence of droplet breakup depends on the balance between the disruptive forces generated by the equipment, which tend to pull the droplet apart, and the interfacial forces, which tend to keep it intact. Breakage occurs when the ratio between them, the Weber number (N_{We}), exceeds a critical value. The critical value of N_{We} above which droplet breakup occurs depends on the viscosity ratio of the dispersed and continuous phase (Bentley and Leal, 1986; Groeneweg et al., 1994). For laminar flow, there is a maximum viscosity ratio above which breakup by laminar shear flow is virtually impossible. This maximum ratio has been confirmed both theoretically and experimentally to be around 4 (Stein, 1996). Equation 27 defines the Weber number for laminar flow. In turbulent flow, droplet disruption is caused by large shear and pressure gradients associated with intermediate-size eddies generated in the fluid (Walstra, 1993). This can be represented by the local turbulence energy dissipation rate ϵ. For isotropic turbulence, the expression for Weber number is given by Eq. 28 (Karbstein and Schubert, 1995). The constant C_3 in this equation is of order unity for the critical Weber number (McClements, 1999).

Due to the highly dynamic nature of an emulsion, droplets move around and frequently collide with each other. When they do, they can coalesce and form a larger droplet unless they are surrounded by a layer of surfactant molecules which prevents coalescence. Disruption of a droplet is always followed by the formation of new surfaces, with an insufficient amount of emulsifier to protect the newborn droplets from coalescing with each other. Therefore, coalescence is determined by the time for surfactant migration and adsorption in the newly formed surfaces, as compared to the time interval between collisions. Coalescence is averted when $\tau_{\text{adsorption}}/\tau_{\text{collision}} \ll 1$. The adsorption and collision times are inversely proportional to the shear rate in laminar flow (Eqs. 29 and 31), so their ratio is independent of shear. In turbulent flow, the ratio $\tau_{\text{adsorption}}/\tau_{\text{collision}}$ decreases with increasing power input, as it is proportional to $\epsilon^{-1/6}$ (Eqs. 30 and 32). Based on these equations, the required shear rate (or energy dissipation rate in turbulent flow) to produce an emulsion with a particular droplet size can be estimated.

There is another mechanism preventing coalescence in turbulence flow, which becomes important at relatively large droplet sizes (Tsouris and Tavlarides, 1994). When two droplets approach each other, a thin film of liquid (the continuous phase) can be trapped between the droplets (Shinnar, 1961). Unless sufficient time is allowed for the liquid to drain, the droplets are not likely to coalesce. In other words, coalescence is prevented when $\tau_{\text{drainage}}/\tau_{\text{collision}} > 1$. An estimate for drainage time is given by Eq. 33. This criterion becomes insignificant when the breakup criterion is met, in which case the droplet size would be controlled by breakup.

For suspensions, we deal with the prevention of aggregation of primary solid particles to form clumps, or the destruction of such clumps if formed. The viscous shear stress that tends to pull the particles apart can be compared with the aggregate strength, which in turn depends on the attraction forces between the particles. The ratio is the fragmentation number N_{Fa} the value of which should be greater than unity for the aggregate to break (Hansen et al., 1998). Assuming the London-van der Waals forces to be the primary attraction force, N_{Fa} is defined as in Eq. 35. For turbulent flow, it can be expressed as a function of ϵ, as in Eq. 36.

Finally, the shear rate or power density can be related to equipment design and operating conditions. Pertinent design equations are summarized in Table 13. In agitated vessels, the average power density is related to the dimensionless power number N_P, which in turn depends on the agitation Reynolds number N_{Re}, and impeller geometry. The required blending time t_b is also a function of N_{Re}. Charts showing the dependence of both N_P and t_b on N_{Re} for various types of impeller geometry can be found in the literature (Oldshue, 1983; Walas, 1988). The constant C_4 in Eq. 37 depends on the vessel geometry. For example, for a cylindrical vessel with diameter T and height H, its value is given by

$$C_4 = \frac{4}{\pi}\left(\frac{D}{T}\right)^2\left(\frac{D}{H}\right). \tag{44}$$

The turbulence energy dissipation rate in an agitated vessel is usually not uniform. Since droplet breakup mainly occurs in the most intense turbulence energy dissipation region, such as near the impeller tip, the maximum value of ϵ should be used instead of the average power density ϵ_{av}. The value of $\epsilon_{\max}/\epsilon_{\text{av}}$ is around 100 (Zhou and Kresta, 1998). If solid particles are involved, it is important to make sure that they are suspended completely and do not sink to the bottom of the vessel. The most commonly used correlation for critical impeller speed for complete suspension is the one proposed by Zwietering (1958) (Eq. 40). In this equation, C_5 is a dimensionless constant which depends on vessel and impeller geometry, and X is the weight fraction of solids in the suspension.

In colloid mills, the shear rate depends on the rotational speed, rotor radius, and the gap width between the stator and the rotor. Taylor instabilities may occur in a colloid mill when the value of the Taylor number, defined in Eq. 42, exceeds a critical value of about 41.2 (Kaye and Elgar, 1958). Under this condition, the resulting emulsion has an almost constant droplet size, regardless of the shear rate (Schubert and Armbruster, 1992). In pressure homogenizers, the average value of energy dissipation rate depends primarily on the homogenizing pressure, as shown in Eq. 43. This equation is derived by assuming proportionality between the potential energy due to the homogenizing pressure and the kinetic energy of fluid elements passing through the valve (Dickinson, 1994). Based on typical working parameter values, the constant C_6 is estimated to be about 10^{-2}.

The operating conditions of the heat exchanger in the chilling step are crucial for emulsions with the continuous phase partially crystallized. To obtain the desired texture, the cooling rate must be such that the crystals have the right size. Generally, slow cooling generates uniform, large crystals, while rapid cooling leads to relatively small, polydisperse crystals. Crystallization kinetics can be used to provide an estimate of the crystal-size distribution for such a melt crystal-

Table 13. Design Equations for Selected Equipment Units

Equipment	*Design Equations*		*Ref.*
Agitated vessel	$\epsilon_{\text{av}} = C_4 N^3 \mathrm{D}^2 N_P$	(37)	Zwietering (1958), Zhou and Kresta (1998)
	$N_P = N_P(N_{Re}, \text{geometry})$	(38)	
	$t_b = t_b(N_{Re}, \text{geometry})$	(39)	
	$N_{CS} = C_5\left(\frac{\mu}{\rho_L}\right)^{0.1} d_p^{0.2}\left[\frac{g(\rho_S - \rho_L)}{\rho_L}\right]^{0.45} D^{-0.85} X^{0.13}$	(40)	
Colloid mill	$\dot{\gamma} = \frac{2\pi N R_r}{b}$	(41)	Wieringa et al. (1996)
	$N_{Ta} = \frac{2\pi N \rho_e R_r^{1/2} b^{3/2}}{\mu_e}$	(42)	
Pressure homogenizer	$\epsilon_{\text{av}} = \frac{C_6 p^{3/2}}{h \rho_e^{3/2}}$	(43)	Dickinson (1994)

Table 14. Typical Deviations from Target Quality Factors and Possible Remedies

	Possible Modifications				
Problem	*Disp. Phase Vol. Frac.*	*Particle or Droplet Size*	*Emulsifier Conc.**	*Thickener Conc.**	*Others*
Viscosity is too high	Decrease	Increase	Decrease	Decrease	Use wider or bimodal PSD
Viscosity is too low	Increase	Decrease	Increase	Increase	Use narrower PSD
Shear-thinning behavior is not strong enough	—	Decrease	Increase	Increase	Use nonspherical particles
Product exhibits shear-thicknening behavior	Increase	Decrease	—	Decrease	Use wider or bimodal PSD
Product is too thixotropic	—	—	—	—	Use a different rheological additive
Shear modulus is too high	Decrease	Increase	Decrease	Decrease	Decrease solid volume fraction
Shear modulus is too low	Increase	Decrease	Increase	Increase	Increase solid volume fraction
Phase inversion occurs	—	—	Increase	Increase	Add the dispersed phase more slowly Reduce agitation

*Instead of modifying emulsifier or thickener concentration, there is always the option of using a different emulsifier or thickener.

lization process, but experimental data is required for parameter estimation.

Step 4: product and process evaluation

The base-case product and process resulting from the procedure above need to be evaluated using bench-scale equipment. Any deviation from the target quality factors specified in Step 1 and the necessary modifications to meet the objectives are identified. The physical models described in Step 3 are again used to provide insights as to what changes are necessary.

At this point we also need to examine the stability of the product. According to the DLVO theory, colloid stability is determined by two opposing effects: the London-van der Waals attraction and the electrical double layer repulsion. Quantitatively, the total interaction energy from these two sources can be expressed as (Gregory, 1993)

$$V_{\mathrm{tot}} = \pi \epsilon_r \epsilon_0 d_p \psi_0^2 \exp(-\lambda z) - \frac{A d_p}{24 z}. \tag{45}$$

The Stern potential ψ_0 cannot be measured and is approximated by the readily-measured zeta potential. When this total energy is plotted against separation distance, a typical curve with a maximum is obtained. Typically, an emulsion or suspension is stable if the height of this maximum is about 20 kT, where k is the Boltzmann constant (Lissant, 1991). A zeta potential of about −40 to −100 mV generally corresponds to a stable emulsion, but experimental testing is recommended (Moses and Ng, 1985). Since it is often impractical to conduct stability tests comparable in length to the product shelf life, accelerated tests, such as storage at elevated temperatures and repeated exposure to freeze-thaw cycles, are often used (Breuer, 1983).

Table 14 suggests some possible modifications to rectify typical problems. If the viscosity of the emulsion is too high (low), we can adjust the thickener concentration, decrease (increase) the dispersed phase volume fraction (Eqs. 7 and 8), or increase (decrease) the capillary number (Eq. 11). If the emulsion is not sufficiently shear-thinning, we can increase the relative magnitude of attraction between particles to the hydrodynamic forces, such that flocculation occurs at low shear. Comparison of forces acting on particles (Wibowo and Ng, 2001) reveals that this can be achieved by reducing particle size. Shear-thickening can be avoided by decreasing particle size or continuous phase viscosity, since these would increase the critical shear rate (Eq. 20). Thixotropic behavior mainly depends on the properties of the rheological additive. Therefore, problems with thixotropy, as well as other viscosity-related problems, can be fixed by changing the rheological additive. If the shear modulus of the emulsion is too high (low), we can decrease (increase) the dispersed phase volume fraction or increase (decrease) the capillary number (Eq. 17). For emulsions with crystallized continuous phase, a possible remedy is to increase (decrease) the solid fraction to increase (decrease) the shear modulus (Eq. 18). Phase inversion can be avoided by widening the ambivalence region.

Conditions in commercial production can be different from the laboratory-scale experiments. Agitated vessels are often used in the pre-emulsification step. For example, if the scale-up rule of constant power density is followed, the required impeller speed would be lower in the large-scale unit compared to the small-scale unit. Consequently, the shear rate experienced by the product is lower in the large-scale unit. For a shear-thinning emulsion, the higher viscosity, if not properly anticipated, may cause problems such as imperfect blending or excessive stress to the equipment at the production scale. Another situation to consider is the shear experienced during pumping and filling to appropriate containers. Depending on the thixotropic properties of the product, excessive shear not experienced in the laboratory can cause product damage. Other issues, such as the trade-off between ease of mixing and energy savings in the application of a low-energy emulsification technique, also need to be considered.

Examples

We now present four examples to illustrate the application of the procedure in the synthesis and development of consumer and pharmaceutical product manufacturing processes.

Example 1: development of a hand lotion manufacturing process

A cosmetic company wants to produce a hand lotion, whose function is to restore and maintain the skin in a fully moisturized condition (Williams and Schmitt, 1992). Based on market research on customers' expectations, the product should be easily applicable and has to rub in quickly. In addition, it has to be smooth and does not feel oily or greasy. Hard bottles would be used as the product container. The product would flow when poured from the bottle, but should not appear runny. Production in 5-tonne batches is planned.

Step 1. To achieve the desirable fast rub-in performance, the product should have a low viscosity when applied to the skin. To achieve the desirable controlled flow upon pouring, a high viscosity at low shear is desired. Based on the heuristics in Table 4, we aim for a shear-thinning product with a viscosity of 0.025 Pa·s upon application.

Step 2. Since the main function is to protect the skin from dryness, the key active ingredient is an emollient. Oily components such as fatty acids, fatty alcohols, and long-chain esters are suitable for this purpose (Mitsui, 1997). Petrolatum, because of its high adhesive power, is used to keep the ingredients on the skin. To maintain the humidity of the lotion itself, a humectant such as glycerol is also necessary (Table 6). The high viscosity is achieved by adding a thickener. Based on company experience, carbomer (a synthetic polymer) is chosen. Carbomer is normally used in dispersed form and needs to be neutralized by a base such as KOH (Clarke, 1993). Preservatives and perfume are also necessary to make the lotion more attractive.

The fact that some ingredients are hydrophilic and others are hydrophobic calls for an emulsion as the proper delivery vehicle. To avoid the greasy feeling when the lotion is applied to the skin, we choose O/W emulsion (Table 5). An emulsifier can be selected using the criteria in Table 7. HLB calculations using data from Fox (1974) point to an emulsifier with an HLB of around 13.

In practice, a number of samples with different compositions are prepared and evaluated to determine the best formula. This is necessary because different ingredients in different amounts can serve the same function. This type of screening is beyond the scope of this article. Instead, we consider the possibility of using different amounts of the thickening agent, assuming the rest of the formula is fixed. The selection of ingredients discussed above agrees with a typical formula of a hand lotion (Williams and Schmitt, 1992), which is assumed to be the recommended formula in this example. Table 15 summarizes the composition, as well as the assumed physical and rheological properties of the continuous and dispersed phases of the emulsion. The continuous phase viscosity data are taken from Pal (1995). The dependence of viscosity on temperature is assumed to follow the Arrhenius relationship (Windhab, 1995; Rao, 1999).

Table 15. Input Information for Example 1: Hand Lotion

Continuous Phase	
Composition	
Purified water (solvent)	80–90%
Glycerol (humectant)	4–8%
Water-soluble polymers (thickener)	x_t % (variable)
Viscosity, μ_c	
K at 25°C	$9.83 x_t^{1.91}$ Pa·s
n	$0.0598 x_t^{-0.97}$
E_a	15,800 J/mol
Density, ρ_c	1,019 kg/m^3
Dispersed Phase	
Composition	
Mineral oil (solvent)	30%
Stearic acid (emollient)	12%
Cetyl alcohol (emollient)	12%
Isopropyl palmitate (emollient)	23%
Petrolatum (emollient)	23%
Viscosity, μ_d	
K at 25°C	6.54×10^{-2} Pa·s
n	1.0
E_a	17,200 J/mol
Density, ρ_d	985 kg/m^3
Emulsion	
Surfactants	
Glyceryl monostearate	80%
PEG-40 stearate	20%
Interfacial tension, σ	2×10^{-2} N/m
Excess surface concentration, Γ	1.0×10^{-6} kg/m^2
Surfactant critical micelle concentration (CMC)	30 kg/m^3
Equipment	
Colloid mill rotor radius	5 cm

Using the Oldroyd model (Table 8), we can estimate the dependence of viscosity on microstructure. In agreement with the heuristics in Table 5, the droplet size and phase volume fraction have little effect on the emulsion rheology. Therefore, the selection of their values should rather be based on other considerations such as smoothness and stability. We select phase volume fraction of 0.15 and mean droplet size of 5 μm. Thickener concentration turns out to be the dominant factor for the emulsion viscosity. Figure 4a shows the viscosity as a function of thickener concentration at two shear rates: 0.01 s^{-1}, representing the rest condition, and 1,000 s^{-1}, the estimated shear applied when the lotion is rubbed to the skin (Table 9). The results show that the desired viscosity of 0.025 Pa·s is achieved at a thickener concentration of about 1.1% with respect to the total mass of the aqueous phase). The low shear viscosity of about 400 Pa·s at this concentration is suitable for a lotion. Figure 4b shows the storage and loss moduli at $\omega = 6.28$ s^{-1}, as a function of thickener concentration. The viscoelasticity of the emulsion, as indicated by the ratio of G' to G'', increases with the amount of thickener. After fixing the thickener concentration at 1.1%, the storage and loss moduli can still be manipulated to a limited extent by varying the phase volume fraction.

Step 3. The flowsheet structure is synthesized next. Figure 5a shows a possible flowsheet alternative. Pre-mixing steps are used due to the various ingredients involved in the continuous and dispersed phases (Table 10). A pre-emulsification step followed by a homogenization step is necessary, because the required droplet size is less than 100 μm. Since the dispersed phase volume fraction is less than 30%, the possibility of using a low energy emulsification process is considered (Figure 5b). In both cases, the homogenization step has to be performed before cooling to avoid permanent reduction in product viscosity (Table 10). Agitated vessels are used for pre-mixing and pre-emulsification. Since the viscosity ratio is about 0.9, which is less than 4, a colloid mill can used for

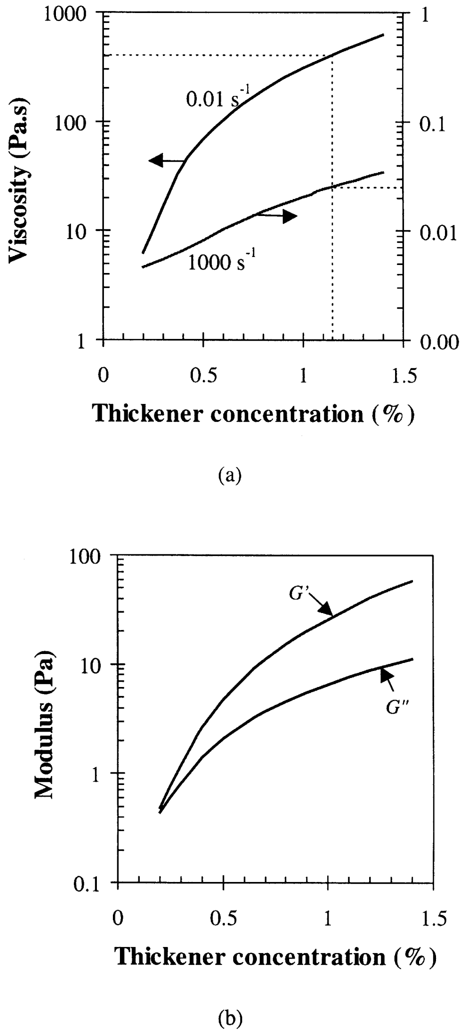


Figure 4. Estimated rheological properties of the hand lotion (Example 1).

(a) Vicosity; (b) shear and loss moduli.

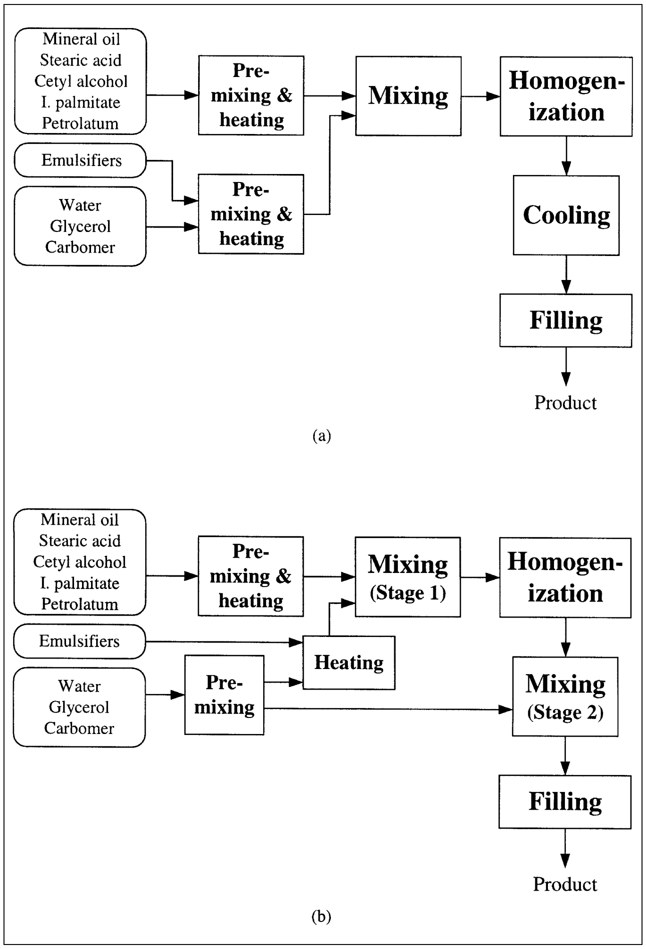


Figure 5. Alternatives for Example 1.

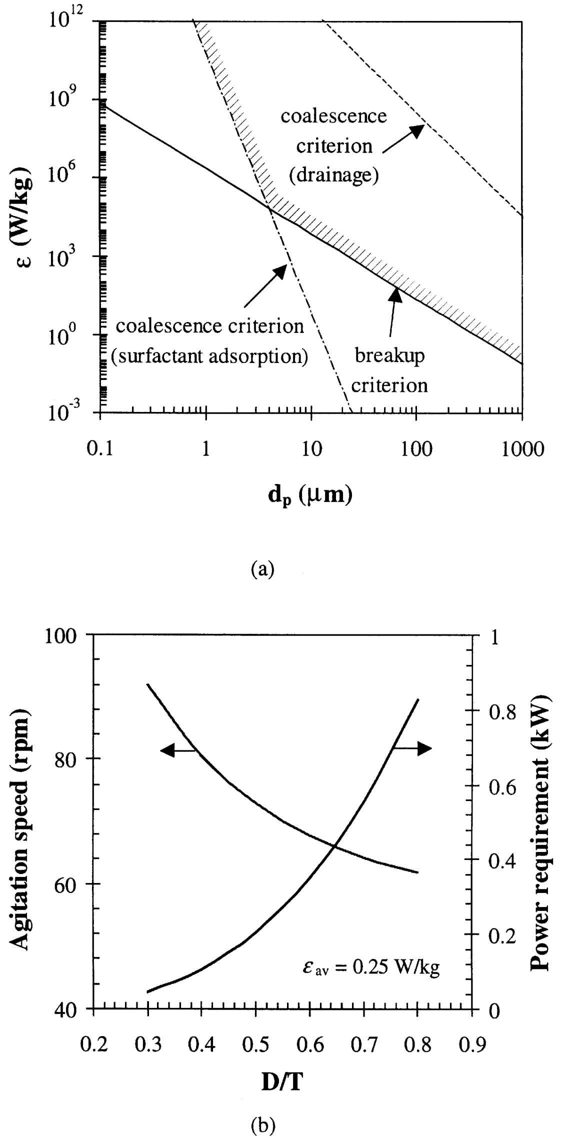
(a) Standard; (b) low-energy emulsification.

homogenization (Table 10). A colloid mill is preferred over a pressure homogenizer because of its lower cost.

An addition policy is then selected. Since an O/W emulsion is to be formed, the oil phase should be added to the aqueous phase (Table 10). If an emulsifier with an HLB of around 13 as recommended in Step 2 is used, then it should be put in the aqueous phase.

Next, we determine the equipment operating conditions. The mixing or pre-emulsification step is performed in an agitated vessel operating in turbulent flow regime. Figure 6 illustrates the breakup and coalescence criteria (from Eqs. 27–32) for turbulent flow. In the calculation, it is assumed that the amount of surfactant used is equal to the CMC. The solid line represents the breakup criterion, where the Weber number (Eq. 28) is equal to the critical value. For a given droplet size, the line indicates the minimum value of ϵ above which the droplet would break. Walstra's coalescence criterion is represented by the dashed line, which gives the maximum value of ϵ below which the surfactant adsorption to the newly formed surface is not fast enough to prevent recoalescence, even though droplet breakup may occur. Thus, when this line is located above the breakup line (that is, for droplet sizes less than 4 μm), the breakup criterion becomes meaningless. The dotted line represents the coalescence criterion obtained by comparing the collision and drainage times (Eqs. 32 and 33). In the region to the right from this line, $\tau_{\text{drainage}}/\tau_{\text{collision}} > 1$, indicating that coalescence is averted. When this line lies below the breakup line, it represents the minimum value of ϵ above which droplets of that size would not coalesce. However, this line is not meaningful when it is located above the breakup line (Shinnar, 1961), as is the case for this system. Therefore, the required value of ϵ to achieve a certain droplet size is indicated by the shaded region in Figure 6.

Assuming a pre-emulsion droplet size of 100 μm, we find from Figure 6a that the required value of ϵ is about 25 W/kg, which corresponds to an average power density of about 0.25 W/kg. We want to perform emulsification at a higher temperature for easier mixing. Considering the boiling points of the ingredients, it is decided that the temperature should not exceed 75°C. At this temperature, the necessary agitation speed with impellers having various values of impeller-to-vessel diameter ratio D/T to obtain this value of ϵ is depicted in Figure 6b. The corresponding power requirement for a 5-



(a)

(b)

Figure 6. Operating conditions for the agitated vessel (Example 1).

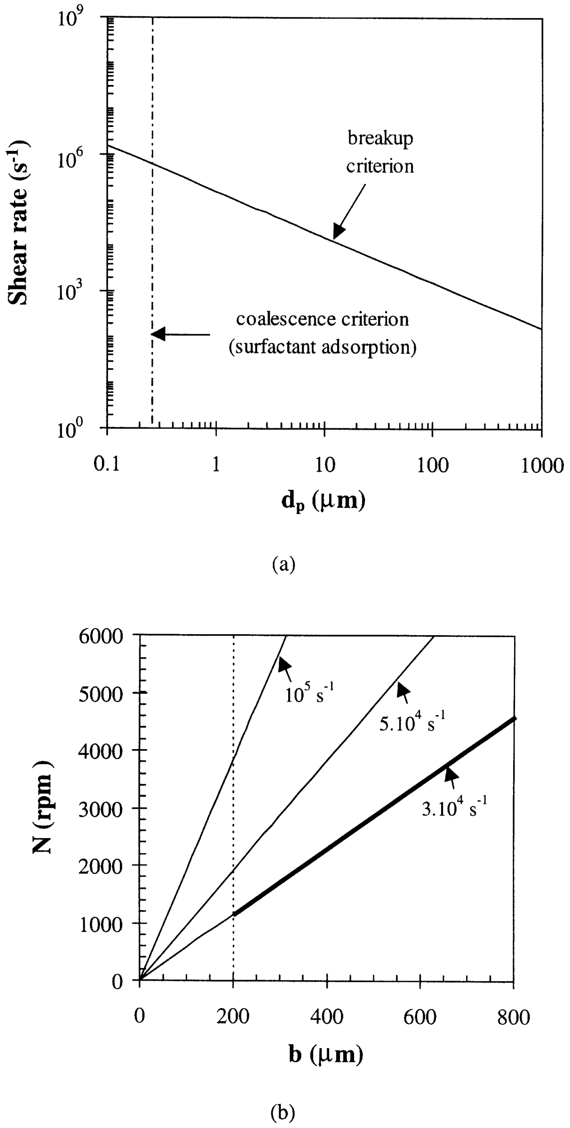
(a) Breakup and coalescence criteria for turbulent flow; (b) required agitation speed to obtain ϵ = 25 W/kg.

tonne vessel is also shown. Due to the shear-thinning property of the emulsion, it is desirable to use high impeller-to-vessel diameter ratio (Table 10). If a value of 0.8 is selected, the shear rate is estimated using Eq. 23 to be about 14 s^{-1}, corresponding to an emulsion viscosity of about 0.37 Pa·s at 75°C.

Figure 7a is used to estimate the required operating conditions for the colloid mill, which operates at the laminar flow regime. Similar to Figure 6a, the solid line represents the breakup condition. The dashed line represents the coalescence condition. In contrast to turbulent flow, the breakup line is vertical, indicating no dependence on shear rate. This is because both adsorption and collision times are inversely proportional to $\dot{\gamma}$ (Eqs. 29 and 31). To obtain droplets with a size of 5 μm, the required shear rate is about $3 \cdot 10^4$ s^{-1}. Figure 7b shows the values of the rotor rotational speed and gap width that provide the necessary shear rate, calculated using Eq. 41. It turns out that the Taylor number is always below 41.3 in this region, so that Taylor eddies are not likely to be present. The lower boundary for the gap width (dotted line) reflects the fact that the gap is seldom narrower than 200 μm in practice.

Step 4. The base-case emulsion is then produced in a 3 L bench-scale unit according to the operating conditions suggested in Step 3. The resulting product is examined to see whether the requirements are met. For illustrative purposes, three possible scenarios are now discussed along with the recommended actions to fix the problem.

Scenario 1. Viscosity measurement shows that the viscosity is lower than predicted throughout the entire range of



(a)

(b)

Figure 7. Operating conditions for the colloid mill (Example 1).

(a) Breakup and coalescence criteria for laminar flow; (b) required rotation speed and gap width to obtain the desired shear rate.

shear observed. In particular, the viscosity at 1,000 s^{-1} is only 0.01 Pa·s, indicating that the product may appear runny when applied to the skin. A possible remedy is to decrease the droplet size (Table 14). Since the droplet size is controlled by the breakup phenomenon in the colloid mill, we should increase the shear rate by reducing the gap width or increasing the rotational speed of the colloid mill (Eq. 41).

Scenario 2. The viscosity at 1,000 s^{-1} is about right, around 0.025 Pa·s. At 100 s^{-1}, the estimated shear for pouring from a bottle, the viscosity is 0.25 Pa·s. In other words, the lotion is too thin at low shear. The corresponding shear stress at pouring is about 20 Pa, which is comparable to that due to the gravity. This indicates that it may be difficult to pour the lotion from the bottle. The consumer may have to shake the bottle to get it out, and, with a relatively low viscosity at low shear, it may run out uncontrollably. Because the emulsion viscosity is dictated by the continuous phase, the problem can be fixed by adjusting the thickener concentration (Table 14). If this does not solve the problem because the viscosity at high shear may become too low, we may want to use another thickener with a different shear-thinning behavior. Another alternative is to increase droplet size, as long as other restrictions such as product stability and texture are not violated.

Scenario 3. The product takes too long to regain its original viscosity. As a consequence, it splashes out the tube and appears runny after being poured out of the bottle. Since thixotropy is typically a property of the thickener, reformulation may be necessary. A nonthixotropic thickener such as methyl cellulose is a potential substitute (Clarke, 1993).

Scale-up is considered to make sure that the desired product can be reproduced in production. Figure 8 shows the effect of scale to the required agitation speed and viscosity of the emulsion, if a constant value of ϵ should be maintained. We assume here that the viscosity of the product (as observed in the trial runs) actually matches the prediction using the Oldroyd model. To achieve $\epsilon = 0.25$ W/kg, the bench unit requires an agitation speed of 228 rpm, compared to 62 rpm in the production unit (5 m^3). Also, the viscosity of the emulsion in the small unit is only about one-third the actual product viscosity. The required blending time in the production unit is 3 times higher and the power requirement, scaling with N^3D^5, is about 1,600 times higher.

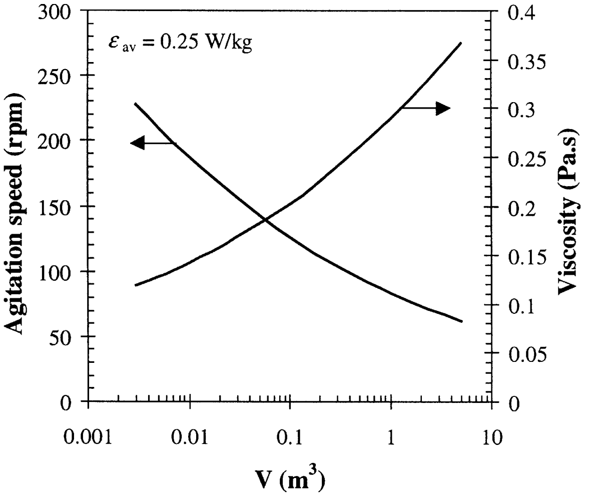


Figure 8. Effect of scale on the required agitation speed and viscosity of the emulsion at constant ϵ (Example 1).

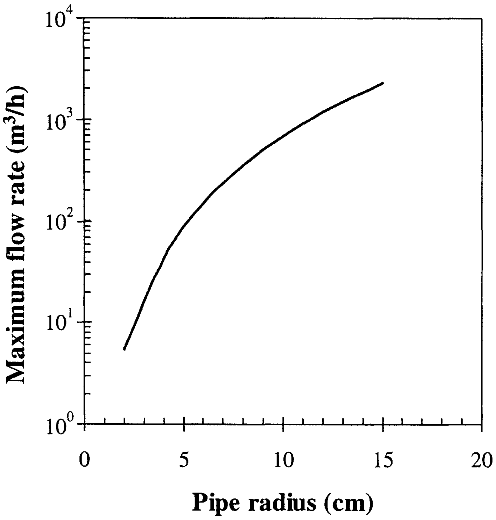


Figure 9. Estimated maximum flow rate as a function of the pipe radius (Example 1).

Let us assess the feasibility of using low-energy emulsification technique. If only 25% of the continuous phase were heated to the emulsification temperature, the dispersed-phase volume fraction of the initial emulsion would be 0.41. At an agitation rate of 62 rpm, the viscosity of this concentrated emulsion is 0.390 Pa·s, compared to 0.367 Pa·s of the original emulsion ($\phi = 0.15$). Such a small increase in viscosity corresponds to only a slight increase in power requirement and blending time. On the other hand, the thermal energy for heating decreases by 75%. Based on this assessment, the low energy technique is favored. However, before making the final decision, more tests are necessary to make sure there is no operational problem such as phase inversion.

We also need to ensure that the product is not exposed to excessive shear during processing. From measurement, it is observed that the product viscosity drops to a constant, low value after operating above a shear rate of 1,000 s^{-1}. This is an indication of structural breakdown. Using Eq. 24, we can estimate the maximum pumping flow rate above which the shear rate exceeds this limit. Figure 9 shows the estimated maximum flow rate as a function of the pipe radius.

Another important point to consider is the filling process. The product is filled to the bottles using a machine operating at 25°C, at which the shear rate is estimated to be 300 s^{-1}. The product viscosity at this shear rate is 0.1 Pa·s, with the corresponding stress of about 30 Pa. We must make sure that this stress does not exceed the strength of the pin of the filling machine, for otherwise it may break (Ward et al., 1974).

Example 2: reformulation of a massage cream

This example illustrates the use of the systematic procedure to determine the necessary modifications to an existing

Table 16. Input Information for Example 2: Massage Cream

Continuous Phase	
Composition	
Purified water (solvent)	83.2%
1,3-butylene glycol (humectant)	16%
Borax (alkali)	0.8%
Viscosity, μ_c	
K at 25°C	2.65×10^{-3} Pa·s
n	1.0
E_a	15,800 J/mol
Density, ρ_c	1,009 kg/m^3
Dispersed Phase	
Composition	
Paraffin (solvent)	65%
Beeswax (cream base)	21%
Petrolatum (emollient)	14%
Viscosity, μ_d	
K at 25°C	4.53×10^{-2} Pa·s
n	1.0
E_a	16,000 J/mol
Density, ρ_d	856 kg/m^3
Emulsion	
Surfactants	
Glyceryl monostearate	50%
POE-20 sorbitan monolaurate	50%
Interfacial tension, σ	4×10^{-3} N/m
Excess surface concentration, Γ	1.24×10^{-6} kg/m^3
Yield value	30 Pa
Viscosity at 25° and 0.03 s^{-1}	1,020 Pa·s
Mixing	
Vessel capacity	5 m^3
Agitation speed	100 rpm
Blending time	5.9 min
Power requirement	1.75 kW
Homogenization	
Homogenization pressure	20 MPa

manufacturing process to produce a new product. For years, a cosmetic company has produced a massage cream, a type of cold cream normally used as a cleansing agent for facial skin. Recently, this product (A) begins to lose market share. Market research reveals that customers have been switching to a competitor's product (C), which they claim to have a stronger cleansing effect. It is decided to reformulate the cream to increase its cleaning power. The information on the properties of product A, as well as existing operating conditions, is summarized in Table 16.

Step 1. Obviously, the desired performance is a stronger cleansing power. Since the texture and flow behavior of product A will remain the same, the droplet size of the modified cream should stay the same. In agreement with the heuristic in Table 4, the maximum viscosity of the modified product (B) should not exceed 3,500 Pa·s.

Step 2. Oily materials are used to dissolve fats and oils that often accumulate on the face (Mitsui, 1997). After analyzing the composition of both products, product C is found to contain about 85% oily components such as fatty acids, fatty alcohols, and long-chain esters, while product A contains only 75%. For this reason, the proposed solution is to increase the oily materials content to 85%. Other ingredients remain the same.

To avoid the greasy feeling upon application to the skin, an O/W emulsion is still desirable (Table 5). This means the emulsion would be highly dispersed, and it is important to use an emulsifier which can support this type of emulsion (Table 7). In particular, phase inversion should not occur. Depending on the phase behavior of the system, the increase in phase volume fraction may require a change in the emulsifier concentration, or if such a high phase volume fraction cannot be supported in the system, a different emulsifier must be chosen. For illustrative purposes, let us assume that a slightly larger amount of emulsifier is necessary, and this addition causes the interfacial tension to decrease to 3×10^{-3} N/m.

In a concentrated emulsion, the droplet size and phase volume fraction have a significant effect on the emulsion rheology (Table 5). Assuming the Princen-Kiss correlation (Eq. 19) holds, we can predict the emulsion viscosity based on the value of N_{Ca}. With a droplet size of 1 μm and an interfacial tension of 3×10^{-3} N/m, the predicted viscosity at a low shear rate (0.03 s^{-1} is about 3,000 Pa·s, which is still in the permissible range.

Step 3. Flowsheet construction and equipment selection steps are skipped in this example. We assume that there is no change to the original process, which uses an agitated vessel for pre-emulsification, followed by a pressure homogenizer. Note that the viscosity ratio is very high (about 17), so that a colloid mill would not have been suitable. Low-energy emulsification is not considered because the dispersed phase volume fraction is high (heuristics in Table 10).

Addition policy is assumed to be the same as the original. We now consider the operating conditions for the pre-emulsification step. In the original operation at 100 rpm, the value of ϵ_{av} is found to be about 0.53 W/kg. If this value is to be kept constant for the production of the new cream (B), the agitation speed has to be about 86 rpm. The emulsion viscosity at this new operating condition would be 6 times higher compared to the production of A, resulting in a blending time of about 1.5 times longer. Alternatively, if the agitation speed is kept constant at 100 rpm, the power requirement increases to 2.5 kW (33% higher than for producing A), and the blending time increases by about 25%.

The homogenization step should also be examined. Since the viscosity ratio is the same for products A and B, the value of the required Weber number should also be the same. According to Eq. 28

$$\frac{\epsilon^{2/3} d_p^{5/3}}{\sigma} = \text{constant}. \qquad (46)$$

If the droplet size is kept constant, Eq. 46 suggests that the power input must be reduced to match the decrease in interfacial tension. Since $\epsilon \propto p^{3/2}$ (Eq. 43), it is suggested that the homogenization pressure be reduced to 15 MPa. This reduction is important, because if the homogenization pressure is higher, the droplets will be smaller, causing the emulsion viscosity to increase and resulting in an undesirably thick product.

Step 4. Similar to Example 1, the base-case product is evaluated and necessary adjustments are made. The two alternatives of operating conditions (decreasing agitation speed and increasing ϵ_{av}) can be compared to come up with the

Table 17. Input Information for Example 3: Toothpaste

Composition	
Solid phase	
Silica (abrasive)	14.0%
Carboxymethyl cellulose (thickener)	0.3%
Silica aerogel (thickener)	8.0%
Polyethylene glycol (thickener)	5.0%
Liquid/aqueous phase	
Sodium monofluorophosphate (active agent)	0.8%
Sorbitol (humectant)	32.7%
Glycerin (humectant)	20.1%
Sodium benzoate (preservative)	0.1%
Dye solution (color)	0.5%
Water (solvent)	14.8%
Others	
Flavors	2.2%
Surfactant	1.5%
Aqueous Phase	
Viscosity, μ_c	0.14 Pa·s
Density, ρ_c	1,100 kg/m^3
Solid Particles	
Hamaker constant, A	8.55×10^{-20} J
Dielectric constant, ϵ_r	48.65
Density, ρ_d	1,600 kg/m^3

best option. For example, if the increase in blending time would cause an intolerable decrease in production capacity, we may prefer to increase ϵ_{av} at the cost of higher power requirement.

Example 3: manufacture of toothpaste

This example illustrates the manufacture of 5-tonne batches of a toothpaste containing a significant amount of solids. A plastic tube is used as the product container. The toothpaste should not flow by itself, but can be squeezed easily out of the tube. It should mix with water, and have a low viscosity when brushed onto the teeth. Only steps 1–3 will be discussed.

Step 1. The toothpaste should have a high viscosity with a yield value above 20 Pa, so that it appears thick and does not flow by itself (Table 4). It should also be shear thinning so that it can spread easily upon application. We also want it to be smooth and moist.

Step 2. The key active ingredient is an abrasive because the main function of the toothpaste is to remove stains from the teeth. Silica is chosen for this purpose. To enhance the cleaning ability, a surfactant such as sodium lauryl sulfate is used. Another desirable active ingredient is a fluoride compound such as sodium monofluorophosphate, which prevents dental caries (Balsam and Sagarin, 1972). To retain moisture, we need to use a humectant (Table 6). A thickener needs to be used to achieve the desired high viscosity and the shear-thinning behavior. Hydrated silica and polyethylene glycol are the most commonly used thickener for toothpaste (Williams and Schmitt, 1992). Since toothpaste is in contact with the tongue upon application, taste is an important factor affecting consumer satisfaction. Therefore, we need to use flavor. We also use color to enhance the performance, and preservative to prevent degradation by bacterial activity. Table 17 summarizes the ingredients along with some relevant physical properties.

The majority of the ingredients are water-soluble or water-dispersible, except the abrasive, which are in solid form. Therefore, the appropriate product delivery system is a suspension. No emulsifier is necessary. Iterations are often necessary to come up with the best formulation. For example, Garlen (1996) documented some case histories on efforts to achieve good toothpaste formulations.

To achieve the desired soft and smooth texture, the solid particles must be small (Table 8). An average solids particle size of 3–20 μm is generally acceptable (Williams and Schmitt, 1992). Using Eq. 20 and taking $d_p = 5\ \mu$m, it is obtained that the critical shear rate above which shear thickening occurs is about 0.4 s^{-1} for $\phi = 0.56$. For the toothpaste, $\phi = 0.273$ (Table 17), and Eqs. 21 and 22 predict a critical shear rate of about 5 s^{-1}. Shear thickening usually occurs over only an order of magnitude of shear rate, and is often followed by shear thinning (Barnes, 1989). Thus, it can be expected that upon application by toothbrush ($\dot{\gamma} \approx 10^4$ s^{-1}, Table 10), the viscosity has decreased again and shear thickening is not a problem.

Step 3. The flowsheet is shown in Figure 10. We use a pre-mixing step to mix the water-soluble ingredients as well as the water-dispersible thickeners, and add the abrasive particles at the mixing step. A size reduction unit is used to reduce the particle size of the solids to submicron size, but a homogenizer is not necessary (Table 10). An agitated vessel is sufficient for the pre-mixing. Due to the large portion of solids to be mixed in the mixing step, a ribbon mixer is used. Because of the intensive mixing of the paste in the ribbon mixer, incorporation of air into the product is likely. The ribbon mixer is operated under vacuum, followed by a deaeration step. The flowsheet in Figure 10 is in agreement with the one reported by Williams and Schmitt (1992).

Obviously, the proper feed addition policy is to add solid particles to the aqueous phase. The flavor and other minor ingredients can be added at any time since the mixture is not heated to a temperature that may cause their destruction. In the presence of surfactant, incorporation of air is much more

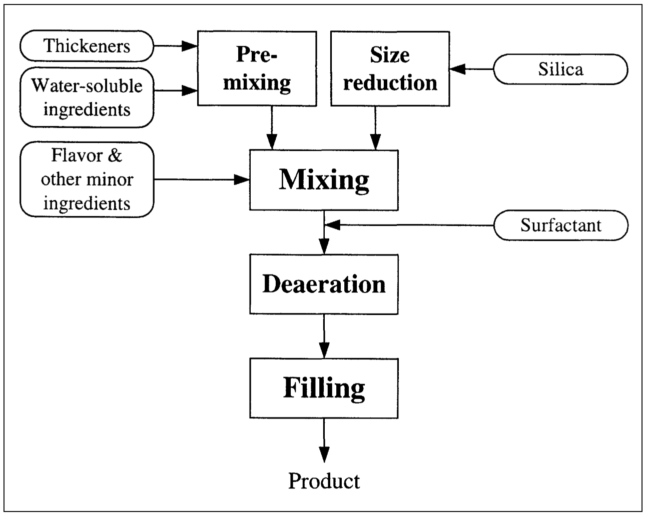


Figure 10. Toothpaste manufacture (Example 3).

likely. For this reason, sodium lauryl sulfate should be added last (Table 10), with gentle agitation to prevent foaming.

We can use Eq. 35 to predict the required shear rate to prevent the solid particles from aggregating. If we assume $\zeta = -50$ mV (stable suspension), the required value of $\dot{\gamma}$ for $d_p = 5$ μm is about 0.002 s^{-1}, which is very small. The shear rate can be related to impeller rotational speed (Ayazi-Shamlou and Edwards, 1985)

$$\dot{\gamma} = \left(34 - 144\frac{c}{D}\right)N, \qquad (47)$$

where c is the clearance between impeller tip and vessel wall. Using a typical value of $c/D = 0.07$, this leads to an estimated impeller speed of less than 0.01 rpm. This indicates that aggregation is not a concern.

Example 4: manufacture of an ophthalmic ointment

This example illustrates the manufacture of a pharmaceutical ointment for treatment of eye infections. To minimize the possibility of contamination during administration, the ointment is to be packaged in small collapsible tubes. Therefore, the ointment should be easily squeezed out of the tube. As in Example 3, we only discuss Steps 1–3.

Step 1. To assure stability, the ointment should have a high viscosity (Table 4). In fact, higher viscosity of an ophthalmic product can lead to increased contact time and pharmacological effect (Bapatla and Hecht, 1996). It should also be shear thinning so that it can flow out of the tube when squeezed. Since the eye is sensitive to particles larger than 20 μm, the particle size of the suspended drug should be about 5–10 μm.

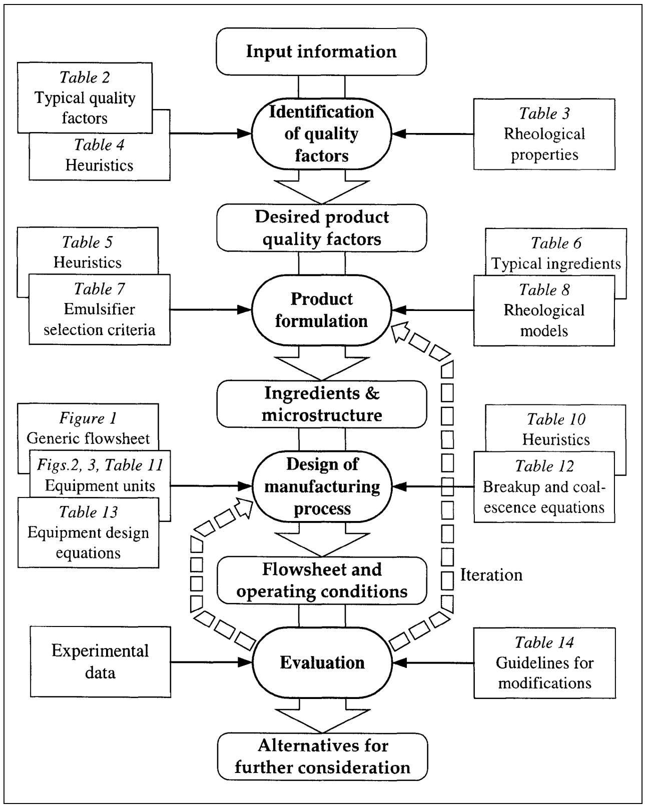


Figure 11. Systematic procedure for synthesis and development of creams and pastes manufacturing processes.

Step 2. Gentamicin sulfate, an anti-infective agent, has been selected as the active ingredient. Preservatives such as methylparaben and propylparaben are used to retard the degradation of the drug (Table 6). A thickener is used to achieve the desired high viscosity and shear thinning behavior. Because the active ingredient is unstable in an aqueous medium, a nonaqueous vehicle such as petrolatum is used (Bapatla and Hecht, 1996). Color and flavor should not be present in an ophthalmic product. Gentamicin sulfate is a solid, while the preservatives are oil-soluble. Therefore, a suspension is an appropriate product delivery system. Using an analysis similar to Example 3, we predict that shear thickening is not a problem.

Step 3. The flowsheet is similar to the one for toothpaste manufacture. A premixing step is used to mix the preservatives with molten petrolatum. The gentamicin sulfate particles is ground to the desired size in a jet mill, and then mixed with the liquid phase. An agitated vessel is sufficient for the pre-mixing, and a ribbon mixer is used in the mixing step. A homogenizer is not necessary. The order of addition is clear: the solid phase should be added to the liquid phase. Since contamination should be strictly avoided for an ophthalmic product, pre-sterilization and aseptic operation are necessary (Table 10).

Conclusions

As the global chemical processing industry redoubles its efforts on high-value-added chemicals, conventional process design is rapidly expanding into product-oriented process synthesis and development (Kind, 1999; Westerberg and Subrahmanian, 2000; Cussler and Moggridge, 2001). Synthesis underscores the importance of process conceptualization at the early stage of a business venture, whereas development signifies the need for a complementary experimental program. For such products, quality is the primary consideration and the manufacturing process demands a high degree of integration of PSE and other basic engineering sciences. We have to consider the plant and equipment scale issues, but equally importantly, the particle scale issues, since product quality is largely determined by the smaller scales. This multiscale perspective is expected to be a mainstay in product-oriented process design (Ng, 2001).

As part of an overall effort to design product-oriented processes, we have presented a systematic procedure for the manufacture of creams and pastes, the entirety of which is depicted in Figure 11. The desired quality factors are related to the product ingredients and microstructure, and then to the process flowsheet and operating conditions. Processing considerations are taken into account from the very beginning, so as to ensure successful development of the product from the laboratory to commercial production. Heuristics, as well as physical models describing relevant phenomena, are used to assist decision-making at each step of the process.

The hierarchical procedure provides the development team with a complete picture of the problem at all times, so that individual efforts can be appropriately channeled towards a faster and more effective development process. The ultimate result would be a better product, shortened time-to-market and reduced cost.

Although the emphasis of this article is on consumer products, the procedure is also applicable for other products in the form of creams and pastes. Examples include food products such as mayonnaise, salad dressings, and margarine. However, performances such as sterility and taste need to be taken into account for those products. The models and heuristics described in this article are limited to creams and pastes. The procedure can be extended to other types of product delivery systems such as concentrated solutions, microemulsions, and foams. Efforts in this direction are now underway.

Acknowledgment

Financial support from the National Science Foundation (Grant No. CTS-9908667) is gratefully acknowledged.

Notation

a = constant in Eq. 2, dimensionless
A = Hamaker constant, J
b = gap width in colloid mill, m
c = clearance between impeller tip and vessel wall, m
$C_1 - C_6$ = constants, dimensionless
d = fractal dimension, dimensionless
d_p = droplet diameter, m
D = impeller diameter, m
E_a = activation energy, $\mathrm{J \cdot mol^{-1}}$
f = vibration frequency, kHz
G = shear modulus, Pa
G^* = complex modulus of viscoelasticity, Pa
G' = storage modulus, Pa
G'' = loss modulus, Pa
h = homogenizer valve gap width, m
H = vessel height, m
k = constant in Eq. 7, dimensionless
k = Boltzmann constant
k_c = constant in Eq. 16, Pa
K = pre-exponential factor of non-Newtonian fluid viscosity, $\mathrm{Pa \cdot s}$
m_s = surfactant concentration, $\mathrm{kg \cdot m^{-3}}$
n = constant in power-law viscosity model, dimensionless
N = rotational speed, $\mathrm{s^{-1}}$
N_{CS} = critical impeller speed for complete suspension, rpm
N_{Ca} = capillary number, dimensionless
N_{De} = Deborah number, dimensionless
N_{Fa} = fragmentation number, dimensionless
N_P = power number, dimensionless
N_{Re} = Reynolds number, dimensionless
N_{We} = Weber number, dimensionless
p = homogenization pressure, $\mathrm{N \cdot m^{-2}}$
Q = volumetric flow rate, $\mathrm{m^3 \cdot s^{-1}}$
r = rate of coalescence, $\mathrm{s^{-1}}$
R_p = pipe radius, m
R_r = colloid mill rotor radius, m
t = time, s
t_b = blending time, s
t_r = relaxation time, s
T = vessel diameter, m
X = weight fraction of solids in suspension, dimensionless
x_t = thickener concentration, % (weight)
z = separation distance, m
$\dot{\gamma}$ = shear rate, $\mathrm{s^{-1}}$
Γ = excess surface concentration of surfactant, $\mathrm{kg \cdot m^{-2}}$
ϵ = turbulence energy dissipation rate, $\mathrm{W \cdot kg^{-1}}$
ϵ_{av} = average power density, $\mathrm{W \cdot kg^{-1}}$
ϵ_r = dielectric constant, dimensionless
ϵ_0 = permittivity of vacuum $= 8.85 \times 10^{-12}$ $\mathrm{C \cdot m^{-2}}$
ζ = zeta potential, V
θ = surface coverage, dimensionless
κ = viscosity ratio, dimensionless
λ = Debye length, m
λ_1, λ_2 = constants in Oldroyd viscosity model, dimensionless
μ = viscosity, $\mathrm{Pa \cdot s}$
ρ = density, $\mathrm{kg \cdot m^{-3}}$
σ = interfacial tension, $\mathrm{N \cdot m^{-1}}$
τ = time, s
τ_0 = yield value, Pa
ϕ = internal phase volume fraction
Φ = solid volume fraction
ψ_0 = Stern potential, V
ω = angular velocity, $\mathrm{s^{-1}}$

Subscripts

c = continuous phase
crit = critical
d = dispersed phase
e = emulsion
hi = upper limit
lo = lower limit
max = maximum
0 = initial value
∞ = final value

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