(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 002 882 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
17.12.2008 Bulletin 2008/51

(51) Int Cl.:
B01F 3/08 *(2006.01)* ***B01F 5/06*** *(2006.01)*

(21) Application number: **07110340.2**

(22) Date of filing: **15.06.2007**

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC MT NL PL PT RO SE SI SK TR
Designated Extension States:
AL BA HR MK RS

(71) Applicant: **Wageningen University**
6703 HD Wageningen (NL)

(72) Inventors:
- **van der Zwan, Eduard Antonius**
  6707 ER Wageningen (NL)
- **Schroën, Catharina Gerarda Petronella Henrica**
  6866 EG Heelsum (NL)
- **Boom, Remko Marcel**
  6712 CG Ede (NL)

(74) Representative: **Swinkels, Bart Willem**
Nederlandsch Octrooibureau
P.O. Box 29720
2502 LS Den Haag (NL)

Remarks:
The references to the drawings are deemed to be deleted (Rule 43 EPC 1973).

(54) Process for manufacturing an emulsion

(57) The present invention relates to a process for manufacturing an emulsion, wherein a feed comprising a dispersed phase, a continuous phase and optionally an emulsifying agent is passed through a packed bed of, preferably essentially non-compressible, particles which are essentially inert to the dispersed phase, the continuous phase and the emulsifying agent, said particles having an average particle diameter in the range of 0.1 - 1000 μm.

EP 2 002 882 A1

Description

Field of the invention

[0001] The present invention relates to a process for manufacturing an emulsion. In particular, the present invention relates to a process for manufacturing an emulsion wherein instead of a membrane a packed bed of particles is employed.

Background of the invention

[0002] Premix membrane emulsification is an emulsion manufacturing process which has received much attention (cf. Suzuki, K.; Fujuki, I.; Hagura, Y., "Preparation of corn/oil and water/corn oil emulsions using PTFE Membranes", Food Sci. Technol. Int. Tokyo 1998, 4(2), page 164). In such process, a coarse premix emulsion having large droplets and a wide droplet size distribution of the dispersed phase is forced through a membrane with pores having a diameter in the micrometer range, wherein the droplet size as well as the droplet size distribution is reduced. Advantages of this process are low energy costs and a relatively high production rate. It is therefore a good alternative for conventional emulsification methods involving high pressure homogenisers, colloid mills and rotator-stator systems. Additionally, this process is a good alternative for nonconventional emulsification methods such as cross-flow membrane emulsification and micro channel emulsification, in particular because of the high production rate. A detailed description of membrane emulsification processes is disclosed in US 2004/0152788. However, the use of membranes in emulsification processes is hampered by in-depth fouling of the pores of the membrane, in particular when biological components are used in the formulations such as proteins which may be used as stabilisers. In-depth fouling must be prevented to maintain a reasonable throughput and a reasonably narrow size distribution of the droplets so that sophisticated pretreatments, maintenance and replacement of the membranes is often necessary. However, preventing in-depth fouling is not always possible, and when possible it often involves costly procedures and harsh cleaning conditions. It therefore limits the applicability of the process.

[0003] US 2006/0102553 discloses an improvement of the membrane emulsification process, wherein the membrane is constructed from two or more superimposed layers having different pore diameters which would prevent blockage of the membrane due to its asymmetric structure. The effect of the asymmetric structure is mostly to reduce the hydrodynamic resistance of the membrane. Since the fouling components are part of the formulation, they have to pass the pores. These components will therefore still foul the membrane. Any reduction of the concentration of the fouling components by rejection or accumulation of the membrane either will alter the final product formulation, or will postpone the problems to a later stage (internal accumulation).

[0004] US 2006/0128815 discloses a method for manufacturing an emulsion, wherein a dispersed phase is forced through a membrane having one or more orifices into a continuous phase, wherein the rate by which the dispersed face is forced through the membrane is interrupted by e.g. a wire or a plate located in the vicinity of the orifice. However, also here the components have to move through the membrane pores and thus will foul an ultimately block the pores.

[0005] Therefore, the techniques disclosed in the art still suffer from fouling problems. The present invention provides a solution to these problems, wherein the system is inherently robust against fouling of pores by the product components.

Summary of the invention

[0006] The present invention relates to a process for manufacturing an emulsion, wherein a feed comprising a dispersed phase, a continuous phase and optionally an emulsifying agent is passed through a packed bed of, preferably essentially non-compressible, particles which are essentially inert to the dispersed phase, the continuous phase and the emulsifying agent, said particles having an average particle diameter in the range of 0.1 - 1000 μm.

Drawings

[0007]

Figure 1 shows a schematic representation of the apparatus used for performing the experiments.

Figure 2 shows a schematic representation of the experimental setup.

Figure 3 shows the pressure drop Δp across the filter against the flux J. The points are measured data. The grey scale indicates the number of passes: black = 1 pass, white = 6 passes.

Figure 4 shows a comparison between data obtained in conventional pre-mix membrane emulsion experiments (circled squares) and data obtained in experiments in the process according to the invention (all other symbols). The grey scale indicates the number of passes: black = 1 pass, white = 6 passes.

Detailed description of the invention

[0008] The verb "to comprise" as is used in this description and in the claims and its conjugations is used in its non-limiting sense to mean that items following the word are included, but items not specifically mentioned are not excluded. In addition, reference to an element by the indefinite article "a" or "an" does not exclude the possibility that more than one of the element is present, unless the context clearly requires that there is one and only one of the elements. The indefinite article "a" or "an" thus usually means "at least one".

[0009] The term "emulsion" is well known in the art and comprises a mixture of two immiscible liquid substances. One substance (the dispersed phase) is dispersed in the other (the continuous phase). Examples of emulsions are butter, margarine and mayonnaise. In butter, a continuous phase (comprising at least a liquid (but also solids)) surrounds droplets of water (water-in-oil emulsion). Emulsions are unstable and thus do not form spontaneously. Energy input through shaking, stirring, homogenization, spraying or other processes are needed to form an emulsion. Over time, emulsions tend to revert to the stable state of oil separated from water. Homemade oil and vinegar salad dressings are examples of unstable emulsions that will quickly separate unless shaken continuously. This phenomenon is called coalescence and happens when small droplets recombine to form bigger ones. Fluid emulsions can also suffer from creaming, i.e. the migration of one of the substances to the top of the emulsion under the influence of e.g. buoyancy.

[0010] The term "emulsifying agent" (also known as emulsifier or emulgent) is to be understood as a component that stabilises the emulsion physicochemically. Usually, they are surface active substances or detergents which increase the kinetic stability of emulsions greatly so that, once formed, the emulsion does not change significantly over storage time. In food applications, egg yolk (contains lecithine) is often used. Emulsifying agents may also stabilise the emulsion by chemical interactions, e.g. as in the removal from grease by using soap.

[0011] An important advantage of the process according to the present invention is that the packed bed of particles can be cleaned very easily. The bed is removed and resuspended by a short backflow; the individual particles can then - in suspension - be easily cleaned and re-used, or replaced by new particles. It is preferred that the particles are essentially non-compressible.

[0012] In addition, the packed bed of the particles may comprise a support, which may be porous itself, e.g. a membrane or a sieve. According to the invention, it is preferred that the packed bed comprises a support, preferably a porous or permeable support. Accordingly, it is preferred that the support is provided with apertures having a mean diameter in the range of 0.1 to 1000 μm, more preferably 1 to 100 μm and most preferably 3 to 50 μm.

[0013] According to the invention, it is further preferred that the particles have an average particle diameter in the range of 1 - 1000 μm, more preferably 1 - 500 μm. The particle size distribution of the particles is preferably such that the smallest particles do not pass the support. Preferably, the size distribution is adapted to the desired droplet size of the droplets of the produced emulsion. In general it is preferred that the standard deviation is about 0% to about 100%, more preferably about 0 to about 20 %

[0014] The invention encompasses the option of applying a number (1 - 20) of successive layers of particles, each with a smaller particle size in the flow direction; thus in effect creating a packed bed with a gradient in particle sizes.

[0015] In the process according to the present invention, a feed is employed wherein the ratio of the dispersed phase to the continuous phase (i.e. dispersed phase : continuous phase) is preferably in the range of 10^{-4} to 10^{4} v/v, based on the total volume of the feed. More preferably, this ratio is 10^{-3} to 10^{3} v/v, even more preferably 10^{-2} to 10^{2} v/v, yet even more preferably 10^{-2} to 1 v/v, yet even more preferably 10^{-2} to 0.5 v/v and most preferably 10^{-2} to 0.20 v/v, based on the total volume of the feed.

[0016] Although not explicitly necessary, it is preferred that the feed comprises an emulsifying agent, preferably in amount of 10^{-4} to 99.99 wt.% of an emulsifying agent, based on the weight of the continuous phase. More preferably, the amount of emulsifying agent is 10^{-3} to 90 wt. %, even more preferably 10^{-2} to 50 wt.%, and most preferably 10^{-2} to 10 wt.%.

[0017] According to the invention, the process can be repeated and preferably comprises 1 - 10 passes. By employing more than one pass, the droplet size and the number of droplets in the emulsion can be further changed. However, it appears that viscosity and permeation behaviour is hardly affected.

[0018] According to the invention, the feed is preferably passed through the packed bed of particles under a pressure of 100 Pa to 100 MPa, more preferably 100 Pa to 10 MPa, even more preferably 1 kPa to 10 MPa.

[0019] The pressure drop ΔP over the packed bed is given by the Ergun relation [Van 't Riet, K., *Basic Bioreactor Design,* 1st Ed., Marcel Dekker, Inc., New York, 1991]. The superficial speed V_{sl} is calculated with:

$$v_{sl} = \frac{J}{1-\varepsilon}$$

wherein J is the flux over the packed bed (in $m^3.s^{-1}.m^{-2} = m.s^{-1}$) and ε is the particle hold-up (dimensionless). The Ergun relation appears to be a good estimation for emulsions.

[0020] The flux J can be calculated from the mass flow Φ_m over the packed bed by:

$$J = \frac{\Phi_m}{\rho_l \cdot A_{col}}$$

wherein ρ_l is the density of the feed and A_{col} is the surface area of the surface of the packed bed.

[0021] It is preferred that the pressure drop Δp over the packed bed of essentially non-compressible particles is 100 Pa to 100 MPa. More preferably, the pressure drop is 100 Pa to 10 MPa and most preferably 1 kPa to 10 MPa.

[0022] According to the invention, the pressure drop

Δp over the packed bed of essentially non-compressible particles as function of the flux J is preferably between 10^4 to 10^8 Pa/m.s^{-1}, more preferably between 10^5 to 10^7 Palm.s^{-1}.

[0023] Obviously, if the packed bed comprises a support, the pressure drop over the support must be taken into account as is apparent to the person skilled in the art.

[0024] The packed bed according to the present invention can also suitably be used for separation purposes. Accordingly, the present invention also relates to a process for separating matter from a liquid phase, wherein the liquid phase is passed over (cross flow operation) or through the packed bed of particles (dead-end operation). The matter can for example be cells, macromolecules, emulsion droplets or other particulate material, wherein the matter is dispersed in the liquid phase. The liquid phase may comprise organic or inorganic liquid material.

Examples

Example 1

[0025] n-Hexadecane (99% for synthesis, MERCK) was used as dispersed phase. MilliQ water was used as continuous phase. As surfactant Tween 20 (for synthesis, MERCK) was used. The concentration was in all cases 0.5% v/w water phase. The hexadecane fraction was in all cases 5% (v/v). The premix was made by stirring the continuous phase, the surfactant, and the dispersed phase with a magnetic stirrer at -60 rpm in a 10 L flask for at least 1 day. The total volume of the premix emulsion varied between 3 and 8 liter, and in that way, a reproducible premix emulsion could be obtained.

[0026] For the particle bed, a fraction of 100HFL hydrophilic glass beads (Pneumix SMG-AF) obtained by sieving between a 53 μm and a 125 μm sieve were used. The average particle diameter (d_{43}) was measured to be 75.9 μm, and the span was 0.677. The particle density (ρ_p) and bulk density (ρ_b) were measured after sedimentation in water and found to be 2518 kg·m^{-3} and 1393 kg·m^{-3} respectively, resulting in a particle hold-up (ε) of 0.553.

[0027] Before the actual experiment started, a certain amount of glass beads (varying from 0 to 8 gram) was put in the column as depicted in Figure 1. The filter on the bottom of the reactor that prevents the glass beads from falling out was a metallic Stork Veco sieve with rectangular pores of 10 by 405 μm and a porosity of 4%. The column wall was made of Plexiglas to allow visual checking of the top surface of the glass bead bed, which is to be horizontal. The column was closed and connected to the rest of the set-up (Figure 2).

[0028] At the beginning of the emulsification experiments, the valves connected to the pressurized nitrogen vessel, the water pressure vessel, and the outlet valve of the column with the particle bed were closed. The other valves were opened. Around 300 mL of the premix was put in the emulsion pressure vessel and by raising this vessel; the hydrostatic pressure difference transported the liquid to the column. Excess air in the reactor could escape through the air outlet. As soon as the column was filled with emulsion all valves going in and out of the reactor were closed. The column was turned up-side-down 3-5 times to disperse the glass beads through the liquid. The column was then placed vertically to let the particles settle to the bottom in a few seconds time. This pre-treatment of the glass bead column lead to reproducible emulsification results, also slightly to our surprise.

[0029] The actual experiment started by pressurizing the emulsion vessel. All valves connecting the nitrogen vessel with the column were opened. The pressure was set with the valve connected to the nitrogen and read with the electronic pressure sensor (P). The outlet valve was opened and emulsification started; the homogenized emulsion was collected in a beaker on a balance connected to a computer, which recorded the mass output every second. The homogenized emulsion was recycled up to six times. The droplet sizes of the premix emulsions, and the homogenized emulsions were analyzed with the Mastersizer 2000 of Malvern. After the entire experiment, the particles were cleaned repeatedly (3-4 times) with hot water.

[0030] The obtained curves (mass flow Φ_m [kg·s^{-1}] versus time) were analyzed and only if a linear relationship was obtained the data were used for further analysis. E.g. if creaming occurs, the curves are no longer linear because the actual viscosity was not constant in time, and therefore, these data were disregarded. In total, 167 experiments qualified for the final analysis. The number of experiments per particle bed mass (m_{bed}), and number of passes (N) are shown in Table 1 together with the symbols that are used in the figures in the results and discussion section to distinguish them.

[0031] The droplet size was fitted for various pressures, mass flows, number of passes, and energy densities as described in the theory and results section. All fits were conducted with the MATLAB least square fit function (lsqcurvefit) of the Optimization Toolbox and with the Mathcad minerr function. When both fits gave the same answer the standard deviation of the fit, the standard deviation of the fit parameters, and the correlation coefficient for the parameters were calculated.

[0032] In figure 1, the reference numbers have the following meaning:

1. Outlet air
2. Screw
3. Inlet feed
4. O-ring
5. Plexiglass top
6. Plexiglass cylinder
7. Glass bead bed
8. Filter
9. Metal bottom
10. Outlet emulsified emulsion

[0033] In figure 2, the reference numbers have the following meaning:

11. Nitrogen
12. Water
13. Feed
14. Reactor with packed bed

Example 2

[0034] The process according to the invention was compared with conventional pre-mix membrane emulsification. Data for emulsion droplet diameter [μm] from pre-mix experiments (Vladisavljević et al., Langmuir 22, 4526 - 4533, 2006) as well from experiments according to the process of the present invention were plotted against energy density E_v [bar] data with:

$$E_V = \frac{P}{\Phi_V} = \frac{\Delta p \cdot \Phi_V}{\Phi_V} = \Delta p$$

wherein P is the power input [W] and Φ_v is the volume flow [$m^3.s^{-1}$]. The data are shown in Figure 4. The circled squares are from Figure 11 of Vladisavljević *et al.* (Tween 20 concentrations = 0.5 wt.%, Δp (membrane) 10^5 Pa); all other symbols are from experiments according to the invention (Tween 20 concentrations = 0.5 wt.%, $0.8 \cdot 10^5 < \Delta p$ (membrane) $< 1.2 \cdot 10^5$ Pa). The grey scale of the symbols indicates the number of passes: black = 1 pass, white = 6 passes. It appeared that the data of the premix experiments coincided with the data of the experiments of the process according to the invention.

Claims

1. A process for manufacturing an emulsion, wherein a feed comprising a dispersed phase, a continuous phase and optionally an emulsifying agent is passed through a packed bed of, preferably essentially non-compressible, particles which are essentially inert to the dispersed phase, the continuous phase and the emulsifying agent, said particles having an average particle diameter in the range of 0.1 - 1000 μm.

2. The process according to Claim 1, wherein the particles have a particle size distribution in the range of 1 to 1000 μm.

3. The process according to Claim 1 or Claim 2, wherein the packed bed comprises a number, preferably 1 - 20, of successive layers of particles, each with a smaller particle size in the flow direction.

4. The process according to any one of Claims 1 - 3, wherein the feed comprises a ratio of the dispersed phase to the continuous phase of 10^{-4} to 10^4 v/v, based on the total volume of the feed.

5. The process according Claim 4, wherein the feed comprises a ratio of the dispersed phase to the continuous phase of 10^{-2} to 0.20 v/v, based on the total volume of the feed.

6. The process according to any one of Claims 1-5, wherein the feed comprises 10^{-4} to 99.99 wt.% of an emulsifying agent, based on the weight of the continuous phase.

7. The process according to any one of Claims 1 - 6, wherein the process comprises 1 - 10 passes.

8. The process according to any one of Claims 1 - 7, wherein the feed is passed through the packed bed of particles under a pressure of 100 Pa to 100 MPa.

9. The process according to any one of Claims 1 - 8, wherein the pressure drop over the packed bed of essentially non-compressible particles is 100 Pa to 100 MPa.

10. The process according to any one of Claims 1 - 9, wherein the pressure drop Δp over the packed bed of particles as function of the flux J is between 10^4 to 10^8 Pa/m.s^{-1}.

11. Use a packed bed of, preferably essentially non-compressible, particles, said particles having an average particle diameter in the range of 0.1 - 1000 μm, in a filtration process.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 07 11 0340

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	DATABASE WPI Week 198514 Derwent Publications Ltd., London, GB; AN 1985-085392 XP002457704 -& SU 1 111 802 A (IRKUT SURVEY METHOD) 7 September 1984 (1984-09-07) * abstract * -----	1-10	INV. B01F3/08 B01F5/06
X	JP 08 057278 A (NANOMAIZAA KK) 5 March 1996 (1996-03-05) * abstract * * figure 6 * -----	1,2	
X	EP 0 022 442 A (EXXON RESEARCH ENGINEERING CO) 21 January 1981 (1981-01-21) * abstract; claims 1,11; figure 1 * -----	1,2	
A	US 3 209 554 A (JOHN MACMANUS) 5 October 1965 (1965-10-05) * column 5, line 40 - column 6, line 31; figure 2 * -----	1-10	TECHNICAL FIELDS SEARCHED (IPC)
A	US 4 511 254 A (NORTH HENRY [CA] ET AL) 16 April 1985 (1985-04-16) * abstract; figure 9 * -----	1-10	B01F

~~The present search report has been drawn up for all claims~~

Place of search	Date of completion of the search	Examiner
Munich	14 November 2007	Muller, Gérard

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons
....
& : member of the same patent family, corresponding document

2

EPO FORM 1503 03.82 (P04C01)

European Patent Office

Application Number

EP 07 11 0340

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- [ ] Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

- [ ] No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- [ ] All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

- [ ] As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

- [ ] Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

- [X] None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

  1-10

- [ ] The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

European Patent Office

LACK OF UNITY OF INVENTION SHEET B

Application Number
EP 07 11 0340

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-10

Process for manufacturing an emulsion.

---

2. claim: 11

Use of a packed bed of particles in a filtration process.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 07 11 0340

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

14-11-2007

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
SU 1111802 A	07-09-1984	NONE	
JP 8057278 A	05-03-1996	NONE	
EP 0022442 A	21-01-1981	DE 2967203 D1	11-10-1984
US 3209554 A	05-10-1965	BE 637771 A	
		CH 404381 A	15-12-1965
		DK 107533 C	05-06-1967
		ES 291951 A1	16-01-1964
		GB 978979 A	01-01-1965
		NL 298440 A	
		SE 308706 B	24-02-1969
US 4511254 A	16-04-1985	NONE	

EPO FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 20040152788 A **[0002]**
- US 20060102553 A **[0003]**
- US 20060128815 A **[0004]**

Non-patent literature cited in the description

- **SUZUKI, K. ; FUJUKI, I. ; HAGURA, Y.** Preparation of corn/oil and water/corn oil emulsions using PTFE Membranes. *Food Sci. Technol. Int. Tokyo,* 1998, vol. 4 (2), 164 **[0002]**
- **VLADISAVLJEVIĆ et al.** *Langmuir,* 2006, vol. 22, 4526-4533 **[0034]**