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**MAKING INDIVIDUAL CAPSULES BY DUAL DEPOSITION (FROM LIQUID)**

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This invention relates to a process for making minute capsules each having a particulate entity of matter as core material, and around each of which particulate core entities, individually, are made successive deposits of protective material, which deposits, together, form a wall of sufficient thickness and strength to enable such encapsulated particulate core entities each to be protected from extraordinary forces encountered in subsequent environmental contacts that without such thickness and strength would tend to cause escape or impairment of such encapsulated entities before they are required for use, and the invention relates further to capsules made by such process.

The process is peculiarly adapted to the collective and simultaneous manufacture of a multiplicity of capsules that, because of their small maximum size, cannot be handled easily, individually, by manual or mechanical means. These capsules may be large enough, when completed, to be seen by the unaided eye, or the core entities thereof may be large enough to be seen by the unaided eye, but, on the other hand, such core entities and their encapsulating walls may be of such dimensions that the completed capsule requires the use of a microscope to be seen. However, the process is chiefly adapted for use in making minute capsules just about large enough to be seen by the unaided eye. Such is not to be deemed to limit the range of sizes of the individual capsules or their core entities, as capsules have been made, by the novel process, in sizes in which the individual largest dimension of the capsules is as much as a half centimeter, but, on the other hand, capsules have been made, by the process of this invention, of which the average largest dimension is of the order of ten microns.

The process by which the capsules of this invention are made employs, as a first step, the phenomenon of the coacervate deposition of film-forming hydrophilic colloid material, from an aqueous solution thereof, around substantially water-insoluble particulate entities, dispersed in said solution, of what are to become core materials, whether such core entities are liquid or solid, or dispersions of solid particulate matter in a liquid. This first deposition step of the film-forming hydrophilic colloid material around the core entities, individually, is brought about by causing a complex coacervation of the molecules of different kinds of colloid material into units, which thus-formed colloid molecular units deposit around the dispersed particulate core material entities that are provided, up to a certain thickness, whereupon such deposition around the core material entities ceases. The thickness of this first deposition, if gelled, is not always sufficient, as regards strength, when gelled, for the purposes for which the capsules are to be used, and, therefore, the solution in which the particulate core material entities have received their first deposited capsular wall deposit is modified and rejuvenated to enable a second step of coacervate deposition around the, then, partially-completed, capsules to be made. The materials still being kept above the gelation point of the gelable colloid material first deposited, the walls are still liquid. Before the second deposition step of the process it is required that the pH of the rejuvenated aqueous solution and contents be above the coacervation region so that coacervation

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cannot occur prematurely. The rejuvenation of the aqueous solution to prepare for the second deposition is attained by supplying more film-forming hydrophilic colloid material to the solution, with the pH of the solution above the coacervation region, said added film-forming hydrophilic colloid material under these conditions again creating a potentially coacervatable condition. Coacervation is then induced, so as to form complex units, by lowering the pH of the aqueous dispersion mixture back into the coacervation region, which complex units, thus formed, then collect around the aforesaid partially-completed liquid-walled capsules to make a second deposit about each of them individually. It is to be understood that the core entity of a particular capsule consists of either a single solid particle, a single liquid droplet, or a single liquid droplet having dispersed therein material of a smaller size, and the invention does not relate to the formation of capsules having multiple capsule entities of core material therein.

In the United States Patent No. 2,800,457, which issued to Barrett K. Green and Lowell Schleicher on July 23, 1957, there has been disclosed a process for causing deposition of complex units of hydrophilic film-forming colloid material around microscopic oil droplets suspended in an aqueous dispersion medium, said deposition being caused by coacervate forces, but according to such disclosure there is only a single deposit of the complex colloid units, which single deposition constitutes the end of the first deposition step of the process of this invention.

In the product produced by the process of this invention, it is to be stressed, and will become apparent in the description to follow, that each individual core entity not only has such a first deposit of hydrophilic colloid film-forming material therearound, but has a second surrounding and coherent deposit of hydrophilic colloid film-forming material over the first deposit, which second deposit in the preferred form of the invention is somewhat different from, but is similar, in the constituents thereof, to that of the first deposit. It is also to be stressed that the capsules made by the process of this invention, by reason of such successive deposits of capsular wall material, are very strong when gelled or when gelled and dried, and the capsules for that reason may be made with relatively large core entities up to sizes visible to the unaided eye.

The core materials which are useful in the manufacture of such capsules not only differ among themselves in their physical state, which may be the solid state or the liquid state, or combinations of solid and liquid state materials, but may differ in their chemical composition and intended use. Of the classes of such liquid and solid core entity materials, among many, may be mentioned foods, drugs, fuels, dyes, chemical reactants, electrical and magnetic materials, and perfumes or flavoring substances. Among the solid materials which are useful, as core materials, may be mentioned magnetic materials such as magnetic iron oxide, powdered substantially water-insoluble inorganic and organic chemical compounds, electrostatic materials such as carbon black pigment and iron powder, and combinations of such materials. To show the wide range of particulate substantially water-insoluble materials adapted for use as core materials for the capsules, there may be mentioned oils and fats in the liquid or solid condition, which may be taken from the general classes consisting of mineral oils, vegetable oils, animal oils, and synthetic oils made by modification of natural oils, or oils of a purely synthetic origin, such as methyl salicylate and the liquid chlorinated diphenyls. To mention a few liquid oils, paraffin oil, kerosene, cotton seed oil, soy bean oil, corn oil, olive oil, castor oil, lemon oil and other fruitskin oils, and turpentine are representa-

tive. Animal oils such as fish oils, lard oil, and other perishable organic oils which may need protection from the atmosphere may be encapsulated by the process of this invention.

If desired, the gelled and hardened thick-walled capsules may be plasticized with water-soluble plasticizers, such as ethyleneglycol, and equivalents thereof, applied externally thereto.

It is within the field of this invention to utilize capsular wall material which is of itself useful by reason of its own characteristics or which carries some other material which has a useful purpose, either with external substances or in combination with the core material, or both. Among such capsule carried materials are bactericidal agents, light-reactant materials, light-filter materials, and coloring materials which, for instance, render the capsules identifiable as to their core content. Such capsule-wall-carried materials may be applied to the capsules after they are made, after any of the steps of gelling, hardening, and drying.

In making of liquid-core entity capsules, the liquid-core drop size may be controlled by the novel manner in which the liquid is dispersed in the aqueous medium as will be described, and the consequent overall capsule size is influenced thereby. Powdered solids, to become core entities, may be sifted to the desired dimensions.

It is within the province of this invention to make use of the capsules as they are suspended in the aqueous medium in which they were made, without solidification so the capsule walls are in the liquid form in which they were deposited out of the dispersion of the film-forming material; or the capsule walls may be solidified, in the aqueous medium, by gelling or other procedures, so that the capsule walls are solid and rigid, and, after such solidifying treatment, the capsules may be hardened to render them incapable of being destroyed by high-pH environments or by heat. The capsules may be used in the aqueous medium of which they were made or dispersed in other liquid or solid vehicles, after gelling or hardening in the aqueous medium. If the capsules are to be used in dry form, as a free-flowing material, the capsular wall material after being solidified and subjected to such further treatment in the nature of hardening as is desirable, are separated from the aqueous medium in which they were made and dried.

As a specific and preferred embodiment of the invention, n-decane, as a liquid, will be used as a typical core material, and it will be dispersed as minute droplets in water in which there has been previously dissolved a mixture of gelatin (preferably having an iso-electric point of about pH 8), gum arabic, and a polyethylenemaleic anhydride copolymer, as capsular wall material. The process, in the beginning, is carried on in an open-top vessel, with the ingredients at about 35 degrees centigrade, such temperature being selected so that the encapsulating wall material ingredients will all be in fluid form during the process. In this specific example, the core material also is in a liquid state. With the particular encapsulating wall material used, the temperature may be lowered after the capsule walls are made to gel and thus solidify the deposit thereof around each core entity, thus to form solid capsules with liquid cores on the completion of the two deposition steps. A further step to the process, as described so far, may be performed, in which the solidified wall material, now encapsulating each core entity, is hardened with cross-linking agents such as formaldehyde, glutaraldehyde, or equivalents. Coming, now, to quantities of materials used in the preferred example, 1,500 cc. of water, maintained at 35 degrees centigrade and agitated from the beginning and throughout the addition of the materials which are added thereto, has dissolved therein 150 grams of an 11%, by weight, aqueous gelatin sol, of the mentioned iso-electric value, and, thereafter, the so-formed solution is adjusted to pH 9 or has been so-adjusted by the pH of the added materials. Next is added 150 grams of an 11%, by weight, aqueous sol of

gum arabic, also adjusted to pH 9. As a third capsular wall ingredient is added 40 grams of a 2%, by weight, aqueous solution of polyethylenemaleic anhydride copolymer having an approximate molecular weight of about 1,000-2,000 as determined by the viscosity of it as a 1% solution in dimethyl formamide, at 25 degrees centigrade, according to Ostwald method "B," such copolymer now being obtainable in the United States of America from Monsanto Chemical Company under the trade designation "DX 843-11," the latter solution also being adjusted to pH 9, if not then at that point. This water solution of the initial wall-forming materials, kept at 35 degrees centigrade, is stirred, so that the liquid rotates about a vertical central axis, and then the core material, which in this example is n-decane, is introduced, or exuded, into the moving liquid, under its surface, by a burette, or other orificed emitter, at a drop-forming station, drop by drop, so that the drops are sheared off and carried away by the rotation of the dispersion, the burette, or emitter, being so controlled that the drops enter the liquid dispersion in such timing, relative to the rotational speed of the dispersion liquid past the end of the burette, that drops of the desired size are formed. In the preferred apparatus, the stirrer, introduced from the top opening of the vessel, includes a vertical, centrally-located stirring rod having radially-extending horizontal stirring blades at the bottom end, the tip opening of the burette being placed beneath the surface of the liquid contents, close to the blades, so that the shearing force against the pendent droplets, as they issue from the burette, better controls the accuracy with which the drops are formed, as regards size. In this preferred example, the drops are so regulated by a burette stopcock and the stirring speed, as to size, that the finished capsules, including the core material and the surrounding capsular walls, may average 500 microns in largest dimension. After the dispersion of the core material droplets into the liquid solution of the capsular-wall-forming materials, the wall-forming materials are caused to make a first deposit onto the droplets by lowering the pH of the aqueous liquid medium to about 4.8, which may be done with a 10%, by weight, aqueous solution of acetic acid. With the concentration of initial ingredients proposed in this specific example, the deposition of the initial wall-forming ingredients which have so far been provided will result in a wall thickness of about 5 microns, whereupon such deposition stops, although some remnants of the wall-forming ingredients in the form of coacervate droplets are left, in the dispersion, undeposited. It is to be understood that this first deposition of wall-forming material, at this stage, is in the liquid state. Next, the aqueous medium, which contains the remnants of the original encapsulating wall material in complex coacervate form, which has not deposited on the liquid droplets, is raised for a short period of time to a pH of about 6.8 by use of a 10%, by weight, aqueous solution of sodium hydroxide, which causes such remnants of encapsulating wall material to return to their original uncomplexed state before substantially disturbing the deposited liquid complex units which have already deposited on the droplet core entities. Continued agitation of the dispersion mixture containing the partially-completed capsules assures that said partially-completed capsules are kept as separate entities and will not coalesce. Next, before the partially formed capsules have been substantially affected by decoacervation, there is introduced into the aqueous medium, containing the partially-formed capsules and the decomplexed remnants of the first encapsulating ingredients, a 2%, by weight, aqueous solution of 40 grams of polyethylenemaleic anhydride copolymer having a substantially higher molecular weight than that used in the initial ingredients, preferably polyethylenemaleic anhydride copolymer having a molecular weight of about 60,000-70,000, as determined by the viscosity method mentioned before, and obtained at present in the United States of America from

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Monsanto Chemical Company under the trade designation "DX 843-31." The separate preliminary step of raising the pH of the dispersion, before adding the second colloid material, may be eliminated if the added colloid material is of a high enough pH naturally, or has been made so, to prevent spontaneous coacervation when added to the solution. After thorough mixing of the newly-added polyethylenemaleic anhydride copolymer solution, the pH of the liquid dispersion mixture is lowered, before the partially formed capsule walls have been substantially affected by deacoacervation, to approximately 5 by the addition of a 10%, by weight, solution of acetic acid, which causes deposition of said newly-added polyethylenemaleic anhydride copolymer and the remnants of the first-added film-forming material, as complex units, around each of the partially-completed capsules, individually, as a second liquid deposit coherent to the first deposit, thus completing a composite wall around each of the droplets of core material, the composite wall then totaling approximately 100 microns in thickness when the second deposition ceases. The capsules are completed, as far as the deposition of the encapsulating wall-forming material is concerned, but the encapsulating walls, at this point, are still in liquid form. In most cases, it is desired to have the colloid capsular walls in a rigid and solid state and, in addition, hardened by cross-linkage, and, therefore, in this preferred embodiment, the temperature of the aqueous dispersion of the liquid-walled capsules is dropped as rapidly as feasible to about 13 degrees centigrade, which is somewhat below room temperature, to make the solidification of the capsule walls proceed rapidly. The capsule walls, then rigid and solid, are still in a reversible state, and the capsule walls will revert to the liquid state upon being heated. To render the capsular walls irreversible in this sense, by being heated, the capsular wall material is cross-linked by treatment with the aforementioned tanning materials, formaldehyde, glutaraldehyde, or equivalent similar materials such as alpha-hydroxy-adipaldehyde. For instance, where formaldehyde is used, for the amount of material under process, .19 milliliter of a 37%, by weight, aqueous solution of formaldehyde per gram of gelatin is stirred in. In case glutaraldehyde is used, .5 milliliter of a 25%, by weight, aqueous solution per gram of gelatin may be used. Amounts of other cross-linking agents may be found by trial-and-error methods. In the event that the formaldehyde solution is used, the aqueous dispersion of capsules should have its pH raised to from between 7 and 9, to render it fully effective, and the pH may be left there until the capsules are ready for use. Where a solution of glutaraldehyde is used, no raising of the pH is necessary.

The capsules, so formed, may be recovered from the aqueous medium by filtration, by centrifuging, or by spraying the dispersed capsules in a preferably hot, gas medium, and, when dry, the capsules may be used as particulate or powdered dry material.

To show the flexibility of the process, encapsulation of droplets of n-decane may be accomplished by the use of gelatin and polyethylenemaleic anhydride copolymer without the additional use of gum arabic. In this modification, 12 grams of gelatin, having its iso-electric point at pH 8, is dissolved in 1,200 grams of water at 55 degrees centigrade. The solution, if necessary, is adjusted to pH 9 with a 20%, by weight, aqueous solution of sodium hydroxide. Into this gelatin solution, while it is being stirred, is dispersed 50 grams of n-decane, the conditions being such as to form core droplets of about 300 microns in average diameter. While the solution is still being stirred at 55 degrees centigrade, there is added 100 grams of a 2%, by weight, aqueous solution of polyethylenemaleic anhydride copolymer of the low molecular weight (1,000-2,000), before specified, the solution being maintained at pH 9. To cause a first liquid deposition of the capsular wall material onto the n-decane droplets, the pH of the mixture is lowered, with

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a 10%, by weight, aqueous solution of acetic acid, to pH 4.8, which, with continued stirring, forms liquid capsule walls around each of the droplets of n-decane to a thickness of about 5 microns, at which thickness deposition stops. To this dispersion of partially-encapsulated n-decane droplets there is added sufficient of a 20%, by weight, aqueous solution of sodium hydroxide to raise the pH to 5.5, after which there is added 50 grams of a 2%, by weight, aqueous solution of polyethylenemaleic anhydride copolymer of the higher molecular weight (60,000-70,000) before specified. If the latter aqueous solution is sufficiently high in pH, no pH adjustment may be necessary. Before the partially formed capsule walls are deacoacervated the pH of the dispersion mixture then is dropped, by use of a 10%, by weight, aqueous solution of acetic acid, to pH 4.6, whereupon the additionally-added higher-molecular-weight polyethylenemaleic anhydride copolymer and the remnants of the gelatin which had not deposited around the partially-completed capsules will deposit around the first deposited wall on each capsule, individually, to form a thick capsular wall around each core entity approximating a thickness of 100 microns. The capsules, which now have the capsular wall material around them in the liquid state, are chilled, to solidify the capsular wall material, and hardened, as before described with reference to the first preferred example.

It is to be understood that polyethylenemaleic anhydride occurs in other molecular weights than those specified herein and the novel process is not limited to the use of polyethylenemaleic anhydride of the weights specified nor in the order of use of the various polymers thereof, as the heavier molecular weight polymer may be used in the first deposit and the lighter weight polymer used to rejuvenate the deposition material for the second deposit, or the same molecular weight polymer may be used both in the original solution and as the addition material preparatory to the second deposit.

Although the two steps of coacervate deposit have been disclosed as controlled by adjustments in the pH of the system, the coacervatable system may be brought into and out of the coacervate zone, and back into the coacervate zone by other means, such as varying the temperature and the compositions or concentrations of the polymer material, as such procedures are known in the coacervate art.

Since it is impossible to make all the liquid core droplets of the same size, or the capsular walls thereof of the same thickness, the figures given as to size are average figures, and, if a more select standard of average size is wanted in the final end product, such selection may be made from the manufactured stock of them. To make smaller or larger droplets than those just specified, regulation of the burette stopcock and of the stirring speed may be resorted to, or other emulsification or dispersion practices may be used. In the event that solid core materials are used, they may be sifted, as mentioned, to obtain the desired maximum average size.

Water-immiscible core materials containing dispersed solids are handled in the same manner as liquids containing no solid constituents. If solid particulate material is to form the core entity, without the use of a liquid vehicle, solid particles of the selected size are beaten into the aqueous solution of encapsulating materials and kept agitated, so as to keep them in dispersed condition while the deposition is made of the encapsulating materials thereon, by adjustment of the pH, as before described in connection with the formation of capsules containing, as core material, only liquid entities. After the liquid deposition of encapsulating material has been accomplished around the solid core particulate entities, the encapsulating wall material may be solidified by cooling and hardening by cross-linking agents, as before de-

scribed. When solid particulate material is dispersed in the wall-forming aqueous medium, the wall-forming materials are adsorbed, to a certain extent, on the surface of the said solid particles of core material and form seed points for the coacervate deposition of capsular wall material thereon, as has been described with regard to the first step of the process.

The particular wall-forming materials which have been specified are not to be deemed as limiting the invention, as other gelable and coacervatable film-forming materials may be substituted therefor and deposited in steps by successive additions of such wall-forming material, with intermediate changes in the pH of the liquid mixture, if necessary.

The invention is not to be deemed limited in regard to materials, amounts of materials, and particularities of the preferred embodiments of the invention disclosed, as it will be apparent that the invention has broad application readily discernible by those skilled in the art.

What is claimed is:

1. A process for the collective and simultaneous manufacture of capsules, each having core material surrounded by capsular wall material, which comprises
  - (a) establishing a system consisting of a dispersion of particulate entities of water-insoluble matter, each of which is to become the core of a capsule, in an agitated aqueous dispersion medium in which the particulate entities are substantially insoluble, said medium containing dissolved therein film-forming hydrophilic colloid materials, at least one of which is gelable, consisting of different kinds of molecules which combine to form coacervate complex units under coacervating conditions;
  - (b) changing the conditions of said system to increase the interaction between the molecules of the colloid materials to effect coacervation, in which said colloid materials contract to form colloid-rich coacervate complex units, some of which units deposit in a liquid state, as a first liquid deposit, around each core entity to a thickness at which such deposition ceases, leaving remnant coacervate complex units of colloid material in solution, and leaving each core entity surrounded by a liquid wall deposit of gelable complex coacervate film-forming hydrophilic colloid material units;
  - (c) changing the condition of the system to cause decoacervation to take place for a time sufficient to decoacervate any remnant undeposited complex units of the hydrophilic colloid material, but insufficient to cause substantial decoacervation of the deposited material;
  - (d) adding to the system and dissolving therein additional film-forming hydrophilic colloid material to form a rejuvenated aqueous colloid-containing medium, which additional film-forming hydrophilic colloid material consists of molecules which combine with the molecules of the colloid materials in the system to form colloid-rich coacervate complex units;
  - (e) again changing the conditions of the system to cause coacervation wherein the interaction between the molecules of the colloid-rich materials in the rejuvenated aqueous medium causes the colloid molecules therein to make new colloid-rich complex coacervate units, which new units deposit in a liquid state onto the first deposit of liquid complex colloid units around each core entity to form a further liquid deposit of colloid material complex units over and around the first deposit, and coherent thereto; and
  - (f) finally, after such second deposit has been made, cooling the so-formed deposited wall of coacervate colloid material around each capsule core entity to gel.
2. The process of claim 1 followed by the step of hardening the gelled capsule wall.
3. A process for the collective and simultaneous manu-

facture of a multiplicity of capsules, each capsule consisting of a single entity of core material surrounded by capsular wall material, which comprises

- (a) establishing an agitated system consisting of an aqueous dispersion medium in which are dissolved film-forming hydrophilic colloid materials to form a solution, the said colloid materials containing heterogeneous molecules which combine to form coacervate complex units when the pH of said colloid-containing aqueous dispersion medium is lowered below a point at which complex coacervation occurs, at least one of the materials being gelable, said aqueous medium and contents being kept at a temperature which keeps the gelable component of the colloid materials in an ungelled state, said colloid-containing aqueous dispersion medium having its pH maintained above said point until it is desired that complex coacervation is to take place, and said colloid-containing aqueous dispersion medium being kept agitated until the process is completed, and in which are dispersed particulate entities of core material which is insoluble in the aqueous medium, each of which entities is to become the core of a capsule;
  - (b) lowering the pH of the colloid-containing aqueous dispersion medium below said pH point until complex colloid units form into a coacervate, some of which coacervate deposits, in a liquid state, around each core entity individually, leaving each core entity surrounded by a liquid wall of gelable complex coacervate film-forming hydrophilic colloid material and the remainder of which coacervate remains in the dispersion medium;
  - (c) rejuvenating the system by adding to and dissolving in the aqueous medium additional wall-forming film-forming hydrophilic colloid material having molecules which can combine with molecules in the system to form coacervate complex units and raising the pH of the medium and contents to a decomplexing pH for a time sufficient to cause any remnant coacervate complex units to be decomplexed but insufficient to cause any substantial decomplexing of the first deposit of colloid material, which additional material and the remnants of the first colloid materials will form further coacervate complex units at said pH point;
  - (d) lowering the pH to the coacervation point, which causes a second coacervation and deposit of complex colloid units onto each partially-formed capsule to form a second liquid deposit coherent with the first deposit to produce thick-walled capsules; and
  - (e) gelling the now-formed thick-walled capsules, by cooling, to make the capsule walls rigid.
4. The process of claim 3 in which the film-forming hydrophilic colloid material is one capable of being cross-linked and the last step is followed by the step of treating the capsules so formed with cross-linking compounds thus hardening the gelable complex coacervate film-forming hydrophilic colloid material.
5. A process for the collective and simultaneous manufacture of a multiplicity of capsules, each consisting of a single entity of core material surrounded by capsular wall material, which includes the steps of
- (a) dissolving film-forming hydrophilic colloid materials in an aqueous dispersion medium, at least one of which colloid materials is temperature-gelable, to form a solution at a temperature which keeps the colloid material in an ungelled state, which temperature is maintained until the last step of the process, the said colloid materials containing different kinds of molecules which combine to form coacervate complex units when the pH of said solution is below the coacervation point, and said solution having its pH maintained above such point until it is desired that complex coacervation is to take place, said solu-

tion being agitated until the process is completed by the remaining steps;

- (b) dispersing particulate entities of water-insoluble matter in said solution, each of which entities is to become the core of a capsule;
- (c) lowering the pH of the solution below the coacervation pH point until complex coacervation takes place to form coacervate complex units of colloid material, certain of which units deposit in a liquid state around each core entity to a thickness at which such deposition ceases, and other of said coacervate complex units remain dispersed and undeposited as remnants in the remaining solution;
- (d) raising the pH of the solution above said coacervation point for a time sufficient to cause decoacervation of the remnant undeposited coacervate complex units of colloid material but insufficient to substantially destroy the first colloid deposit through decoacervation;
- (e) supplementing the solution to a potentially complex coacervatable condition by dissolving more film-forming hydrophilic colloid material in the said solution, which has the said remnants of the first colloid material left therein in a decoacervated state, said additional colloid material containing molecules which can combine with the molecules of the colloid material in said solution to form complex coacervate units;
- (f) lowering the pH of the solution below the coacervation pH point to cause complex coacervation of the colloid materials then dissolved therein, and to cause the deposition of the thus newly formed coacervate complex colloid units in a liquid state onto the first deposit of liquid complex units around each core entity, to form a second and coherent liquid deposit of the colloid material over and around the first deposit on each core entity; and
- (g) finally, when such second deposit has been made, lowering the temperature of the solution to the point where the deposits of gelable complex coacervate film-forming hydrophilic colloid material around each capsular core entity gels.

6. The process of claim 5 in which the gelable hydrophilic colloid material is gelatin and the process is followed by the step of treating the capsules with cross-linking compounds to harden the walls thereof, said cross-linking compounds being selected from the group consisting of formaldehyde, glutaraldehyde, and alpha-hydroxy-adipaldehyde.

7. The process of claim 5, in which the particulate core entities are in a liquid state.

8. The process of claim 5, in which the particulate core entities are of solid material.

9. The process of claim 5, in which the particulate core entities are of solid material dispersed in liquid.

10. A process for the collective and simultaneous manufacture of capsules, each having core material surrounded by capsular wall material, which comprises

- (a) establishing a system consisting of a dispersion of particulate entities of water-insoluble material, each of which is to become the core of a capsule, in an agitated aqueous dispersion medium in which the particulate entities are substantially insoluble, said medium containing dissolved therein film-forming hydrophilic colloid materials consisting of different kinds of molecules which combine to form coacervate complex units under coacervating conditions, at least one of which colloid materials is gelable;
- (b) causing, with agitation, complex coacervation of the colloid materials, by lowering the pH of the system, to form coacervate complex units, some of which units deposit in a liquid state, as a first liquid deposit, around each core entity to a thickness at which such deposition ceases, leaving remnant coacervate complex units of colloid material in solution, and leaving

each core entity surrounded by a liquid wall deposit of gelable complex coacervate film-forming hydrophilic colloid material units;

- (c) raising the pH of the system for a time sufficient to decoacervate any remnant undeposited complex units of the hydrophilic colloid material, but insufficient to cause substantial decoacervation of the deposited material;
- (d) adding to the system and dissolving therein additional film-forming hydrophilic colloid material to form a rejuvenated aqueous colloid-containing medium, said additional film-forming colloid material containing molecules which can combine with the molecules of colloid material already in the system to form complex coacervate units;
- (e) lowering the pH of the rejuvenated aqueous medium to cause complex coacervation of the colloid molecules therein to make new complex coacervate units, which new units deposit in a liquid state onto the first deposit of liquid complex colloid units around each core entity to form a further liquid deposit of colloid material complex units over and around the first deposit, and coherent thereto; and
- (f) finally, after such second deposit has been made, cooling the so-formed deposited wall of coacervate colloid material around each capsule core entity to gel said wall.

11. A process for the collective and simultaneous manufacture of a multiplicity of capsules, each consisting of a single entity of core material surrounded by capsular wall material, which comprises

- (a) dissolving film-forming hydrophilic colloid materials in an aqueous dispersion medium, at least one of which colloid materials is temperature-gelable, to form a solution at a temperature which keeps the colloid material in an ungelled state, which temperature is maintained until the last step of the process, the said colloid materials having opposite electric charges in the solution, which enable the colloid materials to form coacervate complex units when the pH of said solution is below the coacervation point, and said solution having its pH maintained above such point until it is desired that complex coacervation is to take place, said solution being agitated until the process is completed by the remaining steps;
- (b) introducing and dispersing particulate entities of water-insoluble matter in said solution, each of which entities is of a controlled desired size between about ten microns and about 500 microns and is to become the core of a capsule;
- (c) lowering the pH of the solution below the coacervation pH point until complex coacervation takes place to form coacervate complex units of colloid material, which units deposit in a liquid state around each core entity to a thickness at which such deposition ceases, and other of said coacervate complex units remain dispersed and undeposited as remnants in the remaining solution;
- (d) raising the pH of the solution above said coacervation point for a time sufficient to cause decoacervation of the remnant undeposited coacervate complex units of colloid material to an uncomplex state but insufficient to substantially destroy the first colloid deposit through decoacervation;
- (e) supplementing the solution to a potentially complex coacervatable condition by dissolving more film-forming hydrophilic colloid material having one of said electric charges in the said solution, which has the said remnants of the first colloid material left therein in an uncomplexed state;
- (f) lowering the pH of the solution below the coacervation pH point to cause complex coacervation of the colloid materials then dissolved therein, and to cause

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the deposition of the thus newly formed coacervate complex colloid units in a liquid state onto the first deposit of liquid complex units around each core entity, to form a second and coherent liquid deposit of the colloid material over and around the first deposit on each core entity;

(g) after such second deposit has been made, lowering the temperature of the solution to the point where the deposit of gelable complex coacervate film-forming hydrophilic colloid material around each capsular core entity gels; and

(h) hardening the gelled deposit of complex coacervate film-forming hydrophilic colloid material.

12. A process for the collective and simultaneous manufacture of a multiplicity of capsules of a chosen size, each capsule consisting of a droplet of liquid core material surrounded by capsule wall-forming polymeric material, consisting of the steps of (a) providing a solution of capsule wall-forming organic polymeric material and a solvent with which the liquid core material is immiscible; exuding the liquid core material from an orifice of an emitter at a drop-forming station located within the liquid solution, to form droplets and at the same time moving the solution past the drop-forming station at such a speed as to wash the droplets from the orifice when the droplets have reached the desired size, thereby to disperse the droplets of core material in the solution of capsule wall-forming material; and (b) changing the conditions of the

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solution system so the capsule wall-forming material forms a separate phase of polymer-rich liquid droplets which deposit on the dispersed droplets of core material to form liquid-walled capsules.

13. A method of dispersing, in a potentially coacervatable solution of film-forming organic polymeric material, chosen sized liquid droplets of a material immiscible with the solution, the droplets being intended as cores around which the film-forming material deposits when coacervation thereof is induced, to form liquid-walled capsules, including the steps of causing the solution to flow past a drop-forming station within the body of the solution, at a chosen pre-determined speed; and introducing the liquid droplets into the flowing solution at the drop-forming station by a flow-control means, whereby the liquid droplets issuing from the flow-control means are whipped away into the flowing solution, the size of the said whipped-away droplets being determined both by the chosen rate of flow of the solution and the chosen flow control means, in combination.

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