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United States Patent

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Leea Staret Lee

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(12) **United States Patent**
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(54) **CALCIUM CARBONATE MICROTABLETS AND METHOD FOR THE PREPARATION THEREOF**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 510 days.

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C01F 5/24 (2006.01)

(52) **U.S. Cl.**
USPC **423/430**; 423/414; 423/419.1

(58) **Field of Classification Search**
USPC 423/430, 431, 414, 419.1
See application file for complete search history.

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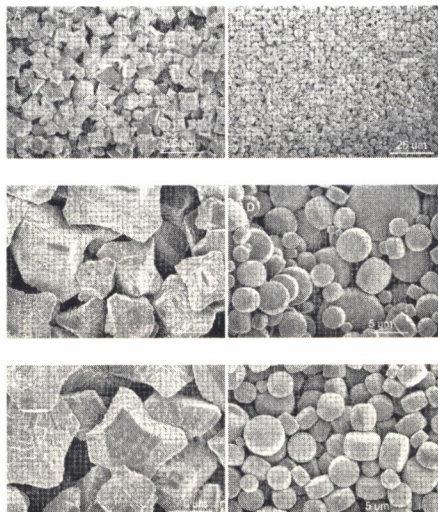
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(57) **ABSTRACT**

The invention discloses a method of preparing monodisperse microtablets of calcium carbonate in aqueous solutions containing calcium, gelatin and urea. Calcium carbonate powders of a unique tablet-like morphology were produced by simply ageing the prefrigerated (at 4° C. for at least 24 hours) CaCl₂-gelatin-urea solutions at 70° C. for 24 h in ordinary glass media bottles. Thermal decomposition of dissolved urea was used to supply aqueous carbonate (CO₃²⁻) ions to the calcium (Ca²⁺) ion and gelatin-containing solutions. Monodisperse CaCO₃ microtablets have the particle sizes from 1 to 8 microns. CaCO₃ microtablets were biphasic in nature and consist of 93 to 98% vaterite and 2 to 7% calcite. Identical solutions used without prefrigeration yielded only trigonal prismatic calcite crystals upon ageing at 70° C. for 24 h.

3 Claims, 3 Drawing Sheets



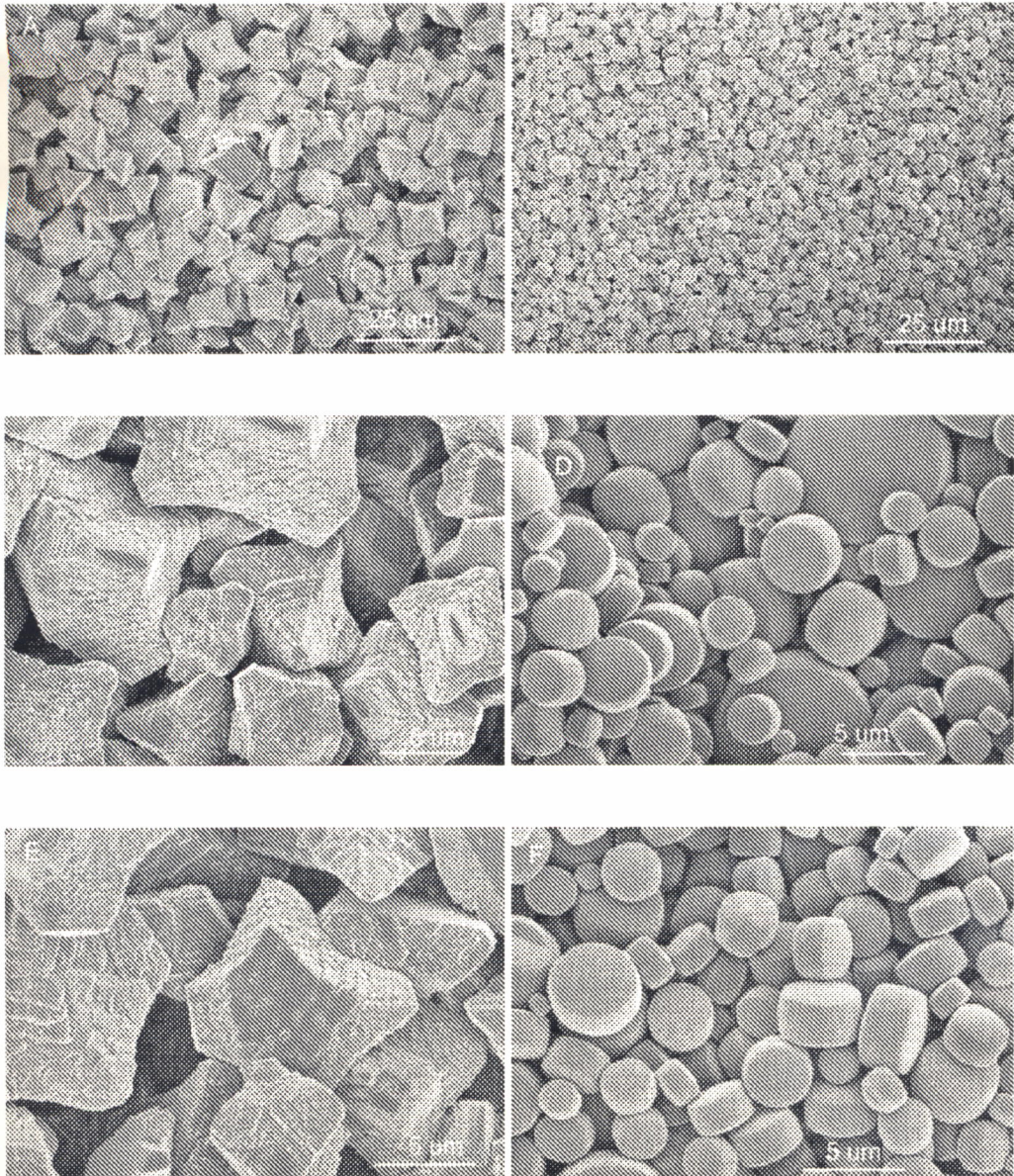


Figure 1

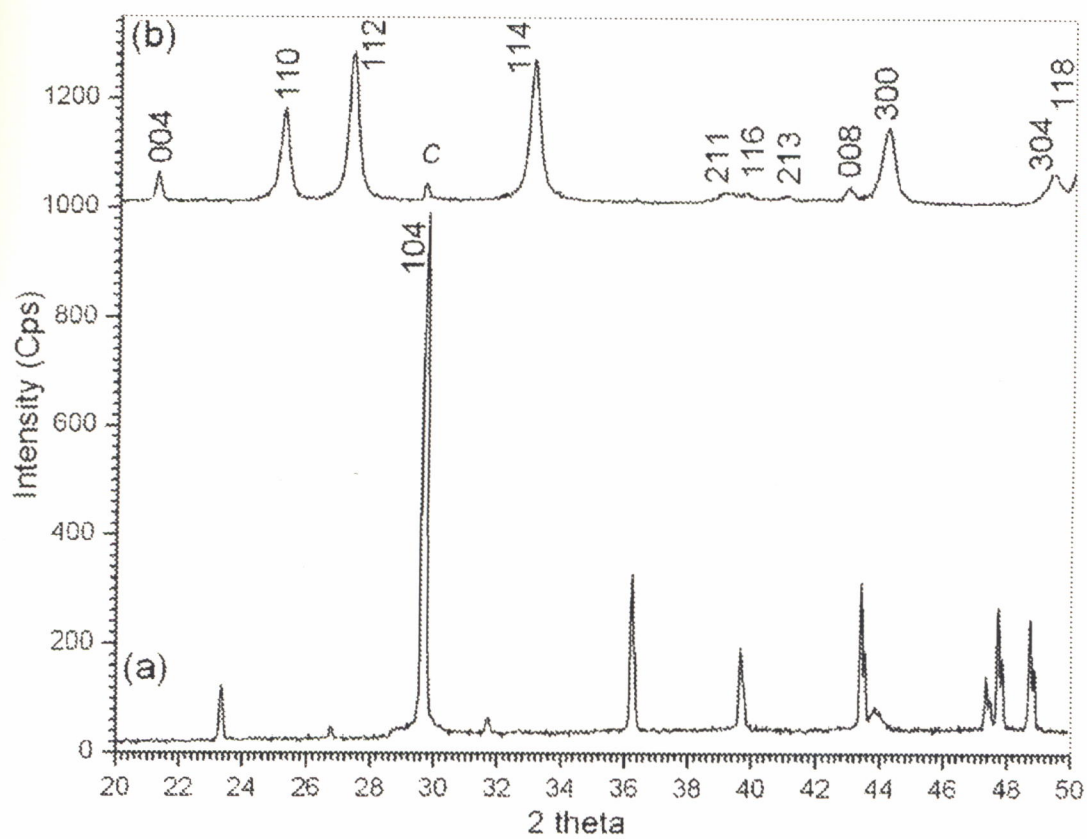


Figure 2

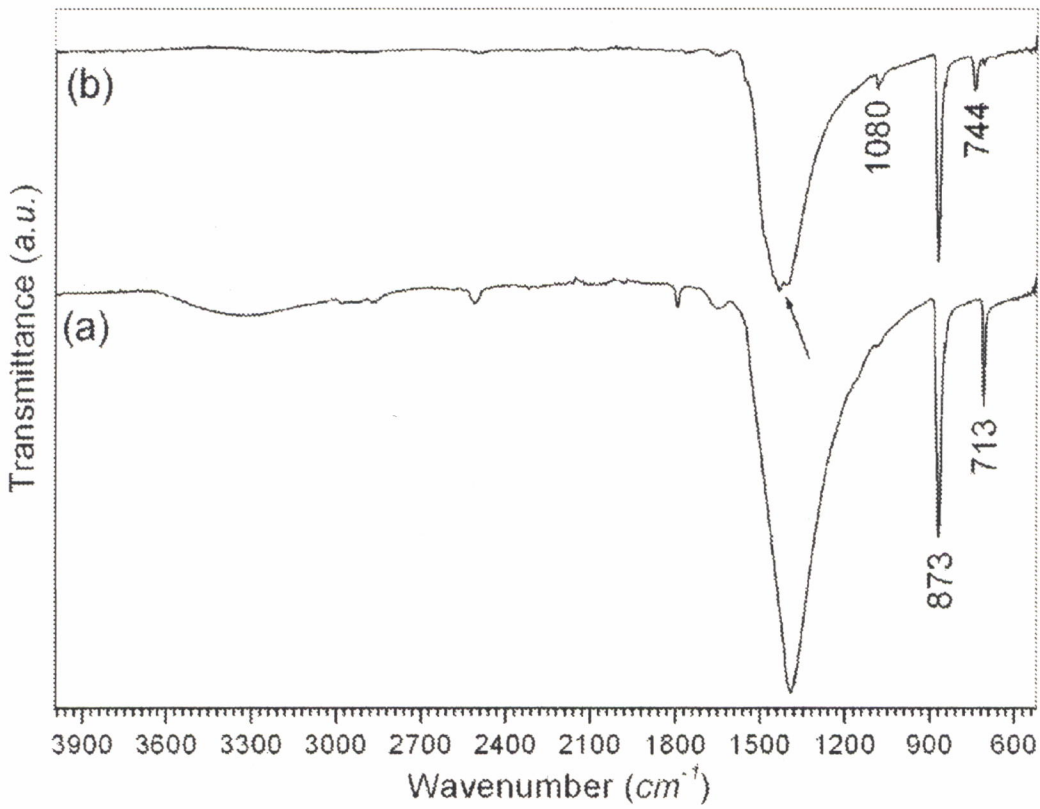


Figure 3

CALCIUM CARBONATE MICROTABLETS AND METHOD FOR THE PREPARATION THEREOF

FIELD OF THE INVENTION

The present invention relates to the monodisperse, non-agglomerated microparticles of calcium carbonate in the form of perfect tablets or pills and their preparation method based on prerefrigerating the solution containing calcium, gelatin and urea.

BACKGROUND OF THE INVENTION

Calcium carbonate (CaCO_3) is an important material of marine and geological biomineralization processes. CaCO_3 powders are also widely used in pharmaceuticals (commonly as a calcium supplement or as an antacid), cosmetics, toothpaste, biomedical, rubber, plastic, paper making, printing ink, and food industries.

Calcium carbonate has three naturally occurring anhydrous polymorphs; calcite, aragonite and vaterite. Amorphous calcium carbonate (ACC), calcium carbonate monohydrate ($\text{CaCO}_3 \cdot \text{H}_2\text{O}$) and calcium carbonate hexahydrate ($\text{CaCO}_3 \cdot 6\text{H}_2\text{O}$) may be regarded as the fourth, fifth and sixth polymorphs of calcium carbonate. At the ambient temperature and pressure, calcite is the most stable and abundant polymorph of calcium carbonate, while vaterite ($\mu\text{-CaCO}_3$), named after Heinrich Vater, is known to be the least stable among the anhydrous polymorphs.

Vaterite, which is regarded as a precursor of calcite or aragonite, has a hexagonal crystal structure with the space group $\text{P6}_3/\text{mmc}$ (No. 194) and $a=b=4.13 \text{ \AA}$, $c=8.49 \text{ \AA}$, $\alpha=\beta=90^\circ$, and $\gamma=120^\circ$. Vaterite has the theoretical density of 2.66 g/cm^3 . Calcite, on the other hand, is rhombohedral with the space group $\text{R}\text{-}3\text{c}$ (No. 167) and $a=b=4.990 \text{ \AA}$, $c=17.061 \text{ \AA}$, $\alpha=\beta=90^\circ$, and $\gamma=120^\circ$. In contrast to that of vaterite, calcite has a theoretical density of 2.71 g/cm^3 . Vaterite has a higher aqueous solubility than calcite and aragonite; however is the least stable polymorph among those. Owing to its instability, vaterite is rare in nature as it would readily convert into one of the more stable calcium carbonate phases, typically, calcite and possibly to monohydrocalcite ($\text{CaCO}_3 \cdot \text{H}_2\text{O}$) or hexahydrate ($\text{CaCO}_3 \cdot 6\text{H}_2\text{O}$). It is known from the prior art that in a solution supersaturated with respect to amorphous calcium carbonate, amorphous calcium carbonate forms first which transforms within minutes into vaterite and into calcite within several hours at room temperature.

Although vaterite is known to be rare in nature, an extremely important discovery was revealed lately that spheres of vaterite 0.5 to $10 \mu\text{m}$ in diameter (of inorganic origin) were forming in situ at a supraglacial sulphur spring located in the Canadian High Arctic. The unusual conditions of the site, including an extremely cold climate and the presence of supersaturated alkaline waters, must be noted for being responsible from preserving this unstable polymorph of calcium carbonate.

Calcium carbonate can be synthesized in the form of spheres (typically in the vaterite form), prismatic/trigonal/scalenohedral crystals (for the calcite polymorph) and needle- or plate-like crystals for its aragonite polymorph. Calcium carbonate synthesis methods involve in common, carbonation of the calcium ion (Ca^{2+})—aqueous solution of a calcium salt in general—by the carbonate (CO_3) ion from a proper carbonate source. A widely used carbonation method in forming calcite/vaterite polymorphs is the carbon dioxide (CO_2) gas bubbling. The method involves bubbling CO_2 gas

through a solution containing dissolved Ca^{2+} ions. A method for producing vaterite particles of spherical, ellipsoidal or plate-like morphology is disclosed in the patent document U.S. Pat. No. 5,275,651. The method involves preparing a mixture containing water, methanol and either unslaked lime or both unslaked/slaked lime, and letting CO_2 bubbles through the said mixture which leads to formation of vaterite particles. The nanofibre and nanoplate type calcium carbonate particles and their preparation method are disclosed in patent application US 2004/0166047. Said calcium carbonate particles are formed by carbonation of milk of lime in the presence of a crystallization controller selected from polyaspartic acid, dioctyl sodium sulphosuccinate, polyacrylic acid and citric acid. The resultant calcium carbonate particles are in the form of nanofibres of nanorosary or faggot type, or in the form of nanoplates of accordions.

Using dissolved sodium carbonate (either Na_2CO_3 or NaHCO_3) as the CO_3^{2-} source, in place of CO_2 gas bubbling, is another practical option to produce calcium carbonate powders of the vaterite or calcite form in aqueous solutions. An example utilizing this method can be found in the patent document RU 2218305. The method includes simultaneous feeding of reagent containing ions of calcium, and the carbonating reagent into a reacting agitated mixture. The reagent containing calcium ions is an aqueous solution of calcium chloride (CaCl_2), and the carbonating reagent is an aqueous solution of sodium carbonate (Na_2CO_3). The resultant product of is the fine-grained calcium carbonate particles with the average particle size of $1.8\text{-}22$ micron with spherical form.

Urea ($\text{CH}_4\text{N}_2\text{O}$) can also be used as the carbonating agent because of its decomposition in aqueous solutions is accompanied by the slow and controlled supply of ammonia (NH_3) and carbon dioxide (CO_2) into the solution. It is known that urea decomposition kinetics is affected by temperature and concentration (of urea and cations present). Therefore, urea was also used (in place of CO_2 gas bubbling or Na_2CO_3 , NaHCO_3 and $(\text{NH}_4)_2\text{CO}_3$ additions) to produce calcium carbonate powders. Wang et al. showed that non-agglomerated calcite, vaterite and aragonite particles can be produced by using the decomposition of urea in CaCl_2 -containing aqueous solutions (50 to 90°C). (Wang L F, Sondi I, Matijevic E. *Preparation of uniform needle-like aragonite particles by homogeneous precipitation. J Colloid Interf Sci* 1999; 218: 545-53)

It should be noted that none of the techniques cited above could go beyond the already known forms of calcium carbonate, "sphere" for vaterite and "rhombohedral/trigonal prisms/scalenohedra" for calcite. The study of Guo et al, on the other hand, which reported the crystallization habit of CaCO_3 in the presence of sodium acrylate (in a solution containing CaCl_2 , $(\text{NH}_4)_2\text{CO}_3$, and $\text{K}_2(\text{SO}_4)_2$ at 30°C .) was quite remarkable that it yielded "disc-shaped" spheres of vaterite or classic rhombohedra of calcite under different experimental conditions. (Guo Y, Yang L, Yang X, Zhang X, Zhu S, Jiang K. *Effect of self-assembly of sodium acrylate on the crystallization of calcium carbonate. Macromol Biosci* 2003; 3:163-68.) Wakayama et al., upon immersing chitosan-coated glass slides into a solution of Ca-acetate and polyacrylic acid (PAA) in the presence of supercritical CO_2 at 50°C and 76.5 kg/cm^2 (7.5 MPa), observed the formation of heavily agglomerated but "rounded, tablet-like" particles of vaterite deposited on the chitosan-coated glass slides. (Wakayama H, Hall S R, Mann S. *Fabrication of CaCO_3 -biopolymer thin films using supercritical carbon dioxide. J Mater Chem* 2005; 15:1134-36). These studies were quite important in the sense that they betrayed the particle morphology is remarkably affected by the experimental conditions.