Development and Application of Salt Crystal as a Capsulation Agent

Yoshihiro Yamaguchi, Koichi Nishioka,and Makoto Chiba

Kinkai Salt Manufacturing Co., Ltd.,
4396 Shirimi, 701-4212 Oku-cho, Oku-gun, Okayama, Japan

Crystallization techniques generally seek to improve the crystallization process, with the primary goal of increasing the purity of a substance obtained through the process. The technique is also employed to control the shape and size of crystals, to enhance the yield of output, as well as to lower the energy consumption.

This paper will introduce the development and application of a crystallization technique to capsulate a foreign substance in a crystal used as a capsulation agent. The application includes the use of a salt crystal to capsulate a chemically unstable substance.

Conventional capsulation typically uses such polymers as gelatin and polysaccharides as a capsulation agent, but its application has been restricted because of their water-solubility, weakness to high temperatures, insufficient air-tightness, and low mechanical strength. Because of these disadvantages, a toothpaste manufacturer in Japan, for instance, had been unable to mix into their products sodium guai azulene sulfonate, which helps allay inflammatory gums but degrades when exposed to air or moisture. As it became possible to enclose this chemical in individual salt crystals and to prevent it from degrading in a toothpaste, however, the toothpaste manufacturer succeeded in developing a new product containing sodium guai azulene sulfonate.

By using salt or other crystallizing chemical compounds as a capsulation agent, chemically or physically unstable substances such as beta-carotene and ascorbic acid, or other substances such as pigments, spices, or seasonings, can be effectively capsulated in individual crystals. This capsulation method may well find other applications.

This paper will focus mainly on the capsulation of sodium guai azulene sulfonate in salt crystals for use in toothpaste manufacturing.

1. Introduction

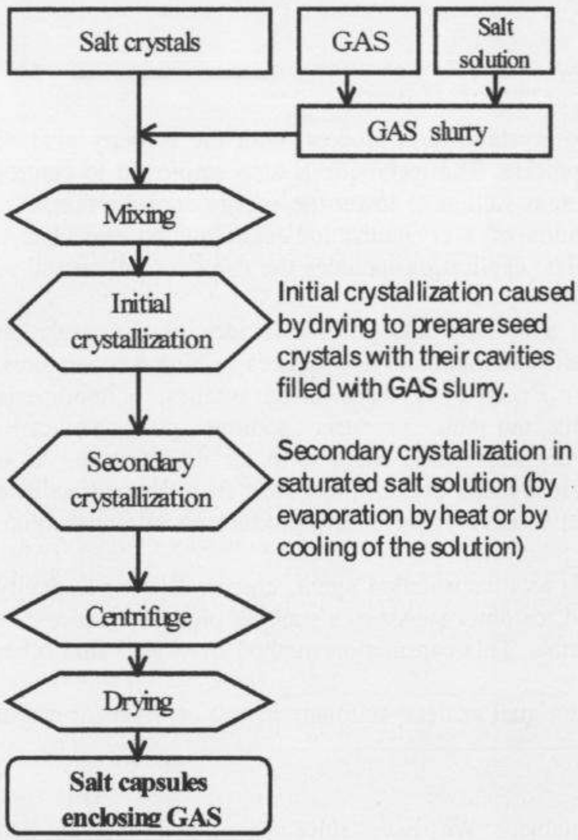
Crystallization techniques have been developed with the primary goal of obtaining various materials of a high purity. The technique has also been employed to control the shape and size of crystals. Further, by improving the equipment used, the output yield can be enhanced and energy consumption reduced. As a manufacturer of food-grade salt made by electrodialysis of sea water with the ion-exchange membrane and a multi-effect vacuum evaporation process, we have been studying techniques for the crystallization of salt. In the process of our research and development, we have established an effective and efficient crystallization technique for encapsulating a chemically unstable foreign substance in individual salt crystals and keep it chemically stable. We have since developed various Salt Capsules, an example of which is that enclosing sodium guai azulene sulfonate (hereinafter called "GAS"). This paper will introduce the production process and characteristics of Salt Capsules containing GAS.

2. Production process

The production of Salt Capsules mainly consists of two crystallization processes-one is to prepare seed crystals coated with a foreign substance and the other to grow the coated seed crystals. In order to achieve a high yield of successfully capsulated product, the coated seed crystals need to be grown as quickly as possible.
In addition, such factors as the number of the

coated seed crystals, the speed of growing these crystals, and the equipment employed in the secondary crystallization process will have an important influence on the growth of crystals and the quality of the final product. Chart 1 shows the production process of Salt Capsules containing GAS.

Chart 1: Production process of salt capsules



2.1. Preparation of seed crystals

Seed crystals are prepared by filling the cavities of salt crystals with a sufficient, appropriate amount of a foreign substance — in this case, GAS slurry. In order to grow the seed crystals thus prepared, the following conditions are important.

2.1.1. Growth of seed crystals

Unless seed crystals are prepared to have their surfaces densely dotted with fine salt crystals, which have been formed from the salt contained in the slurry and become the basis of further crystallization, new crystals with no GAS will form and grow in the crystallization vessel. These crystalls hamper the secondary crystallization of original seed crystals containing GAS.

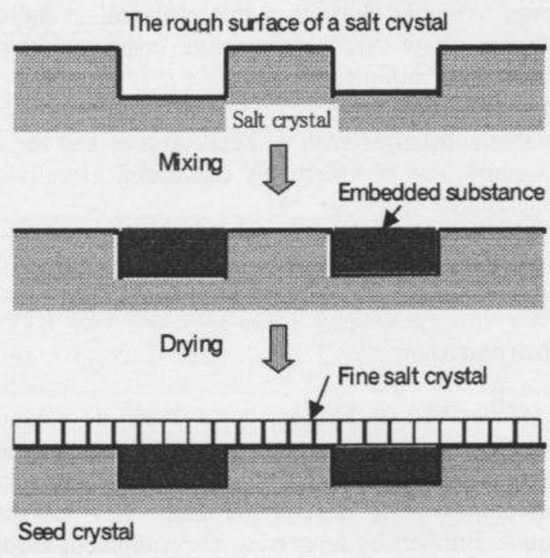
2.1.2. Detachment of a foreign substance

In the secondary crystallization process, seed crystals are agitated for secondary crystallization to occur evenly. It is important that a foreign substance is firmly fixed in the cavities of the seed crystals so that the foreign substance will not be detached from the cavities and a high ratio of successful capsulation will be achieved.

2.1.3. Seed crystals

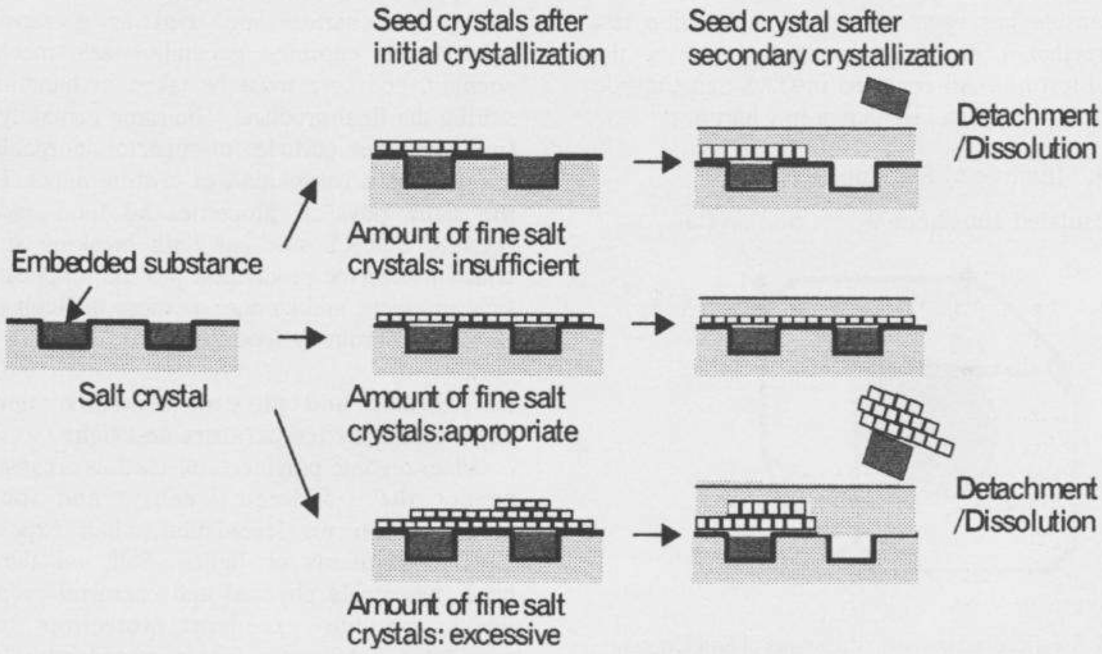
Seed crystals are prepared by drying the salt crystals mixed with the slurry of GAS and salt solution. When the salt crystals have a rough surface, the slurry can be more firmly fixed in the cavities. Chart 2 shows how the slurry is embedded in the cavities of a salt crystal by a process of the salt crystals being mixed with GAS slurry and of the filled cavities being covered by an initial crystallization of salt, contained in the slurry, by drying.

Chart 2: Process of enclosing GAS in the cavities of a salt crystal



When the slurry in the cavities are dried, salt solution crystallizes into fine particles, which cover and fix the GAS, a foreign substance, in the cavities and act as the bases upon which secondary crystallization starts. As Chart 3 shows, the amount of fine salt crystals formed from GAS slurry greatly influences whether seed crystals can be successfully prepared. However, there is no constant relationship between the amount of fine salt crystals and the occurrences of detachment.

Chart 3: Successful and unsuccessful seed crystal preparations



The appropriate amount of a foreign substance is determined by its physical characteristics.

2.2. Secondary crystallization of seed crystals

The foreign substance in the cavities is encapsulated after the secondary crystallization in the crystallization vessel filled with saturated salt solution.

Conventional methods of crystallization, i.e. evaporation by heat or cooling of saturated salt solution, will suffice for this process. It should be noted, however, that some foreign substances decompose or transform at high temperatures, and that, in such cases, crystallization temperatures should be adjusted.

The amount of a foreign substance in Salt Capsule can be adjusted by changing the quantity of the foreign substance in the slurry. When the size of Salt Capsule is specified and the content of the foreign substance cannot be increased beyond a certain level, the size of seed crystals can be reduced to give more space to enclose a greater amount of the foreign substance. The amount of GAS can be increased to around 5% of the total weight of Salt Capsule. To provide greater protection to the enclosed foreign substance, the secondary crystallization process of the seed crystals can be extended.

2.3. Washing, centrifuging and packing

Although the Salt Capsule has a foreign substance encapsulated in it, it has similar physical characteristics to ordinary food-grade salt crystals. Hence no specially designed equipment is required for washing, centrifuging, and packing of Salt Capsules.

3. Characteristics of Salt Capsules

Conventional capsulation typically uses such water-soluble polymers as gelatin and polysaccharides as a capsulation agent. Also, coating with various substances of fine particles is regarded as capsulation. However, the application of these methods is restricted because of possible transformation of capsulation agents at high temperatures, insufficient airtightness, and low mechanical strength. As shown in Chart 4, Salt Capsule, being a crystallized salt, greatly alleviates these problems and facilitates the handling of the finished product.

3.1. Airtightness

Photograph 1-6 shows the process of a seed crystal growing into a GAS-Salt Capsule. The finished product, about 500 μ m in diameter, is a transparent capsule, and the absence of cracks indicates that the enclosed substance is completely sealed up in the capsule. The airtightness of the Salt Capsule has been proven by the elution test using methanol, as shown in Chart 5 and by the survival test of GAS enclosed in GAS-Salt Capsule mixed in a toothpaste, as shown in Chart 6.

Chart 4: Structure of Salt Capsule

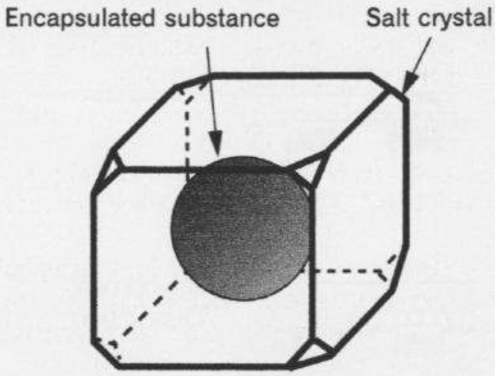


Chart 5: Relationship between thickness of Salt Capsule enclosing GAS after secondary crystallization and GAS elution rate in methanol saturated with salt

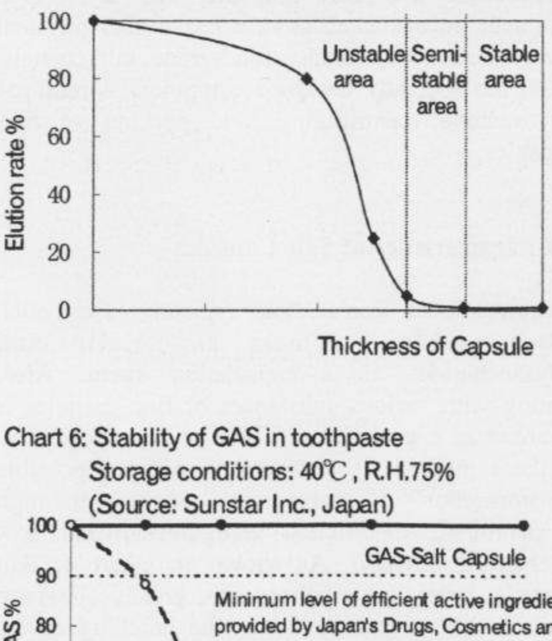
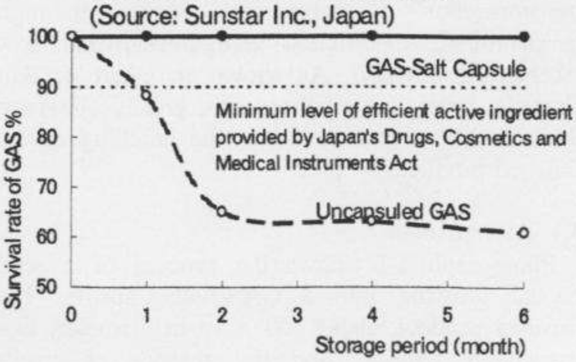


Chart 6: Stability of GAS in toothpaste
Storage conditions: 40℃, R.H.75%
(Source: Sunstar Inc., Japan)



3.2. Mechanical strength

When water-soluble polymers such as gelatin and polysaccharides are used as a capsulation agent, such capsules generally lack mechanical strength, and care must be taken in handling and storing the final products. The same generally holds true when fine particles of sugar or inorganic salts are used as a capsulation or coating agent. Having the same physical properties as food-grade salt crystals, Salt Capsule has high breaking strength, which makes the production process, application to final products, and storage no more difficult than in the case of ordinary food-grade salt.

3.3. Quality and physical transformation and degradation by temperature and light

When organic polymers are used as a capsulation agent, they undergo quality and physical transformation or degradation when exposed to high temperatures or light. Salt, on the other hand, has stable physical and chemical properties, which provide excellent protection to the capsulated substances for a considerably longer period. In the case of GAS-Salt Capsules, little degradation of GAS has been noticed after 5 years of storage.

4. Application of GAS-Salt Capsule

GAS is known to effectively allay inflammatory gums. Sunstar Inc., the co-developer of GAS-Salt Capsule, had had difficulty in developing a toothpaste containing GAS because the oxygen and dissolved oxygen existing in a toothpaste oxidized GAS. As it became possible to manufacture GAS-Salt Capsules on an industrial scale, commercialization of a GAS-containing toothpaste was realized.

4.1. Details of applying GAS-Salt Capsules to a toothpaste

4.1.1. Measures taken to prevent the dissolution and increase the mechanical strength of GAS-Salt Capsules

As salt solution contracts gums by a function of osmotic pressure and helps allay inflammatory gums, salt-containing toothpastes are widely used in Japan.

However, in general, toothpastes contain about 20% moisture, which dissolves GAS-Salt Capsules and renders GAS ineffective. This problem has been resolved by saturating the toothpaste with salt or by increasing the thickness of the Salt Capsule.

Strong mechanical pressure is exerted when mixing the ingredients of a toothpaste and in filling the toothpaste into the tube. But, as Chart 6 shows, no decrease in the survival rate of GAS was observed during the test period, showing the high resistibility of Salt Capsules to mechanical pressure.

4.1.2. Specifications of GAS-Salt Capsules

Purity of NaCl 99.5% minimum (On a dry basis)
Particle size 425-600 μ m 95% minimum
GAS content 945-1,005 mg/kg (Standard deviation for the same production lot is 2.4% maximum.)
GAS elution rate 1.0% maximum (Test method: shaking a test tube containing salt-saturated methanol and GAS-Salt Capsules.)

4.1.3. Protectiveness of Salt Capsules

Chart 5 shows the relationship between the thickness of the Salt Capsule and the elution rate of GAS. The test was conducted by shaking a test tube containing methanol saturated with salt and GAS-Salt Capsules, and measuring the elution rate of GAS. The relationship shows that, when the thickness of the Salt Capsule falls in the range marked "stable area," virtually no elution of GAS occurs. (Thickness data are not shown due to their confidentiality.) Japan's Drugs, Cosmetics and Medical Instruments Act requires that at least 90% of such an active ingredient as GAS contained in a toothpaste should remain effective after three years' of storage at room temperature.

Chart 6 compares the survival rate of the uncapsuled GAS with that of the GAS enclosed in Salt Capsules, both of which were stored in an airtight vessel whose inside temperature was 40 ℃ and relative humidity 75%. Under these conditions, the storage period of one month is equivalent to approximately six month, demonstrating the long-term stability of GAS-Salt Capsules.

5. Other applications of capsulation technique — Salt Capsules and capsules using other materials

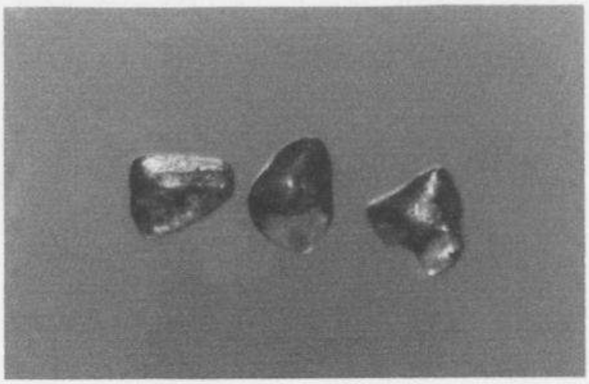
Table 1 lists some of the applications using salt and other materials as a capsulation agent in oder to stabilize chemically or physically unstable substances

It is hoped that capsulation by use of crystallization technique will receive wider attention from various circles, because the process applied to an industrial scale production has a relatively short history and seems to have wider applications.

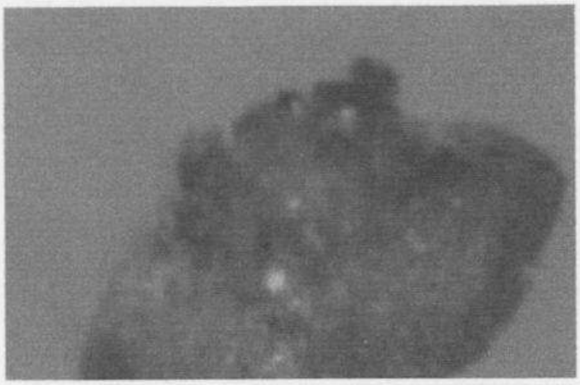
Finally, our special thanks go to the International Salt Symposium for the opportunity to introduce part of our production and research activities, as well as to Sunstar Inc. of Japan who worked with us in the development and application of Salt Capsules.

Table 1: Some applications of capsulation using salt and other materials as a capsulation agent

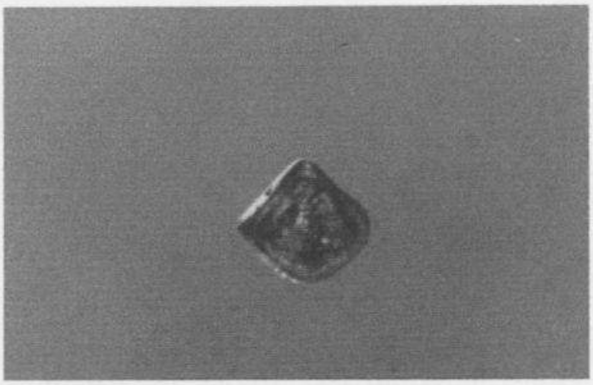
Capsulation agent	Substance to be encupsulated	Application
Salt Potassium chloride Suger	Active medical ingredients	Tablets Quasi-drugs (such as a toothpaste containing active ingredients) Cosmetics
Salt Potassium chloride Suger	Nutrient substances Seasonings & spices	Food products
Sodium bicarbonate	Perfume	Bath chemicals



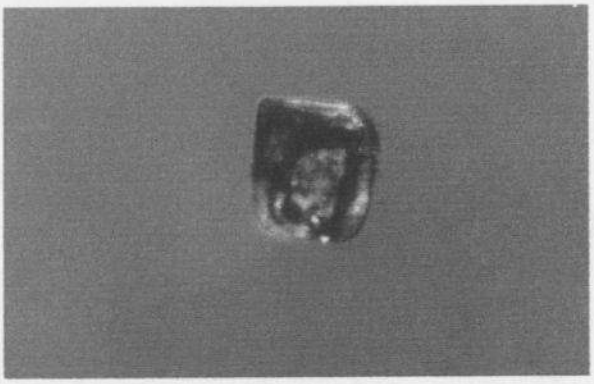
Photograph 1:
Initial crystallization on seed crystals



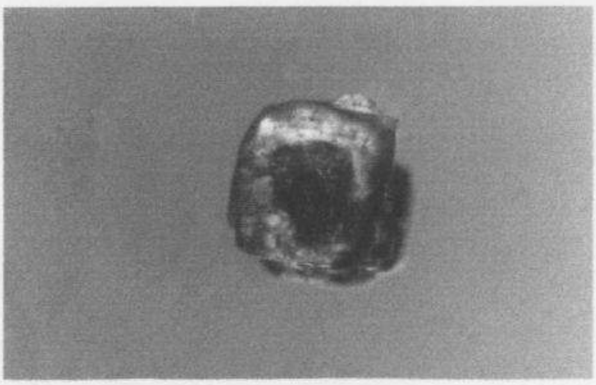
Photograph 2:
Formation of fine salt crystals



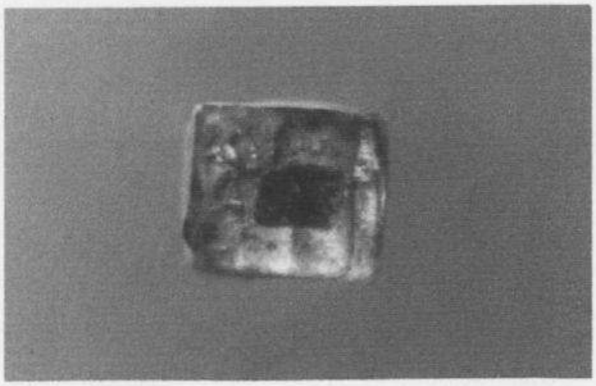
Photograph 3:
Early stage of secondary crystallization
(diameter about 300 μ m)



Photograph 4:
Middle stage of secondary crystallization
(diameter about 400 μ m)



Photograph 5:
Middle stage of secondary crystallization
(diameter about 450 μ m)



Photograph 6:
GAS-Salt Capsule after completion of secondary crystallization (diameter about 500 μ m)