New Preparative Technique for Effervescent Products

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An air suspension coating-reacting technique has been applied to the preparation of effervescent products. Unlike the present method, traditional preparative processes employ cumbersome many-step procedures. The new technique consists essentially of suspending all or certain of the desired materials in a stream of air, then spraying the suspended mass with water or with a solution of the remaining components. Detailed examples are given to illustrate the versatility and advantages of the process described.

EFFERVESCENT salts, ordinarily in the form of powders, granules, or compressed tablets, constitute a well-known class of pharmaceutical preparations. They generally consist of medicinal ingredients, tartaric and/or citric acids, and a gas-generating base such as sodium bicarbonate. Usually they are administered after being put into water, where they effervesce to form a carbonated saline drink. Specific examples of this type of preparation can be found in the official compendia of pharmacy, the "United States Pharmacopeia" and the "National Formulary." The following are examples of such effervescent salts: sodium phosphate, compound salt of potassium bromide, artificial Carlsbad salt, artificial Kissingen salt, artificial Vichy salt, potassium citrate, salt of lithium citrate, salt of magnesium sulfate, and compound effervescent powders (Seidlitz powders).

The following are examples of commercial effervescent products: Bromionyl[1] and Citrocarbonate,[1] Bromo Seltzer,[2] Alka Seltzer,[3] Sal Hepatica,[4] and Brioschi.[5]

Standard processes used to prepare effervescent products consist of mixing the salts, adding a small amount of water to start the effervescence reaction and so obtain a workable mass, quickly drying the mass in ovens or heated dishes to stop the reaction, grinding the mass under dry conditions to form powder or granules, then bottling. Obviously, throughout the procedure the reaction, which liberates carbon dioxide, can be permitted only to proceed minimally, lest the effervescent character of the final product be destroyed.

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[1] Trademarked by The Upjohn Co.
[2] Trademarked by Warner-Lambert Products, Division of Warner-Lambert Pharmaceutical Co.
[3] Trademarked by Miles Laboratories, Inc.
[4] Trademarked by Bristol-Myers Products Division.
[5] Trademarked by Ceribelli & Co.

Control of the amount of water, which is intentionally and unintentionally added to the materials, and hence control of the extent of the reaction has always been difficult to achieve. Techniques such as moistening the materials with 5% water in alcohol, using the water of hydration of citric acid by liberating it *in situ* by heating the salt mix, or using bursts of steam to moisten the material have been used to try to control the extent of the reaction. These techniques have necessarily made the preparation of effervescent pharmaceuticals quite cumbersome.

It is the purpose of this communication to describe a method of preparing effervescent products to facilitate the attainment of control of the reaction just noted; the method also embodies other improvements over standard processes. The new technique consists essentially of suspending the dry sodium bicarbonate and citric acid (or other or all of the composition's ingredients) in a stream of air and spraying the suspended material with water or with a solution of sodium biphosphate or fruit acids. A device such as the Wurster air suspension apparatus (1, 2) or a modified form of it is suitable for this purpose. A satisfactory product can be produced because the following variables can be efficiently, *i.e.*, effectively and rapidly, controlled: the volume and velocity of the air passing through the device, the air temperature and humidity (hence drying capacity), and the liquid feed rate (hence the amount of water and/or other solvent added). Such positive control makes possible complete regulation of the effervescent reaction.

EXPERIMENTAL

The following illustrates the basic technique described. The example shows how the process functions when all of the ingredients are fluidized together, after which water is added to them. The

composition of the formulation made was: sodium biphosphate, 860 Gm.; tartaric acid, 260 Gm.; citric acid, 100 Gm.; flavor, 5 Gm.; sweetener, 13 Gm.; and sodium bicarbonate, 762 Gm.

The 2 Kg. of material was put into the 6-in. Wurster air suspension apparatus chamber as dry solids. Only distilled water was used to cause the ingredients to react slightly and thus form expanded granules. Running characteristics were: air flow = 30–90 c.f.m.; spray nozzle opening = 20/1000 in.; air nozzle opening = 70/1000 in.; atomization pressure = 60 psig; inlet temperature = 120–140 °F.; exhaust temperature = 100–110°F.; inlet fluid pressure = 2–5 psig with a flow rate of 60–70 ml./minute.

The yield was 95%; the granules obtained were in the range 10–30 mesh. The total time needed to process the 2 Kg. was 10 minutes, and the heat cost was about 0.05 cents/lb. of product. Steam could have been used instead of the distilled water to cause the formation of the granules.

The following formula is an illustration of one of the other techniques possible: citric acid, 140 Gm.; sodium bicarbonate, 860 Gm.; and sodium biphosphate, 1000 Gm.

The 6-in. chamber of the air suspension apparatus was charged with the citric acid and sodium bicarbonate; the sodium biphosphate was sprayed as a 40% w/w solution. Running characteristics were: airflow = 30–60 c.f.m.; spray nozzle opening = 20/1000 in.; air nozzle opening = 70/1000 in.; atomization pressure = 60 psig; inlet temperature = 140–160°F.; exhaust temperature = 110–125°F.; inlet fluid pressure = 2–7 psig with a flow rate of 30–40 ml./minute.

The yield was 95%; the granules obtained were in the range 10–30 mesh. Heat costs would be about 0.2 cents/lb. of product.

A similar formula example, but one which illustrates the making of a more complete formula in a larger chamber is: tartaric acid, 1560 Gm.; citric acid, 600 Gm.; sodium bicarbonate, 4572 Gm.; sodium cyclamate, 78 Gm.; water-soluble flavor, 30 Gm.; and sodium biphosphate, 5160 Gm.

The 12-in. diameter Wurster air suspension apparatus chamber was charged with the two acids and the bicarbonate; the sweetener and flavor were dissolved along with the biphosphate, which was sprayed as a 40% w/w solution. Running characteristics were: airflow = 180–300 c.f.m.; spray nozzle opening = 28/1000 in.; air nozzle opening = 70/1000 in.; atomization pressure = 70 psig; inlet temperature = 160–180°F.; exhaust temperature = 130–140°F.; inlet fluid pressure = 10 psig with a flow rate of 60–80 ml./minute.

The yield was 96%; the granules obtained were in the range 10–20 mesh. Heat costs would be about 0.2 cents/lb. of product.

DISCUSSION

Examination of the processes described for making effervescent products with the Wurster air suspension apparatus seems to indicate that the technique has many advantages over the standard preparative processes usually employed for such pharmaceuticals. That the Wurster device can function as a granulator, mixer, fluidized bed drier, and fluid energy mill is central to the attainment of these benefits.

The extent of the effervescent reaction can be controlled during preparation of the mass; this makes possible the regulation and distribution of the water in the mass. Also, the size of the particles can be controlled, and they can be made without the necessity of grinding a dried mass; this eliminates the familiar ovens and trays in addition to the grinders. In addition, segregation of the initial active ingredients is prevented, and fines can be eliminated or minimized.

Since some of the components can be used as filtered solutions, it is possible to eliminate extraneous materials such as specks or fibers, which may contaminate raw materials, even though they meet U.S.P. specifications. With regard to the final product, the stability may be increased because a protective layer of, *e.g.*, biphosphate can be built around the granules. Further, additional ingredients, such as therapeutically active substances or flavors, may be conveniently and uniformly added to the effervescent granules either before or after they are formed. Naturally, the granules can be compressed into tablets after the addition of suitable lubricants.

Advances in air suspension and other fluidized bed technology, such as that recently noted by Scott *et al.* (3, 4), suggest that a method like one described here may be made continuous. This could make the old space and time-consuming batch processes obsolete and create substantial time and cost savings for users of the new method.

SUMMARY

The Wurster air suspension apparatus has been used successfully to prepare effervescent pharmaceutical products. Use of the apparatus for this purpose was illustrated with examples. The advantages inherent to the suggested new method were discussed.

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