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Preparation of direct compressible effervescent components: spray-dried sodium bicarbonate

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Summary

The aim of this work was to benefit from the advantageous technique of tablet manufacture by direct compression for the easy preparation of stable effervescent tablets. In order to overcome the bad flowability and low compressibility of sodium bicarbonate, a common carbon dioxide source in effervescent tablet formulation, a spray-drying technique was applied. The adjustment to achieve different conditions when operating the spray-dryer was described. Some additives such as polyvinylpyrrolidone and silicon oil were found to be essential to obtain direct compressible spray-dried sodium bicarbonate. The prepared spray-dried sodium bicarbonate showed good compression characteristics and excellent compressibility without being transformed into sodium carbonate.

Introduction

Some limited trials were made to apply direct compression technique in the manufacture of effervescent tablets (Lindberg, 1970; Aiache, 1974; El-Banna and Minina, 1981; Saleh et al., 1984). This may be due to the poor compressibility of sodium or potassium bicarbonate and other effervescent tablet ingredients. One of the most important factors on which the successful application of direct compression technique depends is the availability of suitable materials. The problems associated with the materials are mainly concerned with flow and bonding of particles to form a strong compact. The production of various directly compressible grades of effervescent components seems essential to solve most of the problems of the direct compression of effervescent tablets. Sodium glycine carbonate was a trial in this direction (Mendell, 1972).

Spraying-drying has been used pharmaceutically not only as a drying technique but also for many other purposes. It has been used in the production of sustained action tablets by Asker and Becker (1966) and by Kornblum (1969). It has also been applied to the preparation of microencapsulated agglomerates by Kawashima et al. (1972). An improvement of solubility and dissolution rate of poorly water-soluble salicylic acid has been published by Kawashima et al. (1975). Nürnberg and Dolle (1980) reported an improvement of the dissolving behaviour of the cardiac glycosides. Spray-drying has also been applied for preparing

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free-flowing granules for tableting by Scott et al. (1964) and by Fell and Newton (1971).

Spray-drying usually results in the production of free-flowing monodispersed particles which could be directly compressed into tablets, filled into capsules, or put into suspensions (Asker and Becker, 1966). It was the aim of the present work to study the production of spray-dried sodium bicarbonate and to investigate its properties especially its direct compressibility which will facilitate the manufacture of directly compressed effervescent tablets.

Experimental

Materials

Sodium bicarbonate and polyvinylpyrrolidone (PVP) (Prolabo, France). Polyethylineglycol (PEG) 6000 (Merck, F.R.G.). Rhodorsil (silicon oil) fluid 47 V 5000 C (Rhone Poulenc, France). Tween 80 (Merck, F.R.G.). Hydroxypropylmethylcellulose (Pharmacoat 603) (Seppic, France).

Equipment

A spray-dryer (Niro Atomizer Ltd., Copenhagen, Denmark) fitted to an air compressor (Maco Meudon type FP-507 France) and a peristaltic pump (Masterflex, Cole-Parmer Instrument Co., Chicago, U.S.A.).

A JSM-840 scanning electron microscope (JEOL, Tokyo, Japan).

A local made apparatus for determination of angle of repose.

A Turbula T2A mixer (Willy A. Bachofen Mascchinenfabric, Basle, Switzerland)

An instrumented tablet machine (single punch Korsch EK/O, Korch-Berlin, F.R.G.) fitted with 12 mm flat punches and attached to a system of measurement and registration.

An Erweka TBT hardness tester (Erweka Aparatbau, F.R.G.).

Methods

Preparation of solutions. 150 g of sodium bicarbonate was dissolved in 2 litres of distilled water. In the case of incorporating additives, the latter were dissolved in a part of the distilled water and then added to sodium bicarbonate dissolved in the rest of the distilled water. The percentage of the additives was calculated as a function of the weight of sodium bicarbonate, i.e. when it is mentioned that 3% of certain additives was incorporated, this means that 4.5 g of the additive was used with 150 g of sodium bicarbonate.

Spray-drying. The spray-dryer was operated according to the conditions that will be mentioned in each case.

Particle shape. Particle shape was inspected by scanning electron microscopy and photographs were taken to facilitate the comparison between the different spray-dried products.

Particle size. Particle size of the spray-dried products was measured by a photographic counting method.

Test of normal carbonate USP XX. According to the test of the USP XX, 2 ml of 0.10 N HCl and 2 drops of phenolphthalein TS were added to 1 g of sodium bicarbonate, previously dissolved without agitation in 20 ml of water at a temperature not exceeding 5 °C. The solution does not assume more than a faint pink colour immediately.

Angle of repose. The angle of repose of the products was measured according to the "dynamic method" using a local made apparatus which consisted of an aluminium cup with 2.5 cm radius. A carton or paper cylinder that can easily fit on the inverted cup was used. The powder was allowed to flow freely into the cylinder which was then removed and a heap was formed. The height of the formed heap was measured and the angle was calculated. The test was repeated 3 times and the mean value was calculated.

Bulk density. The bulk densities, either before or after tapping, were determined using a measuring cylinder, 100 ml capacity. The method can be described as follows: a known weight of the powder was allowed to flow freely into the measuring cylinder and the volume occupied by this quantity was measured and the apparent bulk density (before tapping) was obtained by dividing the mass by the volume. The packed bulk density (after tapping) was obtained after tapping the measuring cylinder containing the powder onto a hard wood surface from a height of 1 inch at 2 s

intervals until a constant volume was obtained.

Mixing. Mixing was not necessary in the case of the studied spray-dried products as no external lubricant was introduced, whereas the original sodium bicarbonate was mixed with 3% polyethyleneglycol 6000 (250 μm) during 5 min at 25 rpm in a Turbula T2 A mixer.

Compression of tablets. Tablets were prepared using an instrumented Korsch EK/O single punch tableting machine equipped with 12 mm flat punches. Batches, each of at least 100 tablets, were compressed. The compression cycles of 10 tablets, in the middle of each batch, were recorded. From these records, the different compression parameters were calculated.

Hardness. The hardness of 10 tablets of each batch was determined using an Erweka hardness tester. The mean value was calculated in each case.

Results and Discussions

Adjustment of spray-drying conditions

Table 1 summarizes the conditions which were interchanged to determine the optimum conditions for the spray-drying of sodium bicarbonate. The main factors which we could change were: air pressure, liquid feed rate and inlet temperature. In formulation I, the maximum liquid feed rate was used and an air pressure of 3 kg/cm^2 was chosen. A high inlet temperature (170 °C) was used to realize the drying of the chosen high liquid feed rate. These conditions led to an agglomerated damp powder that hardly flowed into the bottle.

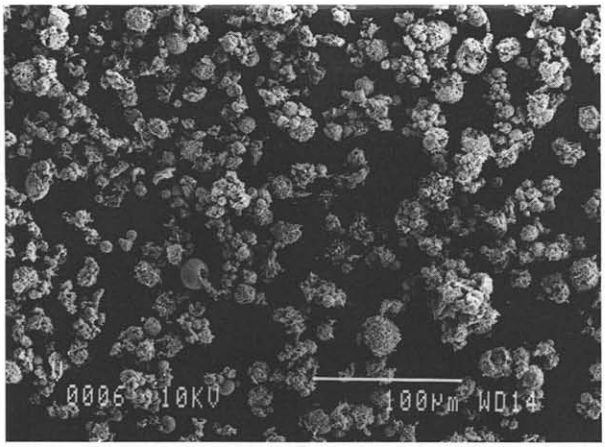
In formulation II, air pressure was increased to 4 kg/cm^2 which means an increased velocity of the spraying disk and means that finer droplets are being formed. In this manner, less agglomerated powder with a lower angle of repose was obtained.

In formulation III, liquid feed rate was decreased to 45 ml/min while air pressure was kept at 4 kg/cm^2; this gave rise to a dry, moderately flowing powder with a low angle of repose. Upon decreasing the liquid feed rate to 28 ml/min and increasing air pressure to 6 kg/cm^2, a powder with a bad flowability was obtained as indicated by its angle of repose (formulation IV in Table 1). This may be due to the smaller particle size which may have resulted.

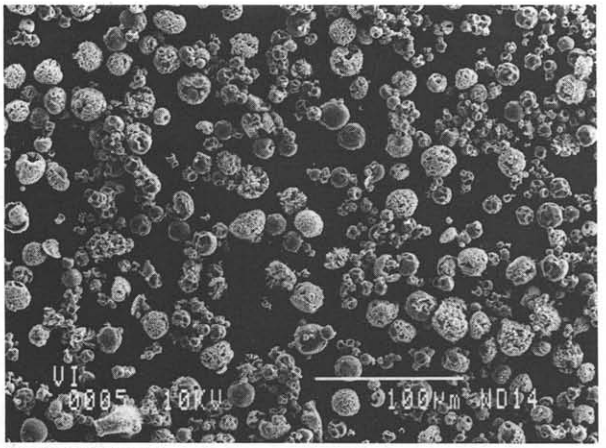
TABLE 1

Adjustment of sodium bicarbonate spray-drying conditions

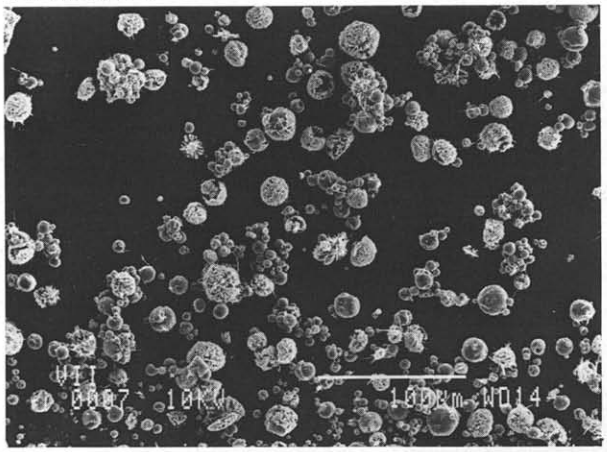
Conditions and properties	Formulation: I	II	III	IV	V
Air pressure (kg/cm^2)	3	4	4	6	4
Liquid feed rate (ml/m)	60	60	45	28	52
Inlet temp. (°C)	170	150	150	150	150
Exit temp. (°C)	70	60	75	87	75
Angle of repose	65	59	58	61	57
General aspect	agglomerated damp powder flows hardly inside the bottle	less agglomerated powder	dry powder flows moderately inside the bottle	agglomerated powder	dry powder flows well inside the bottle



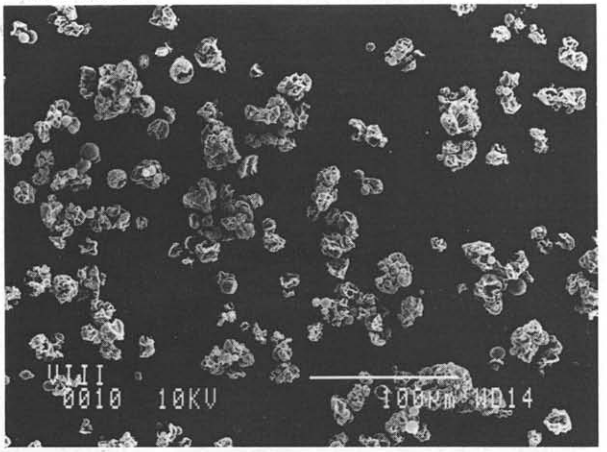
Formulation V



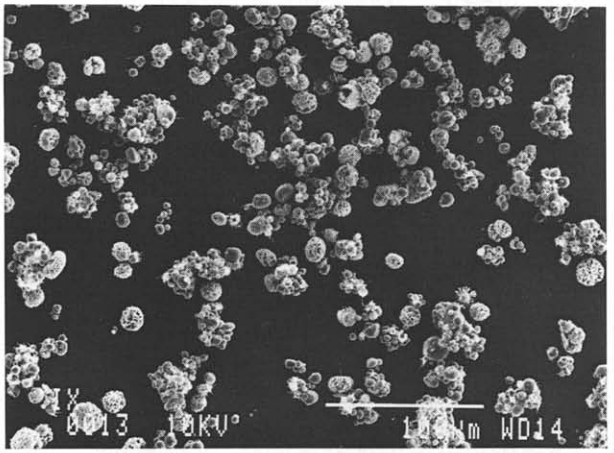
Formulation VI



Formulation VII

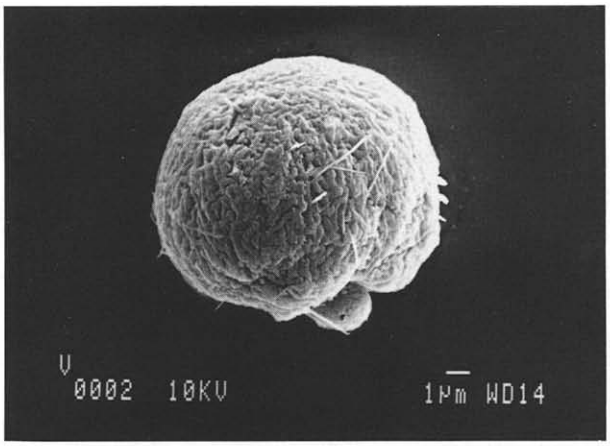


Formulation VIII

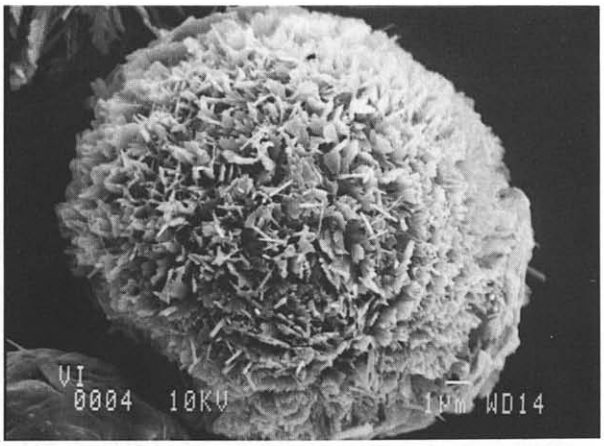


Formulation IX

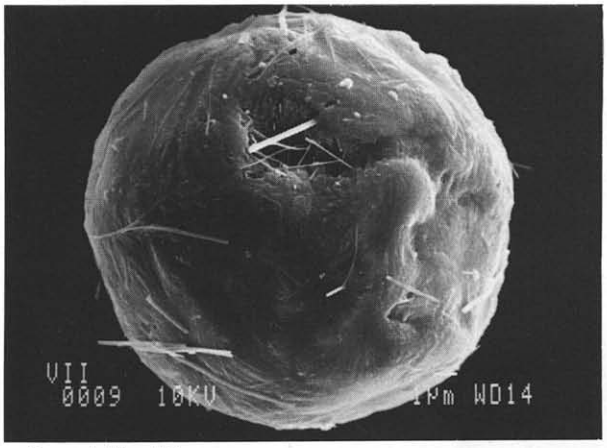
Fig. 1. Scanning electron microphotographs of spray-dried sodium bicarbonate.



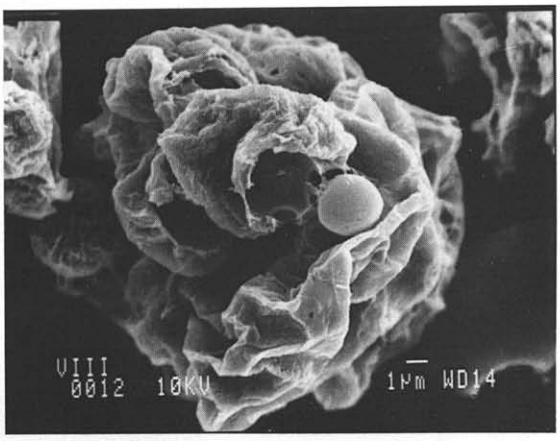
Formulation V



Formulation VI



Formulation VII



Formulation VIII

Formulation IX

Fig. 1 (continued). Scanning electron microphotographs of spray-dried sodium bicarbonate.

TABLE 2

Adjustment of different additives

Properties	Formulation: V	VI	VII	VIII	IX
	$NaHCO_3$	$NaHCO_3$ 5% PVP	$NaHCO_3$ 5%PVP 3% PEG	$NaHCO_3$ 5% Pharmacoat 3% PEG	$NaHCO_3$ 4% PVP 3% PEG 0.5% silicon oil 0.25 Tween 80
Particle size (μm)	12	13.2	15	14	17
Bulk density	0.2	0.28	0.25	0.18	0.26
Packed bulk density	0.35	0.48	0.41	0.30	0.41
Angle of repose	57	56	53	59	48
R	–	0.77	0.78	0.88	0.83
Compression force (dN) for 6 kg hardness tablets	–	650	622	933	847
Difficulties upon compression	difficult to compress due to irregular filling	little chipping and capping	very little chipping at high pressures	irrigular die thin tablets	good tablets no capping no chipping

Resuming an air pressure of 4 kg/cm^2, increasing the liquid feed rate to 52 ml/min and increasing the inlet temperature to 170 °C, led to spray-dried sodium bicarbonate of the best characteristics and flowability as shown in formulation V in Table 1. These basic conditions of air pressure, liquid feed rate and inlet temperature were kept constant hereafter for the rest of our study.

Test of carbonate

Heating of sodium bicarbonate beyond 50 °C normally leads to its transformation into sodium carbonate as patented by White (1963). The USP test of normal carbonate was carried out and indicated that during the spray-drying of sodium bicarbonate no transformation into carbonate took place. This is due to the very short drying time in the process of spray-drying. It was stated by Künanz and Mignat (1980) that because of the short drying times, the product is hardly affected and spray-drying is therefore especially suitable for temperature sensitive products.

Adjustment of different additives

Adjustment of the spray-drying conditions of sodium bicarbonate alone led to a spray-dried powder that flows well inside the bottle but was difficult to compress into tablets due to its small bulk density and irregular die filling. Some products were added to improve the compressibility of the spray-dried sodium bicarbonate such as polyvinylpyrrolidone, Pharmacoat and polyethylene glycol. Although many trials were carried out, Table 2 gives only a few examples containing the best formulation (IX).

Inclusion of 5% PVP (formulation VI) gave rise to an improvement in particle size, bulk density and angle of repose but its corresponding tablets suffered from little chipping and capping. In formulation VII, 3% of PEG 6000 in addition to 5%

TABLE 3

The compression characteristics of normal and spray-dried sodium bicarbonate

Type	Mean compression force (dN)	*R*	Hardness (Erweka) (kg)	Force (dN) for 6 kg hardness tablets
Original sodium bicarbonate	1855	0.88	1.5	6324
	3028	0.90	3.4	
	4415	0.92	4.8	
	6117	0.92	5.4	
Spray-dried sodium bicarbonate	486	0.83	2.6	847
	709	0.82	4.8	
	817	0.83	5.9	
	1234	0.83	9.4	

of PVP were included that led to an improvement in the compression behaviour.

Incorporation of 5% of Pharmacoat instead of PVP (formulation VIII) decreased the bulk density and improved the angle of repose but irregular die filling was noticed upon compression.

In formulation IX, 0.5% of silicon oil was incorporated with the aid of 0.25 % of Tween 80 while the proportion of PVP was decreased to 4%. This formulation was considered to be the best one due to the improvement in particle size, force transmission index (R) as well as the ease with which it was able to be compressed into tablets.

Fig. 1 (A and B; difference in magnifications being 300 and 5000 times, respectively) gives the scanning electron microphotographs of the different spray-dried sodium bicarbonate products (the key of the formulations is the same as in Table 2). They demonstrate the spherical form obtained upon spray-drying of most of the formulations except in the case of including Pharmacoat which gave rise to not completely spherical particles. On the other hand, the inclusion of polyethylene glycol 6000 and silicon oil gave rise to spherical particles with smooth surfaces. These microphotographs also permitted the calculation of the particle size, given in Table 2, and indicated the change in particle size upon including the different additives.

In a previous study, Saleh et al. (1983) failed in trying to compress sodium bicarbonate alone without the addition of direct compression excipients, yet we found with the present sodium bicarbonate (of another granulometry) that we succeeded in directly compressing it into tablets but at the expense of ease of compression as these tablets suffered from capping, picking and chipping. Table 3 shows the compression characteristics of normal (original) and spray-dried sodium bicarbonate. Spray-dried sodium bicarbonate showed better compression characteristics as indicated by the low compression force requirements and accompanying increased hardness, in addition to the ease in tablet compression.

The pressure hardness profiles of normal and spray-dried sodium bicarbonate indicates the superiority of spray-dried sodium bicarbonate and its better compressibility over that of normal one.

Work on spray-dried sodium bicarbonate is being continued in order to study its expected better solubility, its hygroscopicity, stability and its incorporation into effervescent tablet formulation. Moreover, spray-drying of other effervescent tablet components is envisaged.

Conclusions

Spray drying of sodium bicarbonate was achieved with no risk of transformation into sodium carbonate.

Inclusion of some additives was essential to improve bulk density and to increase the particle size of spray-dried sodium bicarbonate to enable its direct compression.

The spray-dried sodium bicarbonate showed excellent compression characteristics compared to the non-spray-dried one; this makes it a future candidate for a source of carbon dioxide in the manufacture of effervescent tablets by direct compression.

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