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Process to manufacture effervescent tablets: air forced oven melt granulation

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In the present study we apply melt granulation in an air forced oven, called "are forced oven melt granulation" to the single-stage manufacture of effervescent granules consisting of anhydrous citric acid (43.2%) and sodium bicarbonate (56.8%) in order to make tablets. This study established that process parameters such as concentration of PEG 6000, residence time in the air forced oven, fineness of PEG 6000, fineness of the initial effervescent mix and efficiency of two lubricants markedly influenced several granule and tablet characteristics. The granules ready to be compressed into tablets were stable for 7 days at 60% RH/18 °C. It is a dry, simple, rapid, effective, economical, reproducible process particularly well suited to the manufacture of effervescent granules which are easily compressed into effervescent tablets. Of all the formulations tested, only formulations B2 and E2 melt granulated for 30 minutes gave tablets which had optimum compression characteristics without processing problems during compression.

1. Introduction

To reduce the problems arising in the manufacture of effervescent granules by the traditional granulation processes [1, 2] (poor flowability and cohesiveness in dry methods [3–5], loss of carbon dioxide, time and energy consumed in wet methods [6–9]) we utilised a one-stage process without solvent called air forced oven melt granulation [10–14], to manufacture effervescent granules comprising anhydrous citric acid, sodium bicarbonate and polyethylene glycol 6000 (PEG 6000) which is a melting material. Anhydrous citric acid and sodium bicarbonate, an effervescent system which produces carbon dioxide more efficiently than other potential effervescent systems, is that for which the one-stage process is most difficult to implement. Nevertheless, our study showed that, air forced oven melt granulation is a simple dry process for the rapid (1 h) and reproducible production of stable effervescent granules which possess good compression characteristics.

2. Investigations, results and discussion

Tables 1 to 4 and Figs. 1 to 5 summarise the results of the investigations.
In the discussion we consider the influence of the process parameters mentioned below on granule characteristics:

- three residence times in the air forced oven (15, 30 and 60 min);
- latent period before screening;
- content of PEG 6000 of two finenesses (very fine and flaked powder);
- two finenesses of the effervescent system (moderately fine and very fine powder);
- two lubricants (sodium benzoate and silicone sodium benzoate).

2.1. Characteristics of raw materials

We determined the particle size distribution, water content, and specific surface area (specific SA) of the raw materials. The results in Table 1 show that for any raw material the greater the subdivision of particles, the greater their specific SA (e.g. ACAmfp : 0.0917 sq.m/g versus ACAvfp : 0.344 sq.m/g) [15]. For both the very fine powder and the moderately fine powder effervescent systems, the particle size distributions of the components are close to each other: this makes it possible to obtain homogenous mixtures. The low water content of the raw materials is in accordance with the manufacturing requirements for effervescent forms [16, 17]. As shown in Table 2, the moderately fine powder effervescent system (mfpES) and the very fine powder effervescent system (vfpES) are unable to form hard tablets by direct compression because of sticking, capping, friction and very poor flow of vfpES. This is the reason for our investigation. The formulations tested are listed in Table 3.

Table 1: Characteristics of raw materials

Raw materials	Particle size distrib. (% w/w)	Water content (%w/w)	Specific SA (m^2/g)
ACAmfp (Roche)	Over 355 μm = 12 355 to 180 μm = 84 Under 180 μm = 4	0.05	0.0917
ACAvfp (Roche)	Under 125 μm = 100	0.09	0.344
SBCmfp (Solvay)	Over 355 μm = 17 355 to 180 μm = 60 Under 180 μm = 23	0.03	0.0912
SBCvfp (Solvay)	Under 125 μm = 100	0.06	0.241
PEGvfp (Contensio)	Under 125 μm = 100	0.04	1.07
PEGf (Hoechst)	Over 1mm = 95 Under 1 mm = 5	0.02	0.01
SBvfp (Mallinckrodt)	Under 125 μm = 100	0.05	1.4
SSBvfp	Under 125 μm = 100	0.05	1.3

ACAmfp = Anhydrous citric acid as moderately fine powder
ACAvfp = Anhydrous citric acid as very fine powder
SBCmfp = Sodium bicarbonate as moderately fine powder
SBCvfp = Sodium bicarbonate as very fine powder
PEGvfp = Polyethylene glycol 6000 as very fine powder
PEGf = Polyethylene glycol 6000 as flake
SBvfp = Sodium benzoate as very fine powder
SSBvfp = Siliconed sodium benzoate as very fine powder

2.2. Influence of process parameters on granule characteristics

On the basic of our results, we identified three groups of granule characteristics.

Table 2: Characteristics of initial effervescent system

Characteristics	Moderately fine powder effervescent system (mfpES)	Very fine powder effervescent system (vfpES)
Flowability (s)	7 (1)	Infinite
Ability to settle (ml)	6 (1)	34 (2)
Tapped density	1 (0.01)	0.89 (0.01)
Water content (% w/w)	0.02 (0.001)	0.04 (0.001)
Mean granule size (μm)	265 (75)	69.8 (18.8)
Friability (%)	2	NA
CO_2 content (mg CO_2/g of granule)	298 (3)	293 (5)
Disintegration (s)	190 (2)	184 (2)
pH of solution	5.6 (0.04)	5.61 (0.05)
Appearance of solution	Clear	Clear
Specific SA sq.m/g	0.0914	0.29
Ability to form strong tablets under apllied pressure	Impossible to make tablet by direct compression	

Mean (SD), n = 3. NA = non applicable

Table 3: Formulations studied

Formulations Components	A	B	C	D	E
Granules					
ACAmfp	43.2	43.2	43.2	43.2	–
ACAvfp	–	–	–	–	43.2
SBCmfp	56.8	56.8	56.8	56.8	–
SBCvfp	–	–	–	–	56.8
PEGvfp*	1	3	5	–	6
PEGf*	–	–	–	3	–

Tablets	A1	A2	B1	B2	C1	C2	D1	D2	E1	E2
SBvfp*	3	–	3	–	3	–	3	–	3	–
SSBvfp*	–	3	–	3	–	3	–	3	–	3

ACAmfp = Anhydrous citric acid as moderately fine powder
ACAvfp = Anhydrous citric acid as very fine powder
SBCmfp = Sodium bicarbonate as moderately fine powder
SBCvfp = Sodium bicarbonate as very fine powder
PEGvfp = Polyethylene glycol 6000 as very fine powder
PEGf = Polyethylene glycol 6000 as flake
SBvfp = Sodium benzoate as very fine powder
SSBvfp = Siliconed sodium benzoate as very fine powder
Formulas A, B, C and D were made with moderately fine powder effervescent system (mfpES). Formula E was very fine powder effervescent system (vfpES)
*Percentages are calculated relative to 100 g of effervescent system

2.2.1. Granule characteristics not affected by process parameters

The physicochemical properties of granules such as water content (0.02%), carbon dioxide content (297 ± 4 mg), pH of tablet solution (5.62 ± 0.02) and appearence of the solution (clear) are not affected by the process since the values obtained for all the formulations tested are almost the same as that of the initial effervescent mixture before granulation (Table 2). Since the physicochemical properties of the granules did not change significantly compared to those of the initial powders before granulation, it proves that the process did not cause deterioration of the initial components of the formulations. Thus air forced oven melt granulation is a milder and more advantageous method compared with wet methods.

2.2.2. Granule characteristics differing from those of the initial effervescent mix but remaining constant with respect to process parameters

The effervescent time and flowability of the granules remaines at 180 ± 3 s and 8 ± 3 s respectively in all formulations tested. Granule effervescent time is in accordance with the Eur. Pharmacopoeial requirements for effervescent granule disintegration, and flowability is adequate to avoid tablet weight variation during compression.
Granule ability to settle remained at 8 ± 2 ml in all formulations tested, except in formulation E in which the value was 24 ± 2 ml (Table 2).

2.2.3. Granule characteristics markedly affected by process parameters

The latent period before screening (cooling) is very important, because when the screening is premature (less than 30 min at 30% RH ± 3/22 °C ± 2 after removal from the air forced oven), the granules adhere to form aggregates which grow, causing flowability to become discontinuous and the weight variation of tablets to increase. When compressing prematurely screened granules, the tablets are pasty instead of being brittle during the crushing strength test. So 30 min is the time necessary to allow the PEG 6000 melt in the granules to harden.
The mean granule size increases with concentration of PEG 6000, fineness of PEG 6000, fineness of initial effervescent mix and residence times in air.
For all formulations investigated, the residence times have notably affected the granule size distribution, characterised in the present study by the mean granule size. The mean granule size increases as residence time increases. So for formulation B, at 15 min, 30 min and 60 min the mean granule sizes are 405 μm, 435 μm and 500 μm, respectively. After 1 h in an air forced oven, the mean granule size did not change regardless of formulation. This observation can be explained by the fact that in the air forced oven, PEG 6000 melts and diffuses progressively through the bed of powder. The phenomenon reaches its maximum after 1 h.
With formulations A, B and C made with moderately fine powder effervescent system and 1%, 3% and 5% respectively of very fine powder of PEG 6000, the mean granule size increases as the concentration of PEG 6000 increases. For example, after 15 min in an air forced oven, the mean granule sizes are 285 μm, 405 μm and 470 μm. With over 5% of PEG 6000 in a moderately fine powder effervescent system, the mean granule size continues to increase and makes flowability irregular and infinite. Granule formation can be explained with the help of the proposed mechanism of melt granulation in Fig. 2: since melt granulation is

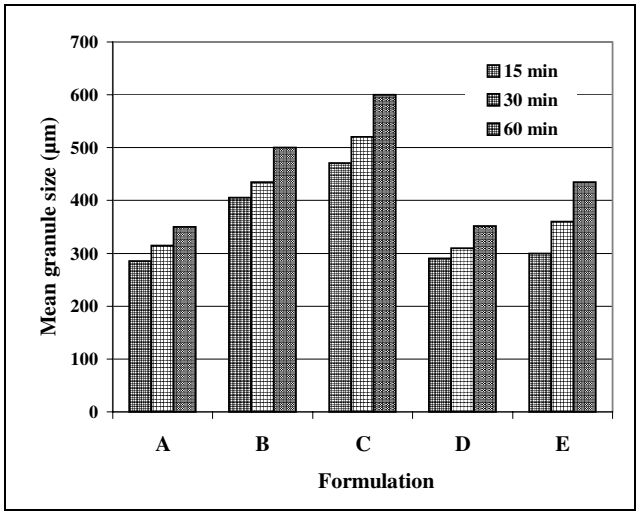

Fig. 1: Influence of process on mean granule size

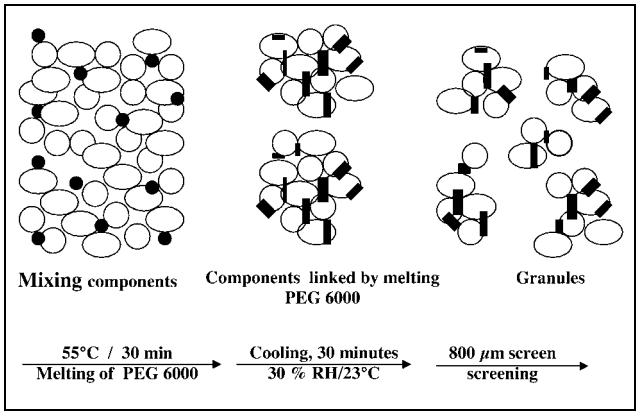

Fig. 2: Mechanism of melt granulation: after mixing and putting components in an air forced oven, PEG 6000 melts and links the particles by the bridges of melting PEG 6000 through the bed of the effervescent mixing to form aggregates which after cooling and screening give granules
◯ Anhydrous citric acid; ○ Sodium Bicarbonate; ● PEG 6000; ◆ Bridges of melting PEG 6000

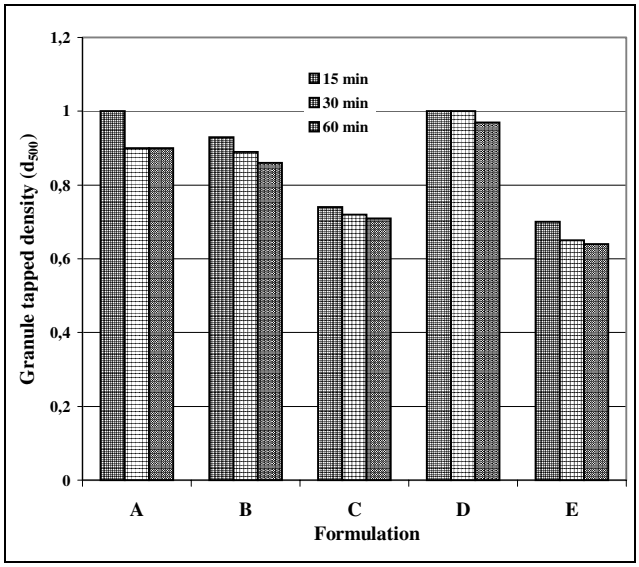

Fig. 3: Influence of process on tapped density

related to the bonding of particles by melting PEG 6000 through the bed of initial effervescent mix to give aggregates which form granules after cooling and screening, the greater the concentration of PEG 6000, the greater the surface area of initial effervescent mix it can cover.

The use of 3% of flaked PEG 6000 in moderately fine powder effervescent mix (formulation D) gave granules with a mean size less than that of granules made with 3% of very fine powder PEG 6000 in moderately fine powder effervescent mix (formulation B). This observation shows the influence of PEG 6000 fineness on the granulability of an effervescent system. The explanation can also be found in the proposed mechanism of melt granulation (Fig. 2): the greater the fineness of PEG 6000, the greater its specific SA and the greater the surface area of effervescent mix it can cover.

In the very fine powder effervescent systems, we studied the effect of concentration of very fine powder PEG 6000 (1%, 3%, 6%, 9%, 15%). We confirmed that, with an effervescent system consisting of very fine powder anhydrous citric acid and sodium bicarbonate, it is not possible to manufacture a granule with a concentration of powdered PEG 6000 less than 6%. With concentrations of 9% and 15% of very fine powder PEG 6000, we obtained after cooling a strong mass that could not be screened with our apparatus. So formulations containing very fine powder effervescent system (formulation E) need more very fine powder PEG 6000 to make a granule than formulations containing moderately fine powder effervescent system (formulation B) (e.g. 6% in formulation E versus 3% in formulation B). This observation demonstrates the influence of fineness of the effervescent system on granule formation. The explanation can also relate to the proposed mechanism of melt granulation: since the degree of subdivision of the particles of very fine powder effervescent systems is greater than that of moderately fine powder effervescent systems, the surface area covered by PEG 6000 (e.g. 0.29 m^2/g versus 0.0914 m^2/g) is greater and the amount of PEG 6000 required to make granules is larger.

Fig. 3 shows that for all formulations investigated, when residence time increases tapped density decreases. When concentration of PEG 6000 increases, tapped density decreases (e.g. formulations A, B and C). Tapped density of granules made with formulation B is lower than that of granules made with formulation D even when the two formulations have the same concentration of PEG 6000. This difference shows the influence of fineness of PEG 6000 on the tapped density of the granules (e.g. very fine PEG 6000 powder in formulation B versus flaked PEG 6000 in formulation D). So tapped density decreases with the fineness of the PEG 6000. The tapped density of formulations made with very fine powder effervescent system (E) is less than that of formulas made with moderately fine powder effervescent system (e.g. E versus C), and this shows the influence of the fineness of the effervescent system. The decrease in tapped density can be explained by the increase in mean granule size when process parameters vary as mentioned above.

As shown in Table 4, when residence time increases, granule friability decreases, except in formulations A and D. The common characteristic of formulas A and D is the lack of sufficient PEG 6000 which acts as a binder.

The decrease in granule friability follows the increase of concentration of PEG 6000 in formulations A, B and C. The influence of fineness of PEG 6000 is demonstrated when comparing formulation D with formulation B which both contain the same concentration of PEG 6000 but have different granule friability. So we can say that fineness of PEG 6000 reduces granule friability. The influence of fineness of the effervescent system on granule friability

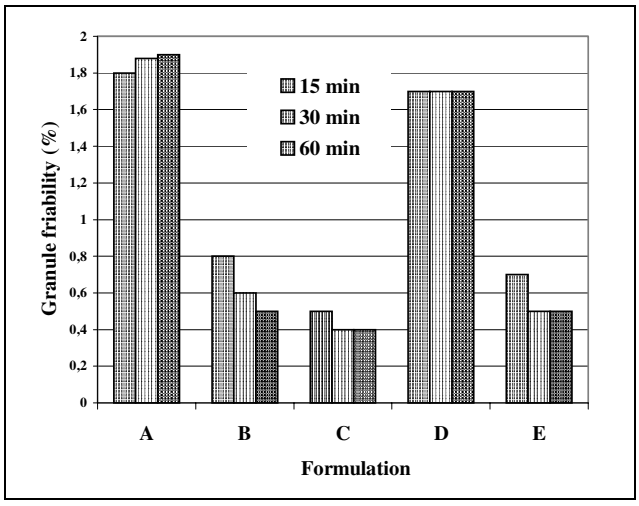

Fig. 4: Influence of process on granule friability

Table 4: Process reproducibility

	Batch 1	Batch 2	Batch 3
Granules characteristics			
Ability to settle	11 (2)	12 (3)	9 (2)
Appearance of solution	Clear	Clear	Clear
CO_2 content (mg CO_2/g of granule	291 (4)	292 (3)	290 (5)
Disintegration (s)	180 (3)	179 (2)	181 (2)
Flowability (s)	7 (1)	6 (1)	6 (1)
Granule friability (%)	0.5 (0.1)	0.6 (0.2)	0.5 (0.1)
Mean granule size (μm)	485 (170)	480 (165)	490 (159)
pH of solution	5.62 (0.02)	5.61 (0.03)	5.62 (0.01)
Tapped density (d_{500})	0.85 (0.02)	0.86 (0.01)	0.85 (0.01)
Water content%w/w	0.02 (0.001)	0.02 (0.002)	0.02 (0.002)
Tablet characteristics			
Appearance of solution	Clear	Clear	Clear
CO_2 content (mg CO_2/g of tablet)	282 (4)	283 (3)	281 (4)
Friability (%), n = 10 tablets	0.5	0.4	0.5
Disintegration (s)	59 (3)	60 (3)	58 (3)
pH	5.64 (0.04)	5.63 (0.04)	5.65 (0.04)
Crushing strength (N)	82 (0.59)	83 (0.57)	81.1 (0.5)
Tablet appearance	Smooth & bright	Smooth & bright	Smooth & bright
Water content % w/w	0.02 (0.001)	0.02 (0.002)	0.02 (0.002)
Weight (g), n = 20 tablets	2.27 (0.01)	2.25 (0.03)	2.26 (0.02)

Mean (SD), n = 3

is not perceptible since the values obtained are comparatively the same as for moderately fine effervescent systems. As PEG 6000 acts as a binder, the greater the concentration of PEG 6000, the greater the hardness of the granule.

The compression at constant volume (depth of lower punch within the die = 6.98 mm) and constant position of upper punch in the die (6.04 mm) permitted us to distinguish 4 categories of formulations:

– Formulations A and D give capping and tablets with poor to crushing strength (< 40 N), with the premature appearance of sticking and friction during compression. Capping and poor crushing strength are due to insufficient of very fine PEG 6000 powder which acts as a binder. Formulation A has only 1% of very fine PEG 6000 powder. Formulation D has 3% of PEG 6000, but it is flaked. As it is flaked the PEG 6000 cannot cover the effervescent mix as homogeneously as very fine PEG 6000 powder. This conclusion was foreseeable from the influence of PEG concentration and fineness on the mean granule size.

– Formulations B1, C1 and E1 give a uniform mass and tablets with good crushing strength (80 to 115 N), but with the premature appearance of processing problems such as sticking and friction. These processing problems come from the fact that sodium benzoate appears to be a poor water soluble lubricant.

– Formulation C2 gives tablets with homogeneous weight and moderate crushing strength (70 N), but the premature appearance of sticking signifies the excess of PEG 6000 in the formulation (5%): under the same conditions, sticking is absent in formulation B2 which contains only 3% of PEG 6000.

Compression characteristics have never been continuous in these first three categories of formulations because of the processing problems mentioned above.

– Formulations B2 and E2 give tablets with uniform mass without processing problems during compression. Their compression characteristics were then evaluated by comparing the crushing strength of tablets manufactured at constant mass (2 ± 0.1 g) at several positions of the upper punch in the die [18].

According to the results shown in Fig. 5, crushing strength increases as the position of upper punch in the die increases from 4.26 mm to 6.66 mm; beyond 6.66 mm the press jams. A small variation of position of the upper punch in the die gives a large variation in crushing strength (e.g. B 2.30 min: with a variation of 1.06 mm, crushing strength increases from 76 N to 143 N). Thirty minutes is a residence time that gives maximum crushing strength to the tablets in both formulations. For an equivalent crushing strength, 15 min residence time requires a deeper position of the upper punch in the die than for 30 min. At 1 h residence time, the crushing strength decreases.

Thus a 30 min melt granulated formulation B2 is the best formulation because it permits us to obtain tablets which possess homogeneous weight and the greatest crushing strength without processing problems during compression.

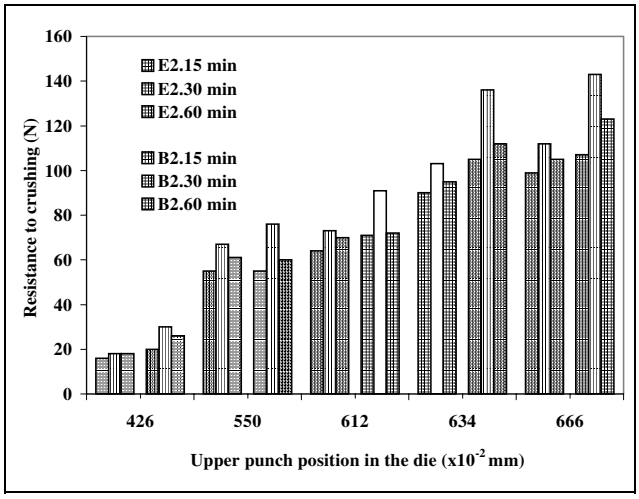

Fig. 5: Compression characteristics of formulation B2 and E2, mean tablet weight = 2 ± 0.1 g

2.3. Reproducibility of air forced oven melt granulation

Three batches of 2 kg of a 30 min melt granulated formulation B2 which was the best formulation were manufactured in order to check the reproducibility of the process. According to the results in Table 4, the granule and tablet characteristics are almost the same for the three batches tested. So analysis of the data establishes that the process is reproducible.

2.4. Moisture intake of granule

We chose a 30 min melt granulated formulation B2, which gives tablets having optimum compression characteristics, to evaluate the equilibrium moisture of effervescent granules.

In all the micro-climates studied, the variation in of equilibrium moisture content after seven days of effervescent granules ready to be compressed into tablets, is less than that of the initial effervescent mix (e.g. at 90% RH/18 °C: 190% versus 226%; at 71% RH/18 °C: 50% versus 74%). At 60% RH/18 °C, the variation in the percentage of equilibrium moisture content after seven days is zero, even though that of the initial mix is 35%. So effervescent granules ready to be compressed into tablets are non-hygroscopic up to 60% RH/18 °C. This observation can be explained by the following facts: since granulation increases the particle size, the specific SA decreases and the contact area of particles with the atmosphere also decreases. As PEG 6000 is a non-hygroscopic material, class I of the hygroscopicity classification [19], when it covers the granule, it also reduces the contact area of the initial material with the atmosphere. The hydrophobic property of siliconed sodium benzoate makes it act as a moisture repellent. So the effervescent granules ready to be compressed into tablets examined here can be handled without moisture uptake in an atmosphere with a relative humidity up to 60% HR/18 °C.

In conclusion, with regard to the granule characteristics of the formulations investigated, only formulations B2 and E2 gave tablets having good compression characteristics, but formulation B2 melt granulated for 30 min was the best. Formulations A1, A2, D1, and D2 gave tablets with very poor crushing strength and capping because of the lack of PEG 6000, which acts as a binder. Formulations B1, C1, C2 and E1 gave tablets with good crushing strength and good weight but with the premature appearance of sticking during compression. We can say that air forced oven melt granulation preserves the stability of the raw materials since the physicochemical characteristics of the granules are almost the same as those of the initial effervescent mix before granulation. Granules ready to be compressed into tablets can be handled in an atmosphere up to 60% RH/18 °C without moisture intake as they were stable for 7 days in a microclimate of 60% RH/18 °C. Air forced oven melt granulation is a simple, reproducible and rapid process because the processing time is 60 min (30 min of residence time in air forced oven and 30 min of cooling). In a future investigation, we will apply air forced oven melt granulation for single-stage granulation of effervescent system mixes and active ingredients in order to make tablets.

3. Experimental

3.1. Manufacturing methods

The single process temperature of 55 °C was imposed by the physicochemical limitations of the components: on the one hand, PEG 6000 melts between 55 °C and 63 °C [20] and on the other hand sodium bicarbonate becomes unstable when heated to about 50 °C [21]. The formulations were made up from 2 kg of a stoichiometric effervescent system (ES) composed of anh. citric acid (43.2%) and sodium bicarbonate (56.8%) as moderately fine powder (mfp) or very fine powder (vfp), and very fine PEG 6000 powder (PEGvfp) or flaked PEG 6000 (PEGf) was added as a melt material. After mixing in a cubic mixer (Erweka FGS) at 24 rpm for 20 min, the effervescent mix was put in the air forced oven, previously adjusted to 55 ± 1 °C. The granules were obtained bonding particles with melting PEG 6000 for 15 min, 30 min or 60 min. After cooling at 30 ± 3% RH/22 ± 1 °C for 30 min, the granules were screened with an oscillating granulator (Erweka FGS) fixed at moderate speed (II), and fitted with a 800 μm screen.

3.2. Study methods

The study methods allowed us to characterise the granules in order to identify the test formulations which have good compression characteristics without processing problems such as sticking, capping, and friction during compression.

3.2.1. Pharmaceutical technical methods

3.2.1.1. Granule flowability and densities

Granule flowability, tapped densities, ability to settle (Volumenometer, JEL/STAV 2003A). were determined as prescribed in the third edition of the European pharmacopoeia (2.9.16, 2.9.16).

3.2.1.2. Granule size distribution

The granule size distribution was analysed using 100 g of granules and a vibrating Retsch Siever (amplitude: 1.5; 10 min) fitted with a European pharmacopoeial series of sieves (710 μm, 500 μm, 355 μm, 250 μm, 180 μm, 125 μm). Mean granule size was determined graphically with a log-normal chart [22].

3.2.1.3. Granule friability

The granule friability was determined with an accurately weighed 25 g sample of the fraction of granules over 180 μm sieve, using a Turbula mixer (28 rpm, 10 min) and a 180 μm sieve. The percentage of weight lost after mixing and sieving was calculated [(weight before mixing and sieving − weight after mixing and sieving)/weight before mixing and sieving × 100].

3.2.1.4. Effervescent granule disintegration

Effervescent granule disintegration was determined with 3 g of granules accurately weighed using the method of the third edition of the European pharmacopoeia (Dosage forms)

3.2.1.5. Granule compression characteristics

For each formulation studied, after mixing 1 kg of effervescent granules with 3% of sodium benzoate or 3% of siliconed sodium benzoate, in a Turbula mixer at 28 rpm for 10 min, we obtained granule mixes ready to be compressed into tablets.

Tablets were manufactured with a single punch press (Frogerais OA) equipped with chromed punches of 24 mm diameter, in a workroom in which air conditioning was adjusted to 30 ± 3% RH and 22 ± 2 °C. Uniformity of mass, resistance to crushing (ERWEKA TBH 28), friability (Pharma Test PTF 1E), and disintegration, were evaluated with third edition of European pharmacopoeial methods (2.9.5, 2.2.8, 2.29.7 and dosages forms). Tablet water content, carbon dioxide content, solution pH and tablet and solution properties were evaluated by the physicochemical methods described below. Sticking to the punch faces and die wall, capping, and friction at the die wall were also evaluated visually. All formulations were first screened by compressing at constant volume and constant position of upper punch in the die. Compression characteristics of formulations that gave tablets of uniform mass without processing problems were then evaluated: For each formulation, the fill volume was first adjusted to obtain tablets of 2 ± 0.1 g. At each position of the upper punch in the die, tablet uniformity of mass was determined. Ten tablets were then collected to determine crushing strength and the means were reported. Upper punch position in the die was measured with a Comparator (Mitutoyo) graduated to 0.02 mm.

3.2.2. Physicochemical methods

3.2.2.1. Water content

Water content was determined with 1 g of sample accurately weighed or one compressed tablet respectively, dried in a desiccator containing activated silicagel. This method was used so as to avoid decomposition of sodium bicarbonate [21] and melting of PEG 6000 [20]. The loss on dry-

ing was calculated after a specified time of 4 h, [(weight of sample before drying-weight of sample after drying)/weight of sample before drying) $\times$ 100)].

3.2.2.2. Appearence and pH of solution

Appearance and pH of the solutions were determined with 3 g of granules or one tablet respectively, in 200 ml of distilled water at 20 ± 1 °C. The appearance of a solution of the sample was assessed visually; the solution had to be clear at the end of effervescence. The pH was determined with a pHmeter AQUADATA APH 1000.

3.2.2.3. Carbon dioxide content

The carbon dioxide content of 3 g of granules accurately weighed or one tablet respectively, in 100 ml of dilute sulphuric acid (R), was determined with a sensitive balance, Mettler PG 503 S [23, 24]. The results were expressed as a loss of weight of the sample at the end of effervescence (mg CO_2 per gram of effervescent system).

3.2.2.4. Granule equilibrium moisture content

In order to study the moisture intake of the granules, granule equilibrium moisture content was obtained for samples of 3 g of granules in three micro-climates containing a saturated salt solution of potassium nitrate (90% RH/18 °C), sodium chloride (71% RH/18 °C), and sodium nitrite (60% RH/18 °C). On the first day and after seven days in the micro-climates, the percentage equilibrium moisture content (EMC %) of the granules was measured with an aqualab CX2 (Decagon) [19].

3.2.2.5. Specific surface area

The specific surface area of the raw materials and initial effervescent mix was measured by laser granulometer (Mastersizer S Ver 2.18, Malvern Instruments). This apparatus measures the diameter of the sphere that possesses the equivalent volume to a particle in order to calculate the specific surface area (specific SA).

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Received December 30, 1999
Accepted April 10, 2000

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