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ORIGINAL ARTICLE

Hot tableting as a new method for obtaining tablets from slow release-coated pellets

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Abstract

Background: Coating of pellets poses difficulties in the tableting process, which is attributed to the fact that ethylcellulose is a fragile polymer having low resistance to compression. This property of ethylcellulose is the reason why obtaining a slow release profile from tableted pellets comparable with that of uncompressed pellets is practically impossible when traditional tableting process is employed. *Method*: This work presents a newly developed method of hot tableting of pellets. The pellets used in the process were tramadol hydrochloride (TH) coated with an Aquacoat ECD aqueous dispersion. A physical property of PEG 3000 (one of the components of the tablet formulation) to liquidify at a given temperature was used in the process of hot tableting carried out at about 56°C. *Results*: During the hot tableting, when a low compression force of about 1 kN was applied, semi-liquid granules containing melted PEG 3000 combined with TH pellets. As the temperature decreases to room temperature, a tablet matrix of good physical parameters was created. In the proposed hot tableting method, granulates containing PEG 3000 provide the tableted pellets sufficient protection from being destroyed. An evidence of such protection is confirmed by the fact that the TH slow release profile from the tableted pellets is comparable to that of uncompressed pellets. *Conclusion*: The hot tableting method allows to obtain the tablets containing compressed pellets with a TH slow release profile comparable to that of uncompresed pellets.

Key words: *Compression; film coating; pellets; slow release; tablets*

Introduction

Hot tableting presents a new concept of producing tablets. The compression force in the hot tableting—as opposed to traditional tableting—is very low and the mechanisms responsible for forming tablet matrix such as fraction of particles, bond formation, and consolidation followed by elastic recovery during the decompression process are not present[1].

During hot tableting process under low compression force, the tablet matrix is formed as a result of the tablet ingredients being bound by a melted excipient present in a tablet composition. The above-mentioned aspects of the process, especially the low compression force, create new possibilities of tableting pressure-sensitive materials, for example, modified and slow release pellets and enzymes[2,3].

Hot tableting also allows to compress moisture-sensitive substances into tablets by completely eliminating water from the granulates. A unique process of creating the tablet matrix during hot tableting allows to use a high percentage of disintegrating substances and to obtain tablets with high porosity, which is favorable during producing orally dispersible tablets[4].

The pellets are composed of the core coated with a film coating polymer, whose characteristics allow the active pharmaceutical ingredients (APIs) to diffuse slowly during the dissolution test. Pharmaceutical technology makes wide and frequent use of ethylcellulose (EC) as a component of the film coating layer. The EC can readily form film coating with proper diffusive characteristics and physicochemical stability[5].

When EC is used as the coating of the pellets, which are to be compressed into tablets, special consideration should be given to mechanical resistance. The film coating should resist the compression force; although it may undergo a slight deformation, it should not break.

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EC coating is brittle and prone to breaking, which is mainly because of strong inner-chain interactions typical of hydrogen bonds[6].

A number of concepts have been tried out in the area of tableting EC film-coated pellets. For instance, part of the tablet formulation was composed of sugar spheres, which—with the API placed on the surface—were then coated with hypromellose and EC and plasticized with triethyl citrate and other plasticizers[7]. A thick EC coating or a multilayer film coating composed of successive applications of different derivatives of EC was also tried[8]. Another approach was introduced to prevent disposition of the cracks on the surface of the coating by curing the compressed pellets for 24 hours at 70°C[9]. Attempts have also been made to influence the degree of pellet deformation by changing the percentage of the EC-coated pellets in the tablet formulation. Other methods of the tableting of pellets involve the use of placebo pellets of differing porosity[10], excipients in powder form [e.g., microcrystalline cellulose (MCC), sucrose, or starch][11], and soft pellets decreasing the release rate[12].

An interesting attempt was to use a combination of excipients exhibiting plastic properties in the compression process—MCC combined with soft excipients, that is, glyceryl behenate[13], glyceryl palmitostearate[14], glyceryl monostearate[15], PEG[16,17], and cellulose fibers soaked with PEG 400 MCC fibers[18].

Wax excipients having low melting point alone or in combination with MCC can produce soft granules especially achieved when hot melt granulation was applied. Beads made without wax (the control formulation) required greater compression forces to form cohesive tablets. As the amount of wax in the bead formulation was increased, the beads become more plastic and compressible.

Similarly, waxes with relatively low melting temperature are used to obtain soft wax granules by means of melt pelletization, which in turn allows to create a tablet formulation where soft wax granules would be compressed and would protect the polymer-coated pellets containing the active substance[19]. However, the methods mentioned above did not allow to achieve satisfactory properties of the tablets, such as disintegration time and dissolution rate.

The API release from the EC film-coated compressed pellets was noticeably higher than the release from uncompressed pellets. This undesired fast release of API occurred as a direct consequence of the damage to the coating caused by the compression force of the punches.

The purpose of this study was to develop a method for tableting coated tramadol hydrochloride (TH) pellets using a hot tableting process where minimal compression force was used to prevent the EC pellet film coating from being damaged and to obtain tablets with good physical properties. The study was also intended to achieve a slow TH release from tableted pellets—possibly closest, which would be as close as possible to that of uncompressed pellets.

Materials and methods

Materials

The following were the materials used: tramadol hydrochloride (Polpharma, Starogard Gdański, Poland), microcrystalline cellulose, Avicel® PH101 (FMC, Brussels, Belgium), glyceryl behenate (Compritol® ATO 888, Gattefosse, St-Priest, France), ethylcellulose (Aquacoat® ECD; FMC BioPolymer, Philadelphia, PA, USA), triethyl citrate (Lancaster, Morecambe, UK), microcrystalline cellulose and guar gum (Avicel® CE-15; FMC BioPolymer, Brussels, Belgium), lactose monohydrate (Pharmatose® DCL-11, DMV International, Veghel, the Netherlands), polyethylenglycol 3000, PEG 3000 (Merck Schunchardt OHG, Hohenbrunn, Germany), mannitol (Parteck® M100, Merck KGaA, Darmstadt, Germany); dibasic calcium phosphate dihydrate as a Emcompress® (JRS Pharma, Rosenberg, Germany), modified starch (Starch 1500®; Colorcon, Indianapolis, IN, USA), croscarmellose sodium (Vivasol®, JRS Pharma, Rosenberg, Germany), sodium stearyl fumarate (Pruv®, JRS Pharma, Rosenberg, Germany), TH reference tablets (Tramal Retard 100 mg, batch no 29L01, Grunenthal GmbH, Aachen, Germany).

Preparation of pellet cores with TH

Pellet cores were prepared by wet granulation of powder mixture followed by spheronization of the extruded mass. On the basis of in the initial experiments, the composition of pellet cores was determined as follows: TH 60.0%, MCC, PH101 35.0%, and glyceryl behenate 5.0%. All substances were granulated with water (30/100 g of the powder mixture) in a high-shear mixer (Glatt VG5, Dresden, Germany). The wet granulate was extruded in an extruder (Caleva model 25; Caleva Ltd., Dorset, UK) through a 1.0-mm diameter sieve. The extrudate (about 30 g) was spheronized for 5 minutes in a 120-mm spheronizer (Caleva model 120; Caleva Ltd.) fitted with a cross-hatch plate rotating at 1800 rpm. The resulting pellet cores were dried at 45°C in a tray oven for 16 hours. Pellet cores of 0.6–1.0 mm in diameter comprised the largest fraction (about 65%) in the given conditions of extrusion and spheronization.

Coating of the pellet cores

The drug-loaded pellet cores (800 g) were coated in a fluidized bed coater using the Wurster bottom spray

(Glatt GPCG3, Binzen, Germany) with an aqueous EC dispersion (Aquacoat® ECD) (680 g). The aqueous polymer dispersion was plasticized with triethyl citrate (42.5 g, 25%, w/w, based on the mass of the polymer) for 2 hours before the coating process to achieve good uptake of the plasticizer by the colloidal polymer particles. The polymer content of the plasticized dispersion was then adjusted to 20% (w/w) by diluting with water (170 g). The coating conditions were as follows: inlet air temperature (55°C), outlet air temperature (42°C), atomization air pressure (1.5 bar), fluidizing air flow (180 m^3/h), and coating rate (6–8 g/min). The pellets were cured at 60°C for 24 hours.

The film coating was sprayed onto drug-loaded pellets to achieve drug release over 8 hours. The film coating thickness of the pellets was determined by cross-sectioning 12 randomly selected pellets with a scalpel. The film coating thickness was measured by placing the hemispheres under a microscope (Eclipse E200; Nikon, Tokyo, Japan) coupled with a digital camera (Altra 20; Soft Imaging System GmbH, Munster, Germany). A computer program (analysis; Soft Imaging System GmbH) was used to calculate—based on the results—an average thickness of the pellet film coating (45 ± 4 μm).

Hot TH pellets tableting

Tablet formulation was composed of a mixture of TH pellets (0.6–1.0 mm) in the ratio of 50% pellets and 50% granulates, which was obtained during wet granulation process conducted in a high-shear mixer using water as a binder (30/100 g of powder). PEG 3000 was an integral component in each of the granulated powders (formulations I–VI), which additionally contained MCC, lactose monohydrate, mannitol, modified starch, MCC, and guar gum and dibasic calcium phosphate dihydrate in the ratio of 1 to 1. The composition of tablet formulations is presented in Table 1.

Each granulate was separately dried in a blow drier (Venticell BMT, Brno, Czech Republic) at 45°C for 16 hours. The dried granulates were then passed through a sieve with a mesh size of 1.0 mm. Then the pellets, croscarmellose sodium, and sodium stearyl fumarate were added, and the mixture was mixed for 5 minutes. Croscarmellose sodium was added as a disintegrating substance to ensure disintegration of tablets into pellets. Sodium stearyl fumarate was used as a lubricant to prevent hot granulates from sticking to the punches. A ratio of 50% pellets and 50% granulates ensured that the tablet formulation had adequate flow, which could otherwise be adversely affected by tackiness of heated tablet formulation.

The resulting tablet formulations were spread evenly on a paper tray and heated in a blow drier to a temperature not greater than 56°C. A tablet press granulate feeder was heated in another blow drier. The feeder was then immediately mounted onto a rotary tablet press (Korsch XL 100, Berlin, Germany) filled with the heated tablet formulation. The formulations were then compressed into tablets via the hot tableting process in the same conditions. During a 3-minute tableting process, the temperature of the tablet formulation dropped from 56°C to 55.2°C. The temperature was measured using an electronic contact thermometer (ETS-D4 fuzzy model; IKA Labortechnik, Staufen, Germany) inserted into the tablet formulation in the tablet press granulate feeder. The tableting parameters were as follows: spherical punches (10.0 mm in diameter), curve radius (9 mm), main compression force (1, 3, 6, and 10 kN), precompression force (0.1, 0.3, 0.6, and 1 kN), and single tablet mass (400 mg). The precompression values were preset by Korsch XL 100 rotary tableting machine as one tenth of the main compression force. Small values from 0.1 to 0.6 kN had no effect on particle rearrangement of the die fill. This is opposite to traditional tableting where (1 kN) precompression force is responsible mainly for rearrangement and deairation of the die fill and plays a key role during the tableting process.

Table 1. Composition (%) of tablet formulations with pellets coated with Aquacoat® ECD.

	Formulation					
Components	I	II	III	IV	V	VI
Pellets[a]	50.0	50.0	50.0	50.0	50.0	50.0
Microcrystalline cellulose	23.6	—	—	—	—	—
Lactose monohydrate	—	23.6	—	—	—	—
Mannitol	—	—	23.6	—	—	—
Modified starch	—	—	—	23.6	—	—
Microcrystalline cellulose and guar gum	—	—	—	—	23.6	—
Dibasic calcium phosphate dihydrate	—	—	—	—	—	23.6
PEG 3000	23.6	23.6	23.6	23.6	23.6	23.6
Croscarmellose sodium	2.5	2.5	2.5	2.5	2.5	2.5
Sodium stearyl fumarate	0.3	0.3	0.3	0.3	0.3	0.3

[a]100-mg pellets containing 45.8 mg TH.

Physical properties of tablets obtained by hot tableting

Tests for disintegration, friability, and hardness of tablets obtained by hot tableting were performed according to USP 31 that specifies requirements for compressed tablets. Spectrophotometric assay for TH in tablets was determined using a tablet powder (20 units) exactly equivalent to 100 mg of the tablets. The TH concentration was read from the appropriate calibration graph.

In vitro release studies

Dissolution test was performed in 1000 mL of water at 37°C (±0.5°C). An automated Hansson Research Sr8+ basket apparatus dissolution tester (Hansson Research, Chatsworth, CA, USA) with an on-line UV/Vis spectrophotometer (Agilent 8453; Agilent Technologies Inc., Wilmington, DE, USA) was used. At different time intervals (1, 2, 3, 4, 5, 6, 7, and 8 hours), the concentration of TH in the samples was analyzed spectrophotometrically at 272 nm. Single tablet mass was 400 mg and contained 91.6 mg of TH. The dissolution results were calculated with reference to 100 mg of TH standard. All dissolution profiles are the mean of 12 dissolution tests performed under sink conditions.

Similarity of dissolution profile of the tablets was compared using model-independent method by linear regression at specified time points and calculating a similarity factor f_2. An f_2 value between 50 and 100 suggests that two dissolution profiles are similar:

$$f_2 = 50 \times \log\left[1+\left(\frac{1}{n}\right)\sum_{t=1}^{n}(R_t - T_t)^2\right]^{-0.5} \times 100.$$

In this equation, f_2 is the similarity factor, n is the number of time points, R_t is the mean percent drug dissolved of, for example, a reference product, and T_t is the mean percent drug dissolved of, for example, a test product[20].

Compressibility

A texture analyzer was used to measure the compressibility of the pellets combined with the PEG 3000-loaded granules at 56°C and at room temperature. The apparatus was equipped with aluminium cylinder probe (TA XT Plus; Stable Micro System, Surrey, UK). The pellets and the granules (tablet formulation V) were heated using magnetic stirrer hotplate (Ret B; IKA WERKE, Staufen, Germany) equipped with an electronic contact thermometer. The test was performed on pellets and granules, a single pellet and a single bead being tested at a time. A single pellet (or bead) was placed on the magnetic stirrer hotplate heated to 56°C. Then a stainless steel cylinder was also placed on the hotplate surrounding the pellet. The use of the cylinder ensured that the entire surface of the pellet would be evenly heated rather than only the point where the pellet was in contact with the hotplate. A probe, fitted with a sensor, was inserted into the stainless steel cylinder and lowered at an even rate toward the surface of the pellet. The speed of the probe moving down the cylinder was 0.1 mm/s. The sensor in the probe automatically was set to detect the surface of the pellet (or granule) and automatically reduced the speed to 0.05 mm/s on a distance of 50% of the pellet's diameter as the pellet was crushed. The ratio between force (N) and distance (mm) was measured. The measurements were performed 12 times. Then Texture Exponent 32 computer program was used to calculate the area under curve as the work of compression 50% (mJ).

Structure characteristics of tablets

The structure and appearance of the tablets were investigated using images obtained by scanning electron microscopy (SEM, Zeiss SUPRA 35VP; Carl Zeiss, Jena, Germany). Extra high tension voltage power of 1 kV was used for pictures A, C, D, E, F and 3 kV for picture B (Figure 2). The 180-fold magnification was used for pictures A, B, E, F and 200-fold magnification for pictures C and D.

Results and discussion

TH pellet cores were obtained by means of extrusion and spheronization. The compressed pellets contained 100 mg of TH. The purpose of extrusion and spheronization was to introduce as much API into the pellets as possible. The results showed that a composition of 60.0% TH, 35.0% MCC, and 5.0% glyceryl behenate gave the extrudate the 'shark skin' effect and that the pellet cores had spherical shape and high durability. An additional amount of glyceryl behenate increased the plasticity of the extrudate and prevented agglomeration of the pellets during spheronization. Water was used as a binder. Initial tests with the use of hydrophilic polymer water solutions of povidone and hypromellose failed because of the high binding properties of the powder mixture.

The polymer coating should have sufficient mechanical resistance and strength to withstand the force of compression applied by the punches during the compression of the slow release pellets[21]. The coating should be capable of deforming plastically in the process, but it should not break as this would lead to immediate release of the API. The major difficulty in compressing pellets was frequent deformation and fragmentation of the film coating and the core when the compression force was applied[19,22]. Deformation and fragmentation had a particular adverse effect on EC film coatings, which were exceptionally fragile and had low stretching and deformation properties[6,23].

Thus, optimum slow release from TH pellets could be achieved by compressing the pellets via a hot tableting method in which it was mainly the fillers and the binder (PEG 3000 in the form of granules) that were deformed and the TH pellets were kept intact. This allowed to obtain a tablet matrix with the required physical properties.

The ability of PEG 3000 to liquidify at 52–56°C was used in hot tableting process to achieve optimum properties of the granules[24]. This was also the reason why the temperature of the tablet formulation (formulations I–VI) and the temperature of the rotary tablet press feeder was 56°C. Under tableting conditions, the use of relatively low compression forces (1, 3, and 6 kN) allowed to create bonds between the TH pellets and the semiliquid granules containing melted PEG 3000. In the final stage, a drop in temperature from 56°C to room temperature allowed to obtain a tablet matrix with good mechanical properties. Semiliquid granules accommodated their shape to the pellets without adverse impact on the coating and the cores of the pellets.

The relationship between the distance and the force needed to obtain 50% deformation of pellets and granules was determined. The area under the curve for the pellets (Figure 1B) and the granules (Figure 1D) obtained in compressibility test preformed at 56°C was larger for the pellets than for the granules. It can be assumed that the granules were more prone to deformation and displacement under the pressure of the punches at 56°C.

Low compression forces applied during the tableting produced a small number of granulate particles and pellets with adhering surfaces. This was sufficient to produce a tablet matrix. The tablets obtained by applying a low compression force (1 kN) had hardness and friability parameters complying with USP 31 requirements except for formulations IV and VI. Tablet hardness and disintegration time (during which a tablet disintegrated into pellets) increased as the compression force was increased, that is, disintegration time from 13 minutes at 1 kN to increase 46 minutes at 6 kN. When the tableting process was conducted at 20°C, similar mechanical properties and relatively short disintegration time of 6 minutes were obtained with a compression force of 10 kN.

Scanning electron microscopy of tablets: formulation V compressed at 56°C with a compression force of 1 kN

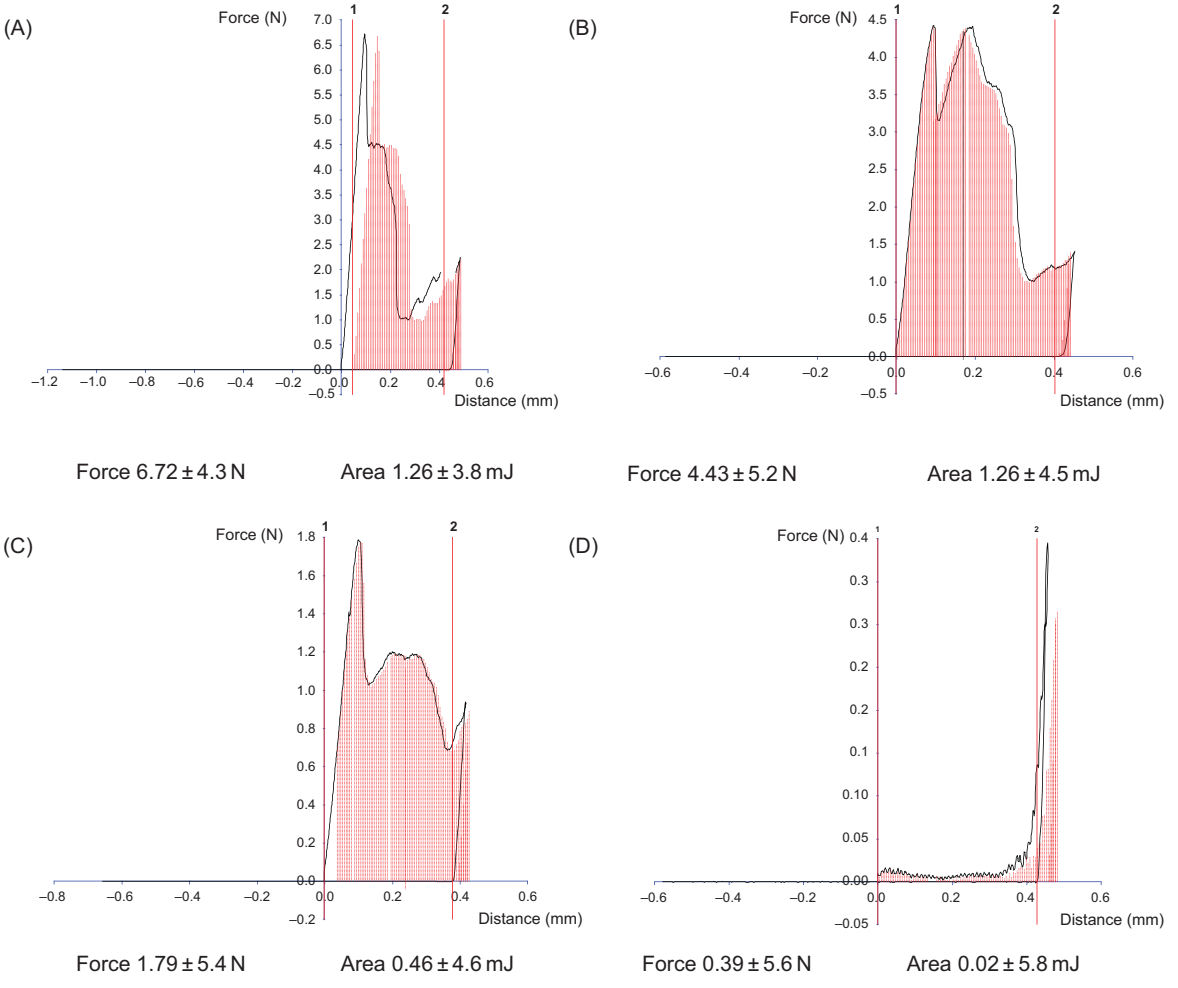

Figure 1. Compressibility of pellets coated with Aquacoat® ECD at 20°C (A) and at 56°C (B) and the compressibility of granules formulation V compressed at 20°C (C) and at 56°C (D).

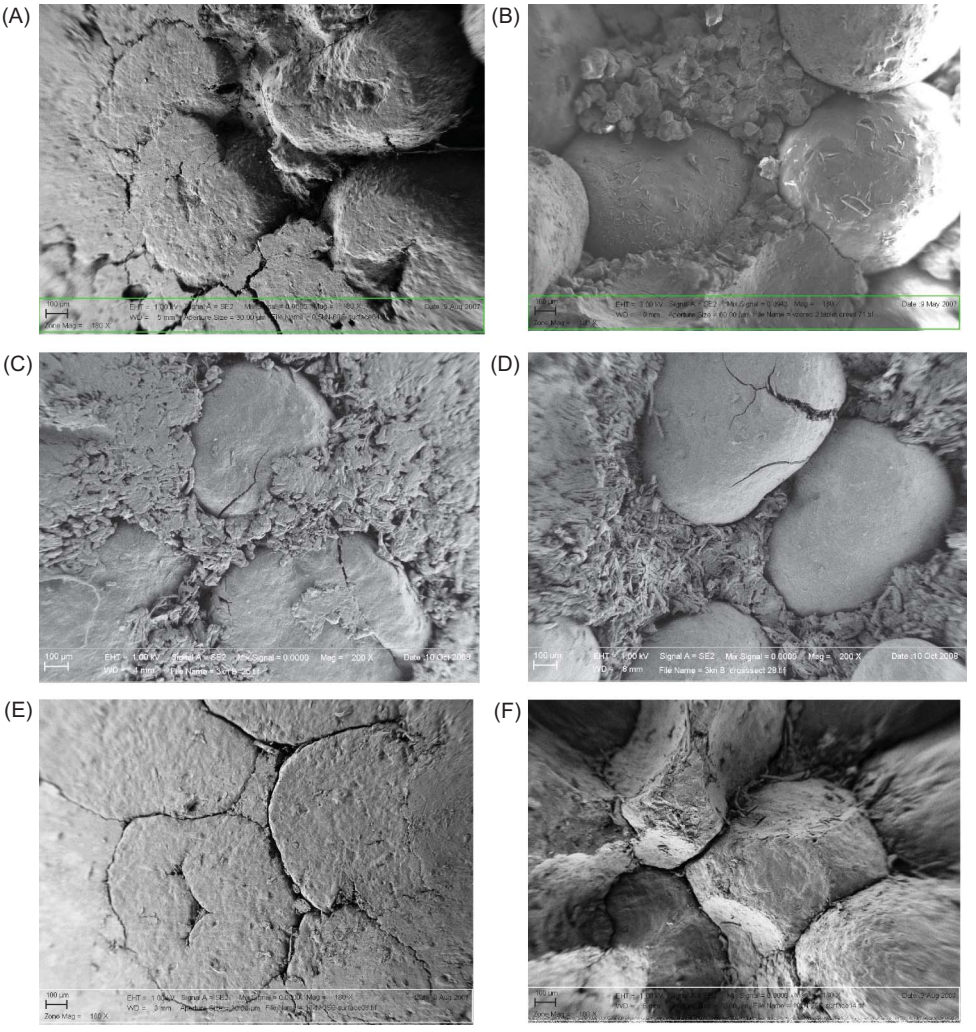

Figure 2. SEM images of compressed pellets (formulation V). Hot tableting, 1 kN/56°C: tablet surface (A) and tablet cross section (B); hot tableting, 3 kN/56°C: tablet surface (C) and tablet cross section (D); traditional tableting, 10 kN at 20°C: tablet surface (E) and tablet cross section (F).

showed an uneven and porous surface (Figure 2A). This appears to be due to the fact that a very low pressure of the punches was applied to hot tablet formulation. This observation was confirmed by the cross section of a tablet shown in Figure 2B, which exhibited a loose structure with undamaged pellets.

Photographs of the surface of traditionally obtained tablets show a typical, smooth surface with visibly compressed and deformed pellets (Figure 2E). A cross section image of such tablets also showed a tablet with a compressed and packed structure where pellets and granules were visibly damaged and deformed (Figure 2F).

The results of TH release profiles from hot tableted pellets (formulation V) confirmed the conclusions obtained by SEM. For tablet formulation V, a comparison (Figure 3) shows the TH release profiles of the pellets compressed at 56°C, the pellets obtained at room temperature, and the pellets that were not tableted. The increase in TH release profiles was achieved by applying higher compression force (3 and 6 kN). The increase can also be attributed to partial deformation and fragmentation of pellets—especially those near the surface of the tablet and in direct contact with the surfaces of the punches and the dies. The degree of pellet fragmentation and deformation was highest at room temperature.

Figure 4 shows the profiles in the discriminating dissolution medium of the reference tablets—Tramal Retard 100 mg, the profiles of the pellets that did not undergo the tableting and a comparison between TH release profiles of pellets obtained by applying a compression force of 1 kN to formulations I–VI (Table 1) during hot tableting process. The TH release profile of hot tableted pellets (formulation V) obtained by applying a compression force 1 kN was similar to that of uncompressed pellets (f_2 = 54). Similarity factor f_2 for the release profiles between hot tableted pellets (formulation V, 1 kN) and Tramal Retard 100 mg was f_2 = 71.

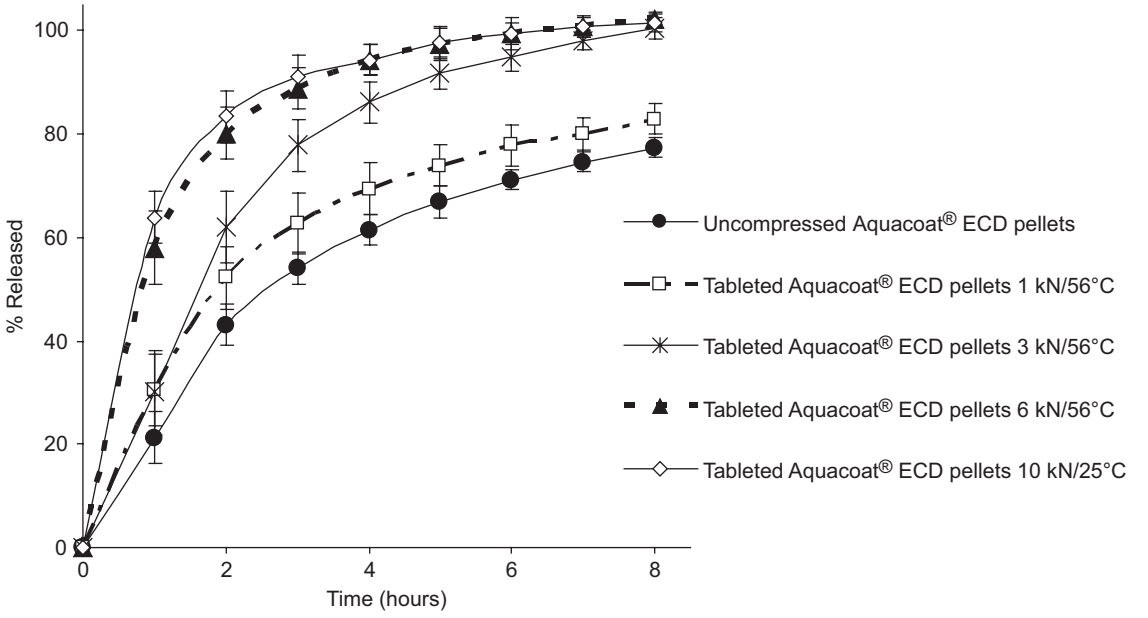

Figure 3. Effect of traditional and hot tableting on tramadol hydrochloride dissolution profile of coated Aquacoat® ECD pellets tableted as such (formulation V).

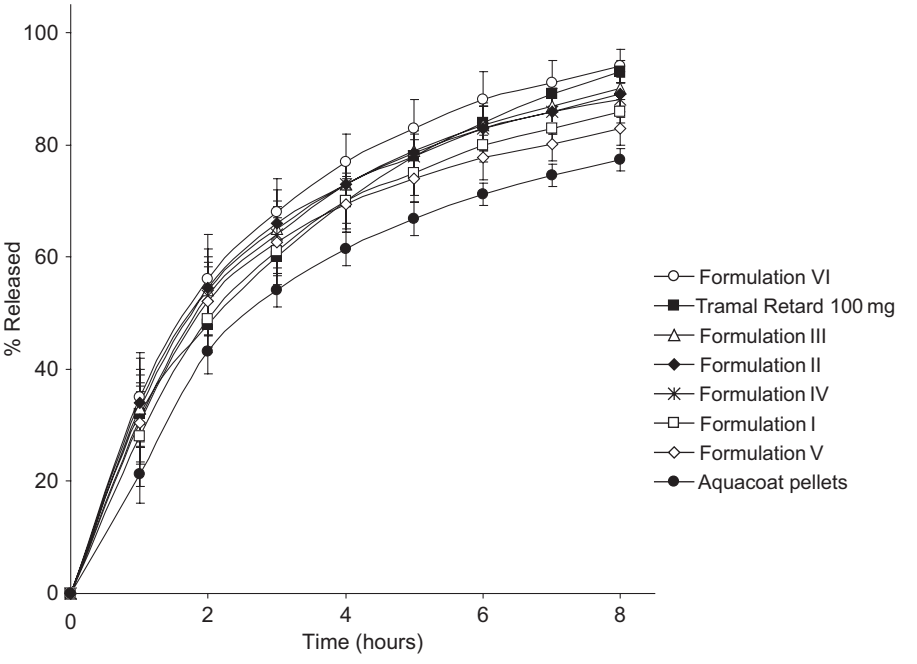

Figure 4. Effect of hot tableting (1 kN/56°C) on dissolution profile tramadol hydrochloride of coated Aquacoat® ECD pellets tableted as such.

TH release rate does not show significant differences in hot tableted pellets, which indicates that the fillers did not have a meaningful impact on hot tableting process. The similarity factor f_2 for the most distinguishable release profile—formulation V and VI—was 59.

The minimal impact of the fillers was due to the fact that the soft granules (melted PEG 3000 combined with the fillers) and the pellets easily create bonds during the hot tableting process, which in turn produces the tablet matrix. The soft granules in a compressed tablet reduce TH pellet deformation and fragmentation. TH release profile, similar to that of uncompressed pellets, was obtained with the tablets from formulation V containing TH pellets, MCC with guar gum, PEG 3000, croscarmellose sodium, and sodium stearyl fumarate. The presence of elastic guar gum definitely increases the cushioning

Table 2. Physical properties of tablets obtained by hot and traditional tableting.

	Compression force/tableting temperature								
	1 kN/56°C						3 kN/56°C	6 kN/56°C	10 kN/20°C
	Formulation								
Parameter	I	II	III	IV	V	VI	V		
Hardness (N)	45 ± 2.1	55 ± 3.3	48 ± 4.4	41 ± 1.7	48 ± 4.2	51 ± 3.0	81 ± 4.0	101 ± 3.8	54 ± 3.1
Friability (%)	1.0	0.9	0.9	1.3	0.7	1.0	0.2	0.0	0.6
Thickness (mm)	6.55 ± 1.8	5.98 ± 2.3	5.91 ± 2.0	6.18 ± 3.7	6.23 ± 1.1	5.71 ± 1.1	5.50 ± 0.9	4.90 ± 1.5	5.30 ± 0.7
Disintegration time (minutes)	8	13	14	9	13	18	35	46	6
Assay (%)	98.1	98.3	97.9	99.0	97.4	96.9	98.1	97.8	99.0
Mass of tablets (mg)	416.0 ± 3.9	402.8 ± 2.8	396.6 ± 3.1	409.6 ± 5.0	392.8 ± 6.1	391.5 ± 1.5	394.6 ± 5.9	398.1 ± 6.7	391.2 ± 5.0

properties of tablet formulation and protects the pellets against the forces of compression applied by the punches.

Creating a tablet matrix by means of hot tableting was not directly connected with the compression properties of excipients but rather with creating the bonds by the PEG 3000 melted in the tablet formulation. The main mechanisms that allowed to create a tablet matrix in the process of hot tableting were based on plastic deformations without fragmentation of the fillers.

During the hot tableting process under 1 kN compressing force, the use of specific types of excipients had direct impact on the tablet thickness. Because of a high bulk density of dibasic calcium phosphate dihydrate in the formulation VI, the corresponding tablets were characterized by the smallest thickness (5.71 mm), whereas the largest thickness was obtained when using MCC as in formulation I (Table 1). Additionally, formulation VI provided tablets of the best granulate flowability during the tableting process, which was also the outcome of the setup's high density.

With formulations I and IV comprising modified starch, the obtained tablets exhibited the shortest dissolution times: 8 and 9 minutes, respectively (Table 2). It was also noted that the dissolution time of the produced tablets was relatively short in comparison to the tablets produced with formulations III (14 minutes) and VI (18 minutes). This was due to the fact that formulations I and IV yielded tablets of a relatively loose structure, where MCC and corn starch triggered a disintegrating effect. This was found to have a negative impact on the hardness of tablets obtained with formulations I (45 N) and IV (41 N), as well as on the tablet friability, which was determined at 1.0% and 1.3%, respectively.

In the process of formulation V employing hot tableting with 3 and 6 kN compression force, the tablets obtained were characterized by different physical properties than those found for tablets prepared using 1 kN compressing force. A higher compression force resulted primarily in producing tablets of a higher physical durability (hardness and friability) (Table 2). That contributed to a higher penetration and filling of the whole tablet matrix with semiliquid granules containing PEG 3000. The surface of the formulation V tablets had a characteristic waxy structure. The degree of the tablet mass ingredient binding in the matrix under the compressing effect determined the tablet thickness. The tablets thickness obtained with 1 kN compression force was of 6.23 mm, whereas applying of 3 and 6 kN compression force resulted in obtaining tablets of 5.50 and 4.90 mm thickness, respectively. This observation seems to be confirmed by the results of friability and hardness tests, 0.2% and 81 N, respectively, for the 3 kN compression force and, 0.0% and 101 N, respectively, for 6 kN compression force.

It was found that the tablet dissolution could mainly be related to the dissolution of PEG 3000, whereas the swelling of disintegrating substances—croscarmellose sodium or MCC—was of secondary importance. The dissolution time of tablets produced with 3 kN compressing force was 35 minutes, whereas with the use of 6 kN compression force the corresponding value was 46 minutes.

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