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Centrifugal die filling system in a new rotary tablet machine

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Summary

This work describes a new tablet machine equipped with an innovative feed system. The system is based on the use of centrifugal force to fill sideway-fitted dies Tablets of good quality, even from mixtures of poor flowability, can be produced Additionally, the segregation of the powders does not appear to be influenced by the new filling system due to the stable packing condition acquired by the powder loaded in the machine. The electronic instrumentation allows one to determine the relationship between compression force and tablet weight in order to establish the correct force limits for the production control chart.

Introduction

The know-how concerning the construction of rotary tablet machines has steadily been improving, thus allowing the rapid production of high-quality tablets. Despite the rapid rate of production, most modern machines are not satisfactory due to the inability to accommodate the variation in properties of the feedstock and to adapt quickly to the changing characteristics of the material being compressed (Rubinstein, 1992).

The feed system has been technically adapted to the increased production rate of tablet machines, however, flowability of the powder often requires optimization in order to meet the performance of high-speed machines. Powder flow to the tabletting machines can vary due to differences in the environmental conditions and characteristics of the raw materials. The development of alternative die-filling methods, which do not rely on good powder flow, as is presently the case, is required (Rubinstein, 1992).

A new rotary tablet machine, equipped with an innovative powder feed system and characterized by having a compression cycle different from that of the usual rotary tablet machines, is under development (IMA, 1993). The novelty resides in the sideways filling of the die with the powdered mixture located at the center of the rotating die table and piped to the dies through special holes. The centrifugal force generated by turret rotation causes the die to fill. Moreover, the instrumentation of the machine allows the operator to produce tablets under safe and rigorous conditions.

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The aim of this work was to study the influence of the new feed system on the properties of the tablets produced. The relationship between applied force and the corresponding tablet weight was also investigated, in view of the development of total tablet quality assurance.

The influence of compression speed, powder flowability and packing properties was evaluated. Weight variation, compression force, physical properties and content uniformity of the prepared tablets were measured.

Materials and Methods

Description of the tablet machine

The current version of the MATIC 3000 tablet machine (IMA spa, Ozzano Emilia, BO, Italy), consists of a rotary machine equipped with 36 punches and instrumented for electronic control of tablet weight. The innovation resides mainly in the shape of the die, which is characterized by the special lateral opening for filling up with the powder mixture. The amount of powder to be compressed is determined by the relative position of the upper and lower punches in the die. Fig. 1 shows the movement of the powder under centrifugal force from the hopper to the die.

The compression cycle starts with the two punches in contact (Fig. 2, panel 1). When the punches separate, a sampling volume is created into which the powder flows from the opening in the die (panel 2). Then the punches move downwards (panel 3), bringing the sampled powder into the closed lower part of the die, where compression takes place (panel 4). The tablet is ejected from the bottom of the die (panel 5) Finally, the two punches return in contact for recovering the initial position (panel 6). As a consequence of this procedure, the filling of the die is driven by two forces: centrifugal force due to the rotation of die table and depression force caused by the rapid separation of punches during the described filling step.

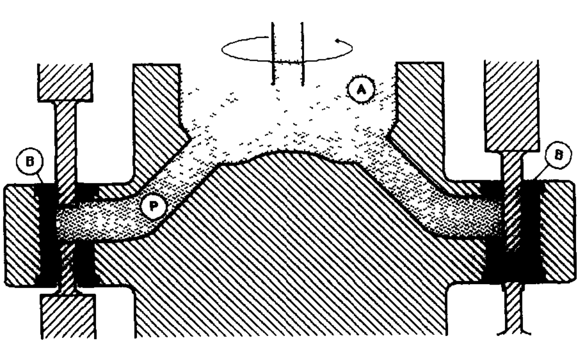

Fig. 1. Schematic illustration of the movement of the powder (P) from the hopper (A) to the die (B) under centrifugal force (left, feeding step; right, compression step).

Materials

Calcium phosphate dihydrate (Emcompress®, Deimos, Milan, Italy), orange soluble colour 4506 (Fratelli Fiorio, Milan, Italy), sodium starch glycolate (Explotab®, Deimos, Milan, Italy), microcrystalline cellulose (Avicel® PH 102, Prodotti Gianni, Milan, Italy), and acetylsalicylic acid FU IX grade (ASA) (two different particle sizes: fine powder < 180 μm and coarse powder 180–840 μm) were obtained from the indicated sources. Aluminum glycinate was supplied by CFM, Milan, Italy. Colloidal silicon dioxide, magnesium stearate, croscarmellose sodium, corn starch and glyceryl behenate were of NF XVII grade. Dihydroxyaluminum aminoacetate and magnesium hydroxide were of USP XXII grade.

The following mixtures were prepared by direct mixing of components: (compositions expressed as percentages) (mixture 1) calcium phosphate dihydrate, 90; color, 5; sodium starch glycolate, 4; magnesium stearate, 1; (mixture 2) calcium phosphate dihydrate, 50; Avicel®, 40; color, 5; sodium starch glycolate, 4; magnesium stearate, 1; (mixture 3) ASA 180–840 μm, 60.2; magnesium hydroxide, 18.5; aluminum glycinate, 9.2; croscarmellose sodium, 4.6; corn starch, 4.2; magnesium stearate, 0.5; glyceryl behenate, 2.8; (mixture 4) ASA < 180 μm, 60.2; magnesium hydroxide, 18.5; aluminum glycinate, 9.2; croscarmellose sodium, 4.6; corn starch, 4.2; magnesium stearate, 0.5; glyceryl behenate, 2.8; (mixture 5) ASA < 180 μm, 59.3; magnesium hydroxide, 18.2; aluminum glycinate, 9.1; croscarmellose sodium, 4.5; colloidal silicon dioxide, 1.5; corn starch, 4.1; magnesium stearate, 0.5; glyceryl behenate, 2.8.

Methods

Mixture control

The static repose angle of the mixtures was measured by growing a powder cone on a suspended disk 87 mm in diameter, until equilibrium height of the cone was attained. Packing properties, as poured and packed densities, were determined using a glass cylinder of 200 ml and a volumetric tapping apparatus. Flow rate of a poured volume of 100 ml of mixture was measured through a funnel (height, 67.6 mm; width, 75 mm) with a hole of 8.8 mm. All measurements

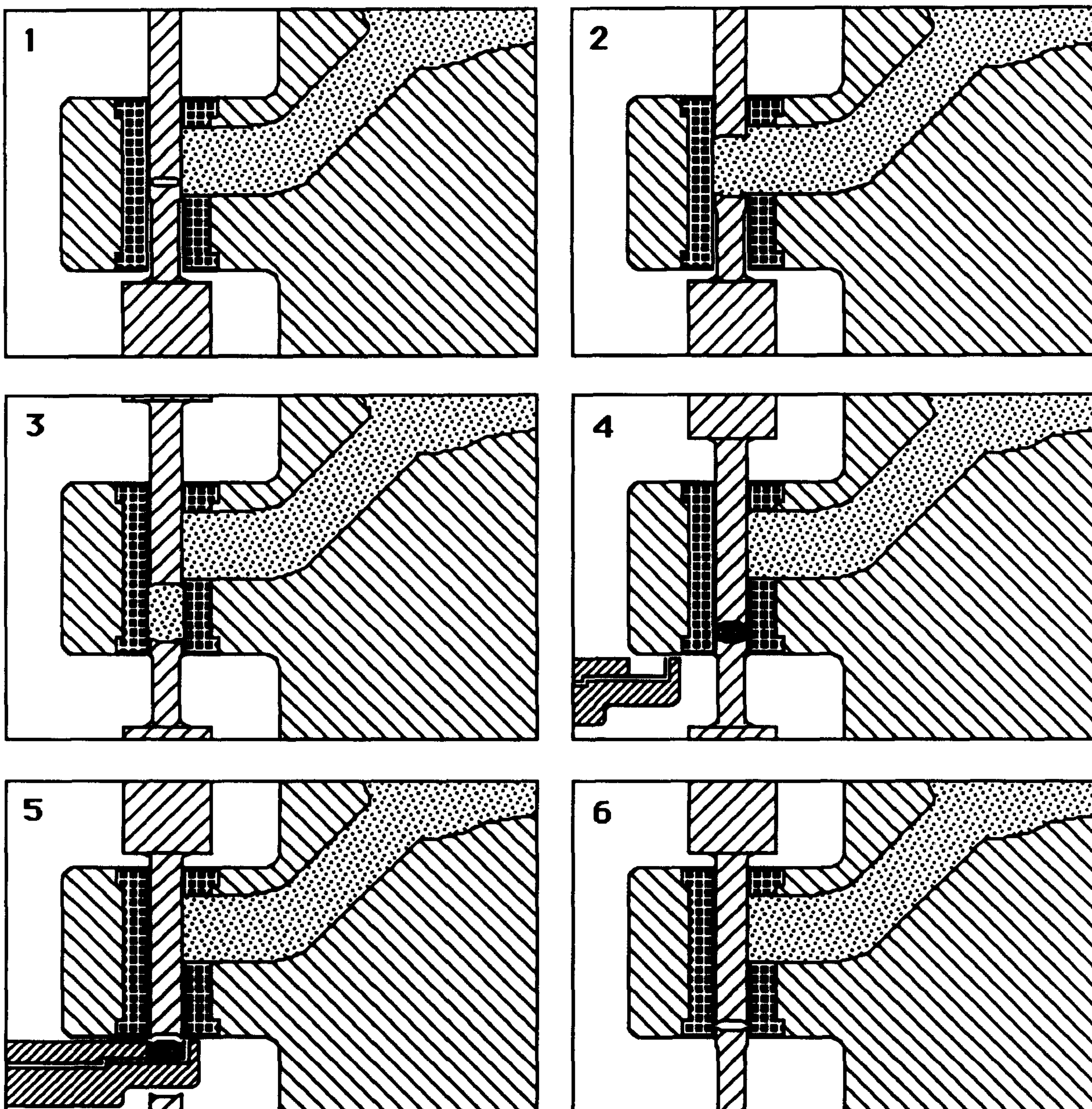

Fig. 2 Tabletting steps of the MATIC 3000 rotary machine (see text for explanation of panels 1–6)

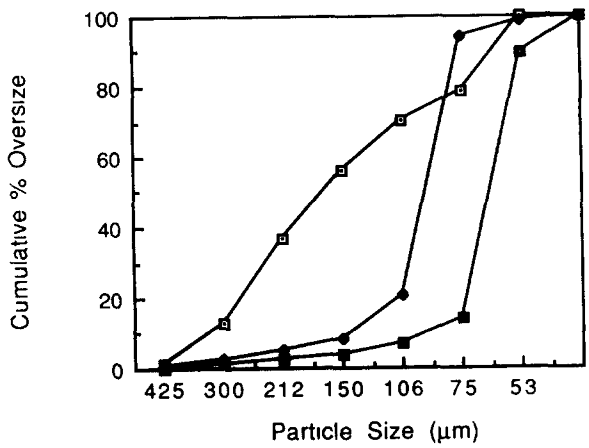

Fig. 3 Particle size distribution of mixture 3 (⊡), mixture 4 (♦) and mixture 5 (■).

were carried out at 20°C and 65% relative humidity (RH).

Tablet preparation

Mixtures were compressed in the MATIC 3000 machine placed in a conditioned room (20°C, 65% RH). Powdered mixtures were loaded into the hopper and the machine was operated for 15 min in order to carefully perform the setting procedures. Then, production was started at 70 and 140 rpm turret rotation. At fixed regular intervals, groups of 100 tablets were sampled for quality control. The automatic weight control system was switched off during these trials.

Disintegration time was measured according to the USP XXII method. Color content of individual tablets was evaluated spectrophotometrically at 440 nm. Tablet hardness was measured using the Monsanto apparatus. All measurements were made on six replicates.

TABLE 1

Packing and flow properties of prepared mixtures

	Mixture				
	1	2	3	4	5
Poured density (g/ml)	0.99	0.66	0.84	0.50	0.49
Tapped density (g/ml)	1.13	0 77	1 04	0 81	0.75
Repose angle (°)	43	38	36	47	37
Flow velocity (ml/s)	14.3	4.8	16 6	[a]	[a]

[a] No flow in the apparatus used.

Results and Discussion

Properties of prepared mixtures

Particle size distributions of mixtures 3–5 are shown in Fig. 3 and packing and flow properties are reported in Table 1.

Effect of compression cycle on mixture segregation

The application of a centrifugal force to a powdered mixture creates a favorable condition for the separation of components having different shapes and densities. In order to investigate the influence of tablet machine compression cycle on segregation, mixture 1, consisting of diluent and a color as tracer, was prepared. The two components possess different shape, density and particle size, which can favor segregation. The possibility of segregation of mixture components was verified, before compression trials, by gently sieving the mixture on a sieve series and checking the color content of the individual fractions. The results showed that a random mixture was obtained and its components could segregate under appropriate mechanical action, as can occur during tablet manufacturing.

Using mixture 1, two compression trials were conducted at 70 and 140 rpm of die table rotation, keeping the machine setting constant. The

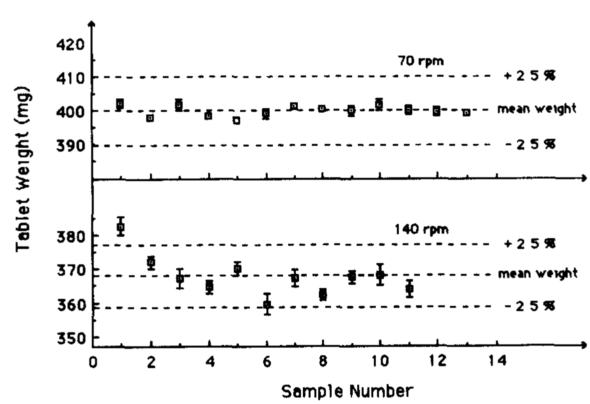

Fig. 4. Tablet weight variation (mean ± SE) obtained with mixture 1 compressed at 70 and 140 rpm die table rotation

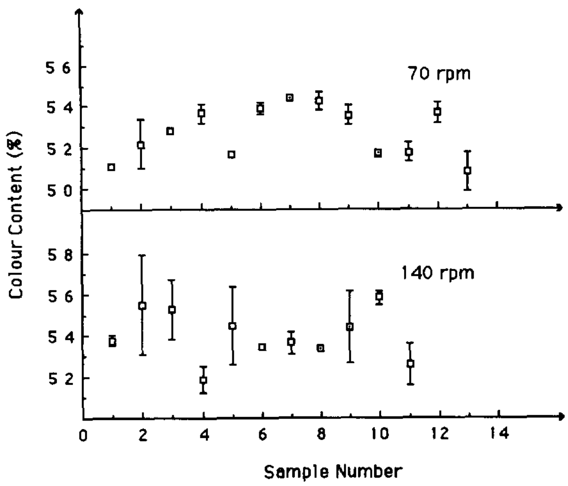

Fig. 5. Tablet color content variation (mean ± SE) obtained with mixture 1 compressed at 70 and 140 rpm die table rotation.

tablets obtained were checked for weight, color content, hardness and disintegration time. Weight variation remained in the ±2.5% range, with a broader spread of the values in the case of the higher compression speed (Fig. 4). Color content uniformity was satisfactory, being better at lower compression speed (Fig. 5).

Careful examination of the prepared tablets revealed a small spot of color on their external lower side, which was attributed to partial percolation of color particles through the diluent granules under centrifugal force. However, a quantitative analysis on the half of the tablet containing the spot, in comparison with the second half, showed no significant difference in terms of color content.

This latter compression trial was repeated using mixture 2 in which a portion of calcium phosphate dihydrate was substituted with microcrystalline cellulose, with the aim of reducing the free space for percolation in the packed mixture. No color accumulation was observed on the tablet surface in this trial and uniform content was achieved, together with low weight variation. Evidently, the shape and particle size of microcrystalline cellulose hinder the percolation of color particles through the diluent particle bed. Technological parameters of the tablet (hardness and disintegration time) were quite close to the mean value, indicating that the compression force did not significantly change during these compression trials.

Effect of powder flowability on weight uniformity

Tablet weight uniformity is strictly dependent on the flowability of the powders from the feeding hopper. In this machine, the particular feed system could reduce the flowability differences of powders, since, during the die-filling step, stable packing of the mixture is achieved as a result of the strong centrifugal force.

In order to evaluate the influence of the powder flowability on the tabletting performance of the machine using powdered or granular components, three buffered ASA mixtures, different with respect to flow and particle size distributions, were prepared. In mixture 3, ASA 180–840 μm and, in mixture 4, ASA < 180 μm were used. Mixture 5 was prepared by adding, as glidant, 1.5% of colloidal silicon dioxide to mixture 4. The values of the packing properties, repose angle and flow rate listed in Table 1 demonstrate the poor flow properties of mixtures 4 and 5.

As a reference, the three mixtures were tabletted on a traditional rotary tablet machine. In this case, mixture 3 was compressed without problems, mixture 4 failed to compress and mixture 5 gave tablets with a large weight variation.

By tabletting the mixtures on the MATIC 3000 machine, acceptable tablets were obtained in all three cases. Fig. 6 shows tablet weight variations determined when keeping the machine setting constant. The best results were obtained with mixture 3 (ASA 180–840 μm), where the weight range is maintained at between ±2.5% of the average. In the worst case (mixture 4), the weight range was between ±5% of the average, which is still acceptable according to pharmacopeial requirements.

The addition of colloidal silicon dioxide to this mixture, in order to obtain mixture 5, improved the weight uniformity of the prepared tablets.

Compression force-tablet weight relationship

Considering the relationship between weight, compression force, crushing strength and disintegration time of pharmaceutical tablets, weight variations within pharmacopeial limits are liable to produce force levels determining undesirable technological properties. The establishment of these relationships is a fundamental step in obtaining uniform production batches as far as weight and, particularly, technological properties are concerned (Colombo et al., 1985).

The compression force values, recorded in the trial relative to mixture 4 and corresponding to the tablet weight reproduced in Fig. 6, are presented in Fig. 7a. It is clearly demonstrated that force variations fit the corresponding weight variations perfectly. However, the range of force variation is much greater than the $\pm 5\%$ of the mean force value. This result strongly indicates that a knowledge of the relationship between weight and corresponding force is essential in order to

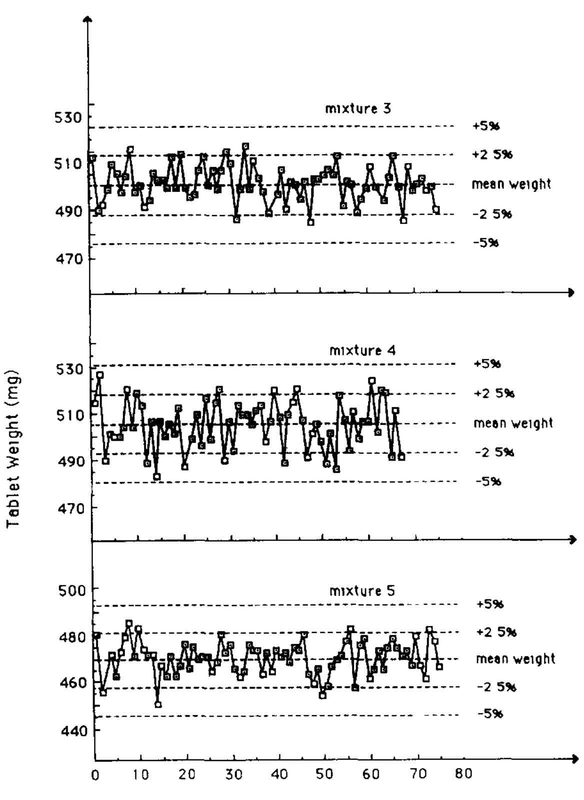

Fig 6 Tablet weight variation obtained with the three ASA mixtures

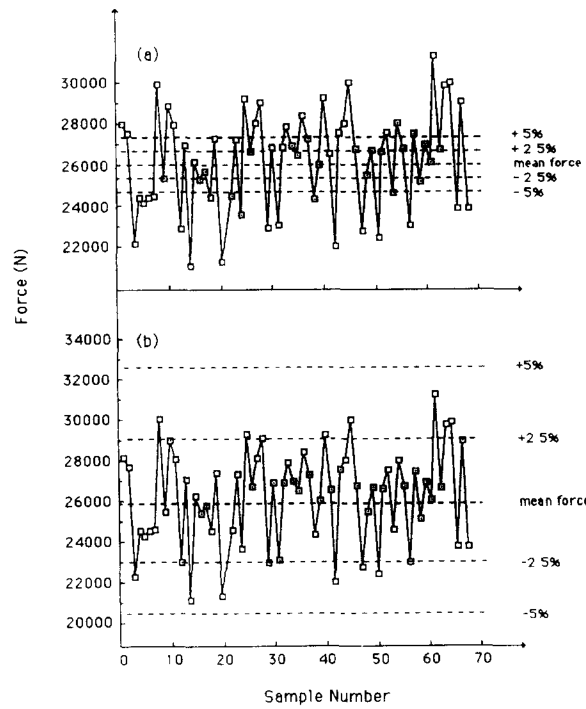

Fig. 7 Tablet force variation with force limits calculated as $\pm 5\%$ of mean force (a) and tablet force variation with force limits calculated from force/weight relationship (b)

set exactly the production force limits for the control of the tablet weight.

Therefore, a trial was carried out on the MATIC 3000 machine in order to establish the relationship between compression force and tablet weight. Fig. 8 displays this relationship as found in the case of mixture 4, in the weight range from 480 to 530 mg, described according to an exponential empirical model (Conte et al., 1988; Dondi et al., 1990). The empirical model allows the calculation of the force values corresponding to the weight limits for a tablet batch accepted by the pharmacopoeia. Fig. 7b shows the correct control chart to be considered for the production of a batch meeting the allowed weight variability: in this case, from the relationship found, tablet force variation corresponding to the 5% weight variation was calculated. Since the machine is capable of automatically eliminating tablets outside these limits, the application of this control chart guarantees the quality of the batch pre-

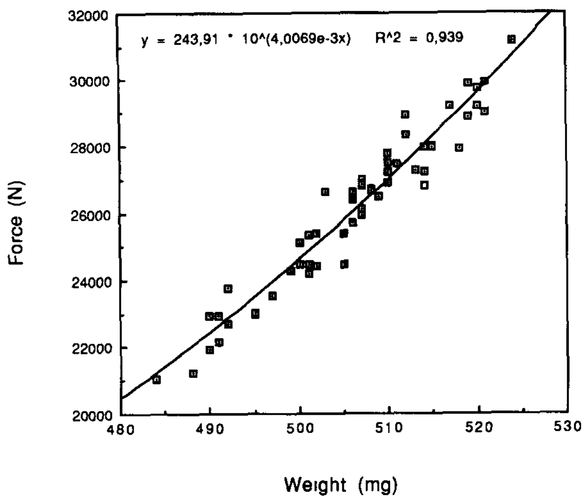

Fig 8. Compression force/tablet weight exponential relationship relative to mixture 4.

pared regarding the weight and properties of the tablets.

Conclusion

The IMA MATIC 3000, as an innovative rotary tablet machine, showed high tabletting capability even in the case of a mixture of poor flowability, which failed on a traditional tablet machine.

The tendency of mixtures of good flowability to undergo separation appears to be reduced with the new filling system based on centrifugal force. That the mixture is maintained under the condition of close packing during production is an advantage in terms of mixture stability. In fact, the new filling system never allows the powder to become a loosely packed bed due to the continuous application of centrifugal force to the powder. The possible percolation of a small amount of fine particles in a larger particle bed appears to be restricted and should be readily avoidable.

As a result of the ability to determine the relationship between tablet weight and compression force, the electronic system improves tablet weight control through the availability of a control chart based on the compression force limits equivalent to allowed weight limits.

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