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Research Article

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Mathematical model of tablet weight control based on middle-die hole error of high-speed rotary pharmaceutical tablet press

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ABSTRACT

Taking the analysis of the filling working procedure on high-speed rotary tablet press as starting point, various influencing factors on tablet weight were analyzed and mathematical formula for tablet weight was derived. Mutual mathematical relation between the tablet weight and the influencing factors were investigated and the main factors which determine tablet weight were found .A conception of compensation equivalent of the depth of middle die hole was proposed. The compensation equivalent of various errors was found out for every individually occurred error. The mathematical formula of the error of middle-die hole depth was found out for alternately occurred errors. The property of various errors was analyzed. By using the mathematical formula of tablet weight and depth error of middle-die hole, a mathematical model for controlling high-speed rotary tablet press was established on the basis of error adjustment of tablet weight. The tablet weight control system designed from this control model was installed on a forty-stroke high-speed rotary tablet press GCP. It was shown by sampling detection at the deviation of tablet weight was higher than that required by National Pharmaceutical Production Administration Norms. The mathematical model for control over error adjustment of tablet weight could provide a reasonable basis for designing the tablet weight control system of high-speed rotary tablet press.

Key words: high-speed pharmaceutical rotary tablet press; tablet weight; error; equivalent; control

INTRODUCTION

When high-speed rotary tablet presses tablet cores, many factors determine the weight of the tablets. In the process of tablets production, the tablet weight is directly affected by filling volume. And the filling volume depends on mechanical factors and factors from particles[1]. The mechanical factors include deviations in the die hole diameter, deviation of the diameters of the upper and lower dies, position deviation of lower dies in the die hole, Mid-plane shaking, remainants on the scraper (without a net) after particles filling, Die wear, deviation of filling guide, deviation of measuring guide, deviation of stroke depth with lower die, bias from adjustment of filling transmission structure and transmission, etc. Factors from particles include physical and chemical properties of the particles, particle spill when upper die the punches into the die hole, particle mobility, particle packing density, particle size and moisture content of the particles, etc[2]. when high-speed rotary tableting machine works, it is empirically difficult to design and operate high-speed rotary tablet machine, to ensure accuracy of tablet weight and to improve the accuracy of the tablet weight due to the presence of a number of factors. In the design of tablet press control system with high speed rotary, there is nowadays no tablet weight mathematical model reasonable to refer to. Starting from working structure at filling station in the high-speed rotary tablet press, this article sets up a mathematical structure that can be utilized to provide a scientific basis for controlling tablet weight accuracy.

EXPERIMENTAL SECTION

Formula derivation of Die hole depth error
The main factors weighing error

When the high-speed rotary tableting machine works at the filling position, suppose the mid-die hole diameter is d , the depth of die hole h , particle packing density ρ , tablet weight W . And suppose error Δd is mid-die hole diameter of d , error Δh in the depth of die hole h , error ΔW in tablet weight. The working structure is shown of the high-speed rotary tableting machine as Fig.1 [3].

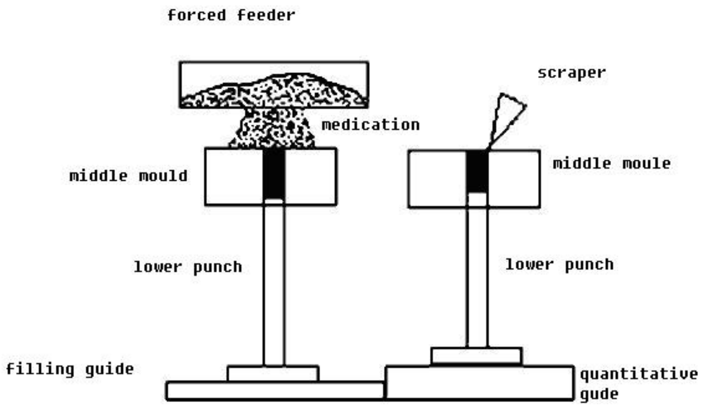

Fig.1 working procedure of filling operation

Lift rail of filling guide is driven by a stepper motor, the filling guide leading to move upward and downwards, and scraper scraping off the excess material. The tablet weight can be deduced from the structure.

$$W = W_\mu + \Delta W = \frac{1}{4}\pi(d_\mu + \Delta d)^2(\rho_\mu + \Delta\rho)(h_\mu + \Delta h) - \sum_{i=1}^{3}(W_{\mu i} + \Delta W_i) \quad (1)$$

W_i、d_μ、ρ_μ、 h_μ are respectively the mathematical expectations of tablet weight, the die diameter, particle packing density and the of depth of the die hole, and $\Delta\rho$ is the error of the density of particle packing. $W_{\mu 1}$ and ΔW_1 are respectively the mathematical expectation of the weight error of materials from position error of the die hole circle with the errors of the diameters in the upper and lower dies and its error variation; $W_{\mu 2}$ and ΔW_2 are respectively mathematical expectation of material weight error from the remainants on the scaper after particulate material filling and its error variation; $W_{\mu 3}$ and ΔW_3 are respectively mathematical expectation of the weight error from particles spill when the upper die punches into the die hole.

Provided:

$$W_\mu = \frac{1}{4}\pi d_\mu \rho_\mu h_\mu - \sum_{i=1}^{3} W_{\mu i} \quad (2)$$

Whenever in trial run or in stable production, $\Delta d << d_\mu$, $\Delta\rho << \rho_\mu, \Delta W_i << W_{\mu i}$ （$i = 1,2,3$）, the relationship between Δh and h_μ varies in the 2 stages. In stable production, $\Delta h << h_\mu$, while in trial run, $\Delta h < h_\mu$ rather than $\Delta h << h_\mu$. It can be concluded from (1) and (2) that

$$\Delta W = W - W_\mu = \frac{1}{4}\pi(d_\mu + \Delta d)^2(\rho_\mu + \Delta\rho)(h_\mu + \Delta h) - \sum_{i=1}^{3}(W_{\mu i} + \Delta W_i) - \frac{1}{4}\pi d_\mu^2 \rho_\mu h_\mu - (-\sum_{i=1}^{3} W_{\mu i}) \quad (3)$$

If higher-order terms $\Delta\rho$、Δd are omitted, then

$$\Delta W = \frac{1}{4}\pi(d_\mu^2\rho_\mu\Delta h + d_\mu^2 h_\mu\Delta\rho + d_\mu^2\Delta\rho + 2d_\mu\rho_\mu h_\mu\Delta d + 2d_\mu\rho_\mu\Delta d\Delta h) - \sum_{i=1}^{3}\Delta W_i \quad (4)$$

From (4), the partial derivatives of the related parameters:

$$\begin{pmatrix} \frac{\partial\Delta W}{\partial\Delta h} \\ \frac{\partial\Delta W}{\partial\Delta D} \\ \frac{\partial\Delta W}{\partial\Delta\rho} \\ \frac{\partial\Delta W}{\partial\Delta W_i} \end{pmatrix} = \frac{1}{4}\pi\begin{pmatrix} d_\mu^2\rho_\mu + d_\mu^2\Delta\rho + 2d_\mu\rho_\mu\Delta d \\ 2d_\mu\rho_\mu h_\mu + 2d_\mu\rho_\mu\Delta h + 0 \\ d_\mu^2 h_\mu + d_\mu^2\Delta h + 0 \\ -1 + 0 + 0 \end{pmatrix} \quad (5)$$

If $\Delta\varphi << \varphi_\mu, \Delta\rho << \rho_\mu, \Delta q_i << q_{\mu i}$ are taken into consideration, (5) can be simplified

$$\begin{pmatrix} \frac{\partial\Delta W}{\partial\Delta h} \\ \frac{\partial\Delta W}{\partial\Delta D} \\ \frac{\partial\Delta W}{\partial\Delta\rho} \end{pmatrix} = \frac{1}{4}\pi\begin{pmatrix} d_\mu^2\rho_\mu + 0 + 0 \\ 2d_\mu\rho_\mu h_\mu + 2d_\mu\rho_\mu\Delta h + 0 \\ d_\mu^2 h_\mu + d_\mu^2\Delta h + 0 \end{pmatrix} \quad (6)$$

It turns out that the relationship between ΔW and Δh is much more important, and Δh is a major factor which determines ΔW .

The mathematical formula of die hole depth error

Error of die hole depth is a major factor determining the tablet weight error, so it is required to figure out the mathematical formula of die hole depth error[4,5].

In practice, Δd、$\Delta\rho$、$(W_{\mu i} + \Delta W_i)$ and Δh are in mutual compensation, it is difficult to work out the relationship between h , ΔW and Δh . The concept of Equivalent is put forward below, and the mathematical formula of die hole depth error is established using it.

If Δd、$\Delta\rho$、$(W_{\mu i} + \Delta W_i)$ occurs individually, which are all compensated through Δh . That is they have an equivalent relationship with Δh when they occur individually.

When Δd occurs individually, if h_1 is the depth of die hole, Δh is the equivalent of compensation for the mold hole depth, then:

$$\frac{1}{4}\pi(d_\mu+\Delta d)^2\rho_\mu h_1-\sum_{i=1}^{3}W_{pi}-\frac{1}{4}\pi d_\mu^2\rho_\mu h_1-(-\sum_{i=1}^{3}W_{pi}) = \frac{1}{4}\pi(d_\mu+\Delta d)^2\rho_\mu\Delta h_1 \tag{7}$$

$$h_1 = h_\mu + \Delta h_1 \tag{8}$$

From (7) and (8), it comes out that:

$$\Delta h_1 \approx \frac{2\Delta d}{d_\mu}h_\mu \tag{9}$$

When $\Delta\rho$ occurs individually, if h_2 is the depth of die hole and Δh_2 is the equivalent of compensation for the mold hole depth, then:

$$\frac{1}{4}\pi(\rho_\mu+\Delta\rho)h_2-\sum_{i=1}^{3}W_{pi}-\frac{1}{4}\pi d_\mu^2\rho_\mu h_2-(-\sum_{i=1}^{3}W_{pi}) = \frac{1}{4}\pi d_\mu^2(\rho_\mu+\Delta\rho)\Delta h_2 \tag{10}$$

$$h_2 = h_\mu + \Delta h_2 \tag{11}$$

It can be derived from (10) and (11) that

$$\Delta h_2 = \frac{\Delta\rho}{\rho_\mu}h_\mu \tag{12}$$

When $(q_{\mu i}+\Delta q_i)(i=1,2,3)$ occurs individually, provided h_3 is the depth of die hole, and Δh_3 is the equivalent of compensation for the mold hole depth, then:

$$\frac{1}{4}\pi d_\mu^2 h_3-\sum_{i=1}^{3}(W_{\mu i}+\Delta W_i)-\frac{1}{4}\pi d_\mu^2\rho_\mu h_3-(-\sum_{i=1}^{3}W_{pi}) = \frac{1}{4}\pi d_\mu^2\rho_\mu\Delta h_3 \tag{13}$$

$$h_3 = h_\mu + \Delta h_3 \tag{14}$$

$$\Delta h_3 = \frac{4\sum_{i=1}^{3}\Delta W_i}{\pi d_\mu^2\rho_\mu} \tag{15}$$

When Δd、$\Delta\rho$、$(W_{\mu i}+\Delta W_i)$ occur alternately, compensation value of the die hole depth error is the sum of the equivalents of their errors. From (9,12,15),

$$\Delta h = \sum_{p=1}^{3} \Delta h_p = \frac{2\Delta d}{d_\mu} h_\mu + \frac{\Delta \rho}{\rho_\mu} h_\mu + \frac{4\sum_{i=1}^{3} \Delta W_i}{\pi d_\mu^2 \rho_\mu} \tag{16}$$

$$h = h_\mu + \sum_{p=1}^{3} \Delta h_p = h_\mu + \frac{2\Delta d}{d_\mu} h_\mu + \frac{\Delta \rho}{\rho_\mu} h_\mu + \frac{4\sum_{i=1}^{3} \Delta d_i}{\pi d_\mu^2 \rho_\mu} \tag{17}$$

Thanks to the introduction of the concept of equivalent of the die hole depth, when Δd、$\Delta\rho$、$(W_{\mu i} + \Delta W_i)$ occur alternately, the formula (16) of die hole depth error can be obtained easily.

RESULTS AND DISCUSSION

Mathematical formula of adjustment of weight error

Analysis of the properties of the errors

Of all the errors, Δd , the error of the die diameter d , is made in processing of die and the die wear seldom occurs in working process, which belongs to the system error[6], and $\Delta W_1, \Delta W_2, \Delta W_3$ also. [7,8].

Affected by such factors as speed, acceleration, vibration and powder particles mobility, $\Delta\rho$, the error in the particle packing density, is random error[9].

According to (16), Δh , the error in die hole depth, derived from the errors above belong to random error. From (3), ΔW , coming from Δh , is random error[10].

Mathematical formula of adjustment of weight error

Based on analysis of the properties of the errors, along with (1) and (16), it comes to:

$$\Delta\rho = \frac{4W}{\pi h_\mu (d_\mu + \Delta d)^2} + \left(\frac{4\sum_{i=1}^{3}(W_{\mu i} + \Delta W_i)}{\pi h_\mu (d_\mu + \Delta d)^2} - \frac{4\sum_{i=1}^{3}\Delta W_i}{\pi d_\mu^2 \rho_\mu} - \frac{2\Delta d \rho_\mu}{d_\mu} - \rho_\mu \right) \tag{18}$$

When the formula (18) is led into (16), then:

$$\Delta h = \frac{4W}{\pi \rho_\mu (d_\mu + \Delta d)^2} + \left(\frac{4\sum_{i=1}^{3}(W_{\mu i} + \Delta W_i)}{\pi \rho_\mu (d_\mu + \Delta d)^2} - \frac{4h_\mu \sum_{i=1}^{3}\Delta W_i}{\pi d_\mu^2 \rho^2_\mu} + \frac{4\sum_{i=1}^{3}\Delta W_i}{\pi d_\mu^2 \rho_\mu} - h_\mu \right)$$

Let

$$g = \frac{4W}{\pi \rho_\mu (d_\mu + \Delta d)^2}$$

$$s = \left(\frac{4\sum_{i=1}^{3}(W_{\mu i} + \Delta W_i)}{\pi \rho_\mu (d_\mu + \Delta d)^2} - \frac{4h_\mu \sum_{i=1}^{3}\Delta W_i}{\pi d_\mu^2 \rho^2_\mu} + \frac{4\sum_{i=1}^{3}\Delta W_i}{\pi d_\mu^2 \rho_\mu} - h_\mu \right)$$

g as their own error equivalent of die hole , s as other error equivalent of die hole. So,

$$\Delta h = gW + s \quad (19)$$

In the production process, W_{μ} is a given value according to National Drug Manufacturing Practice, and W is a timing measurement value from the operators. $d_{\mu,}\rho_{\mu,}h_{\mu}$ are known values through calculations, ΔW and $\Delta d, W_{\mu i}, \Delta W_i$ are all system errors, Δd can be figured out. $W_{\mu i}, \Delta W_i$ are averagely calculated through production volume with introduction of 2 parameters g and s. Also:

$$\Delta h = K_m \Delta N \quad (20)$$

ΔN is the step number with Δh, the die hole error, when the particles are filled in. K_m is conversion constant, leading (20) into (19), then

$$\Delta N = \frac{g}{K_m} W + \frac{s}{K_m}$$

And

$$W = W_{\mu} + \Delta W$$

So

$$\Delta N = \frac{g}{K_m} W + \frac{(s + gW_{\mu})}{K_m} \quad (21)$$

All these above are mathematical formula for error adjustment in accordance with the tablet weight of the high-speed rotary type tableting machine.

Experimental test of error adjustment of the high-speed rotary type tableting machine[11,12]

According to China National Pharmaceutical Manufacturing Practice: Weight variation limit of the tablets weight under 0.3g is $\pm 7.5\%; 0.30g; 0.30g$; that over 0.3g for $\pm 5\%$. If the mathematical expectation of the tablet weight is $W_p = 0.3g, \Delta W_{\max} = 6\sigma = 0.3 \times 5\% g$, so variance is $\sigma = 0.0025g$ [13], the tablet weigh W turns out to be normal distribution $N(0.3, 0.0025^2)$.

After the tableting operators run the machine, the operation steps include: firstly, to adjust the filling volume by their experiences and to adjust the pressure to give out sheet-shaped tablet cores; and then pick out 20 tablets, figure out the average tablet weight, calculating the average error. All these procedures are performed time and time again before it meets national production standards requirements. Finally, provide the proper pressure, yielding reasonable tablet hard value. When the trial is finished, the formal production starts. The operators make timing sampling, checking the tablet weight variation to find the problems and solutions.

According to tablet weight error control model formula (21), prediction and control model of tablet weight is designed. Through tablet weight measurement, tablets variation and output regulation, the production is ultimately achieved in accordance with the tablet weight error control.

The experiment is carried out on a 40-punch on the high-speed rotary tablet press. The samples are divided into 12 groups to check the tablet weight; 20 tablets are taken consecutively out to measure the weight of each tablet. Record the weight errors through comparison to the norm. Pick out anyone from the 12 group, taking Group 6 for example, the tablet weight and its error are shown in Tab.1. $W_{\mu} = 0.3g$ is the tablet weight norm. Tablet weight error divided by its norm is tablet weight variation limit, $\pm 5\%$.

Tab.1 Tablet weight record list

catalogue number	actual tablet weight w/g	tablet weight error △w/g	the difference of tablet weight %
1	0.29941	-0.00059	-0.20
2	0.30198	+0.00198	+0.66
3	0.30022	+0.00022	+0.73
4	0.29916	-0.00084	-0.28
5	0.30121	+0.00121	+0.40
6	0.29808	-0.00192	-0.64
7	0.30221	+0.00221	+0.74
8	0.30255	+0.00255	+0.85
9	0.29908	-0.00092	-0.31
10	0.29895	-0.00105	-0.35
11	0.29930	-0.00070	-0.23
12	0.30201	+0.00201	+0.67
13	0.30041	+0.00041	+0.14
14	0.29911	-0.00089	-0.30
15	0.30133	+0.00133	+0.44
16	0.29707	-0.00293	-0.98
17	0.30523	+0.00523	+1.74
18	0.30285	+0.00285	+0.95
19	0.29808	-0.00192	-0.64
20	0.29788	-0.00202	-0.71

According to Tab.1, the maximum, 0.00523g, of tablet weight error happens to Sample 17, and is +1.74%. The minimum, 0.00059g, happens on the Group 1, and weight variation is -0.20%. The experiment shows that tablet weight differences are within the limits of the national pharmaceutical production management practices, with high accuracy of tablet weight control. The established mathematical model of tablet weight control bears practical and scientific properties.

CONCLUSION

After analysis of the filling working procedure on high-speed rotary tablet press, various influencing factors on tablet weight were analyzed and then mathematical formula for die hole depth was derived according to the equivalent relationship.

Analyze the properties of tablet weight errors, establish mathematical model of error adjustment in accordance with the tablet weights and apply it into practice.

Tablet weight control system has high accuracy by sampling, and the weight variation is much lower than national standards.

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