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Modeling of Mixing Uniformity for Food With Special Medicinal Purposes Based on Chinese Herbal Medicine

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ABSTRACT We developed a recipe based on Chinese herbal medicines for a special medicinal purpose. It is based on the market demand and clinical feedback of formulas for special medicinal uses. The whole nutrient formula contains raw materials in the form of powder and granules, and the finished product is prepared using a dry process. Striking a balance when mixing the powder and granular materials in a uniform manner has always been a critical problem in terms of time and cost when using the dry mixing process. The mixing of the powder and granular raw materials is a complicated process. It involves the mixing of different raw materials, and the physical properties of these raw materials are the main reasons for the hybrid hierarchical nature. A series of experimental studies were carried out on the mass fraction and particle size distribution of each raw material. Using the test data to analyze the influence of different physical properties on the mixing uniformity, we establish a suitable mixing process. On this basis, the experiment was started from the mixing process. Based on the analysis of premixing time, mixed loading amount, premixing speed, total mixing speed, total mixing time, and mixing uniformity, a prediction model based on a genetic hill climbing algorithm is established.

INDEX TERMS Dry process, food for special medical purposes, mixed uniformity model.

I. INTRODUCTION

With peoples' living standards being greatly improved, the malnutrition caused due to hunger has almost been eliminated, however, this does not mean that the problem of malnutrition in China has disappeared. According to statistics, the prevalence of malnutrition in European hospitalized patients is approximately 20%-60%, and in China, it is approximately 35%-65% [1]. The hidden dangers of malnourished patients involve increased mortality, increased hospital stay, delayed wound healing, and increased complications. Clinical patients are prone to be malnourished, and malnutrition is one of the most important factors that cause clinical treatment complications and delay in recovery. Therefore, clinical nutrition support through food for special medicinal purposes is an important component that plays a key role in the clinical treatment process.

Traditional Chinese medicine has been homologous to medicine and food since ancient times. The concept of homology medicines and food refers to some Chinese herbal medicines, which have the properties of food, and also have a preventive effect on certain diseases [2]–[4]. The theory of homology of traditional Chinese medicine has a long history and can be traced back to ancient times. The famous book ''Therapeutics and Materia Medica'' in the history of China is the world's first monograph on medicinal diet. In modern

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day research, medicated diet and diet therapy are one of the important treatment methods of Chinese medicine. This traditional treatment method is being gradually recognized globally. At present, the National Health and Family Planning Commission have published 101 kinds of homologous raw materials for Chinese medicines.

The food with special medicinal purposes, for complete nutrition, has been widely used for clinical nutrition support, but most of its formula-based ingredients are relatively simple, and they have a single source of nutrients [5], [6]. The homology of medicine and food materials of traditional Chinese medicines and foods are highly suitable because they are foods, that have limited side effects, and can be taken for a long time [7]–[10]. To provide healthy, safe, and nutritious food to the target population, the research team has inspected a large number of relevant literature, and combined them with the production situation, hence, developing a food with special medicinal purposes based on Chinese herbal medicine ingredients [7], [11]–[14].

In terms of process selection, the research team mainly compared the dry process and the wet process. The research results are as follows:

TABLE 1. Comparison of dry process and wet process.

item	dry process	wet process
the production cost and period	Low equipment investment, short production cycle, energy saving and cost reduction	Long production cycle, high energy consumption and high cost
nutrition value	Reduce the loss of heat-sensitive nutrients and functional protein activities, and have higher nutritional value	temperature-sensitive nutrients and functional proteins are easily lost during processing and have low nutritional value.
physical and chemical index	Product physical and chemical indicators are easy to control	Product physical and chemical indicators are more difficult to control
production process	The production process is simple, the raw materials can be entrusted to process, and the production site is not affected by material migration.	The production process is complicated, and only some raw materials can be commissioned

Making pharmaceutical drugs is always a complex and long process. The pharmacologists have not only paid attention to the ingredient balance from the side of drug effects (e.g., active ingredients and their interactions, especially for Chinese herbal medicine), but also have considered the mixing uniformity of drugs with complex ingredients from the side of pharmaceutical engineering [15], [16]. It can be seen from Table 1 that the dry process is advantageous than the wet process. Firstly, the basic principle of the dry process is to mix various materials under dry conditions using a two-dimensional (three-dimensional) mixer, and the process does not require the introduction of large, high-cost equipment as in the case of the wet process. This greatly reduced investment, saves energy, and reduces cost. Secondly, the use of dry process avoids high temperature treatment of raw materials, effectively prevents loss of heat-sensitive nutrients, and accurately controls the product quality, thus ensuring the full price of the product. Nutritional efficiency is also maintained. The dry process has a better preservation rate for each vitamin in the whole nutrient powder than that of the wet process. In short, this food with medicinal properties is intended to be produced using a dry process. The whole nutrient formula contains raw materials that are only powder and granules, and the finished product is prepared using a dry process. Striking a balance when mixing the powder and granular materials in a uniform manner has always been a critical problem in terms of time and cost when using the dry mixing process [7], [17]–[21]. From the two aspects of the raw material's granular physical property and the mixing process, reaching a balance of mixing uniformity of powder and granular materials with respect to time and cost is studied.

FIGURE 1. HS-5 three-dimensional motion mixer.

II. EXPERIMENTAL MATERIALS AND METHOD

A. EXPERIMENTAL MATERIALS AND LABORATORY EQUIPMENT

1) PREMIXING EXPERIMENTS AND VARIOUS CHARACTERIZATION EXPERIMENTS

a: MIXING EXPERIMENT

HS-5 type three-dimensional motion mixer, electronic balance, and various standard formula powders.

b: DETERMINATION OF CALCIUM CONTENT

Atomic absorption spectrometer, analytical balance, microwave digestion system (with tetrachloroethane digestion inner tank), adjustable electric furnace, adjustable hot plate, pressure digestion tank (with tetrachloroethane digestion inner tank), constant temperature drying oven, muffle furnace, nitric acid, perchloric acid, hydrochloric acid, and antimony oxide.

c: DETERMINATION OF VITAMIN K1 CONTENT

High performance liquid chromatography, a homogenizer, high speed pulverizer, tissue masher, vortex oscillator, constant temperature water bath oscillator, pH meter, electronic balance, centrifuge, a rotary evaporator, nitrogen blowing instrument, and ultrasonic oscillator. Anhydrous ethanol, potassium carbonate, anhydrous sodium sulfate, isopropanol, n-hexane, methanol, tetrahydrofuran, ethyl acetate, glacial acetic acid, zinc chloride, anhydrous sodium acetate, potassium hydroxide, lipase, amylase, and zinc powder.

d: DETERMINATION OF VITAMIN B1 CONTENT

High performance liquid chromatography, analytical balance, centrifuge, Ph meter, tissue masher, electric thermostat drying oven. N-butanol, potassium ferricyanide, sodium hydroxide, hydrochloric acid, sodium acetate, glacial acetic acid, methanol, phosphorus pentoxide, papain, and amylase.

2) TOTAL MIXING EXPERIMENT AND EACH CHARACTERIZATION TEST

a: MIXING EXPERIMENT

HS-5 type three-dimensional motion mixer, electronic balance, and various standard formula powders.

b: DETERMINATION OF CALCIUM CONTENT

Atomic absorption spectrometer, analytical balance, microwave digestion system (with tetrachloroethane digestion inner tank), adjustable electric furnace, adjustable hot plate, pressure digestion tank (with tetrachloroethane digestion inner tank), constant temperature drying oven, and muffle furnace. Nitric acid, perchloric acid, hydrochloric acid, and antimony oxide.

c: DETERMINATION OF PROTEIN CONTENT

Balance, nitrogen distillation unit, and Kjeldahl analyzer. Copper sulfate, potassium sulfate, sulfuric acid, boric acid, methyl red indicator, bromocresol blue indicator, methylene blue indicator, sodium hydroxide, and 95% ethanol.

d: DETERMINATION OF FAT CONTENT

A Soxhlet extractor, constant temperature water bath, analytical balance, electric blast drying oven, dryer, filter paper tube, and evaporating dish. Anhydrous ethanol and petroleum ether.

e: DETERMINATION OF VITAMIN B2 CONTENT

High performance liquid chromatography, balance, autoclave, pH meter, vortex shaker, tissue masher, constant temperature water bath, dryer, and spectrophotometer. Hydrochloric acid, glacial acetic acid, sodium hydroxide, sodium acetate trihydrate, methanol, papain, and peak amylase.

B. PROCESS DETERMINATION

Through research and verification of the physical properties of the material, the corresponding experimental method has been selected. The physical property verification includes: determining the sieving process with the particle size distribution of the powder particles, determining the stepwise mixing process by mass fraction distribution, and determining the experimental percentage loading amount with the bulk density.

1) SIEVING PROCESS

Many studies have suggested that the size of the powder particles is an important factor that affects the behavior of these particles when the surface characteristics of them are similar [22]–[24]. This is because the particle size index of powder particles often has great differences [25]–[28]. The multiple is much larger than the density and morphology of the powder particles. Therefore, the uniformity of the particle size of the powder mixing system becomes the most important factor when determining the uniform dispersion of different particles, and is also the most important data for detecting the uniformity of product mixing [7], [29]–[31]. In short, the better the particle size uniformity of the powder system composition is, the more similar the motion characteristics of the particles during the mixing process would be, and the better the degree of dispersion between the different types of particles would be when the uniformity of the mixture obtained after the mixing process is higher.

The particle size of the particles is also known as the particle size. A certain method reflects a series of percentages of particles of different particle sizes in mass, quantity, or volume, respectively, as the particle size distribution. In short, the particle size distribution is the particle content of different particle size intervals in the powder. All raw materials were sieved through 20 mesh, 30 mesh, 50 mesh, and 80 mesh to obtain the particle size distribution results of the raw materials as shown in TABLE 2.

As can be seen from the above table, all of the test materials can pass through 20 mesh and 30 mesh sieves. When passing through the 50 mesh sieve, some of the raw materials could not pass completely. Taking into account the validity of the test, the mass fraction data of 50 mesh and 80 mesh sieves of all the test materials were further analyzed to obtain a line graph as shown in the following figure.

It can be seen from the line graph in FIGURE 2 that the particle size of the raw materials after a 50 mesh sieve exhibits a relatively uniform distribution. As it would be difficult for the particle size distribution between the raw materials to be all similar, in the actual mixing process, all the raw materials are preferentially sieved, and the sieved raw materials are in a relatively uniform state, which is more favorable for uniform mixing. Based on the experimental results of the particle size

TABLE 2. Raw material particle size distribution.

Serial number	raw material	mass fraction（%）			
		20mesh	30 mesh	50 mesh	80 mesh
1	non-dairy creamer	0	0	11.2	6.4
2	maltodextrin	0	0	11.2	64.2
3	whey powder	0	0	7.8	53
4	soybean isolate protein powder	0	0	0	44.4
5	sodium citrate	0	0	6	19.8
6	Compound fat-soluble vitamin	0	0	0	3.86
7	Compound water-soluble vitamin	0	0	0.44	8.74
8	jujube powder	0	0	0	1.8
9	Yiren power	0	0	0	64.6
10	calcium carbonate	0	0	2.54	3.9
11	potassium chloride	0	0	1.2	18.8
12	Compound mineral powder	0	0	0	1.8
13	xanthan gum	0	0	0	0

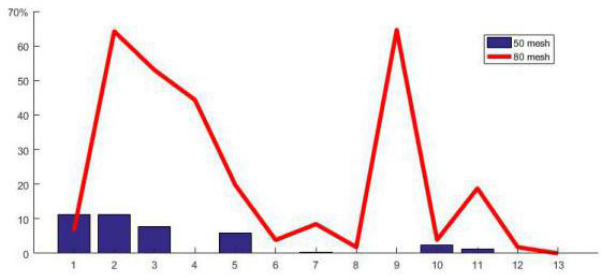

FIGURE 2. Raw material particle size distribution.

distribution, to ensure the reliability of the sieving process, it was decided that all the raw materials passed through a 50-mesh sieve before being mixed.

2) FRACTIONAL BULK

The mass fraction of each material is different. In the mixed system, the material with a small mass fraction is not easily dispersed. The quality scores of all the 13 raw materials of the special medical formula based on Chinese herbal medicines developed in the previous study group are shown in the following fan chart:

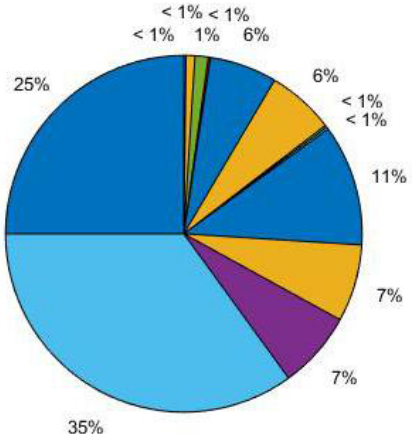

FIGURE 3. Raw material particle size distribution.

In the above mixed system, the mass fraction of non-dairy creamer, maltodextrin, whey protein powder, soy protein isolate powder, sodium citrate, jujube powder (nucleated), and coix seed powder is large. The combined fat-soluble vitamins, complex water-soluble vitamins, calcium carbonate, potassium chloride, complex minerals, and xanthan gum have a small mass fraction. As raw materials with a small mass fraction are not easily mixed uniformly in the integrated mixing system, it is considered that the raw materials having a smaller mass fraction are preferentially mixed by the amplification charging method during the test, and are referred to as premixing throughout the process.

III. RESULTS

This paper proposes an algorithm for optimizing hill climbing using improved genetic operators (hereinafter referred to as IH algorithm). On the basis of automatically adjusting the crossover probability and mutation probability, the automatic selection function of crossover mode and mutation mode is added [32]–[34]. The individual scores are accordance with the current score and the best score. The proximity degree automatically adjusts the crossover probability and the mutation probability; the crossover mode and the variation mode are automatically selected according to the score difference. Automatically adjusting the intersection and variation according to the difference can make the crossover operation and the mutation operation more efficient and effective [35]. Using the improved crossover and mutation operator instead of the subtraction operator in the hill climbing algorithm can avoid the algorithm being trapped in the local optimum by the subtraction operator. To avoid or overcome risks, it is better to expand the global optimization capabilities. Limiting the search space with the maximum support tree can improve the search efficiency of the algorithm [36]–[38]. Finally, the improved algorithm was used to simulate the data of the premixing and total mixing experiments of the formula for the

special medicinal use formula, and the global optimal results were obtained [39]–[41].

A. PRINCIPLE OF IH ALGORITHM

The IH algorithm first uses the principle of mutual information to calculate the mutual information between nodes, and on this basis, establishes the maximum support tree to limit the search efficiency of the search space. The maximum support tree is a tree-like structure calculated using mutual information theory. Mutual information is a measure of the correlation between two variables. Taking variable X and variable Y as examples, mutual information uses I(X, Y). The calculation formula is shown as follow:

$$\begin{aligned} \mathrm{I}(X, Y) &= H(X) + H(Y) - H(X, Y) \\ &= \sum\nolimits_{X,Y} p^{(X,Y)} \log \frac{p(X, Y)}{p(X)\, p(Y)} \end{aligned}$$

The initial support tree is searched by the edge-adding and edge-turning operators. The Bayesian information criterion (BIC) scoring function is used to calculate the current individual score, the highest score F of the record structure and the average score F_{av}, and the individuals whose score is higher than F_{av} are stored in the set C. The individuals are selected from the set C in turn, and the cross mutation probability is automatically adjusted according to the difference between the current individual score and the best individual score: the smaller the difference between the individual score and the best score, the smaller is the crossover probability and the mutation probability, and the individual's superiority can be guaranteed. Sex is not destroyed; the greater the difference between individual score and the highest score, the greater the probability of crossover and mutation, which can increase the diversity of the population and thus, find the global optimal solution faster. The BIC scoring function, the constructed crossover probability P_c, and the mutation probability P_m are as shown as follows:

$$S_{BIC} = \log\left(\theta^{MV}, B\right) - \frac{1}{2} Dim(B, X_i)$$

$$\mathrm{Dim(B)} = \sum\nolimits_{i=1}^{n} Dim(B, X_i)$$

$$P_C = \begin{cases} P_{c1} - \dfrac{K(F - F_1)}{F} & |F - F_1| \le \eta \\ P_{c1} + \dfrac{K(F - F_1)}{F} & |F - F_1| > \eta \end{cases}$$

$$P_m = \begin{cases} P_{m1} - \dfrac{K(F - F_2)}{F} & |F - F_2| \le \eta \\ P_{m1} + \dfrac{K(F - F_2)}{F} & |F - F_2| > \eta \end{cases}$$

where: θ^{MV} is the maximum likelihood estimate of the parameter; Dim(B) is the dimension of the network structure B; P_c is the crossover probability; $P_{c1} = 0.64$; Pm is the mutation probability; $P_{m1} = 0.04$; F is the preliminary search by the hill-climbing operator. The best score obtained; F_1, F_2 are the scores of the current individual; K is a constant; η is the set threshold.

According to the score difference ξ, the intersection mode and the variation mode are automatically selected: set the threshold μ, if the difference between the individual score F_1 and the best score $F_{\xi 1}$ is less than or equal to μ, then a single point crossover is performed, whereas if the difference ξ_1 is greater than μ, then the two points are crossed. After the crossover operation, the score is calculated again and the variation mode is selected according to the difference F_2 between the individual score F_2 and the best score F. If the difference ξ_2 is less than or equal to μ for single point variation, the difference ξ_2 is greater than μ for two points of variation. This is shown as follows. According to the difference between the current individual score and the best score, the intersection method and the variation method are automatically selected, which can effectively avoid the shortcomings of finding the optimal solution speed and easily destroy the superiority of the individual caused by the single crossover mode and the single mutation mode. The individual's superiority increases the diversity of the population, finds the global optimal solution more quickly, and improves the global optimization ability of the algorithm.

$$\begin{cases} single\ crossing\ point\ \xi_1 \le \mu \\ double\ crossing\ point\ \xi_1 > \mu \end{cases}$$

$$\begin{cases} single\ crossing\ point\ \xi_2 \le \mu \\ double\ crossing\ point\ \xi_2 > \mu \end{cases}$$

As each Bayesian structure is represented by an adjacency matrix, the adjacency matrix corresponding to our Bayesian structure is shown as T:

$$T = \begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Through the cross operation and the mutation operation, the adjacency matrix corresponding to the global optimal individual is found, and then the corresponding Bayesian structure is output through the adjacency matrix.

B. SIMULATION EXPERIMENT BASED ON IH ALGORITHM

The simulation experiments of IH, GA, HC, and improved algorithm SHC were carried out based on the standard Asia network, Car network, and Alarm network, respectively [42], [43]. By comparing the average best score, accuracy and running time of the four algorithms, and the advantages and disadvantages of the IH algorithm are comprehensively analyzed. The accuracy is measured by the exact number of edges C and the number of wrong edges W for the calculated structure, where the number of error edges is the sum of redundant edges, missing edges, and inverted edges. The standard Asia network has 8 nodes and 8 edges, and randomly generates data samples with data volumes of 500, 1000, 3000, 5000, and 9000. Four kinds of algorithms, such as IH, GA,

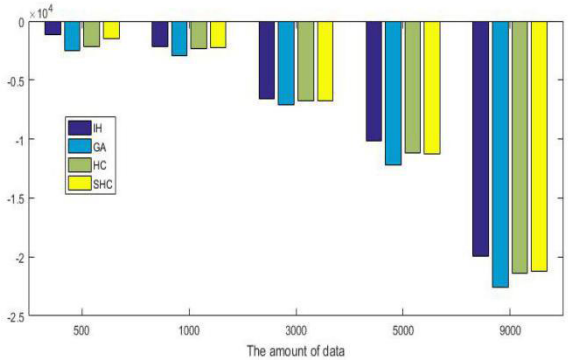

FIGURE 4. Best score comparison of each algorithm.

HC, and SHC, were used for structural training, and the average best scores are shown in FIGURE 4.

It can be seen from FIGURE 4 that the average best scores of GA and HC are small, and the best score for SHC improves to some extent, but the average best score of IH is even higher than that of SHC. The correct number of edges and the number of wrong edges are shown in FIGURE 5 and FIGURE 6, respectively. The algorithm execution time pairs are shown in FIGURE 7.

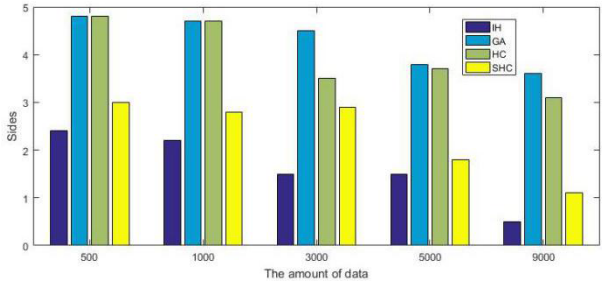

FIGURE 5. The correct number of sides of each algorithm.

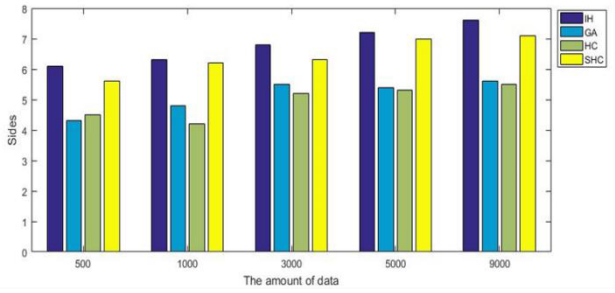

FIGURE 6. The error number of sides of each algorithm.

It can be seen from FIGURE 5 and FIGURE 6 that the exact number of edges obtained by IH is much more than that of GA and HC, and also more than the improved algorithm SHC; on the other hand, the number of error edges generated by IH is much smaller than the other three algorithms.

It can be seen from FIGURE 7 that the SHC has the shortest running time and the running time of IH is slightly longer than that of the SHC. This is because IH has added improved crossover and mutation operators to the traditional

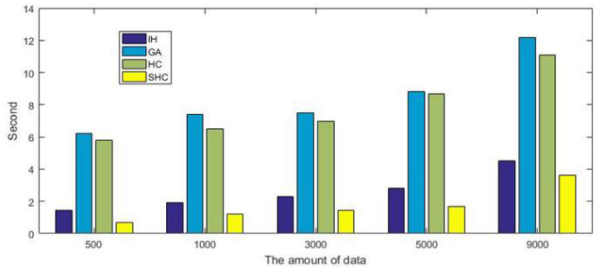

FIGURE 7. Comparison of execution time of each algorithm.

HC to improve its global optimization ability. However, compared with GA and HC, the running time has been greatly shortened. According to the cumulated data from FIGURE 5, FIGURE 6, and FIGURE 7, the average best score, operation speed, and accuracy of IH are much better than that of HC and GA. Compared to the improved algorithm SHC, IH greatly improves the accuracy in less time.

Average best score. The standard Car network has 12 nodes and 9 edges, and randomly generates data samples with data volumes of 500, 1,000, 2,000, 3,000, and 5,000.

Using IH, GA, HC, SHC for structural training. The average best score obtained for structural training using IH is significantly higher than that of GA, HC, and SHC; the running time of IH is much lesser than that of GA and HC, and the time increases compared to SHC.

C. VARIABLE SELECTION AND PROCESS PARAMETER MODELING

The whole process of special medicinal use formula is divided into sieving, premixing, and total mixing. The purpose of the sieving process is to make the particle size uniform, which is beneficial for the uniform mixing between the granules, and is considered a relevant parameter for the process. The final mixing uniformity has little effect, so the process is not considered during the modeling process. There are many process parameters in the process of premixing and total mixing, and the relationship between these process parameters is complicated. If the loading amount is too large, the movement efficiency becomes low within the prescribed total mixing time, resulting in poor mixing effect. When the premixing rotation speed is too low, the uniformity of the premixed raw materials is not good, and the premixed raw materials and the total mixed raw materials are not sufficiently mixed in the prescribed total mixing time, resulting in poor mixing uniformity [44]. According to the mixing process principle, there are six parameters to be analyzed: premixing time (T_y), premixing speed (V_y), loading amount (M), total mixing time (T_z), total mixing speed (V_z), mixing uniformity (C_v), etc. The process parameters with large influences are modeled, and the IH algorithm is used to train the quantitative data of the parameters to obtain the model.

IV. CONCLUSION

The whole nutrient formula powder materials are powders and granules, and the finished product is prepared by using

a dry method. Maintaining the uniformity of mixing of the powders and particulate materials has been a problem, in terms of time and cost, that is difficult to solve by the dry mixing process. The mixing of powder and granule raw materials is a complex process in which pluralities of different powder materials are mixed, and the difference in physical properties of the raw materials serves to be the main reason for the mixed stratification. The particle size distribution and mass fraction of each raw material were studied. A screening production process was established by studying the particle size distribution, and a step-by-step mixing production process was established by studying the mass fraction. On this basis, the experiment begins with the mixing process. Based on the analysis of premixing time, mixed loading, premixing speed, total mixing speed, total mixing time, and mixing uniformity, a prediction model based on genetic hill climbing algorithm was established.

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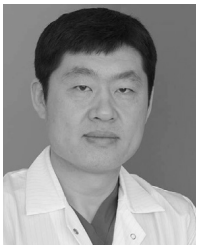

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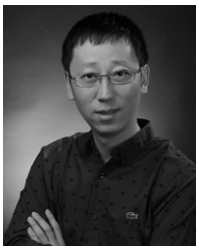

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