Medicine Safety Assessment Method Based on Dynamic Dual Optimization

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Abstract

As people pay more and more attention to medicine safety issues, related medicine safety monitoring platforms are also rapidly popularized. However, previous work has poor accuracy and low efficiency in medicine safety assessment. In this paper, the medicine safety evaluation index system of the medicine safety monitoring platform is determined from four aspects: medicine research and development, medicine market, medicine production, and medicine uses. In order to solve the problems of the medicine safety evaluation model, such as low evaluation accuracy, slow convergence speed, and long training time, the dynamic dual optimization of PSO-BP medicine safety assessment method (OPSO-BP) is proposed. The weights and thresholds of BP neural network are optimized by the PSO algorithm to improve the quality of assessment. In addition, we optimize PSO: use the cosine function to dynamically adjust the inertia weight w and use the average optimal position of the individual in the population to replace the optimal position of the individual. It improves the problem that the evaluation model in the traditional algorithm is easy to fall into the local optimal solution due to the lack of generalization ability. In this paper, the effectiveness of OPSO-BP is verified by comparative experiments with the designed questionnaire data of medicine safety evaluation.

Keywords: Medicine safety assessment system, PSO-BP assessment model, Dynamic adjustment of inertia weight, Individual optimal solution optimization

1 Introduction

In recent years, people have increasingly strengthened the renovation and supervision to address medicine safety and evaluation issues [1-3]. However, compared with the perfect vertical medicine safety supervision system established by the United States, the world is still in its early stage in the aspect of medicine safety supervision and evaluation system. The promulgation of laws and regulations on medicine safety has not been perfect and made specific [4-5].

However, the definition of medicine safety and medicine safety evaluation index is still relatively vague. There is not a relatively authoritative reference standard for the establishment of a medicine safety evaluation index system [6]. In the whole process of medicine sampling investigation and evaluation, there are many factors influencing the results of medicine safety evaluation [7-10]. In general, the medicine safety evaluation can be divided into two categories: risk assessment to medicines after its development and before getting into the market and safety assessment to medicines after getting into market. For the medicine safety assessment before and after marketing, there are a variety of methods to be used domestically and overseas. For example, the FDA in the United States adopts many different ways to avoid risk (Risk Evaluation and Mitigation Strategy) [11-12] in the aspects of medicine classification, assessment standard development, marketing approval, and so on. In the United States, the most used methods for the post-market safety assessment of medicines are black-box warning systems and non-randomized, multi-center clinical trials based on openness [13]. However, medicine safety assessment mainly adopts the method of literature evaluation-pharmacology research-clinical expertise. LPC [14] combines the theoretical research and practical application and adopts the form of a questionnaire survey to evaluate medicines indices at all levels to carry out the random sampling survey on the experts, and to evaluate medicines systematically [15-16]. Safety assessment for nanotechnology and nanomedicine was introduced to further explain the key concepts in nanotoxicology, including the importance of dose, dose rate and biodynamics [17]. Key factors for the successful implementation of toxic genomics in drug discovery and development were illustrated [18]. A comprehensive review was presented to determine visual effects for medical risk and benefit-risk communication [19]. In summary, our contributions mainly include the following three points:

(1) Through literature research, a questionnaire survey, panel discussion, expert consultation, and mathematical statistics, a medicine safety evaluation index system was designed, and medicine safety was evaluated from the aspects of medicine research and development, medicine market, medicine production, and medicine uses.

(2) To solve the problem that the accuracy of the traditional BP medicine safety assessment model is not ideal, the PSO algorithm is used to optimize the weights and thresholds of the BP neural network. Aiming at the issue that the assessment efficiency of the PSO-BP model is not high enough, the dynamic inertia weight control and the method of replacing the individual optimal solution with the average optimal solution of the population were respectively used to

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optimize the model.

(3) We conduct extensive experiments to demonstrate the effectiveness of our OPSO-BP medicine safety assessment model. Experimental results show that our method can achieve superior performance by a large margin.

2 Comprehensive Index of Medicine Safety Assessment

Whether the evaluation index system is scientific and comprehensive determines whether we can correctly evaluate medicine safety. In this paper, through literature research, questionnaire survey, panel discussion, expert consultation and mathematical statistics, the relevant indexes that have an impact on medicine safety are divided into primary and secondary indicators according to the relationship of importance or supplementary conditions. A total of 4 first-level indicators and 13 second-level indicators. As shown in Figure 1. The scoring standards of secondary indicators were determined through consultation with the expert group of Drug safety Assessment, and their corresponding relationships are shown in Table 1.

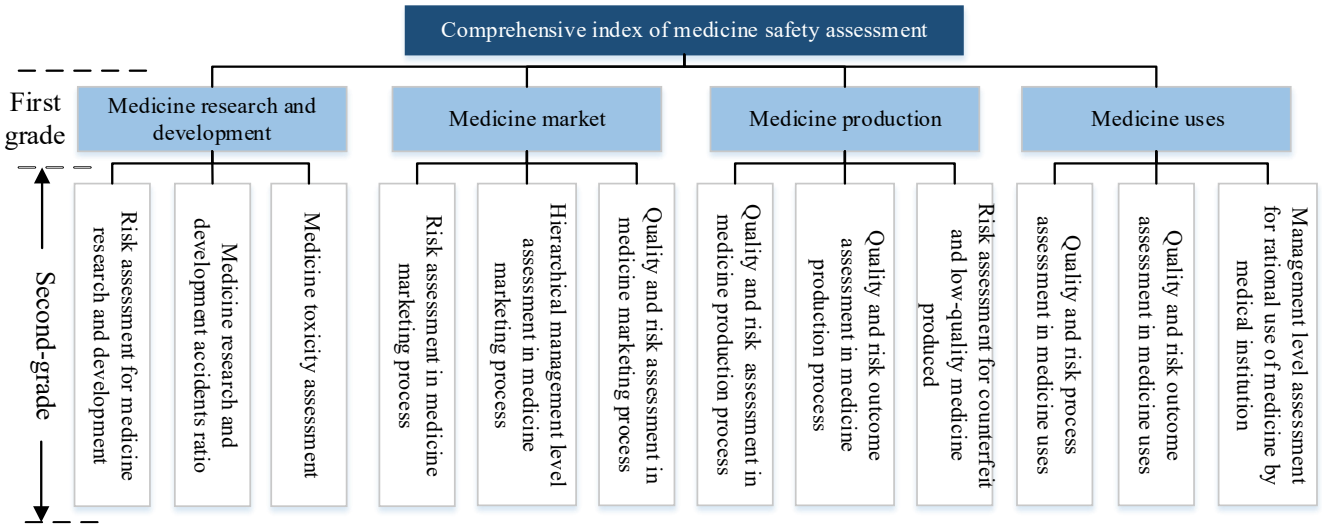

Figure 1. Classification of first-grade and second-grade index for medicine safety assessment

Table 1. Scoring standard of medicine safety questionnaire

First-grade Index	Second-grade Index	Scoring criteria
Personal information indicators (10 scores)	Work address	0-3 scores
	Work seniority	0-3 scores
	Professional title	0-4 scores
Safety indicators during medicine development (20 scores)	Medicine development risk assessment	0-7 scores
	Proportion of medicine development accidents	0-7 scores
	Toxicological assessment of medicines	0-6 scores
Safety index of medicine management (20 scores)	Process evaluation of medicine manufacturing quality risk	0-10 scores
	Evaluation of medicine production quality line management level	0-4 scores
	Evaluation of medicine manufacturing quality risk results	0-6 scores
Safety index of medicine production (20 scores)	Medicine management quality risk process evaluation	0-5 scores
	Evaluation of medicine management quality risk results	0-5 scores
	Risk assessment of counterfeit and inferior medicines	0-10 scores
Safety index of medicine uses (30 scores)	Process evaluation of medicine use quality risk	0-5 scores
	Evaluation of medicine use quality risk results	0-6 scores
	Evaluation of rational medicine use management level in medical institutions	0-4 scores
	Risk assessment of medicine use in medical institutions	0-3 scores
	Public assessment of medicine use risk	0-2 scores
	Risk assessment of adverse medicine reactions	0-5 scores
	Percentage of cases with adverse reactions	0-5 scores

3 BP and PSO Algorithm Principle

3.1 BP Neural Network

BP neural network is a multi-layer feed-forward neural network that uses error back propagation [20-21]. BP neural network includes input layer, hidden layer, and output layer. Each layer can contain multiple neurons. The hidden layer can be a single layer or multiple layers. Generally, only one single

hidden layer is required in regression prediction to obtain relatively accurate results. The BP structure is shown in Figure 2.

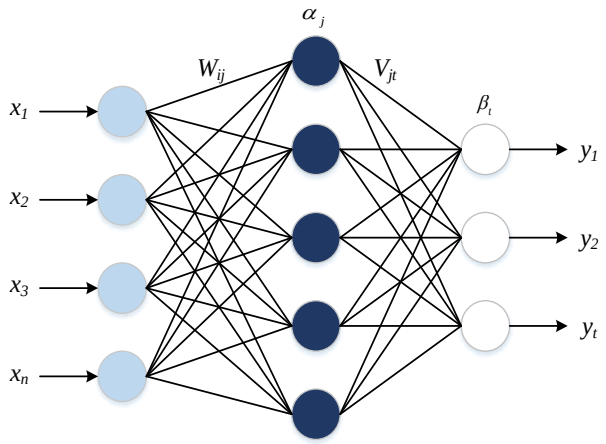

Figure 2. BP neural network structure

Where $X_i = (X_1, X_2, \cdots, X_n)$ is a set of input vectors, $Y_j = (Y_1, Y_2, \cdots, Y_t)$ is a set of output vectors, W_{ij} is the connection weight between the input layer and the hidden layer, and V_{jt} is the connection weight between the hidden layer and the output layer. α_j and β_t are the node thresholds of the hidden layer and output layer respectively.

3.2 Particle Swarm Optimization Algorithm

The main idea of the Particle Swarm optimization algorithm is to find the optimal solution by simulating the foraging behavior of birds [22-26]. The flow of the PSO algorithm is as follows: In a D-dimensional search space, a particle swarm is composed of m randomly initialized particles. According to the individual extreme value $Pbest_{id}^t$ and the group extreme value $Gbest^t$ of the current population of particles, PSO changes the position $(x_{i1}^t, x_{i2}^t, \cdots x_{iD}^t)$ and velocity$(v_{i1}^t, v_{i2}^t, \cdots v_{iD}^t)$ of the particles through repeated iterations to obtain the optimal solution of the population. In each iteration process, the update formula for the velocity and position of particle is as follows:

$$v_{id}^{t+1} = \omega \times v_{id}^t + c_1 \times rand\left(Pbest^t{}_{id} - x_{id}^t\right) + c_2 \times rand\left(Gbest^t - x_{id}^t\right) \quad (1)$$

$$x_{id}^{t+1} = x_{id}^t + v_{id}^{t+1} \quad (2)$$

Where v_{id}^t is the velocity of the particle i in the d-dimensional space after the t-th iteration, x_{id}^t is the corresponding particle position, ω is the inertia weight, c_1 and c_2 are the acceleration coefficients, and *rand*() is a random number that changes between [0,1], $Pbest_{id}^t$ is the historical optimal position of the *i*-th particle in the current iteration, and $Gbest^t$ is the historical optimal position of the population in the *t*-th iteration.

4 Medicine Safety Assessment Method Based on Dynamic Dual Optimization

4.1 Improvement Ideas

Since the weights of BP neural networks are usually determined by the gradient descent method, it is often difficult to find the optimal weights after repeated trials. It has shortcomings such as slow convergence speed, weak network performance, and the inability to guarantee the global optimal value. In addition, even if the number of samples is very small, BP is easier to fall into the local solution optimal, and there will be a situation where the prediction and the expected value have a larger error.

In order to optimize this problem, the BP neural network is connected with the particle swarm optimization algorithm. PSO is characterized by information sharing and co-evolution between groups. The search direction and distance of particles can be continuously changed according to the particle speed and fitness value, and the quality of the particles can be determined according to the particle fitness value. When the particles move in a preset space, it will continuously change the position according to the individual extreme value and the global extreme value to update its own fitness value to achieve the purpose of optimizing it in the preset space. Compared with the BP neural network, the PSO algorithm can search in a larger space, and avoid the BP neural network from falling into the local optimum. PSO improves the performance of the network model by optimizing the connection weights and thresholds of the BP neural network. The inertia weight w of the traditional PSO-BP evaluation model adopts a linear decreasing strategy. This strategy makes the inertia weight w linearly decrease with the increase of the number of iterations in the process of PSO algorithm searching for the optimal solution. This strategy has a strong global search capability in the early stages of iteration. However, if the best point cannot be searched in the initial stage, then as w decreases, the local search ability is strengthened, and it is easy to fall into the local extreme value. In order to maintain the ability of the PSO algorithm to find the global optimization in the early stage of the iteration and the faster convergence speed, and in the later stage of the iteration, it can maintain a certain ability to jump out of the local optimal solution and search for the optimization in the local range. This paper improves the PSO algorithm from two aspects.

4.2 PSO Particle Optimization based On Dynamic Double Optimization

1) Dynamic adjustment of inertia weight based on cosine function

Through the analysis of Formula (1) and (2), the inertia weight has a relatively large impact on the convergence ability of the PSO algorithm and controls the particle's global and local search capabilities. Generally, particles are required to have better global search capabilities in the early stage of the iteration, and particles are required to have better local search capabilities in the later stage of the iteration. Therefore, in order to enable the PSO algorithm to maintain a certain optimization ability and a faster convergence speed during the first and later stages of the iteration, and to improve the evaluation efficiency of the medicine safety assessment model, we design the A method. Through the observation of the standard cosine function image, we compare it with the linear decreasing function.

To make PSO-BP maintain certain optimization ability and faster convergence speed in both early and late stages of iteration, and to improve the assessment efficiency of the medicine safety assessment model, the standard cosine function figure (Figure 3) was observed and compared with the linear decrement function. In the decreasing process of the standard cosine function, it can guarantee a slower change rate in the early phase so that the particles in the PSO-BP can keep a faster flight velocity and a good global search optimization ability in the early stage. It can also reduce the change rate of inertia weight to a certain extent in the late stage so that PSO-BP can maintain a certain local search and optimization ability in the late optimization phase. Therefore, the cosine function was used to dynamically control the inertia weight ω in this paper. As shown in Formula (3).

$$\omega = \left(1+\cos\frac{T*\pi}{T_{\max}}\right)*\left(\frac{\omega_{\max}-\omega_{\min}}{2}\right)+\omega_{\min} \quad \textbf{(3)}$$

Where T denotes the number of current iterations, T represents the maximum number of iterations; and where ω_{max} denotes the maximum inertia weight value $and\ \omega_{min}$represents the minimum inertia weight value that were set respectively.

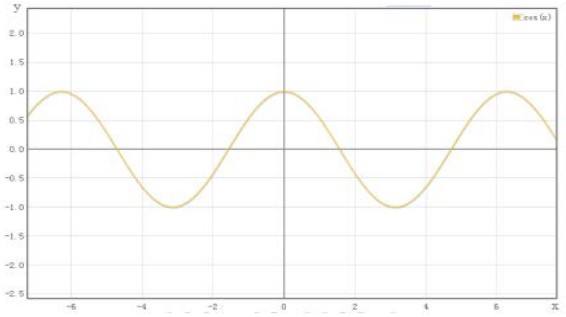

Figure 3. Standard cosine function

2) Population average optimal solution optimization

In the “flying” optimization process of the population, it is possible that the particles in the population go beyond the scope of the global optimal solution because their “flying” velocity is too fast, resulting in that the particles cannot "fly back" to the position of the global optimal solution again in the optimization process. Considering that the use of cosine functions for dynamic control of inertia weights may have an impact on the optimization results, the average value $Pbest_{avg}^{t}$ of the optimal position found by all particle individuals in the population was used to replace the optimal location $Pbest_{avg}^{t}$ found by a single individual particle. By using the global optimal average position of the population $Pbest_{avg}^{t}$ to control the particle optimization, the individual particle can learn from the experience of other particles in the “flying” optimization process and adjust the direction and speed of its own optimization. As shown in Formula (4).

$$v_{id}^{t+1} = w\times v_{id}^{t} + c_1\times r_1\times(Pbest_{avg}^{t} - x_{id}^{t}) + c_2\times r_2\times(Gbest_{avg}^{t} - x_{id}^{t}) \quad \textbf{(4)}$$

The PSO-BP was improved by using cosine function to dynamically control the inertia weight and using global optimal average position $Pbest_{avg}^{t}$ to replace the individual optimal position$Pbest_{id}^{t}$, in the optimization of the model, it is easy to get into the problem of local optimal solution due to the different optimization methods. In order to verify that the optimized PSO-BP neural network model of medicine safety assessment has fast operation speed under the premise of maintaining the accuracy of medicine safety assessment, the same experimental data as the PSO-BP model of medicine safety assessment would be used to carry out the experiment.

4.3 Optimize the Process of BP Neural Network

The main idea of OPSO-BP: The optimal solution obtained by the improved PSO algorithm is used as the initial weight and threshold of the BP neural network. The specific implementation process is as follows:

Step 1. Preprocess the medicine safety questionnaire data.

Step 2. Initialize the weights and thresholds of BP neural network.

Step 3. Initialize the optimized PSO algorithm. The optimized PSO algorithm is used to optimize the weights and thresholds of each layer of the BP model for medicine safety assessment.

1) Initialize the relevant parameters of the population number, number of iterations, learning factor, and inertia weight in the optimized PSO algorithm.

2) Determine the particle fitness calculation function in the optimized PSO algorithm and calculate the fitness of each particle. The fitness calculation formula is Formula (1) and Formula (2).

3) According to the calculation result, judge whether the preset minimum error or the maximum number of iterations is met. If it meets the requirements, go to Step 4; if it does not meet the requirements, go to Step 4.

4) Combine improvement strategy 1 and improvement strategy 2 to update the current speed and position of all particles and return to Step 4.

Step 4. Assign the weights and thresholds calculated by the optimized PSO algorithm to the corresponding nodes of each layer in the BP model for medicine safety assessment and determine whether they meet the output conditions. If the preset accuracy requirement or the set maximum number of iterations are met, then go to Step5; if the preset accuracy or the maximum number of iterations are not met, return to 2).

Step 5. The training of OPSO-BP is completed, input the test data, then output assessment results.

OPSO-BP algorithm flow is shown in Figure 4.

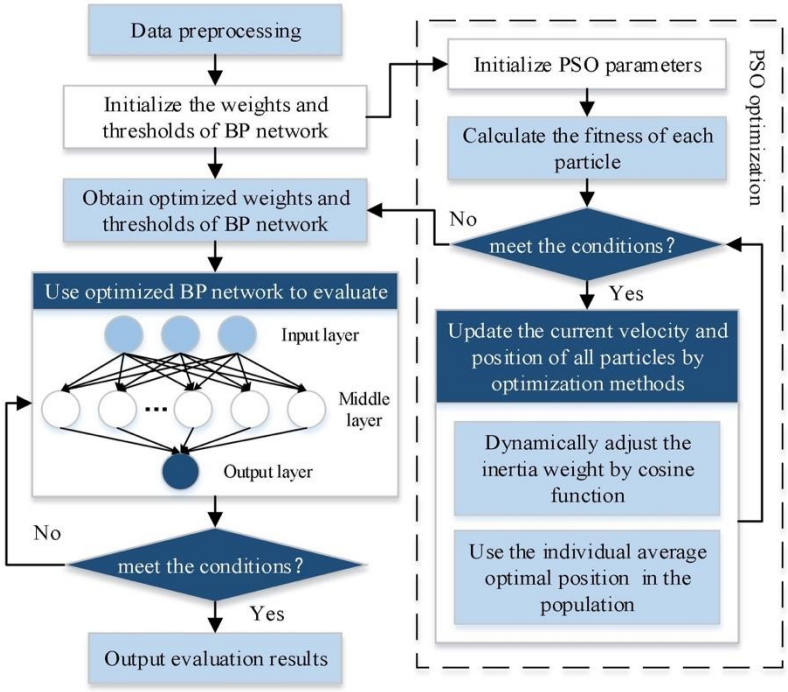

Figure 4. OPSO-BP algorithm flow

5 Experiment Analysis

Experiments are conducted in this section and we aim to answer the following research questions:
RQ1: How are the key parameters of our proposed OPSO-BP set?
RQ2: How does DGCF perform compared with baseline models?

5.1 Experimental Data

We designed the medicine safety assessment questionnaire, then invited medical-related practitioners and experts in the pharmaceutical-related industry to conduct an anonymous survey. A total of 1800 questionnaires were made, and the number of medicine safety questionnaires actually evaluated was 1532, among which 1436 were valid data for evaluation of relevant indicators. 78.39% of the total questionnaires were scored at [70,90], and 6.73% were below 60 scores. This paper randomly selects 1000 questionnaire data of medicine safety evaluation as the training set, and 30 questionnaire data as the test set.

5.2 Evaluation Standard

This paper uses relative error as the evaluation standard for experimental results. The specific calculation formula is

$$Relative\ error = \frac{\Delta x}{x_t} = \frac{x - x_t}{x_t} \quad (5)$$

Where x is the predicted value and x_t is the true value.

5.3 OPSO-BP Parameters Setting (RQ1)

The number of hidden layer nodes of the optimized PSO-BP medicine safety assessment model (OPSO-BP) is determined to be 10. In order to determine the optimal maximum inertia weight ω_{max} and minimum inertia weight ω_{min} of the optimized PSO-BP neural network model of medicine safety assessment, the trial and error method was adopted to carry out the experiment.

(i) The maximum inertia weight ω_{max}

The minimum inertia weight was set to 0.3 and the maximum inertia weight was tested in the interval of [0.6,1.0]. The experimental results are shown in Figure 5.

Training error and running time of OPSO-BP under different maximum inertia weights, as shown in Table 2.

Table 2. Training error and running time of OPSO-BP under different ω_{max}

Maximum inertia weight	Training error	Run time
1.0	0.001084	300s
0.9	0.001062	293s
0.8	0.001033	268s
0.7	0.001035	270s
0.6	0.001042	276s

During the experiment, we found that when the maximum inertia weight ω_{max} is 0.8, the optimized model has a higher running time efficiency on the premise of ensuring accuracy. Therefore, the maximum inertia weight of OPSO-BP model of medicine safety assessment was set to 0.8.

(ii) The minimum inertia weight ω_{min}

The maximum inertia weight was set to 0.8 and the minimum inertia weight was tested in the interval of [0.1,0.5]. The experimental results are shown in Figure 6.

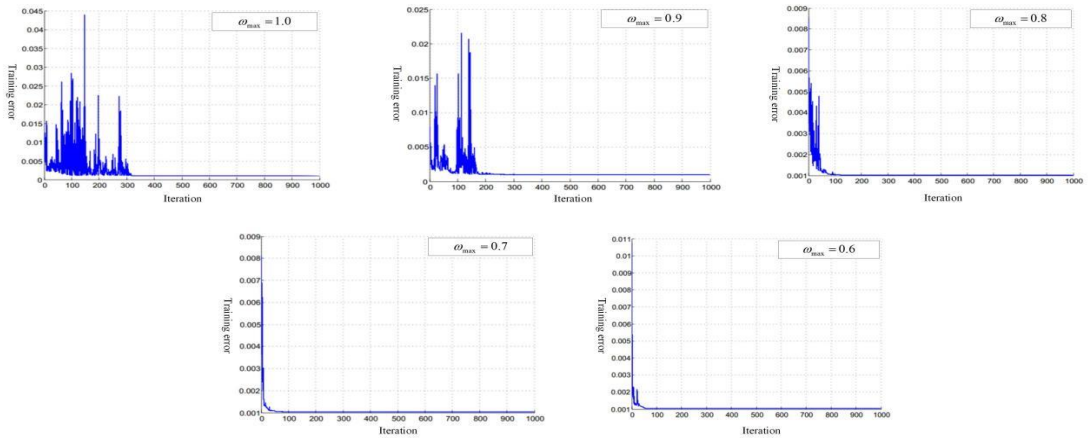

Figure 5. Experimental results under different maximum inertia weights

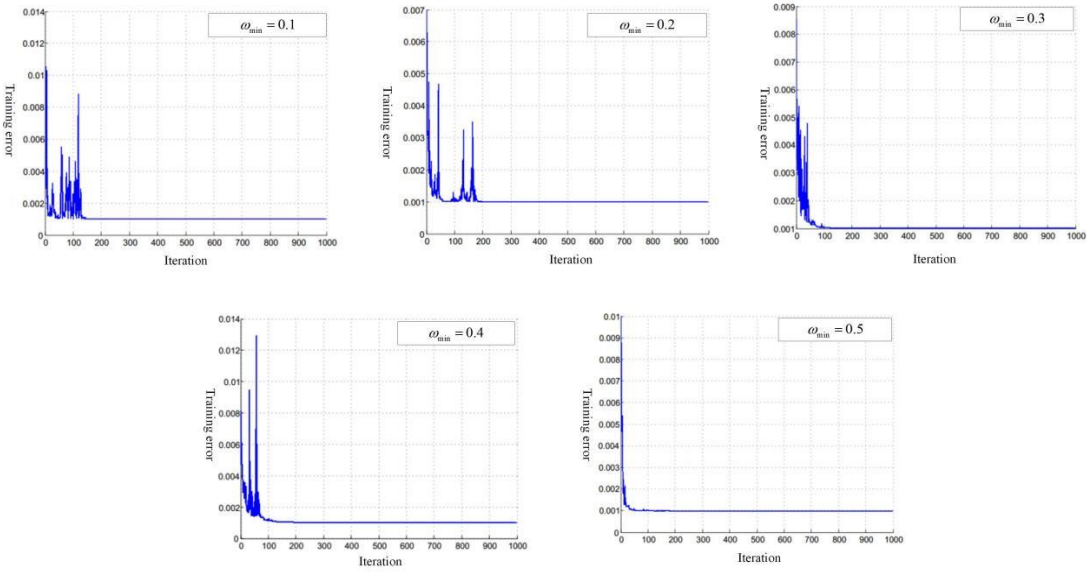

Figure 6. Experimental results under different minimum inertia weights

Training error and running time of OPSO-BP under different minimum inertia weights are shown in Table 3.

After the experiment, it is found that with the increase of the minimum inertia weight, the running time efficiency shows a trend of downward at first and then upward. The minimum inertia weight was set to 0.3 on the premise of achieving the same accuracy.

Table 3. Training error and running time of OPSO-BP under different ω_{min}

Minimum inertia weight	Training error	Run time
0.1	0.001062	297s
0.2	0.001052	301s
0.3	0.001027	267s
0.4	0.001033	273s

After the experiment, it is found that with the increase of the minimum inertia weight, the running time efficiency shows a trend of downward at first and then upward. The minimum inertia weight was set to 0.3 on the premise of achieving the same accuracy.

(iii) Other parameter settings of OPSO-BP

The number of iterations was set to 200, the learning factors C_1, C_2 were both set to 2.05, the inertia weight ω_{max} was set to 0.8, ω_{min} was set to 0.3, the flying velocity was set to 0.8, and the minimum error accuracy was set to 0.0001. The fitness obtained is shown in Figure 7.

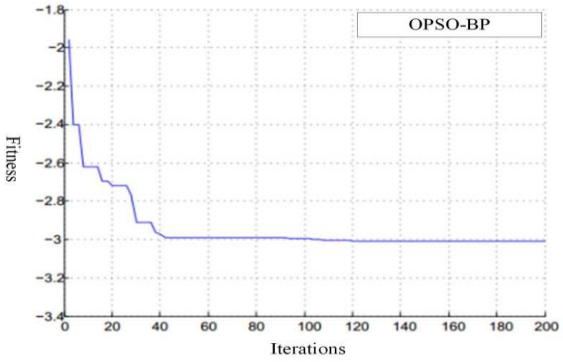

Figure 7. The fitness of optimized PSO-BP neural network

After the experiment, it is found that the optimized model only needs 123 iterations to achieve the minimum error accuracy in the process of finding the optimal solution.

5.4 Comparison of Experimental Results (RQ2)

In the comparative experiment, we set the following benchmark evaluation methods:

(1) BP medicine safety assessment model (BP): This method uses BP neural network to evaluate the safety of medicines.

(2) PSO-BP medicine safety assessment model (PSO-BP): PSO algorithm was used to optimize the weights and thresholds of every layer of BP medicine safety assessment model.

Figure 8 is the comparison between the assessment scores obtained by the three methods and the traditional scores. BP performs the worst. This is mainly due to the influence of BP neural network's own algorithm defects. The network uses the gradient descent method (Gradient Descent) to update the weight operation. In the process of learning and training the sample data, if the network encounters a concave area, it will fall into the area and have no ability to escape. As a result, its convergence accuracy is low. PSO-BP has a certain improvement over BP. OPSO-BP performs the best and is closer to the traditional scores.

Figure 9 is the relative error of the three methods. In the 30 groups of medicine safety evaluation test data, only 3 groups of BP's evaluation results have an error of less than 10%, and 5 groups have an error of more than 20%; PSO-BP has 22 groups of evaluation results with errors of less than 10%. Only one group has an error of more than 20%. Compared with BP, PSO-BP has a greater improvement in accuracy. The relative errors of all OPSO-BP evaluation results are less than 10%, and its performance is still the best.

Figure 10 is the comparison of medicine assessment grades and traditional grades. BP evaluates 14 medicines with the same grade as the traditional grade, accounting for 46.67% of the test samples. PSO-BP has 26 samples with the same assessment grade as the traditional grade. Its assessment accuracy reaches 86.67%, which is a great improvement compared to BP's accuracy. OPSO-BP has 29 samples with the same assessment grade as the traditional grade. Its evaluation accuracy reaches 96.7%.

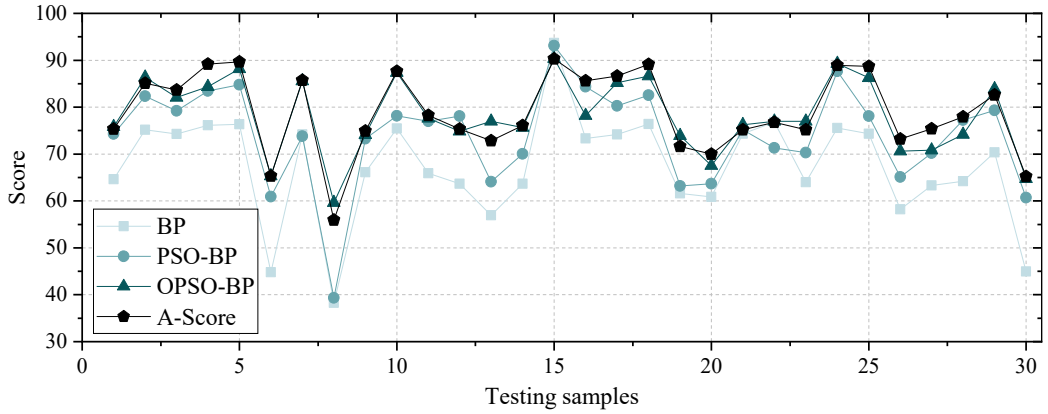

Figure 8. Comparison of assessment scores obtained by three methods with traditional scores

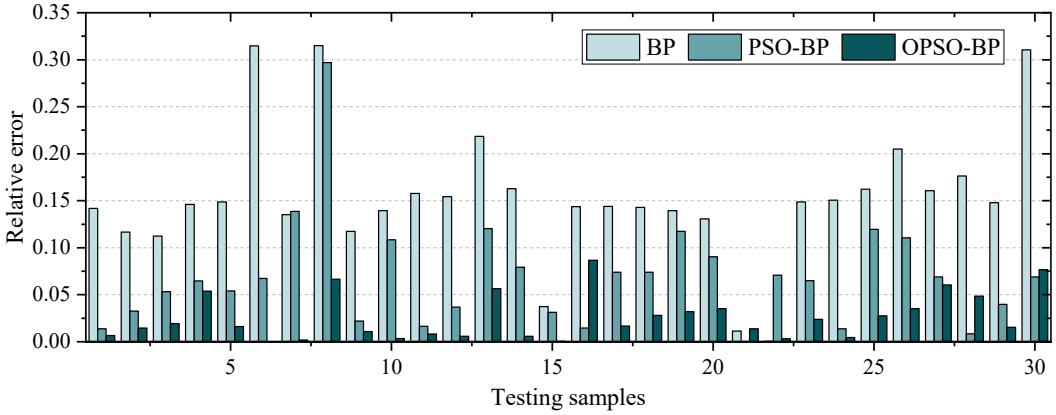

Figure 9. Relative error of the three methods

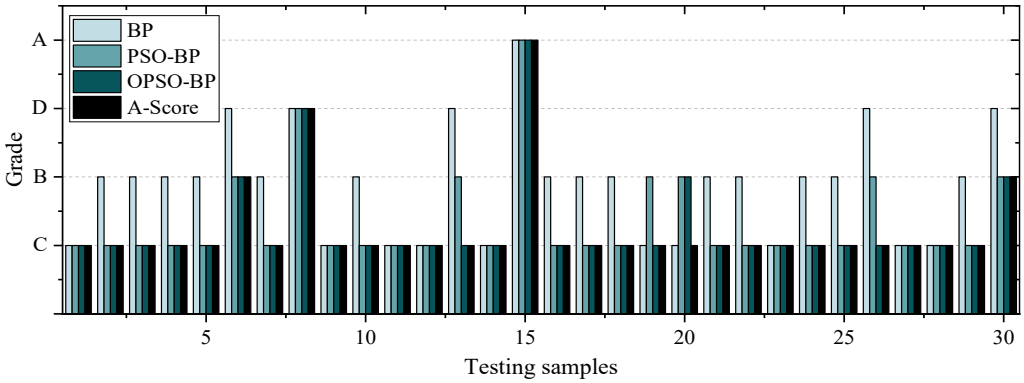

Figure 10. Comparison of medicine assessment grades and traditional grades

We also compare the running time of the three methods, as shown in Table 4. BP takes the shortest time, and it does not have any optimization strategy. OPSO-BP has a shorter running time than PSO-BP. This is because OPSO-BP's inertia weight uses a cosine function to dynamically control its change strategy. This strategy can maintain a good global search ability in the early stage and ensure the local optimization ability in the later stage. Its convergence speed is also faster than that of PSO-BP. In addition, OPSO-BP also uses the average value of the optimal solution of each particle in the population to replace the optimal solution of the individual particle, which enhances its own robustness and fault tolerance. Two strategies improve the situation where it is easy to fall into the local optimal solution. In summary, OPSO-BP has a more balanced performance.

Table 4. Comparison of the running time of the three methods

	BP	PSO-BP	OPSO-BP
Running time	10-40s	230-310s	200s-300s

6 Conclusion

This paper proposed the application of the neural network medicine safety assessment model for medicine safety assessment. The OPSO algorithm is used to optimize the weight and threshold setting. Aiming at the problem that the assessment efficiency of the PSO-BP medicine safety assessment model is not high enough, the optimized OPSO-BP medicine safety assessment model is constructed. The dynamic inertia weight control based on the cosine function and the method of replacing the individual optimal solution with the average optimal solution of the population are respectively used to optimize the model. The experimental results show that the accuracy and efficiency of our OPSO-BP medicine safety assessment model are improved on the premise of maintaining the accuracy of medicine safety assessment. The accuracy is 50% higher than BP and 10% higher than PSO-BP.

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