



## Original article

## Effects of different components of Mao Dongqing's total flavonoids and total saponins on transient ischemic attack (TIA) model of rats

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## ABSTRACT

**Objective:** To study the effects of the different components of the total flavonoids and total saponins from Mao Dongqing's active site on the rats of TIA model, determine the optimal reactive components ratio of Mao Dongqing on the rats of TIA. **Methods:** TIA rat model was induced by tail vein injection of tert butyl alcohol, the blank group was injected with the same amount of physiological saline, then behavioral score was evaluated.

Determination the level of glutamic acid in serum, the activity of Na<sup>+</sup>-K<sup>+</sup>-ATP enzyme, Ca<sup>++</sup>-ATP enzyme and Mg<sup>++</sup>-ATP enzyme in Brain tissue, observe the changes of hippocampus in brain tissue, the comprehensive weight method was used to evaluate the efficacy of each component finally. **Results:** The contents of total flavonoids and total saponins in the active part of Mao Dongqing can significantly improve the pathological changes of brain tissue in rats, improve the activity of Na<sup>+</sup>-K<sup>+</sup>-ATP enzyme, Ca<sup>++</sup>-ATP enzyme and Mg<sup>++</sup>-ATP enzyme in the brain of rats, and reduce the level of glutamic acid in serum. The most significant of the contents was the ratio of 10:6. **Conclusion:** The different proportions of total flavonoids and total saponins in the active part of Mao Dongqing all has a better effect on the rats with TIA, and the ratio of 10:6 is the best active component for preventing and controlling TIA.

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## 1. Introduction

Mao Dongqing is the dry root of the hairy holly. It has the effect of activating blood circulation, dredging collaterals and heat-clearing and detoxifying (Jiao et al., 2015; Yilmazel, 2017). It was used for the treatment of Ischemic stroke and thrombophlebitis (Li, 2011; Gao et al., 2017). Modern research shows that it can promote the ability of anoxia-fast and anti-platelet aggregation of rats (Fang et al., 2016). Previous studies in our laboratory have found that Mao Dongqing has a better effect on the rats with TIA (Miao et al., 2011a,b). The active fraction, total flavonoids and total saponins of Mao Dongqing were divided into 10:5, 10:6, 10:7 three different components for experimental treatment after preliminary screening, so we can study the effects of the different proportion components of total flavonoids and total saponins on rats with

TIA in this experiment (Abbas et al., 2017; Ali et al., 2017). The efficacy of each component was evaluated by using the comprehensive weight method, to determine an optimal proportion of components for preventing and controlling TIA, lay the foundation for the development of new dosage forms of Mao Dongqing.

## 2. Materials and methods

## 2.1. Drugs and reagents

Total flavonoids and saponins of Mao Dongqing, provided by the laboratory of analytical chemistry from Henan university of traditional Chinese medicine, the total flavonoids content is 52%, total saponins is 51%; Yangxueqingnaokeli, provided by Tianjin Tasly pharmaceutical Limited by Share Ltd, batch number: 091005; Nimodipine, purchased from Shandong Xinhua Pharmaceutical Limited by Share Ltd, batch number: 0808170; Tert butyl hydrogen peroxide (t-BHP), produced by the National Pharmaceutical Group Chemical Reagent Co., Ltd., batch number: 20081203; ATP (Adenosine-triphosphate) test kit, completed by the Nanjing Institute of biological engineering, batch number: 20101104; Glutamic acid detection kit, purchased from the Nanjing Institute of Biological Engineering Research Institute of production, batch

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**Table 1**  
The effect of behavioral score of TIA rats ( $\bar{x} \pm s$ ).

Group	Dose (g/kg)	Number	First score	Number	Second score	Mortality (%)
Blank	–	20	0 ± 0**	20	0 ± 0**	0%
Model	–	14	2.9 ± 0.6	9	2.7 ± 0.5	55%
Nimodipine	0.02	14	1.7 ± 1.0**	11	1.5 ± 0.9*	45%
Yangxueqingnaokeli	1	15	1.7 ± 1.0**	10	1.5 ± 0.7**	50%
10:5 high dose	Total flavonoids: total flavonoids = 0.133:0.067	15	1.5 ± 1.0**	11	1.7 ± 1.0**	45%
10:5 middle dose	Total flavonoids: total flavonoids = 0.067:0.033	14	1.9 ± 0.9**	10	1.5 ± 0.7**	50%
10:5 low dose	Total flavonoids: total flavonoids = 0.033:0.017	15	2.4 ± 0.6	10	2.3 ± 0.7	50%
10:6 high dose	Total flavonoids: total flavonoids = 0.125:0.075	15	1.4 ± 0.9**	10	1.5 ± 0.9*	50%
10:6 middle dose	Total flavonoids: total flavonoids = 0.0625:0.0375	15	1.9 ± 0.9**	10	1.8 ± 0.9*	50%
10:6 low dose	Total flavonoids: total flavonoids = 0.003:0.002	15	3.6 ± 5.1	10	1.9 ± 0.9*	50%
10:7 high dose	Total flavonoids: total flavonoids = 0.118:0.082	15	1.6 ± 0.9**	10	1.6 ± 0.8*	50%
10:7 middle dose	Total flavonoids: total flavonoids = 0.058:0.042	15	1.9 ± 0.8**	10	1.6 ± 0.7**	50%
10:7 low dose	Total flavonoids: total flavonoids = 0.029:0.021	14	1.9 ± 1.8*	9	2.3 ± 0.7	45%

\* Compared with model group  $P < 0.05$ .

\*\* Compared with model group  $P < 0.01$ .

number: 20101106; Coomassie Blue, purchased from the Nanjing Institute of Biological Engineering Research Institute of production, batch number: 20101105.

## 2.2. Animals

Wistar rats, half male and half female, weighing 280–300 g, produced by the experimental animal center of Hebei Province. The certificate number: 1010134; laboratory Certificate No. SYXK (Henan 2010-001).

## 2.3. Instrument

UV-2000 visible spectrophotometer, purchased from the unique instruments Co. Ltd. (Shanghai); TGL-16G table centrifuge, produced by Anting Shanghai scientific instrument factory. Enzyme-labeled instrument, the BIO-RAD company, models: BIORAD – 680.

## 2.4. Method

260 Wistar rats, half male and half female rats were randomly divided into 13 groups. In addition to the blank group, the other 12 groups of rats were made into TIA model. The doses of three kinds of proportion of Mao Dongqing total flavonoids and total saponins 10:5, 10:6, 10:7 high, middle and small are 0.2, 0.1, 0.05 g/kg respectively, they are made into 0.02, 0.01, 0.005 g/ml by 0.1% carboxymethyl cellulose sodium (CMC); The dose of Yangxueqingnaokeli group is 1 g/kg, is made into 0.1 g/ml by 0.1% CMC; The dose of Nimodipine group is 0.02 g/kg, is made into

0.002 g/ml by 0.1% CMC; The model group and blank group give the same volume of 0.1% CMC. The dosage was 1 ml/100 g once a day, continuously for 7 days. The rats were induced into TIA for third days and sixth days by tail vein injection 0.11 mol/Lt-BHP5.2 ml/kg. After 10 min, make rats into the 1 L of the wide mouth bottle, sealed, removed out the rats after hypoxia 10 min, conducting a behavioral score. At first, 260 rats were included in the experiment, but there are 64 rat's dead during the two operations. Finally, 196 rats were involved in the result analysis. Behavioral score standard: normal: 0 points; less dynamic: 1 points; jump or flee: 2 points; trembling limbs: 3 points; abdominal post, cannot stand, limb paralysis: 4 points.

On the seventh day, the blood was taken from the orbit immediately after administration of 1H. The blood was centrifuged and serum was taken to determine the content of glutamic acid. Separate the brain from the ice plate and take the sagittal cut. Half of brain put into 10% formaldehyde solution fixed, do the hippocampus pathological section; the other half weighing, made 10% homogenate, determination the activity of  $\text{Na}^+\text{-K}^+\text{-ATP}$  enzyme,  $\text{Ca}^{++}\text{-ATP}$  enzyme and  $\text{Mg}^{++}\text{-ATP}$  enzyme in brain tissue.

## 2.5. Statistics processing method

The data were analyzed by SPSS 13.0 for windows statistical software, all data are expressed by mean  $\pm$  standard ( $\bar{x} \pm s$ ) deviation. Among the groups, the least significant difference (LSD) method was used to test the variance homogeneity and the Games-Howell method was used to test the heterogeneity of variance, ranked data using Ridit test.

**Table 2**  
Effect of SGA (serum glutamic acid) content in TIA model rats ( $\bar{x} \pm s$ ).

Group	Number	Dose (g/kg)	SGA ( $\mu\text{mol/L}$ )
Blank	20	–	115.734 ± 26.930**
Model	9	–	202.325 ± 52.413
Nimodipine	11	0.02	127.641 ± 50.894*
Yangxueqingnaokeli	10	1	142.407 ± 41.004**
10:5 high dose	11	Total flavonoids: total flavonoids = 0.133:0.067	130.358 ± 28.634**
10:5 middle dose	10	Total flavonoids: total flavonoids = 0.067:0.033	157.177 ± 73.956*
10:5 low dose	10	Total flavonoids: total flavonoids = 0.033:0.017	204.882 ± 60.374
10:6 high dose	10	Total flavonoids: total flavonoids = 0.125:0.075	118.373 ± 41.313*
10:6 middle dose	10	Total flavonoids: total flavonoids = 0.0625:0.0375	149.070 ± 31.280*
10:6 low dose	10	Total flavonoids: total flavonoids = 0.003:0.002	185.101 ± 64.120
10:7 high dose	10	Total flavonoids: total flavonoids = 0.118:0.082	132.560 ± 33.391**
10:7 middle dose	10	Total flavonoids: total flavonoids = 0.058:0.042	140.229 ± 28.051**
10:7 low dose	9	Total flavonoids: total flavonoids = 0.029:0.021	181.802 ± 41.370

\* Compared with model group  $P < 0.05$ .

\*\* Compared with model group  $P < 0.01$ .

**Table 3**The effects of plasma LPA level in rats with TIA ( $\bar{x} \pm s$ ).

Group	Number	Dose (g/kg)	LPA ( $\mu\text{mol/L}$ )
Blank	20	–	732.5 $\pm$ 66.4*
Model	9	–	910.0 $\pm$ 35.7
Nimodipine	11	0.02	713.9 $\pm$ 238.7**
Yangxueqingnaokeli	10	1	755.0 $\pm$ 41.2**
10:5 high dose	11	Total flavonoids: total flavonoids = 0.133:0.067	732.0 $\pm$ 206.6**
10:5 middle dose	10	Total flavonoids: total flavonoids = 0.067:0.033	820.0 $\pm$ 21.1*
10:5 low dose	10	Total flavonoids: total flavonoids = 0.033:0.017	848.0 $\pm$ 29.4
10:6 high dose	10	Total flavonoids: total flavonoids = 0.125:0.075	755.0 $\pm$ 61.9*
10:6 middle dose	10	Total flavonoids: total flavonoids = 0.0625:0.0375	786.0 $\pm$ 38.6**
10:6 low dose	10	Total flavonoids: total flavonoids = 0.003:0.002	827.0 $\pm$ 22.6
10:7 high dose	10	Total flavonoids: total flavonoids = 0.118:0.082	795.0 $\pm$ 28.8*
10:7 middle dose	10	Total flavonoids: total flavonoids = 0.058:0.042	817.0 $\pm$ 27.5
10:7 low dose	9	Total flavonoids: total flavonoids = 0.029:0.021	831.1 $\pm$ 22.0

\* Compared with model group  $P < 0.05$ .\*\* Compared with model group  $P < 0.01$ .

### 3. Experimental results

#### 3.1. The effect of behavioral score of TIA rats

As we can see from Table 1: Compared with the blank group, the behavioral score of the model group was significantly increased, indicate that the model building was successful ( $P < 0.01$ ). Compared with model group, Nimodipine group, Yangxueqingnaokeli group, total flavonoids and total saponins of Mao Dongqing 10:5, 10:6 high dose group, 10:7 high and middle dose group, can significantly reduce the behavioral score ( $P < 0.01$ ) of

rats. In the large dose group, the 10:6 ratio was the best; in the middle and small dose group, the 10:7 ratio was the best. From the point of view of mortality, the three components of total flavonoids and total saponins of Mao Dongqing can reduce the mortality rate of the model rats.

#### 3.2. The effect of serum glutamic acid content in TIA model rats

As we can see from Table 2: Compared with the blank group, the serum glutamic acid was significantly decreased ( $P < 0.01$ ) in the model group, indicating that the model building was

**Table 4**The effect on the activity of brain tissue  $\text{Na}^+\text{-K}^+\text{-ATP}$  enzyme,  $\text{Ca}^{++}\text{-ATP}$  enzyme and  $\text{Mg}^{++}\text{-ATP}$  enzyme ( $\bar{x} \pm s$ ).

Group	Number	Dose (g/kg)	$\text{Ca}^{++}\text{-ATP}$ enzyme ( $\mu\text{molPi/mgprot/h}$ )	$\text{Mg}^{++}\text{-ATP}$ ( $\mu\text{molPi/mgprot/h}$ )	$\text{Na}^+\text{-K}^+\text{-ATP}$ ( $\mu\text{molPi/mgprot/h}$ )
Blank	20	–	6.752 $\pm$ 1.131**	5.031 $\pm$ 0.701**	7.210 $\pm$ 1.476**
Model	9	–	2.917 $\pm$ 0.385	2.699 $\pm$ 0.732	4.382 $\pm$ 0.698
Nimodipine	11	0.02	5.114 $\pm$ 1.486**	4.315 $\pm$ 1.079**	6.535 $\pm$ 1.460**
Yangxueqingnaokeli	10	1	5.504 $\pm$ 0.908**	4.714 $\pm$ 0.639**	6.851 $\pm$ 0.820**
10:5 high dose	11	Total flavonoids: total flavonoids = 0.133:0.067	6.251 $\pm$ 1.227**	5.037 $\pm$ 0.616**	7.203 $\pm$ 0.878**
10:5 middle dose	10	Total flavonoids: total flavonoids = 0.067:0.033	5.373 $\pm$ 0.551**	4.129 $\pm$ 0.335**	6.358 $\pm$ 0.564**
10:5 low dose	10	Total flavonoids: total flavonoids = 0.033:0.017	3.235 $\pm$ 0.328	3.261 $\pm$ 0.630	5.588 $\pm$ 0.622**
10:6 high dose	10	Total flavonoids: total flavonoids = 0.125:0.075	6.653 $\pm$ 1.018**	5.161 $\pm$ 0.788**	7.396 $\pm$ 0.726**
10:6 middle dose	10	Total flavonoids: total flavonoids = 0.0625:0.0375	5.450 $\pm$ 0.692**	4.460 $\pm$ 0.629**	6.711 $\pm$ 1.042**
10:6 low dose	10	Total flavonoids: total flavonoids = 0.003:0.002	3.357 $\pm$ 0.900	3.390 $\pm$ 0.385	5.884 $\pm$ 0.622**
10:7 high dose	10	Total flavonoids: total flavonoids = 0.118:0.082	6.305 $\pm$ 1.018**	5.002 $\pm$ 0.241**	7.205 $\pm$ 0.664**
10:7 middle dose	10	Total flavonoids: total flavonoids = 0.058:0.042	5.346 $\pm$ 0.497**	4.006 $\pm$ 0.454**	6.399 $\pm$ 0.642**
10:7 small dose	9	Total flavonoids: total flavonoids = 0.029:0.021	3.224 $\pm$ 0.629	3.244 $\pm$ 0.826	5.278 $\pm$ 0.773

\* Compared with model group  $P < 0.05$ .\*\* Compared with model group  $P < 0.01$ .**Table 5**

The effect of pathological changes in the hippocampus of rats with TIA.

Group	Number	Dose (g/kg)	–	+	++	+++
Blank	16	–	16	0	0	0
Model	10	–	0	0	0	10
Nimodipine	15	0.04	15	0	0	0
Yangxueqingnao	12	2	6	6	0	0
10:5 high dose	13	Total flavonoids: total flavonoids = 0.2:0.1	12	1	0	0
10:5 middle dose	11	Total flavonoids: total flavonoids = 0.1:0.05	9	2	0	0
10:5 low dose	11	Total flavonoids: total flavonoids = 0.05:0.025	2	4	5	0
10:6 high dose	13	Total flavonoids: total flavonoids = 0.19:0.11	13	0	0	0
10:6 middle dose	12	Total flavonoids: total flavonoids = 0.094:0.056	10	2	0	0
10:6 low dose	11	Total flavonoids: total flavonoids = 0.047:0.028	3	4	4	0
10:7 high dose	11	Total flavonoids: total flavonoids = 0.18:0.12	11	0	0	0
10:7 middle dose	12	Total flavonoids: total flavonoids = 0.088:0.062	9	3	0	0
10:7 low dose	11	Total flavonoids: total flavonoids = 0.044:0.031	0	6	5	0

“–” No abnormal changes were found in the brain nerve cells; “+” A small number of nerve cells atrophy; “++” Some nerve cell atrophy and cell cytoplasm decrease; “+++” Most of the nerve cells were significantly decreased or the cytoplasm was significantly decreased.

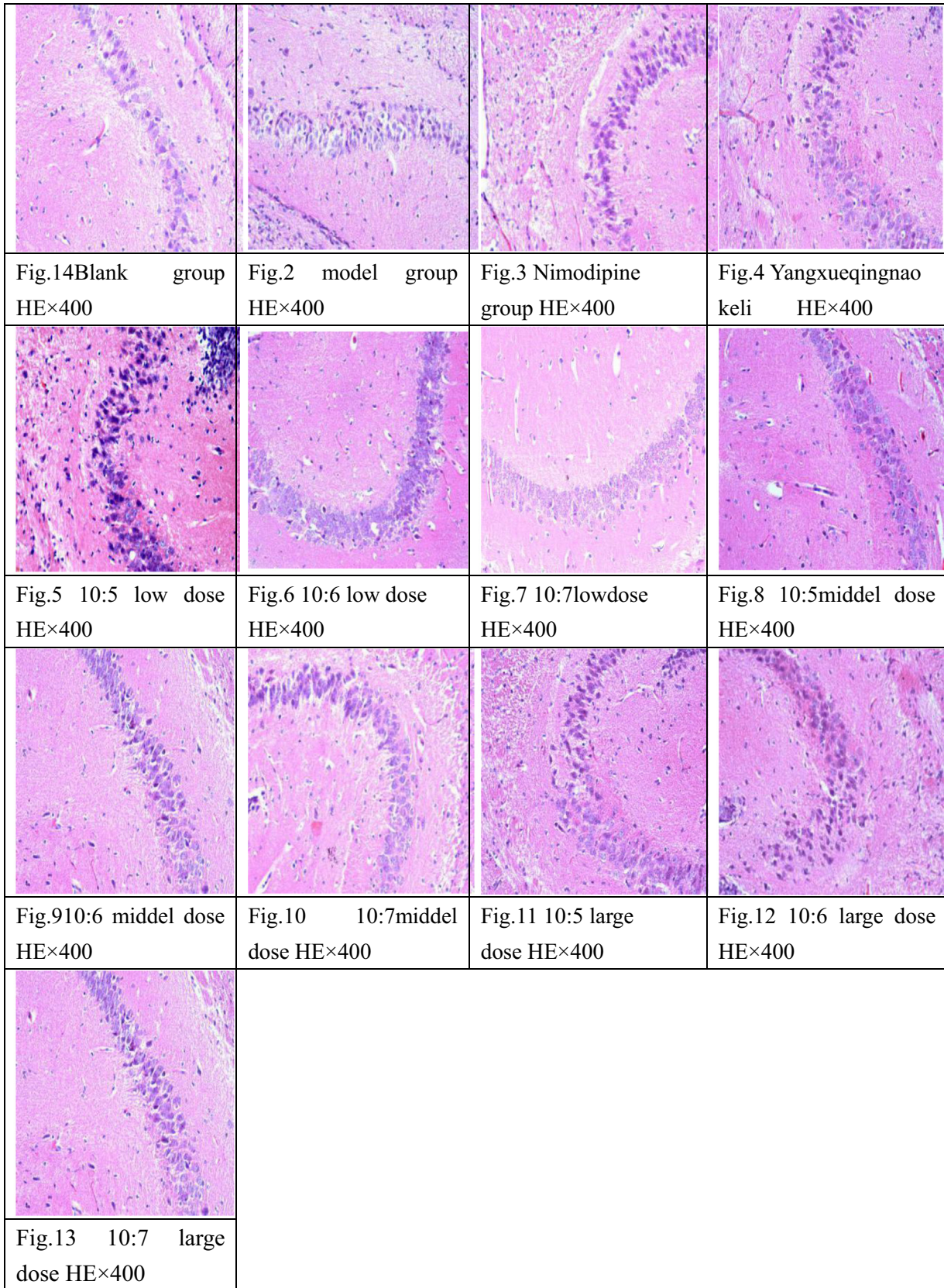


Fig. 1. The effect of pathological changes in the hippocampus of rats.

successful. Compared with model group, Nimodipine group, Yangxueqingnaokeli group, total flavonoids and total saponins of Mao Dongqing 10:5 in high dose group, 10:6 in high dose group, 10:7 in middle, high dose group, all of them can significantly reduce the glutamic acid content ( $P < 0.01$ ); Among of them, in the high dose group, the effect of the 10:6 ratio component is the best; in the middle and small dose group, the effect of the 10:7 ratio component is the best.

### 3.3. The effects of plasma LPA level in rats with TIA

As can be seen from Table 3: Compared with the blank group, the level of plasma LPA was significantly decreased in the model group ( $P < 0.01$ ), indicating that the model building was successful. Compared with model group, Nimodipine group, Yangxueqingnaokeli group, total flavonoids and total saponins of Mao Dongqing 10:5 high dose group, 10:6 middle, high dose group and 10:7 middle, high dose group can significantly decrease the level of plasma LPA ( $P < 0.01$ ), 10:5 middle dose group, 10:7 middle, high dose group can obviously decrease the level of plasma LPA ( $P < 0.05$ ). The results showed that the three components of total flavonoids and total saponins of Mao Dongqing has a good scavenging effect for plasma LPA. Among of them, in the high dose group, the effect of the 10:5 ratio component is the best; in the middle and small dose group, the effect of the 10:6 ratio component is the best.

### 3.4. The effect on the activity of brain tissue $\text{Na}^+ - \text{K}^+ - \text{ATP}$ enzyme, $\text{Ca}^{++} - \text{ATP}$ enzyme and $\text{Mg}^{++} - \text{ATP}$ enzyme

As can be seen from Table 4: Compared with the blank group, the level of  $\text{Na}^+ - \text{K}^+ - \text{ATP}$  enzyme,  $\text{Ca}^{++} - \text{ATP}$  enzyme and  $\text{Mg}^{++} - \text{ATP}$  enzyme was significantly decreased in the model group ( $P < 0.01$ ), indicating that the model building was successful. Compared with model group, Nimodipine group, Yangxueqingnaokeli group, total flavonoids and total saponins of Mao Dongqing 10:5 in low, middle and high dose group, 10:6 in low, middle and high dose group, 10:7 in middle, high dose group, all of them can significantly increase the level of  $\text{Na}^+ - \text{K}^+ - \text{ATP}$  enzyme ( $P < 0.01$ ); Compared with model group, Nimodipine group, Yangxueqingnaokeli group, total flavonoids and total saponins of Mao Dongqing 10:5 middle and high dose group, 10:6 low, middle and high dose group, 10:7 middle and high dose group all of them can significantly increase the level of  $\text{Ca}^{++} - \text{ATP}$  enzyme and  $\text{Mg}^{++} - \text{ATP}$  enzyme ( $P < 0.01$ ). The results showed that the three components of total flavonoids and total saponins of Mao Dongqing could improve the level of  $\text{Na}^+ - \text{K}^+ - \text{ATP}$  enzyme,  $\text{Ca}^{++} - \text{ATP}$  enzyme and  $\text{Mg}^{++} - \text{ATP}$  enzyme. Among of them, in the high dose group, the middle dose

group and the small dose group, the effect of 10:6 ratio was the best.

### 3.5. The effect of pathological changes in the hippocampus of the TIA model rats brain

As we can see from Table 5. The hippocampal neurons were normal in blank control group, the hippocampus area of model group was significantly shrunk and decreased, the brain nerve cells in the hippocampus of nimodipine group were recovered to normal, the brain nerve cells in the hippocampus of Yangxueqingnao granule group were also recovered to normal. The 10:5 low dose group experimental animal hippocampus brain nerve cell were partly atrophy, the 10:6 low dose group experimental animal hippocampus brain nerve cell cytoplasm were partly reduced, the 10:7 middle dose group experimental animal hippocampus brain nerve cell cytoplasm were significantly reduced. The 10:5 middle dose group experimental animal hippocampus brain nerve cell cytoplasm has been restored to some extent, the brain nerve cells in the hippocampus of 10:6 middle dose group experimental animal were recovered to normal, the brain nerve cells in the hippocampus of 10:7 middle dose group experimental animal were recovered to normal. The brain nerve cells in the hippocampus were recovered to normal in the group of 10:5, 10:6 and 10:7 high dose group experimental animal.

By Ridit test, compared with the blank group, the model group had significant statistical significance ( $P < 0.01$ ). Compared with the model group, the nerve cells in the hippocampus of each group had significant statistical significance ( $P < 0.01$ ), which indicating Nimodipine, Yangxueqingnaokeli and Mao Dongqing of the proportion of total flavonoids and total saponin composition has obvious protective effect on nerve cells in the hippocampus. In each group, the effect of nimodipine group, 10:5, 10:6, 10:7 high dose group was the best (see Fig. 1).

### 3.6. The effects of pathological changes in the cerebral cortex of rats with TIA

As we can see from Table 6: The pathological changes of cerebral cortical neurons cell in TIA rats: In the blank group, there were no abnormal changes in the cerebral cortical neurons cell; In the model group, the abnormal changes of cerebral cortical neurons cell were found; In the nimodipine group, the cerebral cortical neurons cell were basic recovery; In the Yangxueqingnaokeli group, the cerebral cortical neurons cell were edema obviously. In the 10:5 low dose group, the cerebral cortex nerve cells were obvious edema; In the 10:6 low dose group, the cerebral cortex nerve cells

**Table 6**  
The effects of pathological changes in the cerebral cortex of rats with TIA.

Group	Number	Dose (g/kg)	–	+	++	+++
Blank	16	–	16	0	0	0
Model	10	–	0	0	1	9
Nimodipine	15	0.04	14	1	0	0
Yangxueqingnaokeli	12	2	0	0	4	8
10:5 high dose	13	Total flavonoids: total flavonoids = 0.2:0.1	2	3	7	0
10:5 middle dose	11	Total flavonoids: total flavonoids = 0.1:0.05	2	4	5	0
10:5 low dose	11	Total flavonoids: total flavonoids = 0.05:0.025	0	1	2	8
10:6 high dose	13	Total flavonoids: total flavonoids = 0.19:0.11	5	2	6	0
10:6 middle dose	12	Total flavonoids: total flavonoids = 0.094:0.056	10	2	0	0
10:6 low dose	11	Total flavonoids: total flavonoids = 0.047:0.028	4	6	1	0
10:7 high dose	11	Total flavonoids: total flavonoids = 0.18:0.12	3	7	1	0
10:7 middle dose	12	Total flavonoids: total flavonoids = 0.088:0.062	2	3	7	1
10:7 low dose	11	Total flavonoids: total flavonoids = 0.044:0.031	1	2	6	2

“–” the cerebral cortex nerve cells were basically normal; “+” individual of the cerebral cortex nerve cells were edema; “++” the cerebral cortex nerve cells were partial edema; “+++” most of the cerebral cortex nerve cells were edema.

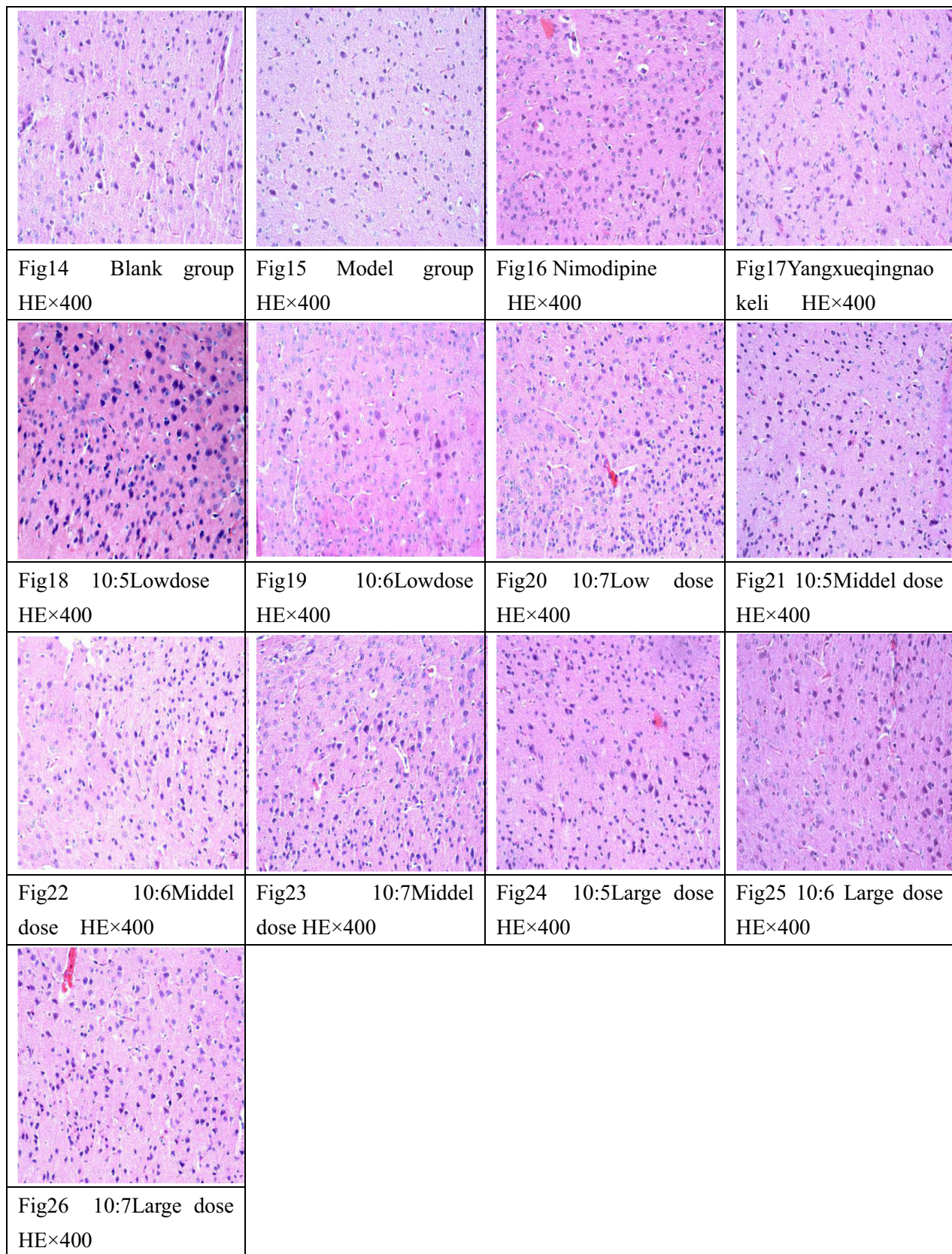


Fig. 2. The effects of pathological changes in the cerebral cortex of rats with TIA.

**Table 7**  
Results of index classification.

Category	I level index (core index)	II level indicators (related indicators)
Index	Behavioral score and pathological findings	ATP, glutamic acid
Weight coefficient	0.7	0.3

were partial edema; In the 10:7 low dose group, the cerebral cortex nerve cells were minority edema. In the 10:5 middle dose group, the 10:6 middle dose group and the 10:7 middle dose group, the cerebral cortex nerve cells were return to normal basically, get recovery obviously and partial edema respectively. In the 10:5 large dose group, the 10:6 large dose group and the 10:7 large dose group, most of the cerebral cortex nerve cells were still edematous, partial of them were edema and individual of them were edema respectively (Atta et al., 2017).

By Ridit test, compared with the blank group, the cerebral cortex nerve cells in the model group had significant statistical significance ( $P < 0.01$ ), which showed that the TIA rat model was successful. Compared with the model group, the cerebral cortex nerve cells in the group of Nimodipine, total flavonoids and total saponins of Mao Dongqing 10:5 large and middle, 10:6 large, middle and small, 10:7 large and middle had significant statistical significance ( $P < 0.01$ ). The protective effect of high dose of 10:6 and nimodipine were the best (see Fig. 2).

### 3.7. Comprehensive evaluation of the different components of total flavonoids and total saponins of Mao Dongqing by comprehensive weight method

#### 3.7.1. Classification of the above indicators, and determine the weight coefficient at all levels (see Table 7)

3.7.2 Based on the improvement of the symptoms and biochemical indexes of the animal model,  $V = |Y - M|/M * 100\%$  (Y was the index value of each drug group, and M was the corresponding

index value of the model group.) Classification of each index value, and determine the weight coefficient of each level (see Table 8).

#### 3.7.3. Comparison of the efficacy of the same dose of total flavonoids and total saponin 10:5, 10:6, 10:7 of Mao Dongqing

In the low dose group of Mao Dongqing's total flavonoids and total saponins of three components, 10:6 is better than 10:7 and 10:5; In the middle dose group, 10:5 is better than 10:6 and 10:7; In the high dose group, 10: 6 is better than 10: 5 and 10:7. Comprehensive evaluation, the effect of total flavonoids and total saponins 10:6 ratio on the improvement of symptoms in TIA model rats was the best (see Table 9).

## 4. Discussion

The transient ischemic attack (TIA) is a kind of recurrent local cerebral blood supply disorder caused by transient neurological deficits. The accepted definition is transient neurological dysfunction caused by focal cerebral or retinal ischemia (Ganzer et al., 2016a,b). The clinical symptoms are sudden, transient, recurrent and so on (Ganzer et al., 2016a,b). Modern research shows that there are many risk factors, such as age, genetic inheritance, sex, hyperlipidemia, diabetes mellitus, atherosclerosis, and so on, which led to the occurrence of TIA (Mazzucco et al., 2017). With the development of society, the deterioration of the environment and the change of people's living habits, the incidence of TIA is increasing, which has seriously threatened the life and health of the people.

Existing drugs for the prevention and treatment of cerebral ischemia (Chen et al., 2016), such as cerebral blood vessel dilation drugs, anti-platelet aggregation drugs, calcium antagonists, statins, etc. (Geary et al., 2017; Ishaq and Jafri, 2017). Because most of the price is more expensive, the way of administration is limited, adverse reactions and side effects and other factors are not suitable for long-term use, so it is urgent to develop high efficiency and low toxicity drugs for cerebral ischemia diseases (Faux et al., 2017). In recent years, scholars have turned their attention to the development of traditional Chinese medicine or Chinese medicine

**Table 8**  
Index improvement rate classification results.

Rat improvement rate classification criteria				
Grade	Significant improvement	Improved	Slight improvement	No improvement
Large dose group	>80%	80–50%	50–20%	<20%
Middle dose group	30%<	30–20%	20–5%	<5%
Low dose group	20%<	20–10%	10–5%	<5%
Weight coefficient	0.4	0.3	0.2	0.1

**Table 9**  
The comparison of the efficacy of the same dose of total flavonoids and total saponin 10:5, 10:6, 10:7 of Mao Dongqing.

Group	Core index				Relevant index				P value
	Behavioral score	Hippocampal area	Cortical area	LPA	Na <sup>+</sup> -K <sup>+</sup> -ATP	Mg <sup>2+</sup> -ATP	Ca <sup>2+</sup> -ATP	Glutamic acid	
10:5 Low dose	++	+++	++	++	++	++	++	–	1
10:6 Low dose	+++	+++	+++	+++	+++	++	++	++	1.51
10:7 Low dose	++	+++	++	+++	++	++	++	+++	1.27
10:5 Middle dose	+++	+++	+++	++	++	++	+++	++	1.44
10:6 Middle dose	++	+++	+++	+++	+++	+++	+++	++	1.5
10:7 Middle dose	++	+++	+++	+++	++	++	+++	+++	1.44
10:5 Large dose	++	+++	+++	++	++	++	+++	+++	1.4
10:6 Large dose	++	+++	+++	+++	+++	+++	+++	+++	1.53
10:7 Large dose	++	+++	+++	++	++	++	+++	+++	
	++	1.37							

$P = I$  level index score \* I level index weight coefficient + II level index score \* II index weight coefficient = (m \* 0.4 + n \* 0.3 + p \* 0.2 + q \* 0.1) \* 0.7 + (m \* 0.4 + n \* 0.3 + p \* 0.2 + q \* 0.1) \* 0.3 (m: the number of +++; n: the number of ++; p: the number of +; q: the number of –; +++: improve significantly; ++: improve; +: improve slightly; -: no improve).

preparation at home and abroad. The traditional Chinese medicine has a long history in the treatment of cerebrovascular diseases, and has the advantages of small side effect, low cost, and so on (Jin et al., 2015). At present, Chinese medicine treatment of the disease is still dominated by the Decoction (Bai et al., 2015; Zhang et al., 2017), limit its application. Although there are pills, Huoxue Capsule and other traditional Chinese medicine, but are not exclusively used for the treatment of TIA, and the efficacy of the treatment also needs to be further improved. So the research and development of the exact effect, fast acting, small dose of the new dosage form is the key to the treatment of traditional Chinese medicine TIA.

In this study, we used the TIA model of peroxide induced seizures, through the application of the different ratio of total flavonoids and total saponins of Mao Dongqing to TIA model animals, showing that it has a very good effect in the TIA control, and according to the comprehensive weight evaluation method, the comprehensive evaluation of each index. Finally, it was concluded that the optimal proportion of total flavonoids and total saponins in the prevention and treatment of transient cerebral ischemia in the Mao Dongqing (Muhammad et al., 2017). To study the etiology and pathological changes of cerebral ischemia, and to provide a new idea for the development of Mao Dongqing as a new dosage form for the prevention and treatment of TIA.

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### References

- Abbas, G., Salman, A., Rahman, S.U., Ateeq, M.K., Usman, M., Sajid, S., Zaheer, Z., Younas, T., 2017. Aging mechanisms: linking oxidative stress, obesity and inflammation. *Matrix Sci. Med.* 1 (1), 30–33.
- Ali, W., Habib, M., Sajid, S., Khan, R.S.A., Mazhar, M.U., Khan, I.U., Saliha, U., Farooq, M., Shah, M.S.U.D., Muzammil, H.M., 2017. A reverse transcription-polymerase chain reaction (RT-PCR) based detection of foot-and-mouth disease in District Faisalabad, Pakistan during the Year 2016. *Matrix Sci. Med.* 1 (1), 27–29.
- Atta, A., Mustafa, G., Sheikh, M.A., Shahid, M., Xiao, H., 2017. The biochemical significances of the proximate, mineral and phytochemical composition of selected vegetables from Pakistan. *Matrix Sci. Pharm.* 1 (1), 06–09.
- Bai, X.Q., Li, J., Li, C.M., et al., 2015. Observation of curative effect of self-resolving phlegm and Blood Stasis Decoction on transient ischemic attack. *Chinese J. Traditional Chinese Med.* 10, 1843–1845.
- Chen, W.W., Sui, H., Ma, L.Y., 2016. Current situation and prevention and treatment of cardiovascular and cerebrovascular diseases in China. *Prevent. Treatment Cerebrovascular Dis.* 02, 79–83.
- Fang, X.Y., Zuo, T., Qiao, J.Y., et al., 2016. Study on the effect of total flavonoids of hairy holly on cerebral ischemic tolerance in rats. *J. Nanjing Univ. Chin. Med.* 05, 442–446.
- Faux, Steven G., Arora, Pooja, Shiner, Christine T., 2017. Rehabilitation and education are underutilized for mild stroke and TIA sufferers. *Disability Rehabil.* 12, 1–5.
- Ganzer, Christine A., Barnes, Andrea, Uphold, Constance, et al., 2016a. Transient ischemic attack and cognitive impairment: a review. *J. Neurosci. Nursing* 48, 322–327.
- Ganzer, Christine A et al., 2016b. *J. Neurosci. Nursing Transient Ischemic Attack and Cognitive Impairment* 48 (6), 322–327.
- Gao, W. et al., 2017. The first multiplication atom-bond connectivity index of molecular structures in drugs. *Saudi Pharmaceut. J.* 25 (4), 548–555.
- Geary, Lukas, Aronius, Jonas, Wettermark, Bjorn, 2017. Sociodemographic factors are associated with utilisation of statins after ischaemic stroke/TIA. *Int. J. Clin. Practice* 71 (3), 3–4.
- Ishaq, S., Jafri, J., 2017. Biomedical importance of cocoa (*Theobroma cacao*): Significance and potential for the maintenance of human health. *Matrix Sci. Pharm.* 1 (1), 01–05.
- Jiao, A.J., Wang, J., Zhang, H.L., 2015. Study on Chinese medicine Mao Dongqing. *J. Guangxi Med. Univ.* 02, 322–325.
- Jin, R., Wang, Y.G., Xue, C.M., et al., 2015. Proprietary Chinese medicine prescription review standard and scale of exploration (two). *Chin. Repeated Admin. Hospital Pharm. J.* 07, 565–570.
- Li, X.R., 2011. An overview of the pharmacological effects of Mao holly. *global. Chin. Med.* 03, 238–240.
- Mazzucco, Sara, Li, Linxin, Tuna, Maria, A., 2017. Time-of-day could affect cognitive screening performance in older patients with TIA and stroke. *Cerebrovascular Dis.* 43 (5), 290–293.
- Miao, M.S., Ming, B., Fang, X.Y., 2011. New application of Mao Dongqing pubescens extract in preparing medicine for improving cerebral ischemia tolerance. *Henan: CN102258550A*, 11–30.
- Miao, M.S., Ming, B., Miao, Y.Y., 2011. Application of total saponin of Mao dongqing in preparation of medicine for preventing and treating transient cerebral ischemia syndrome. *Henan: CN102058635A*, 05–18.
- Muhammad, G., Rashid, I., Firyal, S., 2017. Practical aspects of treatment of organophosphate and carbamate insecticide poisoning in animals. *Matrix Sci. Pharma.* 1 (1), 10–11.
- Yilmazel, G., 2017. Co-existence of lipitension and central obesity: an epidemiologic study of primary care patients. *Acta Med. Mediterranea* 33 (3), 437–441.
- Zhang, H.T., Tian, M., et al., 2017. Effect of *Aster tataricus* on production of inflammatory mediators in LPS stimulated rat astrocytoma cell line (C6) and THP-1 cells. *Saudi Pharmaceut. J.* 25 (3), 370–375.