

The impact of the Uighur medicine abnormal savda munziq on antitumor and antioxidant activity in a S180 and Ehrlich ascites carcinoma mouse tumor model

Ainiwaer Aikemu^{1,2}, Abdiryim Yusup², Anwar Umar^{3,4}, Bénédicte Berké^{3,4}, Nicholas Moore^{3,4}, Halmurat Upur^{2,3}

Departments of ¹Drug Analysis, ²Traditional Uighur Medicine and ³Pharmacology, Xinjiang Medical University, 830011 Urumqi, Xinjiang People's Republic of China, ⁴Department of Pharmacology, University Victor Segalen Bordeaux 2, 33076 Bordeaux, France

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ABSTRACT

Aim: This study was designed to study the antitumor and antioxidant activity of Uighur medicine abnormal savda munziq (ASMq) in the S180 and Ehrlich ascites carcinoma mice tumor model.

Materials and Methods: The serum levels of superoxide dismutase (SOD), malonaldehyde (MDA), and glutathione-catalase (GSH-PX) were analyzed, and the mice were also subjected to a hypoxia tolerance test. Their climbing ability was also analyzed. **Results:** The findings of the study revealed that ASMq-treatment leads to an increase in blood serum SOD and GSH-PX levels but a decrease in blood serum MDA levels. Moreover, ASMq-treatment enhanced the survival time of mice maintained under hypoxic conditions and improved their mice climbing ability.

Conclusions: The results of this study indicate that ASMq has obvious antitumor and antioxidative effects.

Key words: Abnormal savda munziq, antioxidant, antitumor

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INTRODUCTION

The herbal formula known as abnormal savda munziq (ASMq) is a Uighur medicinal herbal preparation, which is composed of 10 medicinal herbs, including *Adiantum capillus-veneris* L., *Albagi pseudoalbagi* Desn., *Anchusa italica* Retz., *Cordia dichotoma* G. Forst., *Euphorbia humifusa* Willd., *Foeniculum vulgare* Mill., *Glycyrrhiza uralensis* Fisch., *Lavandula angustifolia* Mill., *Melissa officinalis* L., and *Ziziphus jujuba* Mill. (Patent No. ZL02130082.8) [Table 1]. The preparation is widely distributed in the Xinjiang region of China and has long been used in traditional Uighur medicine for the treatment of diseases such as cancers of the digestive system, diabetes, cardiovascular diseases or chronic asthma, and south of Xinjiang, it is frequently used as a household remedy for the prevention of cancers.^[1] For 10 years, we have been studying the Uighur medicine and investigating

the underlying properties of ASMq and Mushil by applying molecular, pharmacological, and other modern scientific techniques.^[2,3] To date, research has revealed ASMq as possessing free radical and superoxide anionic cleanup properties, in addition to anti-DNA oxidative damage properties. Previous research from this laboratory has also revealed that ASMq possesses a number of potent effects, including strong free radical scavenging effects. Moreover, ASMq also has the capacity to decrease biological markers of oxidative stress, protect against mitochondria and DNA against OH⁻ induced oxidative damage in a cell-free system, and inhibit the proliferation and viability of cancer cells *in vitro*.^[4-8]

MATERIALS AND METHODS

Chemicals and reagents

The ASMq was provided by the Qikang Habo Pharmaceutical Co., Ltd (Xinjiang; Batch Number: 106060). Cyclophosphamide was obtained from the HengRui Pharmaceutical Co., Ltd (JiangSu under the State food

Address for correspondence:

Mr. Halmurat Upur, Department of Pharmacology, Xinjiang Medical University, 830011 Urumqi, Xinjiang, People's Republic of China. E-mail: halmurat@263.net

Table 1: Ingredient of abnormal savda munziq

| Plant name | Family name | Uighur name | Used parts |
|------------------------------|---------------|---------------------|------------------|
| Adiantum capillus-veneris L. | Adiantaceae | Pirsiyavxan | Whole plant |
| Alhagi pseudoalhagi Desv. | Fabaceae | Yantak xikiri | Branch secretion |
| Anchusa italica Retz. | Boraginaceae | Gavzivan | Aerial parts |
| Cordia dichotoma G.Forst. | Boraginaceae | Serpistan | Fruit |
| Euphorbia humifusa Willd. | Euphorbiaceae | Xahtere | Whole plant |
| Foeniculum vulgare Mill. | Apiaceae | Arpabidiyan | Fruit |
| Glycyrrhiza uralensis Fisch. | Fabaceae | Qüq ük buya yiltizi | Radix or rhizoma |
| Lavandula angustifolia Mill. | Lamiaceae | üstihuddus | Aerial parts |
| Melissa officinalis L. | Lamiaceae | Badrenjibuya hindi | Whole plant |
| Ziziphus jujuba Mill. | Rhamnaceae | Qilan | Fruit |

and Drug Administration, Batch Number: H32020857). The Verapamil Hydrochloride injection preparation was obtained from the Shanghai Hefeng Pharmaceutical Co., Ltd (Batch Number: 090201). The superoxide dismutase (SOD) kit was obtained from Nanjing bio-engineering research institute (Batch Number: 20100420). Similarly, the malonaldehyde (MDA) kit was obtained from the Nanjing bio-engineering research institute (Batch Number: 20100420). The glutathione-catalase (GSH-PX) kit was obtained from the Nanjing bio-engineering research institute (Batch Number: 20100420).

Animals and treatment

Kunming's mice (4–6 weeks old) of the SPF level (body weight 20 ± 2 g) were provided by the Laboratory Animal Center of the Xinjiang Medical University. The mice were bred under regular laboratory conditions, with a controlled room temperature and a 12/12-hour light–dark cycle with free access to standard rodent chow and water. The Laboratory Animal Center of Medicine Animal Care and Use Committee approved all experimental protocols. A total of 120 were randomly divided into six groups with 20 animals in each group: (1) control group, (2) model group, (3) high dose ASMq (8 g/kg) group, (4) medium ASMq dose (4 g/kg) group, (5) low ASMq dose (2 g/kg) group, and (6) cyclophosphamide (CY) group. The S180 cells were supplied by the Laboratory Animal Center of Xinjiang Military Hospital and the Ehrlich ascites carcinoma (EAC)

cells were supplied by the China Center for Type Culture Collection, Wuhan University.

The S180 and EAC xenograft models

With the exception of the control group, a 0.2 mL suspension containing 1×10^7 cells/ml of 7-day-old S180 or EAC cells was transplanted into the right axilla of each mouse. The whole operation was finished in 30 min. The control and model groups were treated with 20 mg/kg physiological saline, and the ASMq and CY groups were treated with their respective doses of drug orally 24 h after tumor inoculation. The animals' general health statuses were monitored daily for 10 days.

Assessment of tumor weight, thymus, liver, and spleen index

Twenty-four hours after their last dosage, the mice were killed by cervical dislocation and the thymus, spleen, liver, and solid tumors were excised and weighed. Anticancer activity *in vivo* was expressed as an inhibitory rate and was calculated using the formula: $[(A - B)/A] \times 100\%$, where A and B indicate the mean tumor weights of the model group and experimental groups, respectively. The spleen, liver and thymus were evaluated by the organ index formula: spleen, liver, or thymus weight (g)/body weight (g).

The effect of ASMq treatment on climbing ability in the S180 or EAC tumor-bearing mice

As previously described, for each cell type 120 mice were randomly divided into six groups. Each group was composed of 20 mice, 10 males and 10 females. Of these six groups, five groups were inoculated with the S180 cells. This process was repeated for the EAC cells. Twenty-four hours after the cells were implanted the mice were treated with the respective drugs. For the ASMq-treated mice, there were three groups who were treated with ASMq daily: a high-dose ASMq group (8 ml/10 g gavage); a middle-dose ASMq group (4 ml/10 g gavage), and a low dose ASMq group, (2 ml/10 g gavage). Animals in the CY group received a 20 mg/kg intraperitoneal injection once daily commencing from the second day following cell implantation. In the model group, the mice received a saline gavage once daily. Animals in the control group received no intervention or tumor inoculation. The mice received treatment for 10 days after the last gavage the mice were challenged with the climbing test, in which a length of bamboo (15 cm) was hung in the air and the mice required to climb from the bottom to the top. Each attempt was timed, and the timer was stopped when the mice fall down. The climbing time for each group was averaged, and the climbing time extension rate was calculated according the formula: $(\text{sample group time}/\text{ASMq group time} - 1) \times 100\%$.

Mouse blood serum SOD, MDA, and GSH-PX target determination

As outlined previously, following cell inoculation and 10 days of continuous drug treatment on the 10th day bloody was obtained via an orbital bleed. The samples were set aside for 30 min, centrifuged at $3000 \times g$ for 20 min and, using the respective kits, the blood serum SOD, MDA, or GSH-PX content was analyzed.

The effect of ASMq treatment in the S180 or EAC tumor-bearing on resistance to hypoxia

For each cell type, the mice were divided into two groups: normal pressure and hypoxia. For each group, 120 mice were randomly divided into six groups of 20 animals as mentioned in the previous section (five treatment groups and one control group). The mice received treatment ASMq, verapamil (Ver; 4 mg/kg intraperitoneal) or saline treatment continuously for 10 days. Twenty-four hours after the last gavage, the mice were placed into a 250 ml wide-mouth bottle containing sodium lime (one mouse/bottle). Vaseline was used to close the bottle and the time until the mouse died was recorded.

Statistical procedures

Using SPSS 17.0, normality and variance homogeneity were tested. The mean and standard deviation were calculated, followed by single-factor variance analysis and card side examination of the results. The groups were compared by ANOVA and $P < 0.05$ was considered statistically significant.

RESULTS

The influence of mice daily activities

Following treatment, the mice's behavior, including their drinking, defecation and urination and general appearance were monitored daily. No secretions from the eyes, ears, nose, or mouth were observed. Animals who received 2 g/kg ASMq showed normal activity, mental status, and clean fur. The tumor growth incubation period (TT) was 3 days, and tumor growth velocity (TS) was faster than the model (saline treatment) group. In the group who received a 4 g/kg dose of ASMq, normal activity, a good mental state (better than 2 g/kg dosage group), and clean fur (better than 2 g/kg dosage group) were noted. In this group, the TT was 3 days; however, TS was slower than in the 2 g/kg dosage group. For the 8 g/kg ASMq dose group normal activity, good mental state (better than both the 2 g/kg and 4 g/kg dosage groups), clean fur (better than both the 2 g/kg and 4 g/kg dosage groups) and a TT of 3 days and slower TS than the 2 g/kg and 4 g/kg groups were noted. In the CY-treated group, normal activity, good mental state (better than 2 g/kg dosage group), clean fur (better than 2 g/kg dosage group), and a TT of 4 days and slowest TS of all groups were observed. The model group (saline treatment only) showed decreased activity, enlarged tumor growth, unclean fur and listlessness behavior with a TT of 2 days and TS fastest of all groups were observed.

Inhibitory rate on the growth of transplanted tumors in S180 and the organ weight ratio

The anticancer effects of ASMq treatment in the S180-

Table 2: Antitumor activity of the ASMq drugs in mice transplanted S180 tumor ($\bar{x} \pm SD$)

| Group | Dosage (g/kg) | Tumor weight (g) | Thymus weight (g) | Spleen weight (g) | Liver weight (g) | Body weight (g) |
|---------|---------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------------|
| Control | 0 | 0.000±0.000 | 0.108±0.008 | 0.097±0.012 | 1.201±0.035 | 30.543±0.657 |
| Model | 0 | 0.600±0.039 | 0.103±0.014 | 0.117±0.011 | 1.288±0.065 | 28.692±0.998 |
| CY | 0.02 | 0.305±0.015 | 0.071±0.008 | 0.073±0.010 | 1.138±0.037 | 24.073±1.015 |
| ASMq | 8 | 0.361±0.061 [*] | 0.108±0.019 ^Δ | 0.107±0.016 ^Δ | 1.229±0.071 ^Δ | 27.279±0.912 [*] |
| ASMq | 4 | 0.279±0.031 [*] | 0.092±0.009 ^Δ | 0.113±0.017 ^Δ | 1.382±0.108 [*] | 27.853±1.163 ^Δ |
| ASMq | 2 | 0.387±0.027 [*] | 0.103±0.014 ^Δ | 0.108±0.008 ^Δ | 1.335±0.080 [*] | 26.862±1.100 ^Δ |

*different from the model group, $P < 0.05$, ^Δdifferent from the CY group, $\Delta P < 0.05$

Table 3: Inhibition of abnormal savda munziq drugs on the growth of transplanted tumors in S180 induced mice and organ weight ratio ($\bar{x} \pm SD$)

| Group | Dosage (g/kg) | Thymus weight / Mouse weight (g/g) | Spleen weight / Mouse weight (g/g) | Liver weight / Mouse weight (g/g) | Inhibitory rate (%) |
|---------|---------------|------------------------------------|------------------------------------|-----------------------------------|---------------------|
| Control | 0 | 0.00358±0.00051 | 0.00409±0.00039 | 0.04497±0.00315 | 0 |
| Model | 0 | 0.00354±0.00029 | 0.00318±0.00041 | 0.03933±0.00125 | 0 |
| CY | 0.02 | 0.00295±0.00036 | 0.00305±0.00045 | 0.04737±0.00264 | 49.84 |
| ASMq | 8 | 0.00394±0.00069 ^Δ | 0.00392±0.00063 ^Δ | 0.04511±0.00314 | 40.63 |
| ASMq | 4 | 0.00329±0.00035 | 0.00406±0.00052 ^Δ | 0.04976±0.00535 [*] | 54.11 |
| ASMq | 2 | 0.00383±0.00060 ^Δ | 0.00401±0.00034 ^Δ | 0.04976±0.00348 [*] | 36.35 |

*different from the model group, $P < 0.05$, ^Δdifferent from the CY group, $P < 0.05$

bearing mouse are shown in Tables 2 and 3. Treatment with the CY and ASMq resulted in a marked suppression of tumor growth, as observed by the decreased tumor weights. Compared with the model group, the inhibitory rate for the high, medium, low dosage of ASMq and CY-treated groups were 40.63, 54.11, 36.35, and 49.84%, respectively. The medium and low ASMq dose groups showed significant inhibition on tumor weight compared with the CY-treated group ($P < 0.05$). However, the spleen, the liver or thymus index in the high and low ASMq dose groups did not decrease significantly compared with the model group [Table 3]. The results indicated that *in vivo* ASMq treatment did not cause any serious toxic effects on the immune systems of the S180-bearing mice.

Xenograft growth rate and organ weight ratio in the mice implanted with EAC cells

The anticancer effects of ASMq treatment in the EAC-bearing mouse are shown in Tables 4 and 5. Treatment with CY and ASMq resulted in marked suppression of tumor weight. Compared with the model group, the inhibitory rate for the high, medium, and low dose ASMq groups and the CY group in EAC-bearing mouse were 46.34, 60.98, 38.86, and 49.73%, respectively. The medium and low dose ASMq groups showed a significant inhibition of tumor weight compared with the CY-treated group ($P < 0.05$). Moreover, the spleen, liver, or thymus index for the high and low ASMq dose groups did not decrease significantly compared with the model group [Table 5]. The results

indicated that *in vivo* ASMq did not cause any serious toxic effects on the immune systems of the EAC-bearing mice.

The effect of ASMq treatment on the climbing ability of S180 tumor-bearing mice

As shown in Figure 1, ASMq-treatment at all doses improved the climbing time. The effect on the middle dose group was the greatest and reached significance when compared with the control group ($P < 0.05$).

The effect of ASMq treatment on the climbing ability of EAC tumor-bearing mice

As shown in Figure 2, when compared with the control group, the different doses of ASMq treatment led to an improvement in mice climbing time; however, the effects were most pronounced in the group receiving the middle dose ($P < 0.05$).

Blood serum SOD, MDA, and GSH-PX levels in the S180 tumor-bearing mice

Blood serum analysis revealed that when compared to the ASMq-treated mice, in the CY-treated mice, the SOD and GSH-PX content were reduced ($P < 0.05$). In the ASMq medium dose group, the SOD and GSH-PX serum levels were the closest to normal, control values [Figure 3]. For MDA levels, dosage of the ASMq medium dose group was the lowest, when compared with the control group ($P < 0.05$) [Figure 4]. Further, when compared against the model group, blood serum SOD and GSH-PX levels in the ASMq high dose groups were significantly reduced

Table 4: Antitumor activity of the ASMq drugs in mice transplanted ECA tumor ($\bar{x} \pm SD$)

| Group | Dosage (g/kg) | Tumor weight (g) | Thymus weight (g) | Spleen weight (g) | Liver weight (g) | Body weight (g) |
|---------|---------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------------|
| Control | 0 | 0.000±0.000 | 0.107±0.005 | 0.094±0.010 | 1.251±0.035 | 30.744±0.632 |
| Model | 0 | 0.606±0.043 | 0.101±0.009 | 0.116±0.013 | 1.284±0.041 | 29.178±0.931 |
| CY | 0.02 | 0.309±0.019 | 0.072±0.008 | 0.075±0.010 | 1.138±0.035 | 24.263±0.900 |
| ASMq | 8 | 0.330±0.044* | 0.103±0.019 ^Δ | 0.100±0.013 ^Δ | 1.227±0.057 ^Δ | 27.565±0.810 ^Δ |
| ASMq | 4 | 0.240±0.012* | 0.093±0.010 ^Δ | 0.115±0.014 ^Δ | 1.367±0.102 ^Δ | 28.095±0.896* |
| ASMq | 2 | 0.376±0.019 ^Δ | 0.103±0.014 ^Δ | 0.106±0.008 ^Δ | 1.319±0.060 ^Δ | 26.790±1.010 ^Δ |

*different from the model group, $P < 0.05$, ^Δdifferent from the CY group, $\Delta P < 0.05$

Table 5: Inhibition of abnormal savda munziq drugs on the growth of transplanted tumors in ECA induced mice and organ weight ratio ($\bar{x} \pm SD$)

| Group | Dosage (g/kg) | Thymus weight / Mouse weight (g/g) | Spleen weight / Mouse weight (g/g) | Liver weight / Mouse weight (g/g) | Inhibitory rate (%) |
|---------|---------------|------------------------------------|------------------------------------|-----------------------------------|---------------------|
| Control | 0 | 0.00346±0.00028 | 0.00396±0.00045 | 0.04404±0.00204 | 0 |
| Model | 0 | 0.00348±0.00016 | 0.00306±0.00034 | 0.04072±0.00187 | 0 |
| CY | 0.02 | 0.00296±0.00038 | 0.00310±0.00045 | 0.04693±0.00197 | 49.73 |
| ASMq | 8 | 0.00375±0.00070 ^Δ | 0.00363±0.00049 ^Δ | 0.04454±0.00250 | 46.34 |
| ASMq | 4 | 0.00329±0.00035 | 0.00410±0.00057 ^Δ | 0.04866±0.00363* | 60.98 |
| ASMq | 2 | 0.00383±0.00050 ^Δ | 0.00396±0.00032 ^Δ | 0.04936±0.00384* | 38.86 |

*different from the model group, $P < 0.05$, ^Δdifferent from the CY group, $P < 0.05$

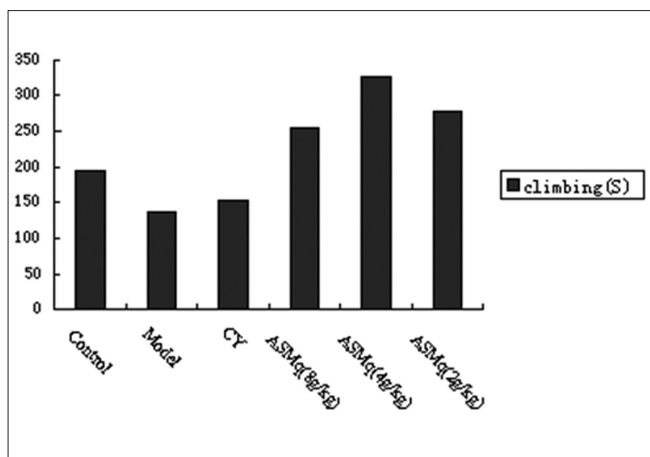


Figure 1: Different dose of ASMq on S180 mice climbing time effects

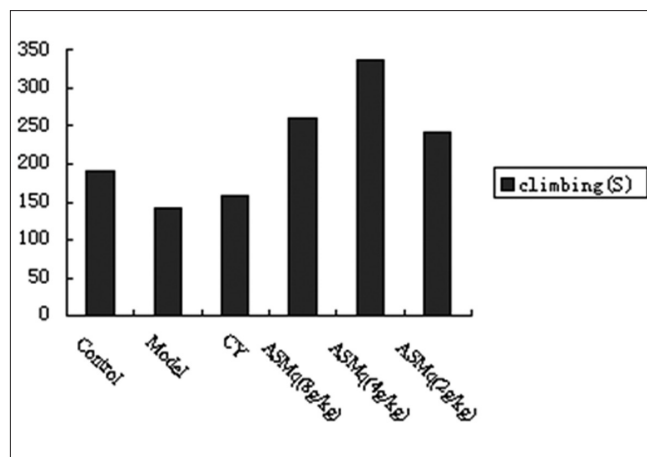


Figure 2: Different dose of ASMq on EAC mice climbing time effects

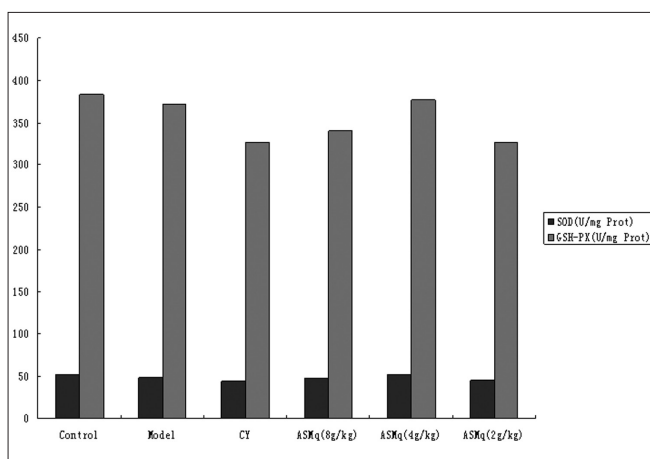


Figure 3: ASMq to S180 tumor-bearing mice blood serum in SOD, GSH-PX target influence

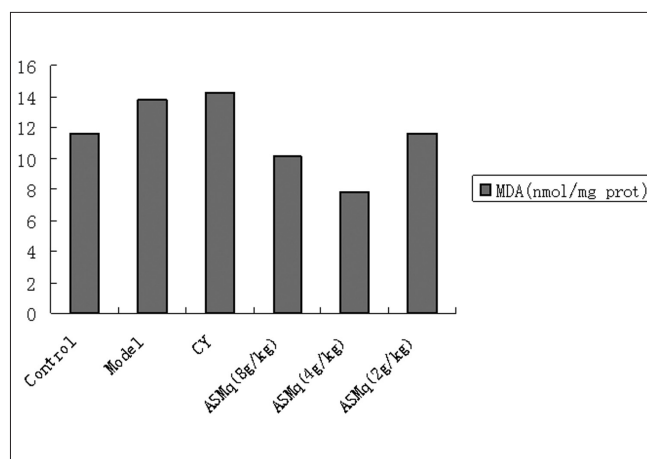


Figure 4: ASMq to S180 tumor-bearing mice blood serum in MDA target influence

($P < 0.05$). In the ASMq medium dose group, SOD and GSH-PX levels were the highest, being close to or surpassing the control levels.

Blood serum SOD, MDA, and GSH-PX levels in the EAC-tumor-bearing mice

Blood serum analysis revealed that when compared to the ASMq-treated mice, the SOD and GSH-PX levels in the CY-treated mice were significantly reduced ($P < 0.05$). In the medium ASMq dose groups, the SOD and GSH-PX content were the highest, falling close to the control value [Figure 5]. For blood serum MDA levels, the ASMq medium dose group recorded the lowest levels when compared against the model group ($P < 0.05$) [Figure 6]. When compared against the model, the SOD and GSH-PX levels in the ASMq high dose groups were significantly reduced ($P < 0.05$). In the ASMq medium dose group, SOD and GSH-PX levels were the highest, being close to or surpassing the control levels.

The effect of ASMq-treatment on S180 tumor-bearing mice subjected to hypoxic conditions

As shown in Table 6, ASMq-treatment can extend the survival time of mice maintained under hypoxic conditions when compared against normoxic conditions. The observed effect was most significant in the middle and high dose ASMq groups ($P < 0.05$). The extension rate in the high, middle, and low-dose ASMq-treated groups and the *verapamil* groups were 23.61, 40.89, 9.04, and 44.16%, respectively.

The effect of ASMq-treatment on EAC tumor-bearing mice subjected to hypoxic conditions

As shown in Table 7, ASMq-treatment can extend the survival time of mice maintained under hypoxic conditions when compared against normoxic conditions, with the effects in the middle and high dose groups being most significant ($P < 0.05$). The extension rate in the high, middle, and low-dose ASMq-treated groups, and the *Vera*

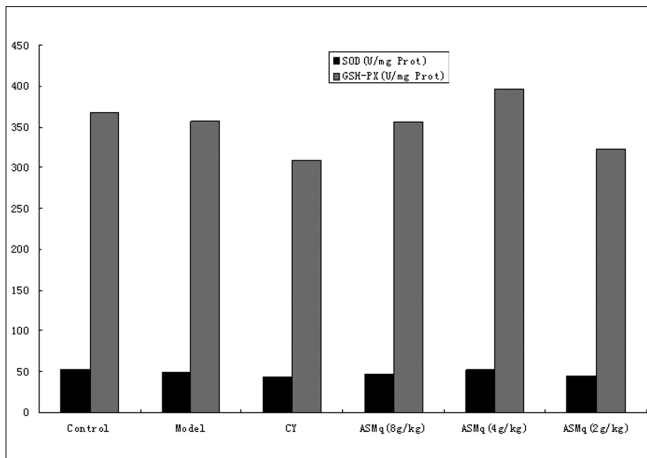


Figure 5: ASMq to EAC tumor-bearing mice blood serum in SOD, GSH-PX target influence

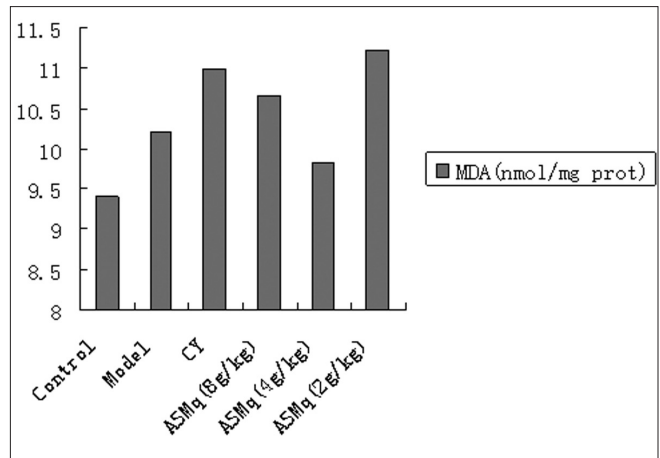


Figure 6: ASMq to EAC tumor-bearing mice blood serum in MDA target influence

Table 6: ASMq's effect on mice hypoxia tolerance

| Groups | N | Dose | Hypoxia(s) | Extension rate (%) |
|---------|----|--------|--------------------------------|--------------------|
| Control | 20 | - | 1374.500±209.615 | - |
| Model | 20 | - | 1262.050±116.234 | - |
| Ver | 20 | 4mg/kg | 1981.500±148.388 | 44.16 |
| ASMq | 20 | 8g/kg | 1699.050±195.207* ^Δ | 23.61 |
| ASMq | 20 | 4g/kg | 1936.600±278.270* | 40.89 |
| ASMq | 20 | 2g/kg | 1498.800±172.356* ^Δ | 9.04 |

Note: compares * $P < 0.05$ with the model group, ^Δcompares # $P < 0.05$ with the CY group

Table 7: ASMq's effect on mice hypoxia tolerance

| Groups | n | Dose | Hypoxia(s) | Extension rate (%) |
|---------|----|--------|-----------------------------|--------------------|
| Control | 20 | - | 1399.55±87.93 | - |
| Model | 20 | - | 1242.10±64.45 | - |
| Ver | 20 | 4mg/kg | 1928.20±65.04 | 37.77 |
| ASMq | 20 | 8g/kg | 1647.35±62.47* ^Δ | 17.71 |
| ASMq | 20 | 4g/kg | 1952.95±57.86* | 39.54 |
| ASMq | 20 | 2g/kg | 1455.45±46.57* ^Δ | 3.99 |

Note: compares * $P < 0.05$ with the model group, ^Δcompares # $P < 0.05$ with the CY group

pamidronate groups were 17.71, 39.54, 3.99, and 37.77%, respectively.

DISCUSSION

Therapy to Abnormal Savda related disease matures and accumulates Abnormal Savada by applying ASMq before expelling it from the body with Abnormal Savda Mushil, thus brings temperament recovery and body fluid equilibrium, supporting the treatment. In this study, the antitumor effects of ASMq were evaluated in two mouse xenograft models. The findings of this study show that ASMq had potent antitumor activity. These findings are compatible with existing research on ASMq,^[9] which shows that ASMq can be applied as an antitumor adjuvant with immunomodulatory effects that has the potential great to be of great clinical significance.

Lipid peroxidization is a process that leads to cell damage. Exposure to different chemicals may induce organism to produce the massive free radicals, causing an accumulation

of toxicity in the cell and leading to lipid peroxidation damage. According to free radical theory, the higher the metabolic rate of an organism, the greater the production of free radicals and the shorter their life span. Conversely, the activity of the antioxidant enzymes has been reported to decrease alongside the aging process, especially with respect to SOD.^[10] It has been reported that age-related SOD decreases^[11] may occur because SOD may be irreversibly inactivated by its product, hydrogen peroxide. Another explanation for the decrease could be an increase in the glycation of SOD. The ASMq dosage has the obvious opposing effect. MDA is a cell membrane lipid peroxidation product and its plasma contents may mirror the amount of lipid peroxidation. Both SOD and GSH-PX can be used to evaluate the oxidation resistance levels as the main biochemistry target.^[12-14] The presence of SOD in the organism can only specifically eliminate the ultra oxygen free radicals, the antioxidant, can the excessive oxygen free radical disproportionate be the hydrogen peroxide, the latter transforms in the catalase and under the GSH-PX catalysis into the water, thus avoids the free radical to cell's harm. GSH-PX is also one kind of important antioxidant.

It may cause the lipid peroxide to return to its original state into fatty acid alcohol, composes the elimination free radical together with SOD the defensive system.^[15-17] The experimental results indicated that the ASMq preparation has the ability to reduce the oxidative damage in the S180 and EAC tumor models.

Hypoxia influences the body's energy supply, and will cause ischemia of the heart brain and other important organs, which will soon lead to death. This experiment shows that ASMq can obviously increase the survival time for the tumor bearing mice living in hypoxic conditions under normal pressure. Moreover, ASMq can extend the climbing time of these two types of tumor-bearing mice, which indicates that ASMq has the effect of postponing fatigue. Hypoxia affects the body's energy supply, and ultimately causes critical organs such as the heart and brain to become ischemic leading to necrosis.^[18-20] Our results show that the ASMq can significantly prolong survival time of tumor-bearing mice under normobaric conditions. The underlying mechanism may be due to ASMq's antioxidant properties that improve the animal's adaptive abilities while under hypoxic conditions. This may consequently aiding in the regulation of various metabolic enzymes, reduced oxygen consumption, free radical scavenging, and increasing the activity of antioxidant enzymes and inhibiting or reducing lipid peroxidation, thereby inhibiting blood rheology degeneration caused by hypoxia. All of these factors may contribute to ASMq's anti-hypoxia effects, but the exact mechanisms remain to be studied in depth. Intragastric administration of ASMq under a normobaric conditions can significantly prolong mouse survival time during hypoxic conditions. This implies that to some extent ASMq has protective effects on cardiovascular and cerebral tissue. In short, ASMq can reduce tumor mass in S180 and EAC tumor bearing mice, inhibit tumor growth, and increase survival time in mice maintained under hypoxic conditions.

The mechanisms leading to these findings may be due to the antioxidant effects of ASMq, leading to an enhanced anti-stress ability, improved adaptation to hypoxic stimuli, improved regulation through adjusting the metabolic enzyme activity, reduced oxygen consumption and free radicals scavenging, enhanced activity of antioxidant enzymes and inhibition or reduction of lipid peroxidation. The net effect of these changes may be to inhibit the changes caused by blood rheology degeneration because of hypoxia and finally an anti-hypoxia effect. However, the mechanism underlying this effect is yet to be fully investigated. In this study, ASMq was applied with a gavage and treatment with ASMq increased the survival time for mice maintained under hypoxic conditions (with normal pressure). These data indicate that ASMq may provide protection for the heart, brain, vessels, and tissues. In conclusion, ASMq can decrease the tumor in the S180

tumor-bearing group and in the EAC tumor-bearing mice, ASMq inhibits the growth of tumors, and strengthens the body's immunity and extends the survival time of mice maintained under hypoxic conditions.

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