Biological Trace Element Research (2021) 199:2201–2207
https://doi.org/10.1007/s12011-020-02342-1

Effects of Nano-copper on Antioxidant Function in Copper-Deprived Guizhou Black Goats

Xiaoyun Shen[1,2,3] · Chunjie Song[1] · Ting Wu[1]

Received: 24 May 2020 / Accepted: 9 August 2020 / Published online: 18 August 2020

Abstract

Guizhou black goats are essential to the production system in the Wumeng prairie in the Western China. This study aimed to determine the influence of nano-copper on antioxidant system in copper-deprived Guizhou black goats. We analyzed mineral contents in soil, forage, and goats' tissues. Blood parameters were also determined. The results showed that copper concentrations in soil and forage were significantly lower, and the iron content was significantly higher in affected compared with healthy area ($P < 0.01$). Copper concentrations in animal tissues (blood, liver, and hair) were significantly lower and iron content was significantly higher in affected compared with healthy goats ($P < 0.01$). After supplementation of nano-copper or copper sulfate, copper concentration in blood was significantly increased and iron content was significantly lower ($P < 0.01$). Compared with nano-copper group, the effect of copper sulfate was slower. Hemoglobin levels, erythrocyte count, and packed cell volume from nano-copper and copper sulfate groups were significantly higher than those in copper-deprived goats ($P < 0.01$). Compared with the copper-deprived Guizhou black goats, serum ceruloplasmin levels in nano-copper and copper sulfate groups were significantly increased, while serum lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and creatinine were significantly decreased ($P < 0.01$). Compared with the copper-deprived animals, serum superoxide dismutase, glutathione peroxidase, catalase, and total antioxidant capacity in nano-copper and copper sulfate groups were significantly higher, while serum malondialdehyde content was significantly lower ($P < 0.01$). The effect of copper sulfate group was significantly lower than that in nano-copper group ($P < 0.01$). Consequently, nano-copper could not only markedly increase the copper content in blood in copper-deprived Guizhou black goats but also much improves the antioxidant capacity.

Keywords Guizhou black goats · Copper deprivation · Copper sulfate · Nano-copper · Antioxidant function

Introduction

The Wumeng prairie is located in the Yunnan-Guizhou Plateau of Southwest China, where the three provinces of Guizhou, Yunnan, and Sichuan meet, and is an important pasture for Guizhou black goats. Goat farming is vital to the production system in the Wumeng prairie in the Western China [1, 2]. In recent years, Guizhou black goats in the Wumeng prairie area have been affected by a locally nutritional and metabolic disease associated with copper (Cu) deficiency, which is characterized by pica, emaciation, anemia, dyskinesia, and neurological disorders such as ataxia; animals are also prone to falls and fractures. The incidence is estimated at 15–25% and the mortality may reach 60%. Similar syndromes have been observed in yaks [3] and sheep [4]. The local farmers suffer seriously from this problem.

Nano-copper (Nano-Cu) is a common artificial material, which has been widely used in the production of intrauterine devices, anti-osteoporosis, anti-aging nano-drugs, lubricant additives, high-efficiency catalysts, and animal feed additives, bringing technological revolution to the development of medicine, industry, and animal husbandry [5–10]. Nano-Cu has the advantages of small particle size and large specific surface area. In addition to the nutritional characteristics of traditional trace element additives, it also has the advantages of small

Xiaoyun Shen and Chunjie Song Equal contributors, they are co-first authors.

✉ Xiaoyun Shen
xyshen@swust.edu.cn

1 School of Life Science and Engineering, Southwest University of Science and Technology, Mianyang 621010, China

2 State Engineering Technology Institute for Karst Desertification Control, Guizhou Normal University, Guiyang 550025, China

3 World Bank Poverty Alleviation Project Office in Guizhou, Southwest China, Guiyang 550004, China

dosage, high bioavailability, and improving animal immune function [11, 12]. Cu is an important mineral for animals, and plays an essential roles in growth and development [13, 14]. Cu is a component of superoxide dismutase (SOD). SOD has the ability to scavenge free radicals [15, 16]. The antioxidant system is the defense system for scavenging free radicals, comprising non-enzymatic and enzymatic systems. The non-enzymatic system includes mainly vitamin E, vitamin C, cysteine, glutathione (GSH), Cu, iron (Fe), zinc (Zn), and selenium (Se). The enzymatic system consists of SOD, glutathione peroxidase (GSH-Px), catalase (CAT), and other antioxidant enzymes [17–19]. The anti-oxidation effect is to remove excess free radicals, maintain the balance between oxidation and anti-oxidation and retain the healthy physiological state of animals. The antioxidant function of animals has an essential relationship with many mineral elements.

The purpose of this research was to explore effects of nano-Cu on blood parameters and antioxidant function in animals and to provide a reference for further study prevention and treatment in Cu deprivation disease in Guizhou black goats.

Material and Methods

Experimental Range

The Cu-deficient ranges were located in Weining County in the Chinese Yunnan-Guizhou Plateau (27°36′–28°26′N, 103°39′–104°47′E), with an average elevation of 2200 m above sea level, annual precipitation of 960 mm, and average atmospheric temperature of 10–12 °C. The grassland vegetation is mainly Puccinellia (*Chinam poensis ohuji*), Siberian Nitraria (*Nitraria sibirica Pall*), floriated astragalus (*Astragalus floridus*), poly-branched astragals (*Astragalus polycladus*), falcate whin (*Oxytropis falcate*), ewenki automomous banner (*Elymus nutans*), common leymus (*Leymus secalinus*), and june grass (*Koeleria cristata*).

Experimental Animals

Sixty Cu-deficient goats, aged 1 year, from Caohai farm in Weining County, were selected. All animals had pica, anemia, depressed appetite, growth retardation, rough coat, and emaciation. Thirty healthy Guizhou black goats were selected from Liangshuigou farm in Weining County, where the diseases had not been reported. All of these animals were judged to be in good health after clinical examination, and they were used as the reference group. All Cu-deficient animals were randomly divided into 2 groups. Group 1 (nano-Cu groups) was supplied with nano-Cu (2 g/goat, once/week). Group 2 [copper sulfate ($CuSO_4$) groups] was supplied with $CuSO_4$ (2 g/goat, once/week).

Collected Sample

Ten soil samples were collected from the surface layer (0 to 20 cm) in each pasture, marking sampling points. Ten samples of mixed herbage were collected from each pasture. In order to reduce soil pollution, forage were cut 0.1 cm above ground level. Samples of hair were taken from necks of Guizhou black goats. Each sample was washed with acetone, rinsed five times with deionized water, and then kept on a silica gel in a desiccator until analyses. Samples of blood were obtained from the jugular vein using a vacuum blood collection tube without anticoagulant and a vacuum blood collection tube containing 1% sodium heparin as an anticoagulant. Samples of liver were taken. Platelets and coagulation were measured 1 day before operation, and the puncture points were located by ultrasound. Vitamin K (10 mg/mL) at a dose of 1 mL/goat was administered by intramuscular injection 15 min before the operation, and the animal was then anesthetized using a local anesthetic agent, typically 3 mL/kg 1% lidocaine. A small incision was made on the right side of the abdomen and a biopsy needle was inserted. During breath holding, insert the needle into the liver, quickly remove the tissue sample, and then place the bandage over the incision. The collected blood and liver samples were returned to the laboratory at a low temperature (4–8 °C) for further processing and analysis within 8 h.

Analysis of Sample

The samples of soil were heated in a microwave in a mixture of nitric acid (HNO_3), hydrofluoric acid (HF), and perchloric acid ($HClO_4$) (5:2:5) mixture to dissolve the sample. The forage and animal tissues were dissolved in HNO_3 and $HClO_4$ (4:1) by microwave heating.

The concentrations of mineral elements in soil, forage, and animal tissue were determined by inductively coupled plasma atomic emission spectrometry (ICP-AES). The elements analyzed were Cu, Zn, Fe, Se, molybdenum (Mo), cobalt (Co), fluorine (F), and manganese (Mn).

Levels of hemoglobin (Hb), packed cell volume (PCV), red blood cell (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobinconcentration (MCHC), and white blood cell (WBC) were determined using an automated hematology analyzer (SF-3000, Sysmex-Toa Medical Electronic, Kobe, Japan). Ceruloplasmin (Cp), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AKP), creatinine (CRT), cholesterol (Chol), blood urea nitrogen (BUN), GSH-Px, SOD, CAT, malondialdehyde (MDA), total antioxidant capacity (T-AOC), sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), and inorganic phosphorus (IP) levels in serum were determined using an automated biochemical analyzer (Olympus AU 640, Olympus Optical Co., Tokyo, Japan).

Statistical Analyses

Experimental data were analyzed by using the statistical package (SPSS, version 23.0, Inc., Chicago, Illinois, USA). Data are presented as means ± S.D., and values were considered to be statistically significant at $P < 0.01$.

Results

Mineral Contents in Soil and Forage

As shown in Table 1, the Cu contents in the soil and forage from the Cu-deprived ranges were significantly lower than those in healthy areas ($P < 0.01$). No significant difference was found in the concentrations of other elements.

Effect of Cu Deficiency on Mineral Contents in Animal Tissues

The concentrations of mineral elements in the blood, hair, and liver are given in Table 2. The Cu concentrations in the blood, hair, and liver from Cu-deprived Guizhou black goats were significantly lower than those in healthy animals ($P < 0.01$), while the concentration of Fe was significantly higher than that in Guizhou black goats ($P < 0.01$).

Effect of Nano-Cu on Mineral Contents in Blood

The concentrations of mineral elements in blood are shown in Table 3, nano-Cu supplementation for up to 10 days, the Cu content in blood significantly increased, and the concentration of Fe significantly decreased ($P < 0.01$). After 20 days of continuous supplement, Cu and Fe content in blood are basically stable. The effect of $CuSO_4$ group was significantly lower than that in nano-Cu group ($P < 0.01$). It can be found that supplementing nano-Cu is the best way to solve Cu deprivation in Guizhou black goats.

Effect of Nano-Cu on Physiological Parameters

As shown in Table 4, compared with the Cu-deprived Guizhou black goats, Hb, RBC, and PCV levels in experimental groups were significantly increased ($P < 0.01$). There was no significant difference between the Nano-Cu and $CuSO_4$ groups.

Effect of Nano-Cu on Biochemical Parameters

As shown in Table 5, compared with the Cu-deprived Guizhou black goats, serum Cp levels in experimental groups were significantly increased, while serum LDH, AKP, AST, ALT, and CRT were significantly decreased ($P < 0.01$). There was no significant difference between the Nano-Cu and $CuSO_4$ groups. Compared with the Cu-deprived animals, serum SOD, GSH-PX, and CAT activities in nano-Cu and $CuSO_4$ groups were significantly higher, while serum MDA levels were significantly lower ($P < 0.01$). There was a significant difference between the Nano-Cu and $CuSO_4$ groups ($P < 0.01$), and nano-Cu had the best effect.

Discussion

Mineral nutrition plays an important role in the evolution, growth, and reproduction of animals [20]. Plant growth cannot be separated from the soil, which provides most of the nutrients needed by herbage [21, 22]. Thus, a better understanding of the mineral characteristics in soil, forage, and animal ecosystem can not only clarify the distribution of mineral elements in soil

Table 1 Mineral contents in soil and forage in studied pastures (μg/g)

Elements	Soil		Forage	
	Cu-deprived range	Healthy range	Cu-deprived range	Healthy range
Mn	315.43 ± 22.52	326.56 ± 35.58	55.72 ± 4.62	53.69 ± 5.41
Zn	51.93 ± 12.35	52.75 ± 14.59	75.92 ± 9.37	79.62 ± 8.93
Cu	2.27 ± 0.19^{a}	16.81 ± 3.26^{b}	2.56 ± 0.48^{a}	10.69 ± 2.79^{b}
Fe	1664.73 ± 126.63^{a}	1375.69 ± 117.56^{b}	395.62 ± 31.55^{a}	307.53 ± 26.71^{b}
Mo	1.81 ± 0.59	1.78 ± 0.61	1.32 ± 0.16	1.29 ± 0.21
Se	0.137 ± 0.017	0.138 ± 0.021	0.12 ± 0.03	0.13 ± 0.04
Co	6.87 ± 0.59	6.83 ± 0.45	1.39 ± 0.57	1.38 ± 0.44
F	11.80 ± 1.77	11.39 ± 1.62	5.42 ± 0.83	5.51 ± 0.77

Different little letters indicate significant difference ($P < 0.01$); the same as below.

Mn manganese, *Zn* zinc, *Cu* copper, *Fe* iron, *Mo* molybdenum, *Se* selenium, *Co* cobalt, *F* fluorine

Table 2 Mineral contents in tissues in Guizhou black goats (μg/g)

Element	Blood		Hair		Liver	
	Cu-deprived animals	Healthy animals	Cu-deprived animals	Healthy animals	Cu-deprived animals	Healthy animals
Mn	0.60 ± 0.02	0.59 ± 0.04	5.98 ± 0.33	5.88 ± 0.40	4.66 ± 0.25	4.67 ± 0.34
Zn	15.88 ± 2.23	15.79 ± 2.37	85.65 ± 4.24	85.75 ± 4.23	55.36 ± 8.53	55.76 ± 7.38
Cu	0.25 ± 0.03[a]	0.87 ± 0.21[b]	2.26 ± 0.33[a]	5.88 ± 0.45[b]	51.33 ± 2.65[a]	106.32 ± 11.65[b]
Fe	577.37 ± 23.31[a]	533.85 ± 25.36[b]	376.87 ± 13.32[a]	357.86 ± 12.78[b]	151.27 ± 12.25[a]	133.27 ± 12.43[b]
Mo	0.34 ± 0.02	0.35 ± 0.03	0.43 ± 0.03	0.42 ± 0.04	1.27 ± 0.25	1.27 ± 0.24
Se	0.06 ± 0.01	0.07 ± 0.01	0.13 ± 0.02	0.12 ± 0.03	0.27 ± 0.23	0.28 ± 0.25
Co	0.36 ± 0.03	0.35 ± 0.02	0.42 ± 0.02	0.44 ± 0.03	0.69 ± 0.23	0.68 ± 0.31
F	0.53 ± 0.03	0.52 ± 0.02	0.13 ± 0.01	0.14 ± 0.01	11.54 ± 0.53	11.49 ± 0.76

Mn manganese, *Zn* zinc, *Cu* copper, *Fe* iron, *Mo* molybdenum, *Se* selenium, *Co* cobalt, *F* fluorine

and forage but also improve our understanding of the health status in Guizhou black goats [23–25]. We analyzed the mineral concentrations of the soil and forage and found that the content of Cu was significantly lower and Fe concentration was significantly higher in affected compared with healthy pasture ($P < 0.01$). Cu deprivation depends not only on the total Cu concentration in the diet but also on other factors which affect Cu absorption and utilization [26]. Li et al. reported that Cu deficiency in Tibetan sheep was induced by S and Fe overdose [27]. The influence of Fe on the absorption and utilization of Cu is mainly due to antagonism between Fe and Cu. As Fe competes with Cu for intestinal protein binding sites, it consequently reduces the rate of Cu absorption [28]. Consequently, many researchers believe that the best ratio of Fe to Cu is 10:1 and excessive Fe will lead to Cu deprivation, consistent with the results of our study.

Cu is an essential trace element for humans and animals. It is present in various enzymes, cofactors, and reactive proteins and plays an important role in its activity, such as Cp, cytochrome oxidase, SOD, and lysyl oxidase. Severe deprivation results in obvious symptoms and Cu deficiency-related diseases of grazing ruminants have been widely reported in the reference. Shen reported a disease of Tibetan gazelle in Qinghai lake watershed of China, which was related to Cu deprivation caused by high S concentration in forage, this disease locally referred to as “shakeback disease” because of an unsteady gait [29]. Yuan et al. reported an illness in Guizhou semi-fine wool sheep related to Cu deficiency by high Mo and S contents in herbage in Guizhou province, China [30]. The main signs of such disorders included pica, emaciation, infertility, growth retardation, ataxia, dyskinesia, and abnormalities in bone development. And these diseases were prevented and cured by oral administration of $CuSO_4$. Compared with those disorders above, this sickness in the study occurred in different animals, region, nutrition deficiency, and characteristics. This was the first report of this disease and was controlled by nano-Cu in the Guizhou black goats.

Nano-Cu particles have an extremely active role in biological systems entering the stomach due to their nanoscale and huge specific surface area. The absorption effect of nano-Cu

Table 3 Effect of nano-Cu on mineral contents in blood (μg/g)

Elements	Nano-Cu group				$CuSO_4$ group			
	0 d	10 d	20 d	30 d	0 d	10 d	20 d	30 d
Mn	0.61 ± 0.06	0.62 ± 0.08	0.59 ± 0.05	0.60 ± 0.07	0.62 ± 0.03	0.61 ± 0.03	0.63 ± 0.05	0.62 ± 0.04
Zn	16.62 ± 1.28	16.41 ± 1.72	15.93 ± 1.57	15.37 ± 1.21	16.62 ± 1.28	16.30 ± 1.54	15.97 ± 1.42	15.53 ± 1.38
Cu	0.25 ± 0.08[a]	0.52 ± 0.03[b]	0.77 ± 0.05[c]	0.89 ± 0.09[c]	0.24 ± 0.07[d]	0.38 ± 0.02[e]	0.57 ± 0.06[f]	0.68 ± 0.07[f]
Fe	576.34 ± 24.36[a]	556.42 ± 26.75[b]	531.85 ± 25.36[c]	529.85 ± 25.65[c]	577.75 ± 24.75[d]	566.38 ± 24.25[e]	544.69 ± 24.35[f]	543.92 ± 25.64[f]
Mo	0.36 ± 0.08	0.36 ± 0.05	0.37 ± 0.03	0.36 ± 0.04	0.35 ± 0.04	0.35 ± 0.06	0.36 ± 0.05	0.34 ± 0.03
Se	0.07 ± 0.02	0.07 ± 0.01	0.09 ± 0.01	0.07 ± 0.01	0.08 ± 0.01	0.08 ± 0.01	0.07 ± 0.01	0.07 ± 0.01
Co	0.36 ± 0.02	0.37 ± 0.05	0.38 ± 0.02	0.35 ± 0.03	0.36 ± 0.02	0.36 ± 0.04	0.37 ± 0.03	0.37 ± 0.02
F	0.53 ± 0.02	0.55 ± 0.02	0.53 ± 0.05	0.54 ± 0.03	0.53 ± 0.05	0.53 ± 0.06	0.54 ± 0.04	0.53 ± 0.05

Mn manganese, *Zn* zinc, *Cu* copper, *Fe* iron, *Mo* molybdenum, *Se* selenium, *Co* cobalt, *F* fluorine

Table 4 Hematological values in Guizhou black goats

Items	Cu-deprived animals	Nano-Cu group	$CuSO_4$ group
Hb (g/L)	92.48 ± 8.27[a]	117.86 ± 9.58[b]	116.39 ± 11.35[b]
RBC (10^{12}/L)	8.69 ± 0.98[a]	11.49 ± 0.73[b]	11.37 ± 0.68[b]
PCV (%)	33.64 ± 2.91[a]	45.28 ± 4.96[b]	43.67 ± 4.58[b]
MCV (fL)	38.71 ± 2.57	39.41 ± 2.33	38.41 ± 2.59
MCH (pg)	10.64 ± 1.06	10.26 ± 1.15	10.23 ± 1.27
MCHC (%)	27.49 ± 3.72	26.03 ± 3.58	26.65 ± 3.24
WBC (10^9/L)	7.43 ± 1.57	7.57 ± 1.49	7.63 ± 1.61

Hb hemoglobin, *RBC* erythrocyte count, *PCV* packed cell volume, *MCV* mean corpuscular volume, *MCH* mean corpuscular hemoglobin, *MCHC* mean corpuscular hemoglobin concentration. *WBC* white blood cell count.

and $CuSO_4$ on Cu-deprived Guizhou black goats was studied, and it was proved that nano-Cu had better absorption effect. RBC is the main carriers of oxygen in the blood [31]. RBC contains Hb, which can combine with oxygen, so that the cells can transport the external oxygen absorbed by the alveoli to the tissue for metabolism [32]. Hb concentrations for healthy animals are 130–150 g/L. Lower contents may be linked to Cu deprivation. And in our study, the Hb, RBC, and PCV from Cu-deprived Guizhou black goats were significantly increased and returned to normal levels by oral administration of nano-Cu or $CuSO_4$. The Cp content was significantly lower in affected compared with healthy Guizhou black goats ($P < 0.01$). Under normal condition, most of the Cu in serum is present as Cp, which plays an essential role in promoting the rate of Fe saturation of transferrin and in the utilization of Fe by bone marrow. So Cu deficiency not only markedly reduces the concentration of Cp, but it causes anemia, which type varies between and within species. In rats, lambs, rabbits, and pigs, the anemia is hypochromic, but in chickens and dogs, it is normochromic and normocytic. In this study, the microcytic anemia was observed in Guizhou black goats. Serum AST, ALT, and AKP activity can reflect the health of the liver, and LDH activity can reflect the degree of liver and muscle damage [33–36]. The activity of AST and ALT in serum in affected Guizhou black goats was significantly reduced, suggesting that the liver cells of Cu-deficient goats may be damaged. Increased serum AKP, LDH, and other enzyme activities suggest that muscle and kidney cells may also be damaged.

GSH-Px is an important peroxidase that is widely distributed in animals, and which can catalyze the reduction of reduced glutathione to hydrogen peroxide and thus help to protect the integrity of the cell membrane structure and function [37, 38]. SOD is one of the main antioxidant enzymes, which can remove excess free radicals in the body and reduce the degree of nucleic acid damage [39–41]. CAT is another important antioxidant enzyme, which can catalyze the

Table 5 Serum biochemical parameters in Guizhou black goats

Parameters	Cu-deprived animals	Nano-Cu group	$CuSO_4$ group
Cp (mg/L)	3.74 ± 1.29[a]	8.53 ± 1.23[b]	7.26 ± 1.66[b]
LDH (U/L)	593.77 ± 72.36[a]	219.57 ± 53.32[b]	247.05 ± 60.19[b]
AKP (U/L)	276.33 ± 39.63[a]	84.84 ± 29.43[b]	91.68 ± 24.58[b]
AST (U/L)	218.31 ± 37.54[a]	73.41 ± 13.73[b]	90.86 ± 17.34[b]
ALT (U/L)	135.42 ± 15.22[a]	35.29 ± 6.31[b]	38.99 ± 7.75[b]
BUN (mmol/L)	5.73 ± 1.92	6.09 ± 1.19	5.85 ± 1.37
SOD (U/mL)	54.83 ± 12.96[a]	147.39 ± 12.72[b]	106.73 ± 9.86[c]
GSH-Px (U/mL)	217.36 ± 28.35[a]	427.63 ± 25.87[b]	393.45 ± 29.77[c]
CAT (U/mL)	9.56 ± 1.76[a]	15.35 ± 1.67[b]	14.97 ± 2.13[c]
T-AOC (U/mL)	3.21 ± 0.62[a]	6.47 ± 0.83[b]	5.95 ± 0.74[c]
CRT (μmol/L)	163.87 ± 21.73[a]	72.91 ± 17.38[b]	82.39 ± 13.72[b]
Chol (mmol/L)	2.79 ± 0.52	2.93 ± 0.35	2.85 ± 0.69
MDA (nmol/L)	32.69 ± 1.05[a]	5.23 ± 1.34[b]	5.92 ± 1.75[c]
K (mmol/L)	3.63 ± 0.54	3.97 ± 0.75	3.74 ± 0.78
Na (mmol/L)	129.23 ± 14.89	121.73 ± 13.97	123.76 ± 15.42
Ca (mmol/L)	2.25 ± 0.28	2.55 ± 0.34	2.57 ± 0.21
IP (mmol/L)	1.79 ± 0.35	1.93 ± 0.41	1.92 ± 0.39
Mg (mmol/L)	0.94 ± 0.28	0.99 ± 0.24	0.97 ± 0.34

Cp ceruloplasmin, *LDH* lactate dehydrogenase, *AKP* alkaline phosphatase, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *BUN* blood urea nitrogen, *CRT* creatinine, *Chol* cholesterol, *K* potassium, *Na* sodium, *Ca* calcium, *IP* inorganic phosphorus, *Mg* magnesium, *SOD* superoxide dismutase, *GSH-Px* glutathione peroxidase, *CAT* catalase, *MDA* malondialdehyde, *T-AOC* total antioxidant capacity decomposition of H_2O_2, thereby playing an antioxidant role. When lipid peroxidation occurs in the body, MDA will eventually form, and excessive MDA will damage the cell membrane structure, resulting in cell loss of function and even apoptosis. Therefore, changes in MDA content cannot only reflect the degree of lipid peroxidation in the body but also reflect the degree of damage to the body. The higher the MDA content, the greater the damage to the body [42]. In the current study, nano-Cu supplementation significantly increased the activities of GSH-Px, CAT, SOD, and significantly decreased the MDA concentration in serum, which could in turn reduce the formation of lipid peroxides and improve the resistance of the organism to oxidative damage. T-AOC can comprehensively evaluate the antioxidant function of the body [43]. Cu deprivation affects the antioxidant function, and causes various diseases in Guizhou black goats. Nano-Cu supplementation can improve the antioxidant function, reduce the production of lipid peroxides, protect the integrity of the cell membrane structure and function, and improve the functions of various tissues and organs in Guizhou black goats.

Conclusion

According to results, Cu deficiency in Guizhou black goats is mainly caused by low Cu concentrations in the soil and forage. Cu deprivation in forage in natural ranges will not only influenced the Cu content in the blood but also severely disrupted the blood parameters and antioxidant function in Guizhou black goats.

Funding information This work was supported by the Project of National Key Research and Development Program of China in 13th Five-year Plan (2016YFC0502601) and the National Natural Science Foundation of China (41671041).

Compliance with ethical standards

Ethics statement The Guizhou black goats that were used in this study were cared for as outlined in the Guide for the Care and Use of Animals in Agricultural Research and Teaching Consortium (Federation of Animals Science Societies, 2016). Sample collections from goats were approved by Southwest University of Science and Technology in China, Institutional Animal Care and Use Committee (Project A00657).

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Liao JJ, Shen XY, Huo B, Xiong KN (2018) Effect of nitrogenous fertilizer on the antioxidant systems of grassland species in the Karst mountains. Acta Pratacult Sin 27(1):169–176
2. Xia YB, Han Y, Chen SC, Wu X (2019) Effects of dietary protein concentration on production performance and rumen fermentation of Guizhou black goats aged 45-105 days. J Grassl Forage Sci 06: 71–79
3. Shen XY, Du GZ, Chen YM, Fan BL (2006) Copper deficiency in yaks on pasture in western China. Can Vet J 47:902–906
4. Huo B, Wu T, Xiao H, Shen XY (2019) Effect of copper contaminated pasture on mineral metabolism in the Wumeng semi-fine wool sheep. Asian J Ecotoxicol 14(6):224–232
5. Jaleh B, Fakhri P, Noroozi M (2012) Influence of copper nanoparticles concentration on the properties of poly(vinylidene fluoride)/ cu nanoparticles nanocomposite films. J Inorg Organomet P Mat 22(4):878–885
6. Lei RH, Wu CQ, Yang BH, Ma HZ, Shi C, Wang QJ, Wang QX, Yuan Y, Liao MY (2008) Integrated metabolomic analysis of the nano-sized copper particle-induced hepatotoxicity and nephrotoxicity in rats: A rapid in vivo screening method for nanotoxicity. Toxicol Appl Pharmacol 232(2):292–301
7. Meng H, Chen Z, Xing GM, Yuan H, Chen CY, Zhao F, Zhang CC, Zhao YL (2007) Ultrahigh reactivity provokes nanotoxicity: Explanation of oral toxicity of nano-copper particles. Toxicol Lett 175(1-3):102–110
8. Griffitt RJ, Weil R, Hyndman KA, Denslow ND, Powers K, Taylor D, Barber DS (2007) Exposure to copper nanoparticles causes gill injury and acute lethality in Zebrafish (Danio rerio). Environ Sci Technol 41(23):8178–8186
9. Chen Z, Meng H, Xing GM, Chen CY, Zhao YL, Jia G, Wang TC, Yuan H, Ye C, Zhao F, Chai ZF, Zhu CF, Fang XH, Ma BC, Wan LJ (2006) Acute toxicological effects of copper nanoparticles in vivo. Toxicol Lett 163(2):109–120
10. Prabhu BM, Ali SF, Murdock RC, Hussain SM, Srivatsan M (2010) Copper nanoparticles exert size and concentration dependent toxicity on somatosensory neurons of rat. Nanotoxicol 4(2): 150–160
11. Liu YZ, Zhu LQ (2012) The biological function and absorption mechanism of nanometer CuO. China Feed 24:31–32
12. Huang JS, Ren S (2001) Development on nanocrystalline powder copper preparation. J Mater Sci Eng 19(2):76–79
13. Zhang CX, Wu HQ, Zhu XP, Jia HT (2012) Analysis of Cd pollution & spatial variability characteristics of typical agricultural soils in Suburbs of Urumqi, Xinjiang. Spectrosc Spect Anal 32:537–540
14. Lai YS (2016) Study on heavy metal pollution of soil and cropper in typical area. Shihezi Univ, Shihezi City
15. Shen XY, Huo B, Wu T, Song CJ, Chi YK (2019) iTRAQ-based proteomic analysis to identify molecular mechanisms of the selenium deficiency response in the Przewalski's gazelle. J Proteome 203: 103389
16. Wu L, Zhang H, Xu C, Xia C (2016) Critical thresholds of antioxidant and immune function parameters for Se deficiency prediction in dairy cows. Biol Trace Elem Res 172(2):320–325
17. Roman M, Jitaru P, Barbante C (2014) Selenium biochemistry and its role for human health. Metallomics 6(1):25–54
18. Chen M, Mahfuz S, Cui Y, Jia LY, Liu ZJ, Song H (2019) The antioxidant status of serum and egg yolk in layer fed with mushroom stembase (*Flammulina velutipes*). Pak J Zool 52:389–392
19. Herena YH, Naghum A, Marla JB, Lucia AS (2019) From selenium absorption to selenoprotein degradation. Biol Trace Elem Res 192(1):26–37
20. Huma V, Singh VK, Singh MP (2017) Heavy metal pollution due to coal washery effluent and its decontamination using a macrofungus, Pleurotus ostreatus. Ecotoxicol Environ Saf 145(4): 42–49
21. Zhao F, Ma Y, Zhu Y (2015) Soil contamination in China: current status and mitigation strategies. Environ Sci Technol 49(11):750–759
22. Popovic MP, Nie H, Chettle DR (2007) Random left censoring: a second look at bone lead concentration measurements. Phys Med Biol 52(17):53–69

23. Shen XY, Jiang ZG (2012) Serum biochemical values and mineral contents of tissues in Przewalskii and Tibetan gazelles. Afr J Bio Technol 11(3):718–723
24. Shen XY, Jiang HM (2013) Study of serum biochemical values and mineral contents of tissues in Guizhou black goat. J Anim Vet Adv 12(5):581–583
25. Shen XY, Chi YK, Xiong KN, Wang HC, Zhang JH (2013) Serum biochemical values and mineral contents of tissues in Guizhou semi-fine wool sheep. J Anim Vet Adv 12(11):1078–1080
26. Spears JW (2003) Trace mineral bioavailability in ruminants. J Nutr 133(5):1506–1509
27. Li SG, Wu JH, Wang QW, Wang ZW, Mo BT (2016) Studies of sulfur-and iron-induced copper deficiency in Tibetan sheep. Agric Sci Technol 17(8):1900–1902
28. Jiang JF, Zhang CS, Jia CY, Gao XJ (2003) The influence of various dietary Fe and Va levels on production performance, apparent deposition of iron, copper, manganese and zinc of broilers. Acta Zoonutr Sin 15(1):31–37
29. Shen XY, Li X, Zhang RD (2010) Studies of "unsteady gait disease" of the Tibetan gazelle (*Procapra picticaudata*). J Wildl Dis 46(2):560–563
30. Yuan R, Li L, Wang Q, Du G (2011) Copper deficiency in Guizhou semi-fine wool sheep on pasture in southwest China karst mountain area. Afr J Biotechnol 10(74):17043–17048
31. Wu T, Song ML, Shen XY (2020) Seasonal dynamics of copper deficiency in Wumeng semi-fine wool sheep. Biol Trace Elem Res. https://doi.org/10.1007/s12011-019-02018-5
32. Meng T, Liu YL, Xie CY (2019) Effects of different selenium sources on laying performance, egg selenium concentration, and antioxidant capacity in laying hens. Biol Trace Elem Res 189(2): 548–555
33. Huo B, He J, Shen XY (2020) Effects of selenium-deprived habitat on the immune index and antioxidant capacity of Przewalski's gazelle. Biol Trace Elem Res. https://doi.org/10.1007/s12011-020-02070-6
34. Wu XZ, Dai SF, Hua JL, Hu H, Wang SJ, Wen AY (2019) Influence of dietary copper methionine concentrations on growth performance, digestibility of nutrients, serum lipid profiles, and immune defenses in broilers. Biol Trace Elem Res 191(1):199–206
35. Chi YK, Zhang ZZ, Song CJ, Xiong KN, Shen XY (2020) Effects of fertilization on physiological and biochemical parameters of Wumeng sheep in China's Wumeng prairie. Pol J Environ Stud 29(1):79–85
36. Huo B, Wu T, Song CJ, Shen XY (2019) Studies of selenium deficiency in the Wumeng semi-fine wool sheep. Biol Trace Elem Res 194(1):152–158
37. Song CJ, Shen XY (2020) Effects of environmental zinc deficiency on antioxidant system function in Wumeng semi-fine wool sheep. Biol Trace Elem Res. https://doi.org/10.1007/s12011-019-01840-1
38. Liu KY, Liu HL, Zhang T, Mu LL, Liu XQ, Li GY (2019) Effects of vitamin E and selenium on growth performance, antioxidant capacity, and metabolic parameters in growing furring blue foxes (*Alopex lagopus*). Biol Trace Elem Res 192(2):183–195
39. Zhao K, Chi YK, Shen XY (2020) Studies on edema pathema in Hequ horse in the Qinghai-Tibet plateau. Biol Trace Elem Res. https://doi.org/10.1007/s12011-020-02043-9
40. Saban C (2019) Effect of dietary vitamin E, selenium and their combination on concentration of selenium, MDA, and antioxidant enzyme activities in some tissues of laying hens. Pak J Zool 51: 1155–1161
41. Liu LN, Chen F, Qin SY, Ma JF, Li L, Jin TM, Zhao RL (2019) Effects of selenium-enriched yeast improved aflatoxin B1-induced changes in growth performance, antioxidation capacity, IL-2 and IFN-γ contents, and gene expression in mice. Biol Trace Elem Res 191(1):183–188
42. Zeng R, Muhammad UF, Zhang G, Tang ZC (2020) Dissecting the potential of selenoproteins extracted from selenium-enriched rice on physiological, biochemical and anti-ageing effects in vivo. Biol Trace Elem Res. https://doi.org/10.1007/s12011-019-01896-z
43. Wang Z, Zhang H, Yang H (2014) Genome-wide association study for wool production traits in a Guizhou black goat population. Plos One 9(9):e107101