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## Influence of mineral water of Remontnensky and Har-Buluk deposits on structural and functional state of gastric mucosa in experimental ulcer genesis of rats

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### Abstract

Identified protective antiulcer effect of mineral water sources “Sour” and “Har-Buluk” of Kalmykia Republic against gastric ulcers is caused by pyloric ligation. Physico-chemical composition of mineral waters of analyzed deposits was studied. It is possible that this water can regulate gastric mucosal homeostasis through the activation of protective mechanisms related to the suppression of activity of aggressive factors such as excess of gastric mucosa acid and pepsin. Thus, the activity of the mineral water was proved by the pathologies of gastrointestinal tract.

**Keywords:** Pylorus ligation; curative mineral water; physico-chemical composition.

### Introduction

According to the modern viewpoints, the guiding link of the peptic ulcer pathogenesis is the disturbance of the balance between the factors of the acid-peptic aggression of the gastric material and gastric mucosa protective elements. Modern experimental investigations are aimed at finding polyfunctioning agents which impact different pathogenetic factors that are the causes of the peptic ulcer. These agents do not cause side effects [1]. A special attention is paid to the role of the natural medical resources in the process of maintaining homeostasis of the gastric mucosa, especially to the role mineral waters influence on the organism [2-4].

The water from natural sources with a sufficiently high content of dissolved substances, definite chemical composition, and having healing properties is called mineral water. Mineral waters are complex of physical-chemical irritants and are subordinated to the general physiological rules. Intake of the mineral water leads to the physiological responses in different organs and systems [2-6].

That is why the goal of this work is to investigate the effectiveness of the influence of the mineral water from the sites “Kisly” and “Har-Buluk” (Republic of Kalmykia) in respect of the

ulcers, caused by the ligation of the pyloric part of the stomach at experimental animals.

According to the results of the recent investigations (2013) which has been carried out in the agrochemical laboratories of the Republic of Kalmykia, the water from the water site Kisly (Remontnensky district, Rostov region) is characterized according to the criteria of the mineral waters assessment as cold (2°C), highly mineralized (25 g/l), acidic (pH 3.8), and mineral, of chloride-sulphate-calcium-sodium-magnesium composition.

Mineral water of the Har-Buluk site is 5 km to South-West of the Har-Buluk settlement. The flow rate of the well is not big; it is 700 l/24 h. The well refers to the hyperpiestic waters. The temperature of the water is +2°C. Due to such temperature, the water of this well refers to the cold waters. Water-bearing materials are clays of maikop type. The water is characterized as highly mineralized, of sulphate-chloride-magnesium composition, with the acid reaction [7].

The performed analyses of the samples of this water showed that the water is siliceous boron highly mineralized of chloride-sulphate-magnesium-sodium composition. Such biological substances are recorded in the water: bromin – 40 mg/l (designation criterion 25 mg/l),

silicic acid – 72 mg/l (criterion – 50 mg/l). Probably the change of seasons influences the chemical composition and water hardness. For example, in spring the water hardness, calcium, and magnesium concentrations increase, and in summer–autumn–winter these decrease. In spring–autumn the concentrations of sulphates, chlorides, weight of the dry residual increase, and in summer–winter these values decrease [7].

## Materials and Methods

The investigation dedicated to the study of the protective antiulcer properties of the mineral waters from Kisly ad Har-Buluk wells were conducted under the conditions of the acute experiment, using 30 white rats, males, weighing 200-300 g. All the experiments with animals were conducted in accordance with the “Work Code for Use of Experimental Animals” (1977).

All the animals were kept under the standard conditions of vivarium having free access to the food and water. Previously they were ranged according to three groups: control, experiment I, and experiment II, 10-15 rats in each group. The animals of the control group during 10 days before initiating ulcers were given main water as drink. The rats of experiment I and experiment II groups within the same period were given 0.9% mineral water solution from Kisly and Har-Buluk wells, respectively (table solution). Moreover, at the beginning of the experiment the weight of the animals of all investigated groups was measured. The volumes of consumed mineral water solutions and drinking water (ml) were also measured.

24 h before the initiating ulcer the animals were subjected to the food and drink deprivation. Ulceration, which was initiated by the ligation of the pyloric stomach region, was conducted according to the standard method [8]. The rats were anesthetized by the ether. Their abdominal cavities were opened and the pyloric part of the stomach was ligated. After the surgery, the animals were not given food and water for 3 h. The euthanasia of the animals was carried out with the help of ether. The gastric mucosa was investigated. To do this, the stomach was taken off, cut along the lesser curvature, the mucosa was everted and thoroughly rinsed with normal saline. The gastric mucosa was investigated using the binocular-micrometer. The area

of ulcers and length of cutaneous condition were calculated for each stomach. After this the average area of ulcers and average length of cutaneous condition were calculated for one stomach in each group.

Statistical processing of the results was performed with the help of the program STATISTICA 6.0 using parametric LSD-tester. The differences were considered as significant when  $p < 0.05$  and  $p < 0.01$ . The data are presented as average values  $\pm$  standard error of the mean.

## Results and Discussion

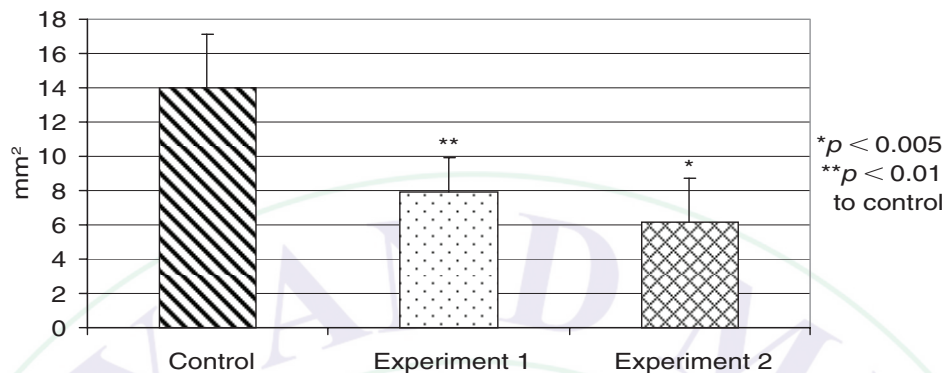
It was stated that the volume of the liquid intake in the group of experiment I and experiment II, where the animals were given 0.9% solution of mineral waters, for the 24 h per every animal was approximately  $82.42 \pm 10.29$  and  $94.31 \pm 5.32$  ml, respectively. In the control group of animals, where the rats were given main water as drink, it was found out that the volume of liquid intake every 24 h was approximately  $110 \pm 4.3$  ml.

Thus, the volumes of mineral waters intake in experimental groups only slightly differ from those of the control group.

During the experiment we used the “Ligation of pylorus” model while watering animals with mineral waters of table concentration. As it is known from the literature, the damages of the gastric mucosa after the pylorus ligation are vast areas of haemorrhage and tissues necrosis the basis of which is the combination of the two mechanisms: perfusion insufficiency in the gastric mucosa due to the excessive stretching of the stomach parries, and drop of pH due to the hyperacidity of the “stagnant” gastric acid and lack of evacuation of the accumulating content [8]. It is known that the hyperacidity of the gastric acid is a risk factor for the development of the acid-dependent diseases of the gastrointestinal tract, including gastro duodenal ulcer [9]. Therefore, this experimental model can be used for the adequate assessment of the antiulcer potential of the mineral waters.

As a result of the conducted investigation, we acquired the following results (Figure 1). Thus, the average area of the damages of the gastric mucosa due to the ligation of pylorus for the animals of the control group was  $14.08 \pm 2.8$  mm<sup>2</sup> ( $n = 10$ ), for the animals of the groups of experiment I and experiment II, which during 10 days before ulcer initiation were given the solutions of

**Figure 1: Effect of 10-day drinking mineral water “Remontnensky” and “Har-Buluk” origin in medical dining breeding on ulceration in the stomach pyloric ligation in rats.**



the medical mineral waters –  $6.43 \pm 1.89 \text{ mm}^2$  ( $n = 10$ ) and  $7.92 \pm 1.47 \text{ mm}^2$  ( $n = 10$ ), respectively. The value of the antiulcer effect for the mineral water of the Kisly well was 54.5%, for the mineral water of the Har-Buluk well – 43.8%. The statistical analysis of the experiment data showed the significance of the antiulcer effects of the mineral waters –  $p < 0.005$  and  $p < 0.01$  for Kisly and Har-Buluk wells, respectively.

The role of the hydrochloric acid hypersecretion in the pathogenesis of the gastric mucosa ulcerous conditions is well studied. However, 30% of all the cases show that the ulcer develops on the background of the partial or complete acidity. Nevertheless, even if the acid itself is not a sufficient etiologic agent for ulcer formation, its corrosive properties are often the cause of increased peptic activity, which is enough to worsen the ulcer [10,11]. Even the normal release of the acid can cause ulcers in the damaged mucosa when there is a disturbance of the balance between the aggressive and protective factors of the gastric mucosa. That is why the use of substances which reduce the release of acid is a common method for the gastro enteric damages [12].

It is known that the homeostasis of the gastric mucosa and its integration are maintained for the account of dynamic processes of the mucosa cells death and their proliferation. Today the leading factor of the mucosa damages development is the oxidative stress [13] and apoptosis [14], since they play an important role in loss of gastric mucosa integrity, caused by the influence of different aggressive factors. In other words, ulcers appear when the oxidative damage and apoptosis prevail over the processes of cell proliferation.

The leading mechanism of the pathogenesis, which causes these damages of the cell membrane structure, is the activation of the lipid peroxidation which leads to the disturbance of balance between the formation and destruction of the hyperoxides and excessive accumulation of the free radicals which are toxic for the cells [15]. Today one can find in the literature data which speak for the active participation of the lipid peroxidation products, in particular such as  $\text{OH}^-$ , in the process of gastric mucosa damaging and apoptosis activation in the area of ulcer effect [16-19]. That is why the use of medical agents that would prevent the consequences of oxidative stress developing due to the inflammation in the ulcer area are one of the possible directions for ulcer treatment.

Based on the acquired results of the investigation using his model of ulcer formation, we can suppose that the mineral water of the Remontnensky and Har-Buluk sites can probably decrease hyperacidity of the gastric acid. One can suggest two ways of such protective activity of mineral waters: the first is the neutralization of the hydrochloric acid of the gastric acid; the second is the blockage of the release with the help of HCl parietal cell in the gastric mucosa which complies with the literature data [1].

However, we cannot exclude the fact that the antiulcer activity of the investigated mineral waters on this ulcer formation model can be explained by their neutralization of the reactive oxygen intermediates which are released as the result of the lipid peroxidation present in any inflammation process.

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