Phytoecdysteroids in the correction of morphological changes of the intestinal mucosa in the model of enteral insufficiency in the growing rats

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ABSTRACT

Aim: to study influence of phytoecdysteroids on the histological structure of the intestinal mucosa in model of chronic enteral insufficiency in the growing rats.

Materials and methods: In the experiments, there were used white pedigree less rats growing under the laboratory conditions of the National University of Uzbekistan. At rats by chronic under-eating there was induced protein-energetic insufficiency. The little rats were divided into two groups on 30 day. One subgroup received phytoecdisteroid ecdisten in dose 2,5 mg/kg for 10 days (studied group), second subgroup received a physiological solution. Control group included healthy little rats. The rats were killed on 40 day of postnatal life. For study of histological structure of the small intestine slices of the size 0,2-0,3 cm were fixed in a solution of Karnua and 10 % solution of formalin and after the appropriate processing were filled in by paraffin. Focused slices of thickness 5-7 microns were stained by hematoxylin and eosin.

Results: The results of morphological study of histostructure of the intestinal mucosa showed that in the rats with enteral insufficiency the mucous membrane was swollen and infiltrate with single atrophic cellular elements. During treatment of enteral insufficiency with ecdisten all morphometric parameters were reliably improved (P<000,1).

Conclusions: Our data indicated that ecdisten may be used as preparation which additionally to known tonic effect has ability to stimulate protein biosynthesis in the body that results in improvement of the processes of membrane digestion and absorption in the small intestine.

Key words: enteral insufficiency, morphology of the mucous membrane, phytoecdysteroids.

INTRODUCTION

The clinical and experimental data available in the literature testify that the formation of functions of various organs and systems during the children's period depends significantly on a mode of feeding and composition of food. The numerous researches which have been carried out in the laboratory of physiology of the Academy of Sciences of the Republic of Uzbekistan showed that the sensitivity of mechanisms of food assimilation to various endo- and exogenous factors is high enough in children's age. In this age disbalance or insufficient nutrition seem to be or cause or predisposition to the damages of the organs and systems including digestion leading to the enteral insufficiency.1,2,3

Enteral insufficiency covers a complex of intestinal and extraintestinal disorders induced by chronic bowel diseases and lesions related to syndrome of polyorgan insufficiency. In spite of the fact that the spectrum of energy tropic preparations also is wide enough, not always there is an opportunity to reveal concrete dot damage of mitochondria and precisely to pick up a suitable medicinal preparation. In this connection, the most effective in wide clinical practice appeared to be the complexes of energy tropic preparations having ability to influence at once on some of key stages cellular energy metabolism. The previous
researches confirm efficiency of phytoecdysteroids for stimulation of protein synthesizing processes in the body.\cite{4,5} This fact assumes an opportunity of use them as stimulators of enzymatic structures of the intestine mucosa as with anabolic steroids. As modulators of a power exchange the interest is represented by researches of the domestic researchers on use of phytoecdysteroids isolated from Leuzea carthamoides and Turkestan lively creature for on biopower of liver cells under the conditions of hepatitis, characterizing, first of all, by sharp changes in mitochondria functioning (M.A.Tashmukhamedova and co-author, 1987). The similar researches were not performed at correction of the states due to chronic enteral insufficiency, in particular we were interested in the effect of phytoecdysteroids on the histological structure of the intestinal mucosa in experiment.

**AIM**

To study influence of ecdisten on the histological structure of the intestinal mucosa in model of chronic enteral insufficiency in the growing rats.

**MATERIALS AND METHODS OF RESEARCH**

In the experiments there were used white pedigreeless rats growing under the laboratory conditions of the National University of Uzbekistan (Head of the Department of Biochemistry prof. Kuchkarova L.S.). At rats by chronic under-eating (quantitative reduction of a vivarium diet by 50 % from norm) there was induced protein-energetic insufficiency. The little rats were divided into two groups on 30 day. One subgroup received phytoecdysteroid ecdisten in dose 2.5 mg/kg for 10 days (from 30 till 40 day of life) (studied group), second subgroup received a physiological solution. For preparation of solutions of phytoecdysteroids 10 mg were dissolved in 10 ml of physiological solution. The volume of received solution was 0,1-0,2 ml. The preparations were given every day at the same time - from 9.00 a.m. to 10.00 a.m.

Control group included healthy little rats. The rats were killed on 40 day of postnatal life.

The morphological researches were performed at the department of anatomy with operative surgery of Tashkent Medical Academy (prof. Sagatov T.A.).

For study of histological structure of the small intestine slices of the size 0.2-0.3 cm were fixed in a solution of Karnua and 10 % solution of formalin and after the appropriate processing were filled in by paraffin. Focused slices of thickness 5-7 microns were stained by hematoxylin and eosin.

The basic morphological criteria were the following changes observed in a mucous environment of the duodenum: a) flattening of the cells of absorbed epithelium covering villi, thinning of the brush border; b) atrophy of the mucosa membrane with moderate thinning and marked shortening of its villi; c)crypt deepening; d) sharp change of ratio “villous length :crypt deepening” due to marked shortening villi and crypt deepening; e) increase in number of interepithelial lymphocytes (IEL), number of enterocytes in the longitudinal slice of the villous in the crypt, number of goblet cells in the villus and in crypt.

In order to improve histomorphological parameters of the small intestine there was used local phytoecdysteroid Ecdisten as preparation improving processes of membrane digestion and absorption in the small intestine. Ecdisten is natural compound of steroid structure, isolated from the roots and rootstocks of Leuzea carthamoides, created by Institute of Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan.

**RESULTS AND DISCUSSION**

The results of morphological study of histostructure of the intestinal mucosa showed that in the rats with enteral insufficiency the mucous membrane was swollen and infiltrate with single atrophic cellular elements. The thickness of the mucous membrane was, on the average, by 25% less than norm. Morphometric measurements of the small intestine in the control group of animals showed absence of changes of morphological and functional structures in the intestinal mucosa (Fig. 1). In group of animals with enteral insufficiency there were noted significant changes in the morphological picture of the small intestine mucous membrane (Fig. 2).

![Fig.1. Morphometric picture of the small intestine in the control group.](image-url)
resulting in dystrophy of the villi and crypt. In the atrophic villi there was also found decreased number of enterocytes to 57,0±3,1 (by 32% in comparison with control). In some areas there was observed desquamation of the brush enterocytes. At the same time with shortening of villus there was noted reliable deepening of the crypt.

**Fig. 2.** Morphometric picture of the small intestine in the group of animals with enteral insufficiency.

**Table 1. Morphological parameters of the histostructure of the small intestine mucous membrane**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control-1</th>
<th>P1</th>
<th>Control-2</th>
<th>P2</th>
<th>Ecdisten</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucous membrane</td>
<td>690±35,0</td>
<td>0,001</td>
<td>524,0±25,4</td>
<td>0,001</td>
<td>700,0±28,7</td>
</tr>
<tr>
<td>Villi length</td>
<td>491±27,0</td>
<td>0,001</td>
<td>304,0±11,3</td>
<td>0,001</td>
<td>507,5±17,8</td>
</tr>
<tr>
<td>Crypt deepening</td>
<td>201±7,6</td>
<td>0,02</td>
<td>220,0±8,4</td>
<td>0,05</td>
<td>201,0±7,6</td>
</tr>
<tr>
<td>V/C (Villi/Crypta)</td>
<td>2,4</td>
<td>1,4</td>
<td></td>
<td>2,5</td>
<td></td>
</tr>
<tr>
<td>Enterocyte number on the longitudinal villus slice</td>
<td>84,0±4,5</td>
<td>0,001</td>
<td>57,0±3,1</td>
<td>0,001</td>
<td>84,0±5,0</td>
</tr>
<tr>
<td>- Crypta</td>
<td>36,0±1,0</td>
<td>0,001</td>
<td>33,0±0,9</td>
<td>0,001</td>
<td>36,9±0,60</td>
</tr>
<tr>
<td>Number of goblet cells on the longitudinal slice -in the villus</td>
<td>14,8±0,4</td>
<td>0,02</td>
<td>16,0±0,4</td>
<td>0,05</td>
<td>14,8±0,50</td>
</tr>
<tr>
<td>- Crypta</td>
<td>17,9±0,5</td>
<td>-</td>
<td>19,0±0,9</td>
<td>-</td>
<td>17,9±0,5</td>
</tr>
</tbody>
</table>

**Note:** P1 - reliable differences between data of control and enteral insufficiency. P2 - reliable differences between data of enteral insufficiency and after treatment with ecdisten.

In the literature there are found descriptions only of single experimental and clinical investigations lightening questions of the state of cellular energetics in bowel diseases.

The investigations performed by Francoise Briet et al (2003) showed decrease in activity of 1 complex of the respiratory chain in the patients with chronic inflammatory disease of the intestine on the background of insufficient nutrition. The authors suggest that mitochondrial insufficiency of 1 complex of the respiratory chain, established in the mononuclears of the peripheral blood is a marker of insufficient nutrition.3 Approximately such results were obtained in experimental investigations of Nieto N et al (2000). The purpose of their study was to evaluate effect of the serious under-eating of protein on the antioxidative defensive system in the small and large intestine of rats. The results showed that chronic diarrhea and serious under-eating of the protein promoted inhibition of antioxidative defensive system both in the small and in the large intestine that may play important role in the pathogenesis of this pathology and supporting of the circulus vituosus of malabsorption-diarrhea-malnutrition in the first ages of life. Mitochondrial dysfunction and changes in the energy metabolism, on the whole, were involved during onset and development of inflammatory intestinal diseases. However, this is the first investigation devoted to search for ways of improvement of the mitochondrial insufficiency.
Thus, in this work on the animal models there has been performed simultaneous study of the histomorphological structures of the small intestine in the growing rats with enteral insufficiency and after receiving phytoecdisteroids. We demonstrated that changes due to malnutrition in the intestinal mucosa may be flattened after ecdisten administration.

Our data indicated that ecdisten may be used as preparation which additionally to known tonic effect has ability to stimulate protein biosynthesis in the body that results, as we showed, in improvement of the processes of membrane digestion and absorption in the small intestine.

CONCLUSIONS

1. Deficit of the protein in the nutrition results in significant changes in the histological picture (decrease in thickness of the mucosa, reduction in number of villi and enterocytes) in the jejunum and finally in deficit of body mass.
2. It was established that under the effect of ecdisten there was achieved reliable improvement of histomorphological data.

ACKNOWLEDGMENTS

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REFERENCES