



## MORPHOLOGICAL AND MORPHOMETRIC PARAMETERS OF THE ESOPHAGUS OF WHITE OUTBRED RATS 3-6 MONTHS UNDER THE INFLUENCE OF THREE DIFFERENT ANTI-INFLAMMATORY DRUGS IN CONDITIONS OF POLYPHARMACY

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### ABSTRACT

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most influential and widespread means of pathogenetic therapy for acute or chronic pain. However, NSAIDs have a specific adverse effect on the gastrointestinal tract. In recent years, the number of studies on damage to the esophagus due to NSAID use has increased. In this work, the morphological and morphometric parameters of the esophagus of 50 white outbred rats aged 3 to 6 months under the influence of 3 different anti-inflammatory drugs on polypharmacy were studied and analyzed.

**KEYWORDS:** esophagus, polypharmacy, morphology, morphometry, anti-inflammatory drugs.

### INTRODUCTION

The **relevance** of studying diseases of the upper digestive tract associated with using non-steroidal anti-inflammatory drugs (NSAIDs) is due to the high

frequency of use in clinical practice. The problems related to the widespread use of NSAIDs are interdisciplinary and are discussed at numerous national and international congresses [1,2,4]. In recent years, the number of works devoted to esophagus lesions due to NSAID use has been increasing. There is evidence that taking NSAIDs (including low-dose aspirin) significantly (approximately doubles) the likelihood of developing peptic esophagitis with the risk of ulceration, bleeding or stricture formation [10]. In this case, the damaging effect of NSAIDs is mainly due to an indirect decrease in the effectiveness of protective antireflux mechanisms and the resistance of the esophageal mucosa to the detrimental effects of this class of drugs.

A significant aspect of this problem is the risk of developing dangerous complications (peptic ulcers, bleeding, and stricture of the lower third of the esophagus). B. Avidan et al. (2001), in a large-scale case-control study, when analyzing possible factors influencing the development of erosive esophagitis, found that taking NSAIDs was statistically significantly associated with the development of esophageal ulcers [3,5,6]. In addition, according to M. Bigard (2004), severe complications of the esophagus (stricture and bleeding) are much more common in older people [7-9]. Thus, given the common upper gastrointestinal side effects of NSAIDs, an important task is to select the most effective and safe drug. It must be remembered that the success and safety of any therapy depends on taking into account the characteristics of each patient and a well-founded and rational approach to a specific clinical situation.

**Purpose of the study.** Study of morphological and morphometric parameters of the esophagus in rats 3-6 months old under the influence of various anti-inflammatory drugs under conditions of polypharmacy.

## MATERIAL AND METHODS

The micromorphology of esophageal tissue was studied on 50 white 3-month-old rats under normal vivarium conditions. Before the start of the experiment, all mature rats were kept in quarantine for one week. After eliminating somatic or infectious diseases, they were transferred to the usual vivarium regime with three daily feedings.

In experimental animals, the following anti-inflammatory drugs were used to study the effect of polypharmacy: aspirin (NSAIDs - salicylic acid derivatives), paracetamol (NSAIDs - anilide derivatives), ibuprofen (NSAIDs - propionic acid derivatives), dexamethasone (synthetic glucocorticosteroid). White rats received four anti-inflammatory drugs in the following dosage: paracetamol 15 mg/kg, aspirin 5 mg/kg, ibuprofen 6 mg/kg. Doses of the drugs were calculated empirically and administered daily intragastrically as a solution for 10 days.

The studies were carried out in compliance with the rules of humane treatment of animals, which are regulated by the “Rules for carrying out work using experimental animals,” approved by the ethics committee of the Bukhara State Medical Institute named after Abu Ali ibn Sino (No. 18 of 01/16/2018).

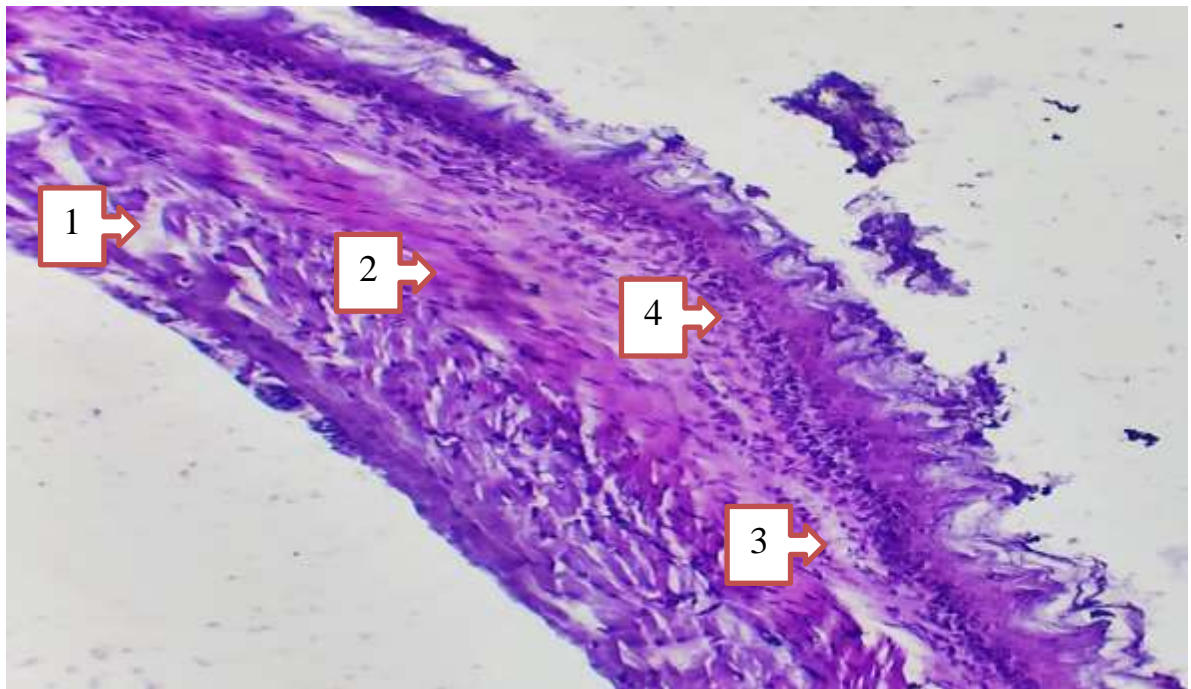
Of the 50 rats used, only one animal died during the experiments. Animals were slaughtered at appropriate times in the morning, on an empty stomach, by instant decapitation under ether anesthesia. A total of 12 esophaguses were examined macroscopically and microscopically. For general morphology, 3 pieces of tissue measuring 1.5x1.5 cm were cut out from the upper, middle and lower parts of the esophagus, which were fixed in 10% neutralized formalin. After washing for 2-4 hours in running water, the samples were dehydrated in alcohols of increasing concentrations and xylene, then embedded in paraffin and blocks were prepared. Paraffin blocks were cut at 5–8  $\mu\text{m}$  and stained with hematoxylin and eosin.

## RESULTS

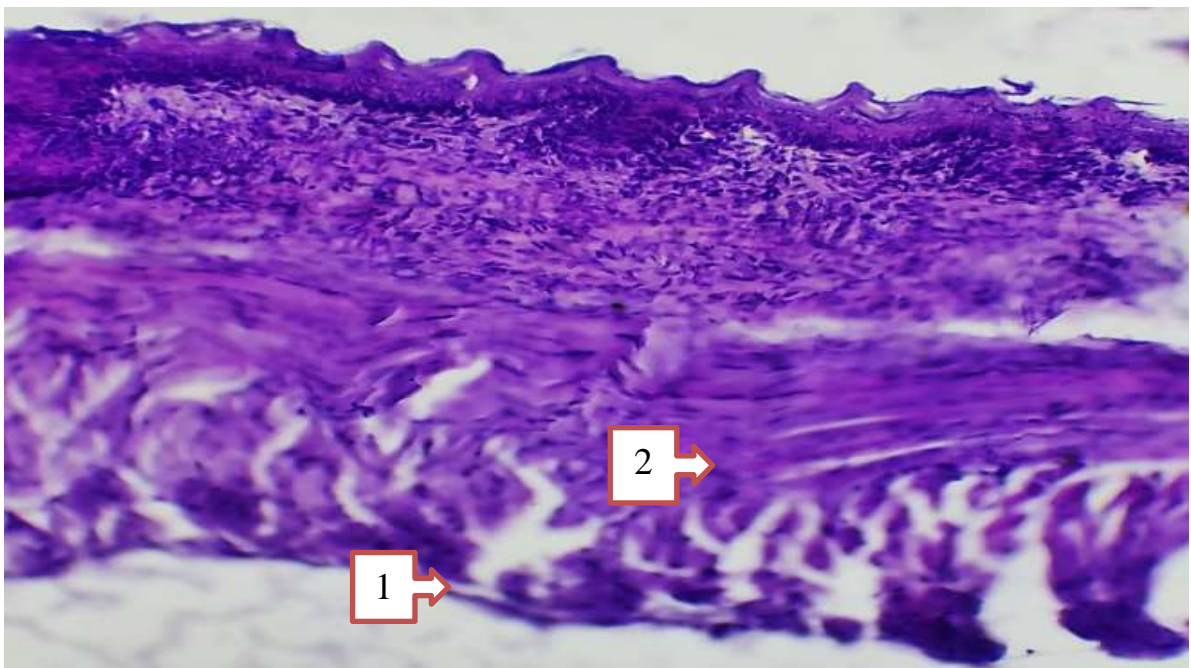
On macroscopic examination, virtually no visible changes in the esophageal wall were observed. Microscopic examination revealed hyperemia of the esophageal wall, muscle tissue swelling, axillary layer hypertrophy, hyperplasia of cells in the submucosal area, and mucous membrane swelling.

Results of a morphometric study of the esophagus muscles of white rats,  $\mu\text{m}$ :

| Norm                                   | In conditions of polypharmacy          |
|--|--|
| Muscular plate (MP) 13.10              | Muscular plate (MP) 14.2               |
| Mucosal layer (ML) 0.34                | Mucosal layer (ML) 0.42                |
| Circular layer (CL) 134.38             | Circular layer (CL) 135.18             |
| Muscle layer (ML) 2.69                 | Muscle layer (ML) 2.78                 |
| Longitudinal muscle layer (LML) 118.45 | Longitudinal muscle layer (LML) 118.48 |
| Muscle layer (ML) 2.47                 | Muscle layer (ML) 2.52                 |

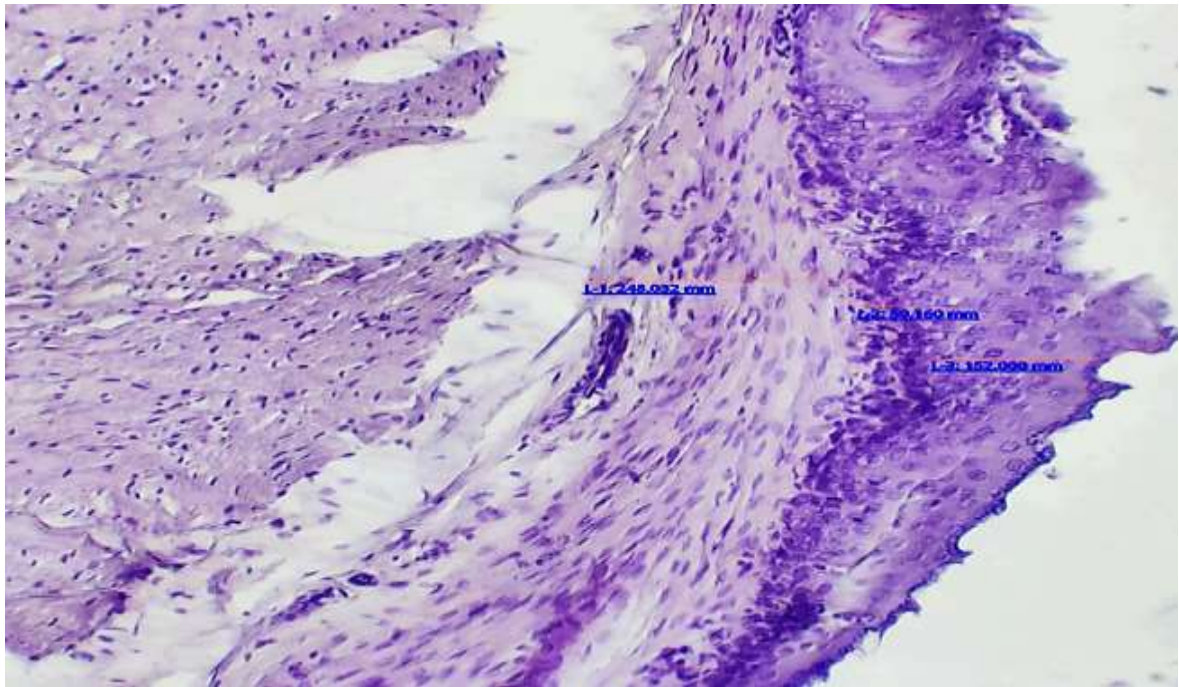


**Fig. 1.** Microscopic view of the esophagus. Edema of muscle tissue (1), hypertrophy of the axillary layer (2), hyperplasia of cells in the submucosal region (3), edema of the mucous membrane (4). G-E. Ob. 20×20.

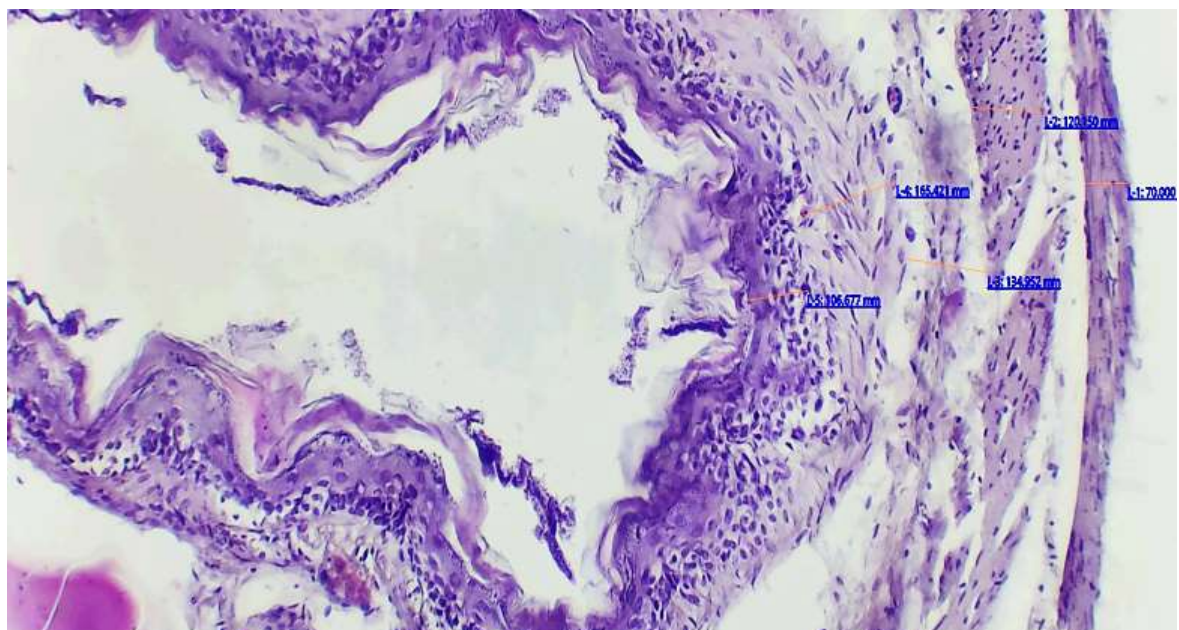


**Fig. 2.** Microscopic view of the esophagus. Edema of muscle tissue (1), hypertrophy of the axillary layer (2), hyperplasia of the submucosal region (3), hypertrophy of the mucous layer (4). G-E. Ob 20×20.

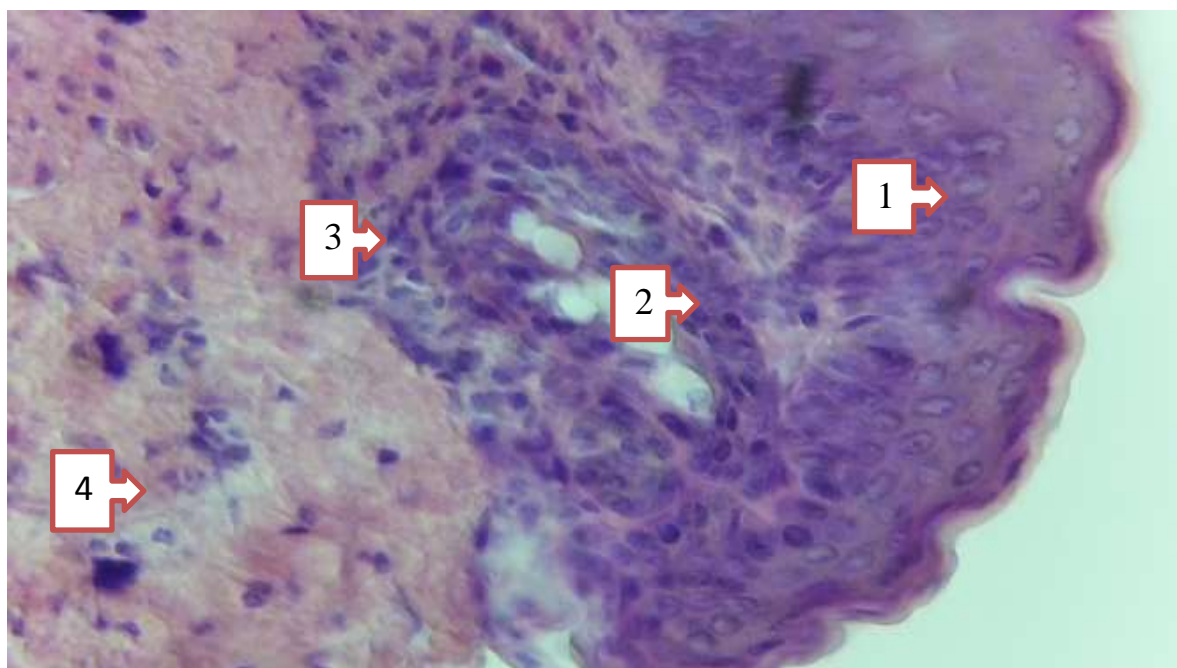




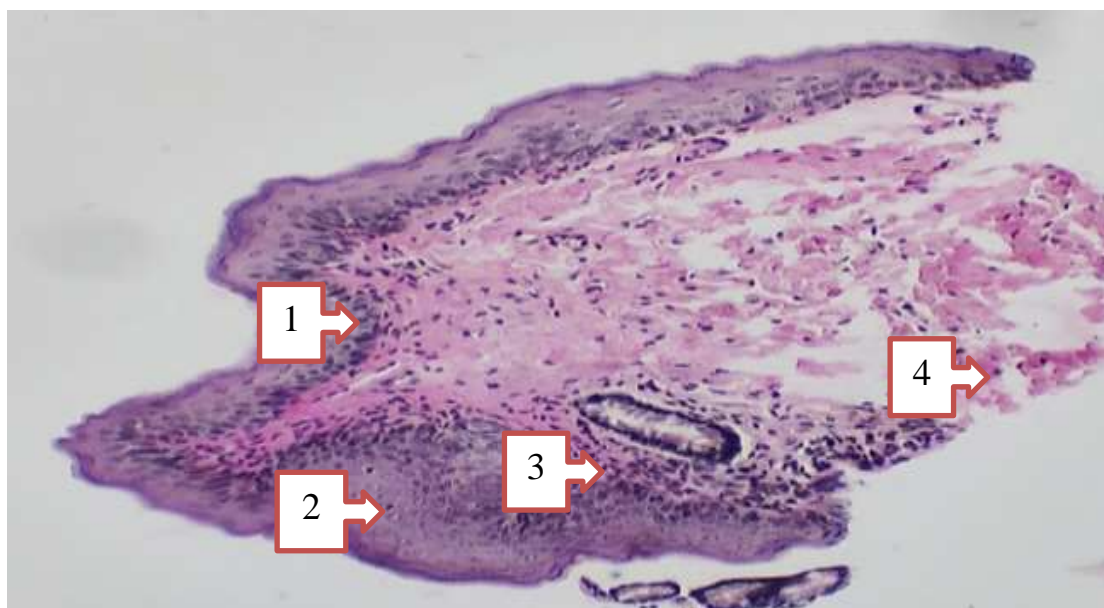
**Fig. 3.** Morphometric parameters of the esophagus. Enlargement of the walls, mucous membranes and submucosa as a result of edema. G-E. Ob. 20×20.



**Fig. 4.** Morphometric parameters of the esophagus. Enlargement of the wall, mucous membranes and submucosal layers as a result of edema. G-E. Ob. 20×20.



**Fig. 5.** Esophagus. Hyperplasia of mucous and submucosal cells (1,2), swelling of the muscle area (3), hypertrophy of the muscle layer (4). Van Gieson staining. Ob. 20×20.



**Fig. 6.** Esophagus. Hyperplasia of mucous and submucosal cells. Van Gieson staining. Ob. 10×10.

## CONCLUSION

When comparing the components of the esophageal wall of experimental laboratory rats 3-6 months of age and animals of the control group, it is clear that the muscular plate of the esophageal wall increased by 1.1  $\mu\text{m}$ , the mucous layer - by 0.08  $\mu\text{m}$ , the circular layer - by 0.8  $\mu\text{m}$ , muscle layer – by 0.09  $\mu\text{m}$ , longitudinal muscle layer – by 0.03  $\mu\text{m}$ . Microscopic examination reveals hyperemia of the



esophageal wall, muscle tissue swelling, axillary layer hypertrophy, hyperplasia of cells in the submucosal area, and mucous membrane swelling.

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