# THE ROLE OF THE ESOPHAGEAL PROTECTIVE DRUG ALFASOXX IN MODERN GASTROENTEROLOGICAL PRACTICE

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**Abstract**

**Objective.** The aim of this review is to determine the role of the esophageal protective drug Alfasoxx in the treatment of gastroesophageal reflux disease, non-erosive reflux disease and refractory forms of reflux-associated pathology based on experimental and clinical data.

**Research materials and methods.** An analytical review of relevant literature and publications, primarily published between 2013 and 2025, focusing on the use of hyaluronic acid and chondroitin sulfate-based medications in gastroenterology, was performed. The results of randomized clinical trials, experimental studies, as well as reviews and meta-analyses, evaluating the mechanisms of action and clinical efficacy of Alfasoxx and other similar esophageal mucosal protective agents, were analyzed.

**Results.** Current evidence indicates that impaired esophageal mucosal integrity is a key mechanism in the pathogenesis of gastroesophageal reflux disease. The esophageal protector Alfasoxx, which contains hyaluronic acid and chondroitin sulfate in a bioadhesive carrier, promotes the formation of a protective barrier on the surface of the esophageal mucosa, thereby reducing epithelial permeability and alleviating the severity of reflux symptoms. The use of Alfasoxx in combination with proton pump inhibitors provides faster symptom relief, improved quality of life, and increased treatment efficacy in patients with non-erosive reflux disease and partial resistance to proton pump inhibitors.

**Conclusion.** Alfasoxx represents a promising approach to mucosal protective therapy in gastroenterology. The use of esophageal protectors allows physicians to simultaneously target two targets: gastric acid secretion and restoration of the esophageal mucosal barrier function. This is especially important in patients with refractory gastroesophageal reflux disease and non-erosive reflux disease.

**Keywords:** Alfasoxx, gastroesophageal reflux disease, non-erosive reflux disease, esophageal protection, hyaluronic acid, chondroitin sulfate

## INTRODUCTION

Gastroesophageal reflux disease (GERD) remains one of the most common gastrointestinal disorders worldwide. According to epidemiological studies, the prevalence of the disease in Europe and North America reaches 20–30% of the adult population [1, 2]. GERD significantly reduces patients' quality of life, is characterized by a chronic, relapsing course, and is associated with the risk of complications, including erosive esophagitis, Barrett's esophagus, and esophageal adenocarcinoma [3].

Over the past decades, acid-suppressive therapy, primarily proton pump inhibitors (PPIs), has been the mainstay of GERD treatment. Despite the high efficacy of PPIs, approximately 30–50% of patients continue to experience reflux symptoms even with adequate treatment [4, 5]. A particularly challenging category is patients with non-erosive reflux disease (NERD), in which the severity of symptoms does not always correlate with the level of acid exposure [6].

Current understanding of the pathogenesis of GERD has expanded significantly. In addition to the acid-peptic factor, significant attention is now being paid to damage of the esophageal mucosal barrier, increased permeability of intercellular junctions, inflammatory response, and increased visceral sensitivity [7]. To solve this pressing medical problem, in recent years a strategy for protecting the esophagus has been actively developed, that is, protecting the esophageal mucosa by creating a mechanical barrier and stimulating reparative processes [8]. One of the most studied esophageal protective agents is Alfasoxx, a medicinal product based on hyaluronic acid and chondroitin sulfate in a bioadhesive matrix. The components of the drug form a protective film on the surface of the esophageal mucosa, reducing the damaging or irritating effects of hydrochloric acid, pepsin and bile acids [9]. Interest in Alfasoxx stems from its potential to pathogenetically affect damaged esophageal mucosa, which is particularly important in NERD, refractory GERD, and extraesophageal manifestations of the disease.

## RESEARCH MATERIALS AND METHODS

An analysis of the scientific literature devoted to the use of hyaluronic acid and chondroitin sulfate in the treatment of reflux-associated diseases was performed. Publications were searched in the PubMed, PMC, Scopus, and Google Scholar databases. The review included clinical studies, experimental works, systematic reviews, and international guidelines published during the above-mentioned period. Scientific articles that met the main inclusion criteria were: (1) studies devoted to the mechanisms of esophageal protection; (2) clinical trials of drugs based on hyaluronic acid and chondroitin sulfate; (3) publications on the problems of NERD and refractory GERD; and (4) studies evaluating the efficacy of combination therapy with esophageal protectors in combination with PPIs. The following parameters were analyzed in these publications: (1) effect on the esophageal mucosa and severity of symptoms; (2) rate of clinical response; (3) indicators of improvement

in quality of life; and (4) safety and tolerability of therapy.

**RESULTS AND DISCUSSION**

To understand the problem, we need to recall modern concepts about the pathogenesis of GERD. Traditionally, GERD was considered an acid-related disease caused by pathological gastroesophageal reflux. However, modern research has shown that the severity of symptoms is determined not only by the level of acid aggression but also by the condition of the esophageal mucosal barrier [10].

Patients with NERD exhibit dilated intercellular spaces with defective tight junctions between epithelial cells, increased permeability of the esophageal mucosa, and activation of inflammatory mechanisms [11]. These changes lead to increased sensitivity of sensory nerve endings and the development of clinical symptoms even with moderate acid exposure.

This is why the sole use of acid-suppressant therapy, particularly PPIs, does not always provide sufficient effectiveness. Therefore, there was a need to develop drugs that could restore the protective properties of the esophageal mucosa.

Alfasoxx is a combination drug containing hyaluronic acid and chondroitin sulfate, incorporated into a bioadhesive base (Poloxamer 407). Hyaluronic acid is involved in tissue repair processes, promotes epithelial cell migration, and accelerates the healing of damaged mucous membranes [12]. Chondroitin sulfate has cytoprotective and anti-inflammatory properties and inhibits the damaging effects of pepsin [13].The bioadhesive base (matrix) ensures long-term contact of the active components with the esophageal mucosa, forming a mechanical barrier against the aggressive effects of refluxate [14]. Experimental studies have shown that esophageal protective drugs reduce epithelial permeability and prevent damage to the mucous membrane under the influence of hydrochloric acid and pepsin [15].

One of the first clinical trials to examine the effectiveness of a combination of hyaluronic acid and chondroitin sulfate was a randomized, double-blind, placebo-controlled study by B. Palmieri et al. [16]. This combination therapy was shown to significantly reduce the severity of heartburn and the degree of regurgitation in patients with NERD.

Later, V. Savarino et al. conducted a multicenter study involving 154 patients with NERD [17]. The addition of a combined esophageal protector to PPI therapy provided a more pronounced reduction in symptoms compared to PPI monotherapy. Particularly important was the rapid onset of clinical effect and improvement in patients' quality of life.

According to current data and concepts, disruption of the esophageal mucosal barrier and visceral hypersensitivity significantly contribute to the pathogenesis of NERD. Therefore, the use of esophageal protective agents is considered one of the most promising treatment options for this form of the disease.

The problem of refractory GERD remains relevant despite the widespread use of PPIs in gastroenterological practice. According to various studies, up to 40% of patients continue to experience symptoms despite standard acid-suppressive therapy [18]. Reasons for the insufficient effectiveness of PPIs may include: (1) weakly acidic or alkaline reflux; (2) impaired esophageal motility; (3) increased mucosal sensitivity; and (4) impaired mucosal and epithelial barriers.

In such cases, the use of esophageal protectors, in particular Alfasoxx, allows for the impact on additional links in the pathogenesis of the disease, reducing the contact of aggressive components of the refluxate with the esophageal mucosa, which helps reduce the severity of inflammation and epithelial reparation.

Modern reviews highlight the stated advantages of combination therapy with PPIs in combination with esophageal protectors in patients with NERD and GERD and incomplete response to acid-suppressive treatment [19].

Of particular interest is the potential use of Alfasoxx for the treatment of extraesophageal symptoms of reflux-associated disease. These include chronic cough, laryngitis, hoarseness, a feeling of a lump in the throat and other ENT symptoms.

A study by G. Pellegatta et al. showed that the combined use of PPIs in combination with hyaluronic acid and chondroitin sulfate helps to reduce the severity of extraesophageal symptoms of GERD [20]. The mechanism of this effect is likely associated with a reduction in damage to the mucous membrane of the upper gastrointestinal tract and a decrease in the inflammatory response.

One of the advantages of Alfasoxx is its high safety profile. Since the drug acts primarily locally, the risk of systemic side effects is minimal. In clinical trials, serious adverse events were observed extremely rarely [16, 17].

This is particularly important in the context of growing concerns about long-term use of PPIs, which may be associated with a small but still increased risk of intestinal infections, hypomagnesemia, bone metabolism disorders and other complications [21].

In recent years, the concept of mucoprotective therapy has been actively developing, supplemented by increasingly new clinical trial results. Data from large studies indicate that restoring the mucosal barrier may become a key treatment option for acid-related diseases [22].

Therefore, esophageal protectors can potentially be used: (1) in NERD; (2) in refractory GERD as an adjunct to PPIs; (3) in extraesophageal manifestations of reflux-associated disease; and (4) after endoscopic interventions on the esophagus.

Further large randomized studies are needed to evaluate the long-term effectiveness of esophageal protectors and to develop optimal treatment regimens using these drugs, and in particular, Alfasoxx.

**CONCLUSION**

Current understanding of the pathogenesis of GERD indicates a significant role for impaired esophageal mucosal barrier function in the development of this disease and its complications. Therefore, esophageal protective therapy is becoming increasingly important in gastroenterological practice.

Alfasoxx is a combination mucoprotective therapy that includes hyaluronic acid, chondroitin sulfate, and a bioadhesive matrix, thereby combining the clinically significant properties and benefits of these components. The drug promotes the protection and restoration of the

esophageal mucosa, reduces the severity of reflux symptoms, and enhances the effectiveness of standard PPI therapy.

The most promising applications of Alfasoxx appear to be in patients with non-esophageal reflux disease (NERD), as well as those with partial resistance to PPIs and extraesophageal manifestations of GERD. This combination treatment regimen, aimed at both reducing acid aggression and restoring the esophageal mucosal barrier, is consistent with the latest understanding of the pathogenesis of reflux disease.

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