



## ASSESSMENT OF CLINICAL SIGNS OF XEROSTOMIA IN PATIENTS WITH DISEASES OF THE CARDIOVASCULAR SYSTEM CAUSED BY TAKING MEDICATIONS

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<https://doi.org/10.5281/zenodo.15647871>

### ARTICLE INFO

Received: 06<sup>th</sup> June 2025

Accepted: 11<sup>st</sup> June 2025

Online: 12<sup>nd</sup> June 2025

### KEYWORDS

*Xerostomia, clinical manifestations, cardiovascular diseases, medications, salivation.*

### ABSTRACT

*Xerostomia, or dry mouth, is a common and often underestimated clinical condition that can significantly impair patients' quality of life. This condition can be associated with various diseases, as well as with the negative effects of medications used to treat them. This is especially important for patients with diseases of the cardiovascular system, as many of them receive medications that can cause changes in salivation. Symptoms of xerostomia include discomfort, difficulty swallowing and speaking, and an increased risk of dental disease. Despite the significant impact of xerostomia on the health of patients, the issues of its assessment and management remain insufficiently investigated.*

**Introduction:** As you know, the number of people taking the drug is constantly increasing all over the world. At the same time, the drugs they use for the prevention or treatment of various diseases can cause the development of adverse drug reactions. It is possible that the quantity and quality of medicines prescribed by a doctor or independently taken by a patient affects the state of oral health, which means that a dentist should pay great attention to the possible effects of pharmacological drugs in the diagnosis of inflammatory diseases of the mucous membrane, periodontal tissues and other changes in the oral cavity of questionable origin. The presence and severity of undesirable drug manifestations in the oral cavity and its diverse clinical picture are determined by both the individual characteristics of the patient and the effects of medications. A wide range of medications can lead to xerostomia. According to numerous researchers [Navazesh M, Kumar SK, 2009; Villa A, Abati S., 2011] medications can cause complications such as dry mouth, taste changes, dysphagia, speech disorders, dental caries, and susceptibility to infections (for example, candidiasis and sialoadenitis). At the same time, drug-induced xerostomia is a reversible phenomenon, and discontinuation of medication can lead to normalization of salivary gland function. In addition to hyposalivation (xerostomia), hypersalivation (ptyalism or sialorrhea) may occur, in which the amount of saliva released in the oral cavity increases [Gorobets S. M., Romanenko I. G., Jerelei A. A. et al., 2018]. Drugs that usually induce this condition are: antihypertensive drugs (especially B-blockers, angiotensin converting enzyme (ACEI) inhibitors) and antiretroviral drugs. It should be noted that elderly people often take one or more medications as prescribed by a doctor. This situation requires dental practitioners to know about the dental manifestations of drug side effects. In this regard, the dentist should be familiar with the general medical history of the patient, the medications



that the patient uses, their side effects, which will help in establishing a dental diagnosis and determining a treatment plan.

**The purpose of this study** was to study the frequency of xerostomia in patients with diseases of the cardiovascular system, where these disorders are associated with the effect of medications.

**Research materials and methods.** The study was conducted in 7 women and 14 men aged respectively with a disease of the cardiovascular system. The control group consisted of 16 healthy volunteers, who were comparable in age and gender. Individuals with a burdened allergic history, who scored 2 points or more on the CAGE questionnaire, and who were constantly taking medications were excluded from the study. On the day of the study, the patients took 20 mg of propranolol and saliva was collected (3 ml) 6 hours after ingestion. Saliva samples were stored frozen at  $-20^{\circ}\text{C}$  before analysis. In each saliva portion, the propranolol concentration was determined by HPLC using our own method. Taking into account the lipophilicity of propranolol, it was extracted in 10 ml of ether from 1 ml of saliva, alkalized with 0.2 ml of 1M NaOH. The ether layer was re—extracted into 100  $\mu\text{l}$  of diluted  $\text{H}_2\text{SO}_4$  Chromatographic conditions: column 100 x 4.6 mm Separon Super C18. Eluent acetonitrile - water (70 : 30, v/v) + 0.1%L”F(N”F), pH2.5 ( $\text{H}_3\text{PO}_4$ ), flow rate 500  $\mu\text{l}/\text{min}$ , the pressure is 200 psi. UV detection at 224 nm. Individual bisoprolol solutions and an internal standard sample (BC) solution were prepared by taking an accurate sample corresponding to 10 mg of the analyte, taking into account purity, and dissolved in methanol (bisoprolol) up to a concentration of 1 mg/ml. The standard samples were stored at a temperature of  $< -65^{\circ}\text{C}$ . Working standard analyte solutions were prepared by successively diluting the initial solutions in an acetonitrile/water mixture (1/1).

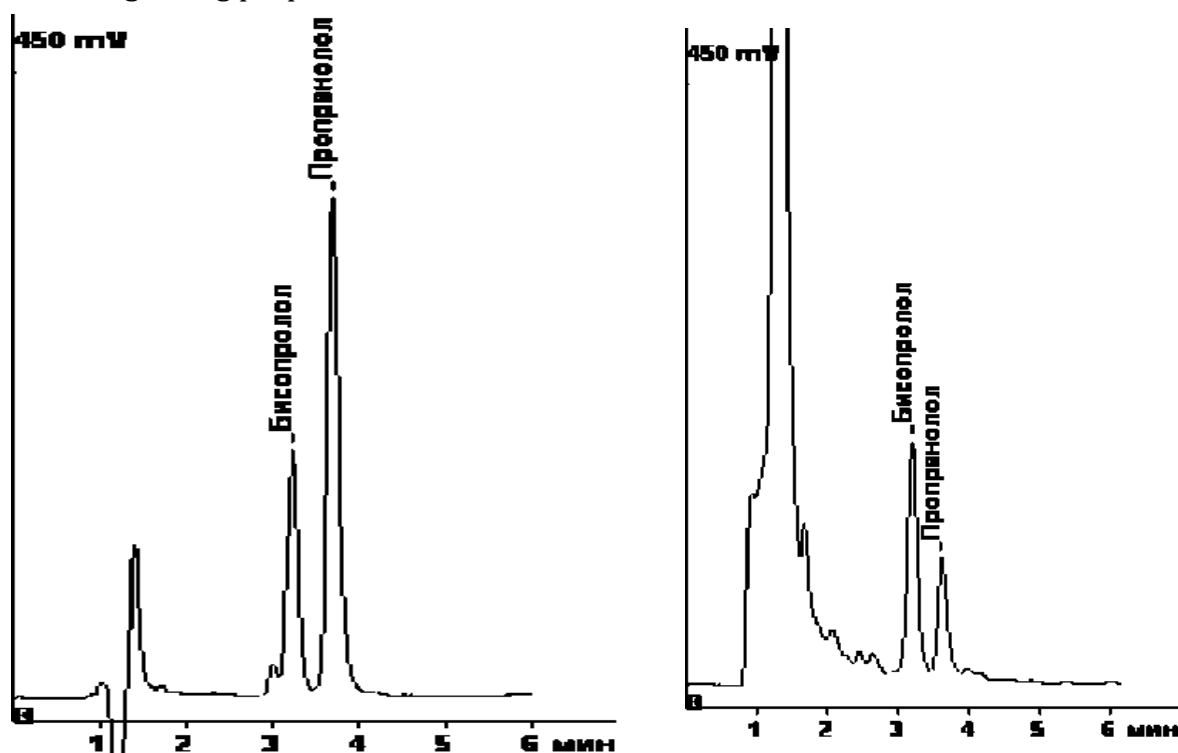
The statistical analysis was performed using the STATISTICA Soft v. 6.0 software package. Taking into account the normal distribution of data (the distribution of groups was checked by the Shapiro-Wilk criterion), when comparing groups, the Student's t-test was used for independent samples, the differences were considered significant at  $p < 0.05$ .

**Research results and their discussion.** As you know, the salivary glands are located under the control of the autonomic nervous system, so their effect is influenced by various medications. Dry mouth is a common complaint in patients treated for diseases of the cardiovascular system due to the occurrence of a large number of medications and polypragmasia. Some antihypertensive drugs cause symptoms of xerostomia without actually reducing salivation. How antihypertensive drugs actually cause xerostomia is unknown, although it is suspected that xerostomia may be associated with increased fluid content and loss of electrolytes, secondary to frequent urination [Thomson V.M., Chalmers J.M., Spencer A.J., Slade G.D., 2000]. Finally, medications can also cause salivation to decrease, causing vasoconstriction of the salivary glands. There is a strong association between dry mouth and the duration of pharmacotherapy. In our studies, the questionnaire revealed that the prevalence of xerostomia was higher among those who took antihypertensive drugs, beta blockers, or angiotensin converting enzyme inhibitors.

Based on the above, the patient was prescribed one dose of 20 mg of propranolol, and 6 hours after taking it, saliva was taken from them. It should be noted that xerostomia was higher among patients taking two or more medications than those taking only one medication. In the

oral cavity with hypertension, changes are sometimes noted that correspond to the picture of the vesicovascular syndrome. It is characterized by the appearance of hemorrhagic blisters on the mucous membrane due to its injury (abnormal bite, foreign objects, destroyed teeth, etc.). Hemorrhagic blisters are most often observed on the mucous membrane of the soft palate, the floor of the oral cavity, cheeks, less often on the mucous membrane of the gums and hard palate. The bubbles are usually single, fixed in one area. The connection of hemorrhagic blisters with vascular changes as a result of cardiovascular diseases is not excluded.

Figure.1. Chromatograms of propranolol 20 mg standards (left) and the patient 6 hours after taking 20 mg propranolol.



As is known, according to N.A.Desrosies et al., the secretion of salivary glands contains a "free" medicinal substance, and drugs that bind strongly to plasma proteins can be detected only in trace amounts. Medicinal substances enter saliva through the transport system of the salivary glands, the mucous membrane of the oral cavity, along with gum fluid. Preparations with lipophilic properties are passively secreted into saliva by cells, which depends on the degree of their dissociation and pH. By competing for the transport systems of the salivary glands, drugs can affect the formation of salivary molecules, which can lead to a change in the volume of secretions secreted.

**Conclusions:** Thus, an accurate and sensitive method for determining the concentration of bisoprolol in mixed saliva may be promising in laboratory diagnostics. This method is highly likely to be used in practical medicine to control the excretion and dosage of drugs and to study the effect of this drug on the condition of the oral mucosa. It should be noted that using this method, it is possible to observe a close relationship between the use of drugs in cardiovascular diseases, which is accompanied by various changes in the organs and tissues of the oral cavity. At the same time, the dentist should pay great attention to the possible effect of



pharmacological drugs in the diagnosis of inflammatory diseases of the mucous membrane, periodontal tissues and other changes in the oral cavity of questionable origin.

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