

Article

Creation of an antioxidant gel for the prevention of viral diseases of the oral mucosa.

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Abstract: This article examines the effects of an antioxidant gel with astaxanthin on the elements of damage to the oral mucosa caused by the herpes simplex virus. The anti-inflammatory, immunomodulatory and wound-healing effects of this drug have been noted.

Keywords: astaxanthin, herpetic stomatitis, gel, ingredients, composition

1. Introduction

Viral diseases of the oral mucous membrane is one of the most important problems in dentistry. Acute herpetic stomatitis occupies a special place in this problem, primarily because this stomatitis accounts for more than 80% of all oral mucosal diseases in children [1,3,4,5]. In addition, acute herpetic stomatitis occupies one of the leading places in the pathology of the oral mucosa, occurring more frequently than scarlet fever, measles, and only slightly inferior to chicken pox.

Recently, scientists of different specialties have come to the conclusion that the basis of many pathological processes in the body, in particular the oral cavity, leading to various diseases, is the same phenomenon. It is the damage of cell membranes and other structures inside the cell by free oxygen radicals. Depending on which structures are damaged: - The hereditary substance (DNA) or the outer membrane, either cancer develops or other disorders are observed[3]. As the body ages, free radical activity increases and the risk of various age-related diseases increases. Now that the cause of these negative changes is known, many medical centers are developing substances that can counteract the effects of free radicals. Free-radical oxidation (FRO) processes are constantly going on in cells and are necessary for the body to carry out a number of important functions, including respiration. However, in a healthy body, free-radical oxidation (FRO) processes are under the control of the antioxidant defense system (AOD), which includes an enzymatic system (superoxide dismutate, glutathione peroxidase, catalase) and bioantioxidants [2,6,7].

Herpes simplex virus is a genus of the alphaherpesvirus subfamily. It is neurotropic and neuroinvasive, which means that the virus cells migrate into the nervous system. This peculiarity allows it to establish itself in the host for the rest of its life after primary infection [1,5]. Viruses are intracellular infectious agents. Viral diseases affect cells that are already impaired, which the pathogen takes advantage of. Modern studies have proven that this only occurs when the immune system is severely weakened and is no longer able to deal with the threat at the proper level [2,6,8]. A huge role with regard to the protective function and the fight against infectious agents belongs to antioxidants. The strongest of them is natural astaxanthin [3,7].



In our study, we decided to create an antioxidant gel based on natural astaxanthin and test its effect on the lesion elements in acute herpetic stomatitis.

2. Materials and methods:

Included the development and technology of obtaining dental gel based on natural astaxanthin. In full accordance with the requirements of the State Pharmacopoeia of the Russian Federation XIII in the manufacture of prophylactic gel for the standardization of the dosage form was carried out to develop a method of quantitative determination of astaxanthin [8].

Astaxanthin is a carotenoid and belongs to the xanthophylls. The chemical name is (6S)-6-hydroxy-3-[(1E, 3E, 5E, 7E, 9E, 11E, 13E, 15E, 17E)-18-[(4S)-4-hydroxy-2,6,6-trimethyl-3-oxo-1-cyclohexenyl]-3,7,12,16-tetramethyloctadeca-1, 3, 5, 7, 9, 11, 13, 15, 17-nonaenyl]-2,4,4-trimethyl-1-trimethyl-1-cyclohexa-2-ynon. The chemical formula is C₄₀H₅₂O₄. In Fig. 1. the structural formula of astaxanthin is presented [8].

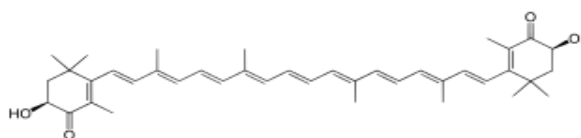


Figure 1: Structural formula of astaxanthin

We used astaxanthin obtained biotechnologically from the yeast *Xanthophyllomyces dendrorhous*. Astaxanthin was an oily liquid of bright orange color that mixes well with the hydrogel base to form a homogeneous microemulsion. Vitamin E and coenzyme Q were chosen as the main components of the prophylactic gel as gas pedals and synergists of astaxanthin.

To create a soft dosage form with astaxanthin in the form of a gel, the excipients presented in Table 1 were used.

Table 1. Composition of a soft drug formulation with astaxanthin

Component	ND	Component assignment
Carbopol	Eur.Ph.	Structure maker
Purified water	FS 42-2619-97	Solvent, the main component of the gel base dispersion medium
Triethanolamine pure	ThU 6-09-2448-86	Neutralizing agent
Nipazole	FS 42-2079-91	Conservative
Nipagin	FS 42-1460-89	Conservative

For the standardization of the gel dosage form, we carried out work to develop a method for the quantitative determination of astaxanthin, in full compliance with the requirements of State Pharmacopoeia of the Russian Federation XIII.

Carbopol, a sparsely crosslinked acrylic polymer with suitable technological characteristics, was used as structure-forming components. Gels based on sparsely crosslinked acrylic polymers are widely used in pharmacy as bases for soft dosage forms. They are white flaky hygroscopic powders of weakly acidic reaction, swelling in water and other polar solvents after dispersion, which form stable gels after neutralization with solutions of basic substances [8].

Nipagin and nipazole were selected as preservatives in the soft dosage form. Nipagin (FS 42-1460-89) is a methyl ester of para-hydroxybenzoic acid. The propyl ester of parahydroxybenzoic acid is known as nipazole (FS 42-2079-91). Nipagin and nipazole are white crystalline powders,



hardly soluble in water, soluble in oils and easily soluble in organic solvents. Nipagin has the best solubility, so it is more often used in aqueous solutions.

Purified water (FS 42-2619-97) is a colorless transparent liquid without taste or smell, used as a solvent.

The composition of the gel (N 2599026 RF MPK7A61Q11/00 "Composition for healing oral tissues") is presented in Table 2.

Table 2. Composition of dental gel based on natural astaxanthin

Name of raw material	Quantity, g
Astaxanthin	0,13-0,26
Carbopol	1,0
Triethanolamine	1,0
Propylene glycol	1,5
Nipagin	0,1
Nipazole	0,05
Purified water	until 100,0

The proposed composition differs from the analogues in the simplicity of production. The dental gel is prepared on the basis of natural astaxanthin, which is the most powerful natural antioxidant with strong anti-inflammatory, immunomodulatory and wound-healing effects. The gel is applied both by the doctor and the patient himself into the oral cavity on the elements of lesions in the mouth.

Instrumental analysis of astaxanthin substance and finished dosage form in the form of gel was performed using the following equipment: Cary 50 UV/Vis spectrophotometer, JEOLJNMECA 600 NMR spectrometer (Japan), with a working frequency for ^1H nuclei of 600 MHz. Mass spectra were recorded on an Agilent 6430 (QQQ) triple quadrupole mass spectrometer equipped with an ion source with chemical ionization at atmospheric pressure. Development of a method for quantitative determination of astaxanthin was performed using an Agilent 1290 high-performance liquid chromatograph equipped with a diode array detector.

All reagents and solvents used for qualitative and quantitative analysis were used.

The composition is prepared as follows. Preservatives (methyl and propyl esters of 4-hydroxybenzoic acid ester) are dissolved in propylene glycol. Then the carbopol gel is prepared. Small portions of carbopol are added to water, left to swell for 2-4 hours, then triethanolamine is added while stirring. A solution of preservatives is added to the carbopol gel while stirring, then the active ingredients are stirred until a homogeneous gel is obtained, including astaxanthin. Vitamin E and coenzyme Q serve as gel pedants of natural astaxanthin in the dental gel [8].

For the purposes of standardization, the use of the finished dosage form in the form of a gel seems convenient because there is no need to introduce conversion factors and allows obtaining an integral value of the quantitative content of astaxanthin when using HPLC method for its analysis [8].

Antioxidant gel with astaxanthin was given to the patient. It was applied to the mucous membrane in the area of the secondary lesion element in acute herpetic stomatitis. The patient applied the obtained gel independently, 2 times a day. It was recommended to use the preparation for 5 days. The result of the study was noticed after two days of use.

Results

The resulting invention No. 2599026 Bulletin No. 28 of 08.09.2016 belongs to medicine, namely to dentistry and can be used for the prevention and treatment of viral diseases of the mucous membranes of the mouth and lips.



The technical result of the invention is the creation of a new composition that allows to increase the effectiveness of prevention and treatment of patients with viral diseases of the oral mucosa, due to the ease of use and improvement of local immunity, without causing allergic reactions and side effects [8].

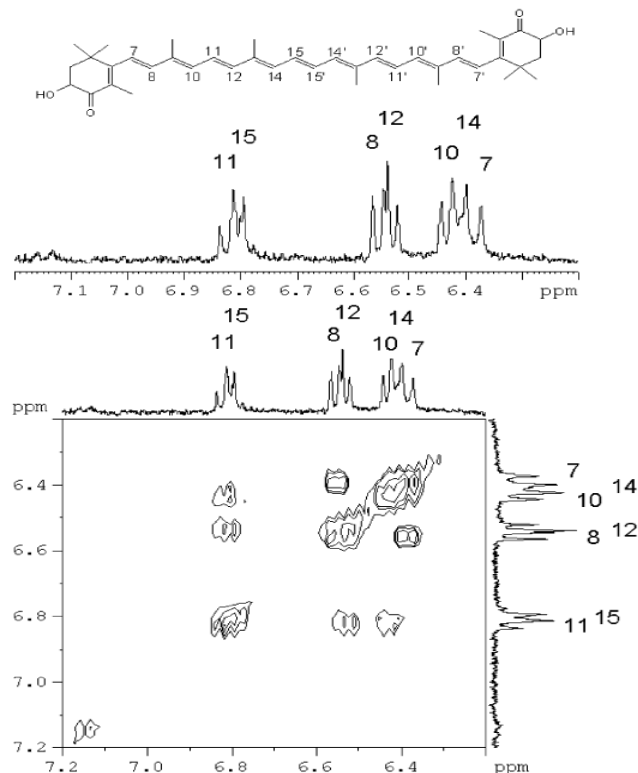


Figure 2. 1H nuclear magnetic resonance spectrum (A) and two-dimensional COSY nuclear magnetic resonance spectrum of trans-astaxanthin

The technical result is achieved by the fact that the composition for healing oral tissues contains in wt%:

Table 3: Composition of Astaxanthin Dental Gel

astaxanthin	0,12-0,26
vitamin E	1,4-2,2
coenzyme Q	0,8-1,5
propylene glycol	0,4-0,7
methyl ester of 4-hydroxybenzoic acid	0,07-0,12
propyl ester of 4-hydroxybenzoic acid	0,02-0,05
carbopol	0,4-0,7
triethanolamine	0,5-0,8
purified water	the rest

The proposed composition differs from the analogues in the simplicity of production. The dental gel is prepared on the basis of natural astaxanthin, which is the most powerful natural antioxidant with strong anti-inflammatory, immunomodulatory and wound-healing effects. The gel is applied both by the doctor and the patient himself into the oral cavity on the elements of lesions in the mouth. The composition of the gel does not cause unpleasant sensations - neither mechanical nor gustatory [8].



3. Conclusion:

The prepared antioxidant gel with astaxanthin has a powerful antioxidant, wound healing effect.

The developed gel belongs to the innovative development, as innovation is an implemented innovation that provides a qualitative increase in the efficiency of processes or products, demanded by the market.

Conflicts of Interest: The authors declare no conflict of interest

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