RESEARCH HYALURONIC ACID COMPLEXATION WITH BIOACTIVE METAL IONS

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Abstract: The paper contains some results for obtaining complex salts (associates) of some 3d-metal ions (Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}) with hyaluronic acid (HA) or sodium salt HA, which can be used in pharmaceutical, cosmetic, and food industry. Substances were studied by IR spectroscopy.
Keywords: hyaluronic acid, complex compounds, bioactive metal ions, importance

1. Introduction

Ever-increasing demands of hyaluronic acid (HA) for pharmaceutical, cosmetic and food industry imposes researches to study and investigate its properties; seek local sources of hyaluronic acid; develop cost-effective methods of production of hyaluronic acid; search new chemical derivatives, medicinal and cosmetic preparations on its base.

Hyaluronic acid gaining more and more popularity in medicine and cosmetics. Many cosmetic products contain hyaluronic acid, due to its ability to moisturize and smooth the skin. Clinical studies show that hyaluronic acid speeds healing of wounds and promotes the disappearance of old and new scars. Hyaluronic acid injections do less visible wrinkles and blemishes caused by acne or injuries.

One of the important properties of HA is that its macromolecules can be conjugated with bioactive compounds for pharmaceutical industry. So, hyaluronic acid can be a vehicle for topical medicines, which drives their absorption. Interesting properties have sodium, potassium, iron, zinc, copper and other salts of HA, which are successfully used in cosmetic and pharmaceutical industry.

2. The properties of hyaluronic acid and its complex – compounds with metal ions

Hyaluronic acid was discovered about 70 years ago in vitreous of bovine eyes. It is a natural biopolymer, class proteoglycans, whose molecule is formed from the remains of β-D-glucuronic acid and N-acetyl-β-D-glucosamine linked by β-glucosidic bonds (1–3) - and β-(1–4), the long unbranched chains (Fig.1.) [1].

From the primary structure of the macromolecule it can be seen that HA has a repetable disaccharide unit in which glucuronic acid is linked to glucosamine with β-glycosidic link between atoms C_1 and C_3, respectively. Basic structural unit is repeated in macromolecular chain is a very rigid chain segment with a length of 11.98 Å. Spatial distribution of anionic groups and their degree of ionization contribute to the conformation of the molecule due to mutual electrostatic rejection of negative duties along the polysaccharide backbone. Tertiary structure of HA in concentrated solutions, gels and solid, is influenced by the large number of hydrogen bonds inter- and intramolecular polar groups of abundant, such as: –OH, –COC–, >C=O, –NH–, –COO–. Structure can be influenced also by hydrophobic interactions of protein fragments. The degree of polymerization and molecular weight varies by tissue type.

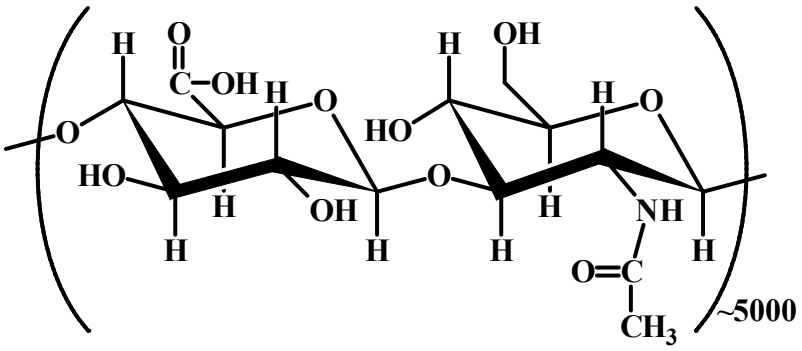

Fig. 1. Structure of hyaluronic acid

HA content in the human body is an important factor on which the physiological process of aging and immunity of the body depends upon. To strengthen the immune system and prevent various diseases including cancer various "food additives" are prepared in which HA is used as an ingredient or as compound. HA is called "star" of cosmetology, "hope" of rejuvenation and "pledge" of beauty. Benefits of HA supplementation – Cosmetic effect: skin hydration from the inside out, correcting in this way wrinkles. – Anti-arthritic: lubricate joints, especially knees and hips ones. – Rejuvenate, anti-aging effect: for men and women between 30 and 40 who are beginning to see signs of aging mirror. The effects are felt quickly after first supplementation with hyaluronic acid.

HA is present in all tissues of the body and performs several important functions. HA is involved in the transfer of nutrients into cells and in the removing toxins from the cells. Important role in the detoxification of the body belongs to d-metal ions, such as Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Mn^{2+}, Zn^{2+} participating in the various enzymes. To ensure the cells micronutrients are necessary such forms of transport, which prevent non-specific absorption of ions of these elements and selectively forward them to the cells. A mode of transport is hyaluronic acid, which easily penetrates into the cell by endocytosis.

Interesting properties complex-compounds of hyaluronic acid with d-metal ions are described in the paper [2, 3].

3. Complexation of some 3d-metal ions with hyaluronic acid

Complexes of hyaluronic acid (HA) with some d-metals increases resistance to chemical irritants and toxins. Moreover, in case of intoxications with heavy metals, the use of HA will facilitate the removal of these metals from the body, due to its ability to bind the metals in stable complexes. This causes a high interest in the study and use such complexes.

In this paper we investigate the complexation of HA with ions of some 3d-metals, such as Co^{2+}, Cu^{2+}, Fe^{2+}, Fe^{3+}. HA for the study was extracted from rooster combs [4]. Complexes were formed with 1N solutions of chlorides respective metals and 1% solutions of HA. The reaction products were washed with water, then with 96% ethanol and dried.

The compounds were studied by IR spectral analysis (Fig. 2).

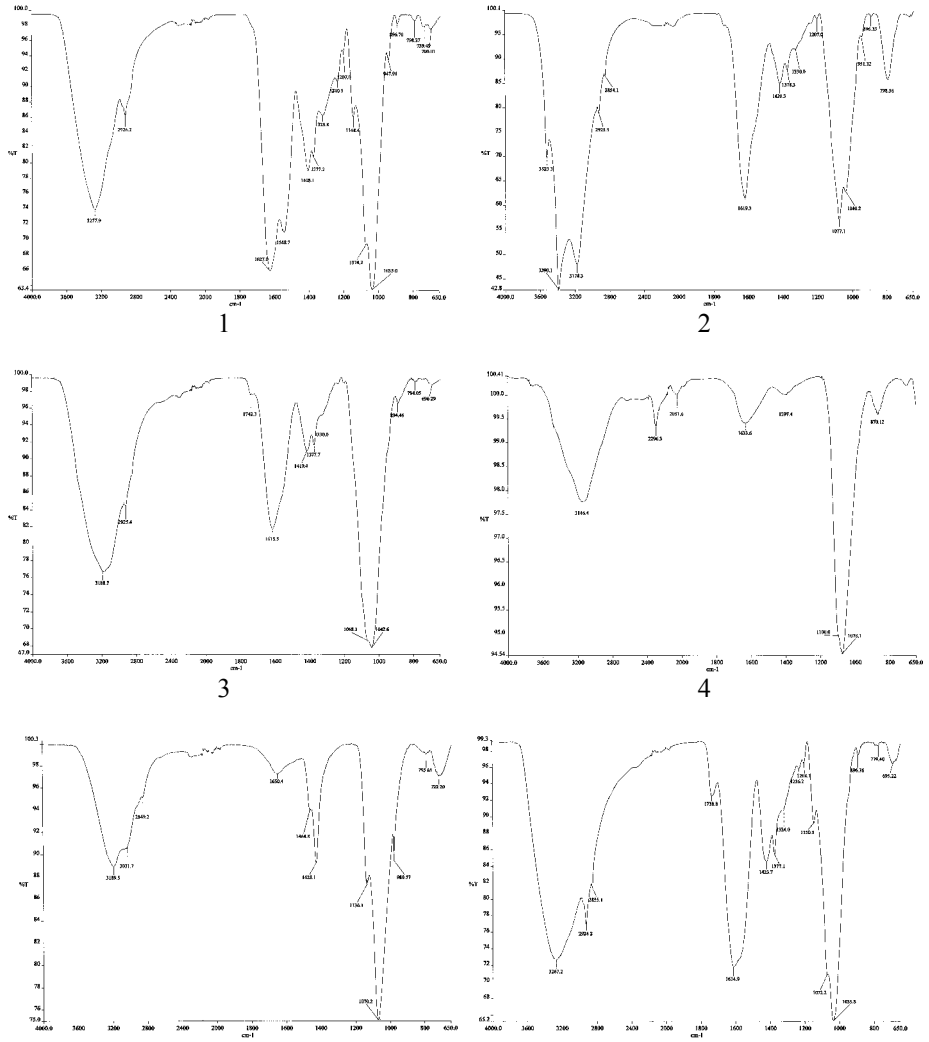

Fig. 2. IR spectra of HA (1) and associates of HA: with Co^{2+} (2), with Cu^{2+} (3), with Cu^{2+}(it never was washed with ethanol) (4), with Fe^{2+} (5), with Fe^{3+} (6).

IR spectra of hyaluronic acid and its associates with the metal ions show that the formation of associates accompanied by a shift of the absorption bands in the region 1740-900 cm^{-1}. This suggests that the formation of associates is due to the interaction of metal ions with electron donor atoms (O, N) of hyaluronic acid.

According to IR spectroscopy of the products, the ions Cu^{2+} and Fe^{2+} form stable complexes with the amide and the carboxylic group, whereas Fe^{3+}, Co^{2+} form less stable complexes.

The study of complex HA with metal ions continues.

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