

SOME ASPECTS OF RATIONAL UTILIZATION OF ANIMAL RAW MATERIALS FOR MEDICINAL PREPARATIONS PRODUCTION

R.V. ILUKHINA, E.Yu. KULIKOVA, I.P. NEMCHINOVA, L.A. MINOSYAN, I.V. ISAYEVA, N.P. LARIONOV
All-Russian Meat Research Institute, Talalikhina 26, 109316 Moscow, Russia

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Introduction: The existing drugs for atherosclerosis treatment are not efficient: they are able to remove only about 30% of lipids from the organism, and side effects are possible (creation of choleliths, deterioration of vision). In connection with this, there is a need in medicinal preparation that has no effect on coagulation system of blood, but maintains antilipemic effect. The substances, similar to heparin, a high molecular sulfopolysaccharide, to which the activator of lipoproteidlipase belongs, have such effect. The raw materials used for the production of the preparation contributing to lipids isolation and decrease of the level of cholesterol, were duodenums of pigs, having a complex of biologically active substances, which previously had not been used for the production of medicinal preparations.

Experimental procedure: Properties of duodenums of pigs and a preparation - activator of lipoproteidlipase - which was named "aliprol", were studied using a number of indices, as well as the methods, used in biological, organic chemistry, microbiology and toxicology. Appearance, solubility, mass fraction of moisture, ash, sulfur, pH value were determined using the methods of State Pharmacopoeia. Anticoagulant activity of aliprol and heparin were determined by their ability to delay coagulation of citrate bovine or lamb plasma, as induced by calcium chloride. Specific optical rotation of aliprol and heparin were measured by the value of angle of rotation of 4% solution of substance in water on polarimeter of type "POLATAT". Molecular mass was determined by gel-filtration method. Calibration of columns was carried out using standard compounds. The structure - by IR-spectrophotometry at IR-spectrophotometer 180 "PERKIN-ELMER" in a tablet of potassium bromide.

Results: At initial stage we worked at procedures of collection, processing and preservation of duodenums of pigs. The duodenums were collected after evisceration of the carcasses. Intestines with the length 40-50 cm were removed from pyloric part of stomach. By light pressing their content was displaced and external fat separated. In connection with quality certification of the products, the investigations have shown that the content of heavy metals and arsenic (lead - 0.01 mg/kg, cadmium 0.03 mg/kg, mercury 0.01 mg/kg, copper - 1.02 mg/kg, zinc 13.98 mg/kg, arsenic < 0.1 mg/kg) were not greater than the critical values. Sulphate ash characterizing the extent of contamination of materials did not exceed 2.0%. The collected raw materials were preserved by two methods: by freezing at not higher than -20°C and by drying in a sublimator up to the temperature not higher than 35°C . The intestines met standards by their organoleptical and physical and chemical indices (Table 1). Based on the developed processing technology involving such stages as dewatering, extraction, heating, separation of cake, treating with proteases, concentration of solution, precipitation of heparinoide, drying of the sediment, a substance of aliprol is obtained. The quality of obtained lots of aliprol substance was determined according to established requirements (Table 2). The substance of aliprol, as produced under production conditions completely meets the established requirements including microbiological ones. The substance of aliprol is heparinoid and contains glycosaminoglycans (acid mucopolysaccharides), as a main pharmaceutical active component. By its structure, aliprol is similar to heparin, which is obtained from mucous membrane of small intestines. The comparative characteristics of composition and properties of heparin and aliprol, as obtained by us are presented in Table 3.

Table 1

Parameters	Characteristics of duodenums of pigs	
	Frozen	Dried
Appearance	Frozen slabs, not over 5.0 cm thick	Dried brittle slabs or their parts
Colour	Brown with yellowish-grey tint	Slightly grey with yellowish tint
Odour	Specific without putrefactive	Specific without putrefactive
Internal temperature of slab, °C, not over	-20	-
Mass fraction of fat, %, not more	-	12.0

Table 2

Parameters	Quality characteristics of preparation	
	Established requirements	Substance of aliprol
Description	Yellowish to grevish or grey to yellowish powder	Grey to yellowish powder
Solubility	Practically non soluble in water, ether, chloroform	Practically non soluble in water, ether, chloroform
Weight loss during drying, %	Not over 25%	18.0
pH value	6.5-8.0	7.6
Toxicity test	Non toxic	Non toxic
Authenticity:		
Mass fraction of hexosamine, %	Not below 8.0	14.8
Total nitrogen, %	Not over 8.0	6.2
Sulphate ash, %	Not over 23.0	17.3
Heavy metals, mg/kg	None	None

Table 3

Compared parameters	Composition and properties	
	aliprol	heparin
Mass fraction of sulfur, %	0.2-0.4	10.0-12.0
Mass fraction of uronic acids, %	1.0-2.0	40.0-70.0
Mass fraction of hexosamine, %	10.0-20.0	not below 20.0
Mass fraction of nitrogen, %	5.0-7.6	2.0-3.0
Specific rotation (+ or -)	minus	+48.0+52.0
Anticoagulant activity, Units/mg	10.0-12.0	150.0-185.0
Average molecular mass, thous. Dalton	about 100	30.0-40.0

The results have shown discrepancies in some parameters. In samples of heparin molecular mass is lower, and anticoagulant activity and sulfur content is higher, than in samples of aliprol.

Discussion: It is known from literature that relative amount of uronic acids and a degree of sulfation are important for anticoagulant activity. A direct proportional relationship is between sulfur content and anticoagulant activity. An increase in sulfur content up to 12.6% in heparin from mucose results in increase of anticoagulant activity (activity 173 Units/mg - sulfur content is 10.2%, respectively, 185 Units/mg - 12.2%). Thus, the heparinoid, which was obtained by us, did not contain sufficient amount of main functional groups to show anticoagulant activity. Infrared spectroscopy method allowed us to identify the substance of aliprol from other glycosaminoglycanes - heparin, chondroitinsulfate, hyaluronic acid, as well as assess the degree of purity of aliprol samples.

Conclusions: Raw materials for aliprol production don't contain heavy metals. An original technology for production of the preparation substance, having antiatherosclerotic action from meat by-products, which previously had not been used, was developed. Physical and chemical properties of the compared preparations have shown, that aliprol doesn't contain sufficient amounts of main functional groups, which are responsible for anticoagulant activity.

The substance of aliprol is safe and non toxic.

Reference: Bartkova L.K., Isayeva I.V. Development of method of quantitative determination of glicosaminoglycanes (mucopolysaccharides) in glandular preparations. In: Rational utilization of endocrine and enzyme materials for medicinal purposes. VNIIMP, M. 1986