

PRODUCTION OF HIGH QUALITY SODIUM IODIDE PREPARATIONS LABELLED WITH CARRIER FREE IODINE-125

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Work is related to the problem of high-quality Sodium ^{125}I /Iodide preparation production and to the choice of the peptides iodination methods with the purpose of control test developing to determine the biological activity of the above mentioned preparation.

The achievements in modern biochemistry became possible due to development and improvement of analytical methods including radioimmunoassay methods. It allows to determine quickly and reliable the content of hormone, enzymes, protein receptors and other components in biological liquids. The specific biological objects labeled with Iodine-125 isotope are used in the base of the methods. Biological objects (mainly peptides) labeled with Iodine-125 are widely used in the other spheres as well. The mechanisms of Iodine-125 isotope entering into peptides molecules had being researched during many years. However some aspects of the problem are undecided.

One of the main criteria of successful iodination is the availability of high-quality preparation of iodine-125 isotope. The preparation should satisfy to the following conditions: high (up to theoretical) specific radioactivity; low (not more than the thousandth part of percent) contents of isotopes with hard radiation (mainly it is Iodine-126 isotope); high (not less than ninety nine percent) contents of main compound (radiochemical purity); pH value preventing the iodide conversion into the free Iodine and together with that leaving possibility of its reducing to the value that is required for the iodination reactions performance (within the range from 8,0 to 10,0 usually); the absence of inhibitors of electrophilic substituting reaction in the preparations as well.

High specific radioactivity is especially important for the iodination of small peptides, which as a rule have one (rarely two or three) point for Iodine-125 isotope introducing. By using preparation with low specific radioactivity they can be occupied by inactive Iodine what causes the decreasing of quantitative yield of the labeled peptide. Low contents of the isotopes with hard radioations is necessary at iodination of biological objects that are sensitive to the action of hard radiation (enzymes, hormones, antibodies and ets.) Radiochemical purity of Iodine-125 preparation is also the important factor by the reason that only Iodide ions are activated by means of activating agents. They are able to enter into electrophilic substitution reaction. The Iodate-ions present mostly in preparation with low radiochemical purity and they do not enter into electrophilic substitution reaction. By this reason the radiochemical purity of Iodine-125

preparation also greatly affects on quantitative yield of iodinated objects. pH value of the reaction solution has the main role at iodination of peptides and some other objects often. So as just at definite pH values the peptide has spatially available groups for electrophilic substitution reaction. pH value of ambiances is very important at processing of enzymatic iodination when some enzymes are used as catalisator. Usually the iodination of peptides is effected at pH 7.5.

High specific radioactivity, low contents of isotopes with hard radiation and the absence of the inhibitors are achieved by means of performance of the technology process. Sodium Iodide labeled with Iodine-125 isotope production is based on the reactions :



As it is seen from reaction some part of Iodine-125 after dissolving should be the form of iodate. It was supposed before that the preparations mature during several days is reducing the Iodate ions contents to the acceptable level. Nevertheless the practice has shown that it does not always happen.

The range of experiments have been effected to study the influence of high temperature on velocity and completeness of iodate-ions into iodide ions conversion. By the experiments had been shown that optimal themperature of heating is 105-110°C and time of heating in the range 85-90 minutes. More long heating and further increasing of temperature are not desirable because the influence of alkali on the vial's glass can affect on quality of preparation.

Iodine-125 preparations keeping at air admission decreases its radiochemical purity. Method can be used for increasing of radiochemical purity of such preparations up to acceptable level and restoration of their efficiency.

At present time there are many different ways of the Iodine-125 isotope entering into molecules of proteins and peptides. For creation of control system for biological activity of Iodine-125 preparations it is necessary to choose those methods which could allow to work with small amounts of Iodine-125 and could be reliable and simple in performance and could be compared with the results of iodination in research works and in wide range of iodining objects as well.

Three methods were chosen: a) entering of Iodine-125 isotope in the molecule of Adrenocorticotrophic hormone by activation of Iodine-125 by means of Chloramine-T with the following reaction of electrophilic substitution in the Tyrosine aminoacid residue; b) entering of Iodine-125 isotope into the molecule of Adrenocorticotrophic hormone by means of enzymetic reaction by meands of Lactoperoxidase at the presence of Hydrogene Peroxide traces; c) entering of Iodine-125 isotope into the molecule of Bolton-Hunter reagent with the use of Chloramine-T as an activator as well.

As the object for determination of biological activity of Iodine-125 preparations Adrenocorticotrophic hormone has a range of advantage: absence of spatial difficulties at iodination, presence of the unique Tyrosine residue, simplicity and reliability of iodination method.

As already had been noted a lot of biological objects are very sensitive to the action of oxides. By this reason the method of conjugation is used for their iodination. For estimation of the quality of Iodine-125 isotope the entering into the molecule of

Adrenocorticotrophic hormone by means of Lactoperoxidase reaction is used at the presence of Hydrogene Peroxide traces.

The Bolton-Hunter reagent (ether of N-hydroxysuccinimide and 3-(p-Hydroxyphenyl)-propionic Acid) is used for entering of Iodine-125 isotope into molecules of peptides by the method of conjugation after intermediate entering of the label into the molecule of peptides by labeled organic molecule that is able to join to the N-end of protein to be iodinated. One of the most important stages of this method is iodination of the Bolton-Hunter reagent. By this reason it is important to estimate incorporation of Iodine-125 isotope into this reagent. Simple structure and presence of one phenoxy-group at a correctly created conditions of iodination allow to determine efficiency of Iodine-125 preparation very exactly.

Biological activity for high-quality Iodine-125 preparations (as I-125 incorporation into above mentioned acceptors) is usually not less than 85% for all three methods of the control.