BIOTECHNOLOGICAL METHOD OF OBTAINING HYALURONIC ACID USING RECOMBINANT MICROORGANISMS

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Hyaluronic acid is a naturally occurring linear glycosaminoglycan consisting of repeating disaccharides of glucuronic acid and N-acetylglucosamine, with unique biological and physicochemical properties. It is present in living organisms, in connective tissues such as skin and cartilage, in the umbilical cord, vitreous humor, synovial fluid and skin [1]. Hyaluronan has good biocompatibility and does not cause a reaction to a foreign body or an allergic reaction during implantation, which allows it to be used in medicine and cosmetology.

Biotechnological method of obtaining hyaluronic acid is the most promising, it is based on the cultivation of microorganisms-producers of hyaluronate. The creation of recombinant systems in various microorganisms to obtain hyaluronic acid, allows the study of enzymes. The main producers are microorganisms of the genus *Streptococcus*, as well as genetically engineered strains of *Bacillus subtilis* and *Escherichia coli*. Literary sources were reviewed to describe the complete manufacturing process.

The species of microorganism-producer *Streptococcus equi* BP-879 was selected. This microorganism is subjected to aerobic fermentation on a nutrient medium, which contains mineral salts with the addition of bacteriolytic enzyme, sources of nitrogen and carbon, surfactants, also not a significant amount of cattle blood. The fermentation process takes place 24-48 hours, at a temperature of 25-40 °C and pH 6.5-8.0. Subsequently, the obtained biomass is centrifuged and chromatographic purification of the target product on ion exchange resins. At the end of the process, pure hyaluronic acid is obtained by molecular weight $0{,}6\times10^6$ Da, protein content of 0.5% and a viscosity of 12-17.3 dl/g [2].

The obtained microorganisms for the manufacture are highly compatible with the human body, because the structure of hyaluronan is preserved among different species. This method of obtaining hyaluronic acid is promising because it does not require purification of proteins and related glycosaminoglycans, and the characteristics are fully consistent with the product synthesized by human.

References:

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