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Tandem Redox Agent Method Useful for Improving Proinsulin-S-sulfonate Folding Yield

A new method using synergistic folding agents significantly increases the production yield of correctly folded proinsulin, offering substantial cost savings for industrial-scale insulin manufacturing.

Insulin is a therapeutic protein that is produced to treat diabetes mellitus. In 2011, global insulin sales reached $16.7 billion, with a large part being produced in E. coli. In such systems, insulin is expressed as the precursor proinsulin and stored in the E. coli cells as inclusion bodies. To produce insulin, the inclusion bodies must be isolated, denatured, undergo sulfitolysis, and be refolded to form proinsulin. During the in vitro folding of Methionine-Arginine Lyspro-Proinsulin-S-sulfonate (MR-KPB-hPSS), a significant fraction of the folding intermediates aggregate through intermolecular disulfide bond formation, resulting in a yield loss near 40 percent. Therefore, reducing aggregation during in vitro folding can increase the production yield of insulin.

Researchers at Purdue University have developed a new method using two synergistic folding agents in tandem to convert MR-KPB-hPSS to correctly folded Methionine-Arginine-Lyspro-Proinsulin with an average folding yield of approximately 72 percent. This method uses redox agents in tandem to simultaneously refold MR-KPB-hPSS and reduce aggregation. If purchased at $749/100g, the additional cost to the insulin production process is $1.48 per gram. With the per-unit cost to produce insulin estimated at $50 to $75 per gram, the additional cost to this process is largely offset by the increase in yield. Thus, the proposed changes to conventional proinsulin folding methods can result in significant cost savings for industrial scale insulin manufacturing.

Advantages:

-Average folding yield increased from 53 percent to over 73 percent

-Significant cost savings for industrial-scale insulin manufacturing

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-Pharmaceutical Industry

-Medical/Healthcare

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