

OPTIMIZATION OF GLUTATHIONE BIOSYNTHESIS IN YEAST: TOWARD EFFICIENT BIOTECHNOLOGICAL PRODUCTION OF ANTIOXIDANTS

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Cell protection against reactive oxygen species is ensured by antioxidant molecules, among which the key compound is reduced glutathione (GSH). It is the most abundant non-protein thiol in cells, with a concentration of about 15 mM. Approximately 99% of it exists in the reduced form, while only about 1% is present as oxidized glutathione [1].

GSH is a tripeptide composed of glycine, cysteine, and glutamic acid. It performs essential functions in the body, including maintaining redox homeostasis, neutralizing oxidative stress, participating in the metabolic detoxification of xenobiotics and endogenous compounds, and regulating immune responses. Impaired GSH metabolism can lead to the development of central nervous system disorders, infections, sarcopenia, chronic liver pathologies, as well as metabolic, cardiovascular, and pulmonary diseases. The growing prevalence of such disorders highlights the scientific and industrial interest in studying and producing GSH as an important antioxidant [2].

Based on the analysis of current scientific publications, comparative evaluation of nutrient medium costs, cultivation duration and conditions, and GSH yield, the strain *Saccharomyces cerevisiae* HBSD-W08 was selected as the most economically viable option for industrial production. Compared with other studied strains, this producer exhibits a higher level of GSH biosynthesis: GSH and biomass concentrations reach 3.73 g/L and 16.7 g/L, respectively (48 hours, 30 °C, 200 rpm).

Special attention was given to optimizing the nutrient medium composition to improve the productivity of the biotechnological process. According to the results, the optimized medium for inoculum accumulation (g/L) includes: glucose – 34.0; peptone – 2.5; MgSO₄ – 10.0; (NH₄)₂SO₄ – 10.0; KH₂PO₄ – 0.13. At the production stage, it is advisable to additionally add glutamic acid (0.10 g/L) as a direct precursor of GSH biosynthesis [3]. Although *S. cerevisiae* is a facultative anaerobe, aerobic conditions are required during microbial synthesis. The presence of oxygen promotes more intensive biomass growth and enhances GSH biosynthesis efficiency.

Since the nutrient medium contains magnesium and phosphorus salts, their interaction may lead to the formation of insoluble precipitates. Auxiliary processes include the preparation of appropriate titration agents (hydrochloric acid and sodium hydroxide) to adjust pH during sterilization of the salt composition and subsequently restore it to the optimal level for producer growth – pH 6.0. The use of concentrated (15%) solutions prevents excessive dilution of the medium. The *S. cerevisiae* HBSD-W08 strain effectively performs GSH biosynthesis, underscoring the potential of producing a dietary supplement capable of supplying the body with sufficient amounts of this vital antioxidant.

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