

**Evaluation of the estimation capability of response surface methodology and artificial neural network for the optimization of bacteriocin-like inhibitory substances production by *Lactococcus lactis* Gh1**

**ABSTRACT**

Bacteriocin-like inhibitory substances (BLIS) produced by *Lactococcus lactis* Gh1 had shown antimicrobial activity against *Listeria monocytogenes* ATCC 15313. Brain Heart Infusion (BHI) broth is used for the cultivation and enumeration of lactic acid bacteria, but there is a need to improve the current medium composition for enhancement of BLIS production, and one of the approaches is to model the optimization process and identify the most appropriate medium formulation. Response surface methodology (RSM) and artificial neural network (ANN) models were employed in this study. In medium optimization, ANN ( $R^2 = 0.98$ ) methodology provided better estimation point and data fitting as compared to RSM ( $R^2 = 0.79$ ). In ANN, the optimal medium consisted of 35.38 g/L soytone, 16 g/L fructose, 3.25 g/L sodium chloride (NaCl) and 5.40 g/L disodium phosphate ( $\text{Na}_2\text{HPO}_4$ ). BLIS production in optimal medium ( $717.13 \pm 0.76$  AU/mL) was about 1.40-fold higher than that obtained in nonoptimised ( $520.56 \pm 3.37$  AU/mL) medium. BLIS production was further improved by about 1.18 times higher in 2 L stirred tank bioreactor ( $787.40 \pm 1.30$  AU/mL) as compared to that obtained in 250 mL shake flask ( $665.28 \pm 14.22$  AU/mL) using the optimised medium.

**Keyword:** Response surface methodology; Artificial neural network; Optimization; Bacteriocin-like inhibitory substances; *Lactococcus lactis* Gh1