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Bioprospecting and rational engineering of new L-asparaginase to present a better biopharmaceutical for blood cancer treatment

Tales A Costa-Silva[1], **I M Costa**[1], **G S Agamez-Montalvo**[2], **A Pessoa**[1] and **G Monteiro**[1]
[1]University of Sao Paulo, Brazil
[2]Federal University of Ceara, Brazil

L-asparaginase (E.C.3.5.1.1) produced by bacteria is used in the treatment of acute lymphocytic leukemia (ALL). However, innumerable side effects were registered by the usage of bacterial L-ASNase during ALL treatment. Other drawbacks associated with prokaryotic L-asparaginase treatment are hypersensitivity reactions, low thermal stability, human proteases degradation and rapid clearance. Some techniques have been used to overcome these downsides such as bioprospecting eukaryotic sources or modification of commercial bacterial L-asparaginases by site-directed mutagenesis. In order to find eukaryotic sources of L-ASNase, 20 filamentous fungi were used in this study, which were isolated from the microbiome of the jellyfish Olindias sambaquiensis. Six fungi samples isolated from jellyfish tentacles (brown structures in jelly fish responsible to toxin production) showed L-asparaginase production by submerged fermentation process. The highest activity was shown by Strain OS02 with 2.7 U/g. This strain was selected for optimization of L-asparaginase production by central composite design of response surface methodology. For maximum enzyme production (11.45 U/g), the best condition was modified Czapek–Dox medium supplemented with L-asparagine and adjusted to pH 7.4 at 32.5 °C and 190 rpm. Regarding protein engineering of commercial bacterial L-asparaginases we used site-directed mutagenesis to obtain L-asparaginase protease-resistance: a new Escherichia coli L-asparaginase (EcAII) variant, triple mutant. The preliminary results showed that mutant enzyme was expressed in E. coli BL21 (DE3) and preserved original L-asparaginase activity. These L-asparaginases proteoforms may be alternative biopharmaceuticals with the potential of further improving outcome in ALL treatment.

Biography

Tales A Costa-Silva has completed his Graduation in Biological Sciences at Federal University of Alfenas, Brazil and is pursuing his PhD at Sao Paulo University, Brazil. He has experience in Microbiology, focusing on Industrial Microbiology, acting on the following subjects: Industrial Enzymology (Production, Purification, Immobilization, Characterization and Application) and Pharmaceutical Biotechnology.

talesmilleto@yahoo.com.br

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