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Enhancement of Lovastatin Production using Gamma Irradiated *Aspergillus terreus*

Thesis

Submitted to the Faculty of Science- Ain Shams University
In partial fulfillment for the Degree of Doctor of Philosophy (Ph.D.) in Science in Microbiology

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This thesis has not been previously submitted for any other universities.

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Abstract

The role of hypercholesterolemia as a risk factor for atherosclerosis, and ischemic heart disease was indicated by the clinical, epidemiologic and pathologic studies. Lovastatin ($C_{24}H_{36}O_5$) is the first compound of its kind to become available for treatment of hypercholesterolemia. The present work has been devoted to study the effect of different parameters on lovastatin production by the local isolated gamma irradiated strain of *Aspergillus terreus*, in an attempt to maximize the production, and also to develop a potential fermentation process for the production of lovastatin using ppww as cheap production medium. Response surface methodology (RSM) was employed to study the effect of culture medium on the production of lovastatin in SmF cultures by *A.terreus* S3γ8. Under response surface methodology (RSM) design, high concentration of lovastatin (540 mg/L.) was achieved at initial pH 6, incubation temperature 30 °C, agitation rate 150 rpm. 4% soluble starch and 0.3% yeast extract as carbon and nitrogen sources, respectively, after 8 days when the production medium was inoculated with 48 hr. age from 10% seed culture inoculums.

Furthermore, the results showed supplementation of amino acid methionine (0.1 g/L.) and vitamin nicotinamide

(1 mg/L.), as well as, antibiotic tetracycline (50mg/L.) to the production medium after 48 hr. of inoculation increased the yield of lovastatin to 813.66 mg/L.

Immobilized *A. terreus* S3γ8 spores in sponge cubes produced the highest amount of lovastatin reached up to 962.66 mg/L. Agro-industrial waste (potato processing wastewater, PPWW) was tested as the main culture medium for lovastatin production by this immobilized fungus under optimizing culture conditions for repeated 5 cycles. The results showed that, high amount of lovastatin production (787 mg/L.) was recorded at the second cycle.