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ORIGINAL ARTICLE

Optimization of lovastatin production from *Aspergillus fumigatus*

Foukia E. Mouafi [a], **Ghada S. Ibrahim** [a,b], **Mostafa M. Abo Elsoud** [a,*]

[a] *Microbial Biotechnology Dept., Genetic Engineering and Biotechnology Division, National Research Centre, El-Bohouth Street, Dokki, Cairo, Egypt*
[b] *King Abdulaziz university, Saudi Arabia*

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Abstract The present investigation, focused on screening of various fungal species for Lovastatin production using different agro-based wastes, also, for maximizing lovastatin productivity by isolated *Aspergillus fumigatus* using response surface methodology (RSM). The following substrates (Olive cake; Pea pods; sugarcane bagasse; wheat bran; rice hulls; beet peel; Potato peel and groundnut shells) were screened to evaluate their effectiveness for lovastatin production, using different fungal species, (*Aspergillus niger; Rhizopus oligosporus; Penicillium citrinum* and isolated *Aspergillus fumigatus*) under solid state fermentation (SSF). Wheat bran was the most suitable substrate for lovastatin production with all fungal species. Optimum conditions of lovastatin production by wheat bran have been attained efficiently by response surface methodology (RSM) using isolated *Aspergillus fumigatus* under solid state fermentation (SSF). The lovastatin yield of (3.353 mg/g DFM) was obtained at an optimum temperature of 28 °C; pH of 5.00; initial moisture content of 70% and incubation period of 12 days. This Lovastatin has the possibility to use in different therapeutic applications.

1. Introduction

Lovastatin is produced as a secondary metabolite of the polyketide pathway by various fungi including *Penicillium* spp. [5]; *Monascus* spp. [12]; *Trichoderma* spp. [4] and *Aspergillus terreus* [8]. *A. terreus* is known to be the best lovastatin-producing species [23]. Statins (e.g. lovastatin) are fungal secondary metabolites, also considered a group of medically important inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA reductase), which catalyzes the rate limiting step of cholesterol biosynthesis [19,22]. Clinically, statins are used as lipid-lowering drugs that effectively lower LDL-cholesterol levels and reduce the risk of cardiovascular events in dyslipidemic patients [3,10]. It decreases LDL level more than other cholesterol lowering drugs, [13]. Lovastatin does not only find a role as anti-cholesterol agent but also plays a key role as an anti-inflammatory agent; cancer cell apoptosis; renal function restoration; treatment for bone disorders and suppressed production of tumor necrosis factor [19]. There is also an increased interest in statins non-lipid activities such

* Corresponding author.
E-mail address: masnrc@gmail.com (M.M. Abo Elsoud).
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as, protection of host cellular damage [27]. In addition, lovastatin has been used in the biomedical applications such as treating coronary heart diseases; Alzheimer's disease [25]. For statin production an alternative strategy for submerged fermentation is the solid state fermentation process (SSF), where solid state fermentation is more advantageous, which offers a good environment for fungi to grow, therefore high mycelia density and high lovastatin production can be expected [19]. According to Pandey et al. [16] solid state fermentation is a process where a wide range of agricultural wastes can be used for growing fungal species and to minimize the overall valuable product cost. Also, it eases optimization parameters, as it involves lower media cost; stability of the product; increased yield and better substrate porosity [2,21]. The present study aims to optimize and demonstrate the effect of different factors and factor–factor interactions on Lovastatin production by isolated *Aspergillus fumigatus* using response surface methodology (RSM) under solid state fermentation.

2. Materials and methods

2.1. Organisms

Different fungal species were selected for the production of Lovastatin using solid state fermentation (*Aspergillus niger* NRRL 595; *Rhizopus oligosporus* NRRL 2710 and *Penicillium citrinum*). The three strains were purchased from NRRL: Northern Regional Research Laboratory, United States Department of Agriculture, Peoria Illinois, USA. In addition, twenty-two fungal isolates were purified from mangrove tree sediments grown along the shores of Red sea, Makadi village, Hurghada region, Egypt.

2.2. Identification of the most efficient lovastatin producer isolate

The most potent fungal strain, isolated from (mangrove trees sediments grown along shores of Red sea, Makadi village, Hurghada region, Egypt) was identified by its morphological and conidial features in the culture growth and DNA partial sequencing. DNA sequencing of the most potent fungal strain was carried out with PCR amplicon. The 28S r DNA sequence D1/D2 region was amplified by PCR from fungal genomic DNA using PCR universal primers:

DR-5′-GGTCCGTGTTTCAAGACGG-3′ and DF-5′-ACCCGCTGAACTTAAGC-3′ respectively, where it has been identified as *Aspergillus fumigatus* (Fig. 1). Identification has been performed at Macrogen Company, Korea.

2.3. Culture maintenance and inoculum preparation

Cultures of all tested fungi were maintained on potato dextrose agar (PDA) at 28 °C for 10 days. Spores that formed were then scrapped and suspended in sterile dist. Water with 0.1% (v/v) Tween 80 and vigorously shaken for 1 min, 2 mL spore suspensions were used as the inoculums for the present investigation [20].

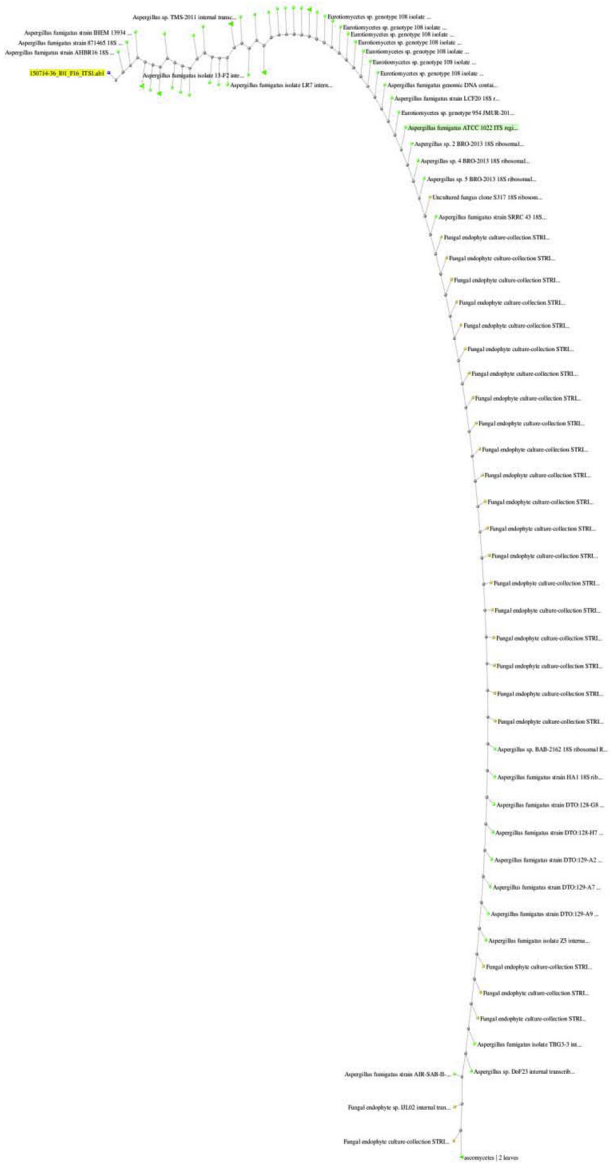

Figure 1 Screening for lovastatin production using different agro-based waste.

2.4. Culture preparations and conditions

Eight agro-wastes (Olive cake; Pea pods; sugarcane bagasse; wheat bran; rice hulls; beet peel; Potato peel and groundnut shells) were dried at 70 °C for 24 h., cooled and grounded. Ten grams of each solid substrates was taken separately in 250 mL Erlenmeyer's flasks and was moistened with distilled water containing ($MgSO4{\cdot}7H_2O$ (0.15 g/l); (NH4)2HPO4 (0.25 g/l); NaCl (1 g/l) to maintain the moisture content of 70% (v/w) [9]. Then, substrates were autoclaved at 121 °C for 20 min, cooled to room temperature and flasks were inoculated with 2 mL of fungal spore suspension. The contents in the flask were mixed thoroughly to ensure uniform distribution of the inoculum and flasks were incubated at 28 °C for 10 days [6].