Bio-synthesis and screening of nutrients for lovastatin by *Monascus* sp. under solid-state fermentation

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Abstract In this study *Monascus* strains were screened for lovastatin production. These strains namely *Monascus purpureus*, *Monascus sanguineus* and their co-culture were able to produce lovastatin in solid state fermentation. Sensitivity of lovastatin was tested on *Saccharomyces cerevaceae* and *Candida* sp. where the former exhibited large zone of inhibition as compared to the latter. Presence of lovastatin was confirmed by thin layer chromatography (TLC) and high performance liquid chromatography (HPLC). Quantification of lovastatin was done with UV spectrometer at 238 nm. Further, Plackett-Burman methodology was applied for screening of nutrients for lovastatin production. Different substrates were screened and amongst them, wheat bran was found to be the best substrate for lovastatin synthesis. Seven nutrients were screened according to the Plackett-Burman design for lovastatin yield. $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ showed the positive impact on lovastatin yield whereas lactose showed the

maximum negative effect with *M. purpureus*. For *M. sanguineus*, $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ displayed the dominant negative effect and soybean the significant positive. With co-culture, the effect of lactose was positive whereas that of malt extract was negative and dominant. The maximum lovastatin yield for *M. sanguineus*, *M. purpureus* and co-culture was estimated to be 0.402, 0.27 and 0.26 mg/g respectively.

Keywords Plackett-Burman · Co-culture · TLC · Lovastatin · *Monascus* sp

Introduction

In many countries, coronary heart disease is a common cause of death in human beings. Major reason for this disease is hypercholesterolemia, which is the accumulation of cholesterol in the blood leading to atherosclerosis. HMG-CoA reductase is a major enzyme responsible for the biosynthesis of cholesterol and it is believed that statins, which are used as prominent preventive drug in clinical practices, are potent inhibitor of HMG-CoA reductase, (Jesús et al. 2009).

Mevastatin, followed by lovastatin were few of the initial statins, reported as secondary metabolites from fungal source. Lovastatin (mevinolin) was the first hypocholesterolemic drug, which was approved by FDA, USA (Manzoni and Rollini 2002). A number of organisms such as *Aspergillus terreus*, *Monascus ruber*, *Penicillium* sp. and *Trichoderma* sp. are known to be potent producer of lovastatin (Valera et al. 2005).

M. ruber and *M. purpureus* are non pathogenic fungi and most exploited strain in South East Asia for the production of red mold rice and lovastatin. Maximum reports present in literature talk about the production of lovastatin using monocultures of these *Monascus* sp. or co-culture of these strains (Panda et al. 2010a). There is a need to explore other

Research highlights

- Lovastatin, known to be a potent cholesterol-lowering drug in humans is being attempted for production from *Monascus purpureus*, *Monascus sanguineus* and their co-culture.
- *Monascus sanguineus* still an unexplored species of *Monascus* was explicitly explored for the production of lovastatin.
- Presence of lovastatin was confirmed by thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) and quantification was carried out with UV spectrometer at 238 nm.
- Plackett-Burman design was used to screen the nutrients for optimized yield of lovastatin.
- Lovastatin yield from *Monascus sanguineus* was found to be almost double as compared to *Monascus purpureus* and its co-culture.

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Monascus strains in relation to fungal secondary metabolites such as lovastatin etc. The aim of this study was to explore another strain namely *Monascus sanguineus*, which is still not exploited for secondary metabolites. Solid-state fermentation (SSF) has been used as a potent technology for higher yield of enzymes and secondary metabolites from microorganism in recent years. SSF shows distinct advantages over submerged fermentation such as higher and faster product yield and improved processing. Biocon India Ltd. has also started production of three valuable fungal secondary metabolites, including lovastatin using SSF on an industrial scale (Suryanarayan 2003). The number of nutrients to be screened and optimized is greater in fermentation process. Plackett-Burman (PB) design is an effective tool for screening of several components which can significantly influence the yield on particular experiment (Subhagar et al. 2010).

The aim of the present study was to screen the lovastatin production from *Monascus* strains. *Monascus purpureus*, *Monascus sanguineus* and the co-culture of these two strains were used for this work. Rapid screening was done with zone of inhibition on *Saccharomyces cerevaceae* and *Candida* sp. and was confirmed with TLC and HPLC method. Solid substrates were tested for screening of lovastatin production and the substrate which produced larger quantity of lovastatin was chosen for further study. Plackett-Burman (PB) design was used for screening of nutrient components in solid state fermentation.

Material and methods

Culture

Pomegranate (*Punica granatum*) was used to isolate the wild strain of *Monascus* which was identified as *Monascus sanguineus* (Rashmi and Padmavathi, 2013).

Reference culture

The reference culture *Monascus purpureus* MTCC 410 was obtained from the Microbial Type Culture Collection, IMTECH, Chandigarh, India.

Both the strains were maintained on Potato Dextrose Agar (PDA) medium. They were incubated at 30 °C for 7 days and preserved at 4 °C. Both the strains were sub-cultured once in every 4 weeks (Rashmi and Padmavathi 2012).

Inoculum preparation

One loop of sporulated culture was diluted in distilled water. The spores were scraped off under aseptic conditions to produce a spore suspension. Spore suspension (5 ml) of *M. purpureus* and *M. sanguineus* was inoculated separately

in conical flasks containing 50 ml of potato dextrose broth. This was incubated at 30 °C for 5 days with shaking at 150 r/min. These cultures were used as inoculum for both the *Monascus* sp. For co-culture, these seed cultures were mixed in the ratio of 1:1 (Panda et al. 2010a).

Solid-state fermentation

Ten grams of different substrates were taken viz. wheat bran, tamarind seed, rice bran and jack fruit seed. These substrates were placed in a 250 ml conical flask to which 30 ml of basal media was added. The basal media composition included 100 g dextrose, 10 g peptone, 2 g KNO₃, 2 g NH₄ H₂ PO₄, 0.5 g MgSO₄·7H₂O, and 0.1 g CaCl₂·2H₂O in 1,000 ml distilled water. The pH of the medium was adjusted to pH 6.0 (Su et al. 2003).

Plackett-burman design for screening of nutrients

Screening of nutrients was done according to Plackett-Burman design (Plackett and Burman 1946). As the maximum lovastatin yield was found with wheat bran, it was used as a substrate for screening of nutrients. The Plackett-Burman technique allows evaluation of N number of variables in N+ 1 experiment and assumes that there are no interactions between different media components (Kammoun et al. 2008). For this study 7 media components viz. Lactose, Dextrose, Malt Extract, Soybean, MnSO₄·7H₂O, MgSO₄·7H₂O and CaCl₂·2H₂O were chosen that were known to significantly influence the production of lovastatin for *M. purpureus*, *M. sanguineus* and the co-culture (Table 1). Though dextrose, lactose and malt extract act as carbon sources, the effect of these on the production of lovastatin is not expected to be alike due to their dissimilar chemical properties and the involvement of two different strains of *Monascus* and their co-culture. As far as malt extract is concerned, it acts as a nitrogen source also and helps in maintaining the pH of the medium. It also contains proteins, ash, lipids, fatty and organic acids, sulphur compounds, vitamins such as biotin, folic acids, nicotinic

Table 1 Levels of factors tested for the production of Lovastatin using Plackett-Burman design

Component Code	Component	Unit	Lower Level (–)	Higher Level (+)
C ₁	Lactose	g/l	80	160
C ₂	Dextrose	g/l	80	120
C ₃	Malt Extract	g/l	3	12
C ₄	Soybean	g/l	3	12
C ₅	MgSO ₄ ·7H ₂ O	g/l	0.045	0.45
C ₆	MnSO ₄ ·H ₂ O	g/l	0.045	0.45
C ₇	CaCl ₂ ·2H ₂ O	g/l	0	0.075

Table 2 Plackett-Burman experimental design matrix for lovastatin production with *M. purpureus* (M₁), *M. sanguineus* (M₂) and Co-culture (M₃)

Run No.	C ₁	C ₂	C ₃	C ₄	C ₅	C ₆	C ₇	M ₁ (mg/g)	M ₂ (mg/g)	M ₃ (mg/g)
1	+	+	+	–	+	–	–	0.057	0.135	0.108
2	+	+	–	+	–	–	+	0.102	0.087	0.156
3	+	–	+	–	–	+	+	0.084	0.108	0.057
4	–	+	–	–	+	+	+	0.123	0.171	0.093
5	+	–	–	+	+	+	–	0.351	0.114	0.261
6	–	–	+	+	+	–	+	0.18	0.222	0.078
7	–	+	+	+	–	+	–	0.237	0.111	0.069
8	–	–	–	–	–	–	–	0.258	0.246	0.111

acid, riboflavin, thiamine etc. (Fluckiger et al. 1994). The Plackett-Burman design was applied for the screening of these media components and only 8 runs were carried out. Since this design takes into account only the linear effect of the media components the interaction effects for the design are not considered. The design is represented by the following polynomial equation of first order:

$$\text{Lovastatin Yield} \left(\frac{\text{mg}}{\text{g}} \right) = \alpha_0 + \sum_{i=1}^n \beta_i x_i \quad (1)$$

Where α_0 is the model co-efficient, β_i are the linear co-efficients, x_i are the variables and n is the number of media components (7 for this study). Each of the media components were represented in two levels, one high (represented by positive sign in Table 2) and one low (represented by negative sign in Table 2).

Table 1 illustrates the factors under investigation as well as levels of each factor used in the experimental design. Table 2 represents the design matrix used to analyze the experimental Plackett-Burman design.

The effect of each of the media components was calculated by the following equation:

The response value effect of the tested variable E_{x_i}

$$= \frac{\sum M_{i+} - \sum M_{i-}}{N} \quad (2)$$

Table 3 Yeast inhibition zone (in diameter) and Rf value of *Monascus* sp. extracts and lovastatin standard

Sample	<i>Candida</i> sp.	<i>Saccharomyces cerevisiae</i>	TLC result (Rf value)
Lovastatin std.	18.00	20.1	0.63
<i>M. sanguineus</i>	20.6	22.1	0.64
<i>M. purpureus</i>	17.1	18.5	0.64
Co-culture	15.3	13.8	0.65

Where the first term of the numerator denotes the summation of the response values at positive (high) level and the second term is the summation of the response values at negative (low) level and N is the number of runs carried out.

Extraction of lovastatin

Fermented dry substrate was taken with 20 ml methanol and kept in a shaker incubator for 2 h at 180 rpm and 70 °C. It was then filtered with Whatman filter paper and filtrate was centrifuged at 3,000×g for 8 min. (Panda et al. 2010a).

Lovastatin detection by TLC

Lovastatin from *Monascus* sp. extracts was analyzed by TLC. This was performed on Silica gel 60F254 aluminium sheets (Merck, Germany) with Benzene: Acetone: Acetic acid (70:30:3, by volume) as the mobile phase (Babu et al. 2011).

Fig. 1 Plate showing the inhibition zones against *Saccharomyces cerevisiae*

Fig. 2 TLC plate showing the presence of lovastatin

Yeast growth inhibition bioassay

Yeast growth inhibition bioassays were performed on *Saccharomyces cerevisiae* and *Candida* sp. Yeast inoculated medium was poured into a 15 cm diameter glass Petri dish.

Fig. 3 Chromatography for the Lovastatin produced by *M. sanguineus* (S), *M. purpureus* (P) and Co-culture (CO) along with pure Lovastatin (Std.)

Yeast inhibition zone was observed by disk diffusion method. 50 μ l (approximately 15 μ g in 50 μ l) of acetonitrile extracts from *Monascus* sp. and pure lovastatin standard were transferred on to 6-mm.diameter disk. After drying these disks were carefully shifted on bioassay plate (Babu et al. 2011).

Estimation of lovastatin by UV spectrophotometry

Purified spots from TLC were scrapped and transferred into glass tubes. Acetonitrile was further added to this. It was then centrifuged, filtered and the filtrate was estimated at 238 nm using UV-Visible spectrophotometer (Sreedevi et al. 2011).

HPLC condition for lovastatin

The High Performance Liquid Chromatography (HPLC) analysis was carried using 250 $\times$ 4.6 mm ID Lichrosper® 100 C18 column of particle size 5 μ m, loop injector of 20 μ l, and Shimadzu CLASS-VP version 5.032 software. The mobile phase was Acetonitrile/water (65:35 v/v and 3.5 pH), acidified with ortho-phosphoric acid. The flow rate was set to 1.0 ml/min with pressure settings as 2,500 psi and the detection was carried out using the wavelength of 235 nm by UV detector (SPD10A VP) (Panda et al. 2010a).

Results and discussion

Screening and identification of lovastatin

Purified lovastatin from *Monascus* extracts and pure lovastatin were subjected for inhibition bioassay for yeast. Both yeast strains *Saccharomyces cerevisiae* and *Candida* sp. had shown clear and proportional diameter of inhibition zone (Table 3 and Fig. 1).

TLC results also showed the presence of lovastatin from *Monascus* extract sample. The Rf values of extracts were found similar to the pure standard lovastatin (Fig. 2 and Table 3). For further confirmation of lovastatin, samples were subjected to HPLC along with pure lovastatin. Retention time for peak of standard lovastatin, *Monascus purpureus*, *Monascus sanguineus* and co-culture was found to be 6.0, 5.9, 5.9 and 6.1 respectively (Fig. 3).

Lovastatin is known to possess anti yeast and anti fungal activity. Kreier et al. (1993) had concluded that lovastatin in the concentration of 0.1–0.5 μ g/ml can inhibit the growth *Rhodotorula rubra*. In *Mucor racemosus*, it was found to trigger an apoptosis like cell death (Roze and Linz 1998). It is also known to inhibit the nuclear division by reducing the activity of HMG-CoA reductase in myxomycetes *Physarum polycephalum* (Engstrom et al. 1989; Sitaram et al. 2000). Babu et al. (2011) found that lovastatin purified from

Table 4 Response value effect of the variables for the two *Monascus* sp. and co-culture

Component	<i>M. sanguineus</i>			<i>M. purpureus</i>			Co-Culture		
	$\Sigma (M_{i+})$	$\Sigma (M_{i-})$	Effect	$\Sigma (M_{i+})$	$\Sigma (M_{i-})$	Effect	$\Sigma (M_{i+})$	$\Sigma (M_{i-})$	Effect
Lactose	0.594	0.798	−0.051	0.444	0.75	−0.0765	0.582	0.351	0.05775
Dextrose	0.519	0.873	−0.0885	0.504	0.69	−0.0465	0.426	0.507	−0.02025
Malt Extract	0.558	0.834	−0.069	0.576	0.618	−0.0105	0.312	0.621	−0.07725
Soybean	0.87	0.522	0.087	0.534	0.66	−0.0315	0.564	0.369	0.04875
MgSO ₄ ·7H ₂ O	0.711	0.681	0.0075	0.642	0.552	0.0225	0.54	0.393	0.03675
MnSO ₄ ·H ₂ O	0.795	0.597	0.0495	0.504	0.69	−0.0465	0.48	0.453	0.00675
CaCl ₂ ·2H ₂ O	0.489	0.903	−0.1035	0.588	0.606	−0.0045	0.384	0.549	−0.04125

Aspergillus terreus had shown yeast growth inhibition against *Saccharomyces cerevisiae*.

Screening of substrates and nutrients

Different substrates were screened for lovastatin production of which wheat bran was found to be the best substrate. Maximum yield was achieved with wheat bran (0.094 mg/g), tamarind seed (0.075 mg/g) and jack fruit seed (0.071 mg/g), whereas the rice bran (0.045 mg/g) produced the minimum yield. Wheat bran was then subjected to the screening of nutrients according to Plackett–Burman design. The response value effect and t-value analysis of the media components was carried out for both the *Monascus* sp. and their co-culture (Table 4). Significance of the media component on lovastatin production was analyzed with the help of t-value. It was found that for *M. sanguineus*, only soybean, MgSO₄·7H₂O and MnSO₄·7H₂O showed positive effect on the lovastatin production whereas the rest of the media components showed the negative effect. As far as the magnitude of the effects was concerned, CaCl₂·2H₂O, dextrose and soybean had the dominant effect (Fig. 4). For *M. purpureus*, it was observed that only MgSO₄·7H₂O showed the positive effect on the lovastatin production whereas the rest of the media components showed the negative effect. The magnitude of the effects of lactose, dextrose and MnSO₄·7H₂O, were found dominant (Fig. 4). For co-culture, the response was mixed. Lactose, soybean, MgSO₄·7H₂O and MnSO₄·7H₂O showed the positive effect on lovastatin production whereas dextrose, malt extract and CaCl₂·2H₂O showed the negative effect. The magnitude of the effects of malt extract, lactose and soybean was found dominant (Fig. 4).

To visualize the effect of the dominant variables on the lovastatin yield and to find the optimum test condition for the

lovastatin production with different media, the equation used for Plackett–Burman design was exploited.

The equation for Plackett–Burman design for the lovastatin production with *M. sanguineus* can be elaborated as:

$$\begin{aligned} \text{Lovastatin yield} \left(\frac{\text{mg}}{\text{g}} \right) \text{ with } M. \text{ sanguineus} &= 0.4737 - 0.0006 \\ &\times \text{lactose} - 0.0022 \times \text{dextrose} - 0.0077 \times \text{malt extract} + 0.0097 \\ &\times \text{soybean} + 0.0185 \times \text{MgSO}_4 \cdot 7\text{H}_2\text{O} + 0.1222 \\ &\times \text{MnSO}_4 \cdot 7\text{H}_2\text{O} - 1.38 \times \text{CaCl}_2 \cdot 2\text{H}_2\text{O} \end{aligned} \quad (3)$$

The equation for *M. purpureus* can be written as:

$$\begin{aligned} \text{Lovastatin yield} \left(\frac{\text{mg}}{\text{g}} \right) \text{ with } M. \text{ purpureus} &= 0.4322 - 0.001 \\ &\times \text{lactose} - 0.0012 \times \text{dextrose} - 0.0012 \times \text{malt extract} - 0.0035 \\ &\times \text{soybean} + 0.0556 \times \text{MgSO}_4 \cdot 7\text{H}_2\text{O} - 0.1148 \\ &\times \text{MnSO}_4 \cdot 7\text{H}_2\text{O} - 0.06 \times \text{CaCl}_2 \cdot 2\text{H}_2\text{O} \end{aligned} \quad (4)$$

The equation for the co-culture can be presented as:

$$\begin{aligned} \text{Lovastatin yield} \left(\frac{\text{mg}}{\text{g}} \right) \text{ with co-culture} &= 0.0984 + 0.0007 \\ &\times \text{lactose} - 0.0005 \times \text{dextrose} - 0.0086 \times \text{malt extract} + 0.0054 \\ &\times \text{soybean} + 0.0907 \times \text{MgSO}_4 \cdot 7\text{H}_2\text{O} + 0.0167 \\ &\times \text{MnSO}_4 \cdot 7\text{H}_2\text{O} - 0.55 \times \text{CaCl}_2 \cdot 2\text{H}_2\text{O} \end{aligned} \quad (5)$$

The effect of various combinations of the dominant variables on lovastatin production while keeping other variables at their central level of the Plackett–Burman experimental design is shown in the response surface plots illustrated in Figs. 5, 6 and 7. These plots are a commendable tool in determining the lovastatin production at intermediate levels of different

Fig. 4 t- effects for the media components for Lovastatin yield for all three strains

combination of media components and also for the optimization of lovastatin production.

From Fig. 5 it can be seen that the lovastatin yield from *M. purpureus* decreased with addition of carbon components either of the lactose or the dextrose. Similar trend was seen with $\text{MnSO}_4 \cdot 7\text{H}_2\text{O}$ also. Hence it can be concluded that out of the experimented media components, lactose, dextrose and MnSO_4 have the negative dominant effect on the lovastatin production with *M. purpureus*. For *M. sanguineus*, the lovastatin yield decreased with $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ and dextrose, but increased with soybean as depicted in Fig. 6. For co-culture, the lovastatin yield increased with lactose and soybean (Fig. 7) whereas it decreased with increasing concentration of malt extract.

The Eqs. 3 to 5 were utilised to find the optimum target values of the media components for maximum lovastatin yield. The equations were solved by

generating a grid of 30 equidistant points for each of the variables covering their range. Thus 210 test conditions were evaluated mathematically and the lovastatin yield for these were calculated using the above equations. The maximum lovastatin yield with the optimum values of the media components for all the three cultures are presented in Table 5.

According to Sayyad et al. (2007), maximum lovastatin yield was obtained with $\text{MnSO}_4 \cdot 7\text{H}_2\text{O}$ concentration of 0.19 g/l in submerged fermentation with *Monascus purpureus*. $\text{MnSO}_4 \cdot 7\text{H}_2\text{O}$, glucose and peptone were found more significant medium components for lovastatin yield with *Monascus purpureus* (Subhagar et al. 2010). Panda et al. (2010b) had attempted screening of the nutrients with Plackett–Burman design for lovastatin production and concluded that it was greatly influenced by the concentration of malt extract,

Fig. 5 Response Surface plots showing the effect of dominant variables on lovastatin yield for *M. sanguineus*

Fig. 6 Response Surface plots showing the effect of dominant variables on lovastatin yield for *M. purpureus*

Fig. 7 Response Surface plots showing the effect of dominant variables on lovastatin yield for co-culture

$\text{MnSO}_4 \cdot \text{H}_2\text{O}$ and $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$. Yeast extract, corn steep liquor and soybean meal were the most favorable organic nitrogen source for lovastatin synthesis (Lopez et al. 2003). According to the literature, widely used carbon sources for lovastatin production are lactose, glycerol and glucose. Glucose has been regarded as the best carbon source for lovastatin production (Sayyad et al. 2007; Chang et al. 2002). Glucose concentration of 30 g/l was found optimum for lovastatin synthesis by *Aspergillus terreus* (Silvia et al. 2002). Manzoni et al. (1998) had also endorsed similar glucose concentration for lovastatin yield from *Monascus paxii*.

In our experiment both carbon source viz. dextrose and lactose had shown negative effect in tested range of concentration for mono-cultures. Increasing lovastatin yield was found till the concentration of 80 g/l and thereafter a decrease in the yield was observed. However in the case of co-culture, effect of these

carbon sources was positive. This may be due to the reason that in case of monoculture, these carbon sources might be inhibiting the lovastatin yield after above mentioned concentration. The results differ for co-culture because of coexistence of the two organisms and the likely reason may be that, these organisms require more concentration of carbon as well as nitrogen source for survival and production of secondary metabolites.

From the present study we can conclude that lovastatin can be produced by another *Monascus* strain viz. *M. sanguineus*. This strain is also an efficient producer in comparison to other explored *Monascus* sp. The co-culture with these strains had not shown significant increase in lovastatin yield. Panda et al. (2010a) has reported increase in yield with co culture of two *Monascus* strain (*Monascus purpureus* and *Monascus ruber*). Our results disagree with Panda et al. (2010a) as the co-culture technique may not be compatible with each other for *M. sanguineus* and *M. purpureus*.

Conclusion

Lovastatin, which is an important secondary metabolite, is known to be a potent cholesterol-lowering drug in humans produced by the filamentous organism such as *Aspergillus* sp., *Monascus* sp. etc. There is lot of literature available regarding lovastatin production from *Monascus purpureus*, *Monascus ruber* and other *Monascus* sp. but not much work has been reported on *Monascus sanguineus*. This study can be regarded as an attempt to screen and identify the lovastatin production from *Monascus sanguineus*, *Monascus purpureus* and their co-culture. Results revealed that the yield of lovastatin was almost double as obtained from *Monascus sanguineus*, when compared to *Monascus purpureus* and its co-culture. Hence the results obtained from this study can be considered as resourceful and innovative in nature. As per the best of our knowledge, this is the first report highlighting the production of lovastatin from *M. sanguineus*. The results are reliable enough to conclude that the fungus *Monascus sanguineus* is a good source for lovastatin production. This species like other *Monascus* sp. can be treated as a potential source for the production of lovastatin and need to be exploited to its potential in future.

Table 5 Optimum conditions for maximum lovastatin yield from the experimental data

Component	Unit	For <i>M. sanguineus</i>	For <i>M. purpureus</i>	For Co-Culture
Lactose	g/l	80	80	160
Dextrose	g/l	80	80	80
Malt Extract	g/l	3	3	3
Soybean	g/l	12	3	12
$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	g/l	0.45	0.45	0.45
$\text{MnSO}_4 \cdot \text{H}_2\text{O}$	g/l	0.45	0.045	0.45
$\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$	g/l	0	0	0
Maximum Lovastatin Yield (mg/g)		0.402	0.27	0.26

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