

STUDIES ON COEXISTENCE OF MONASCUS SECONDARY METABOLITES - RED PIGMENTS AND MONACOLIN K

黃育輝、張耀南

E-mail: 9015654@mail.dyu.edu.tw

ABSTRACT

IN THIS STUDY, MONACOLIN K WAS PRODUCED BY MONASCUS RUBER CCRC 31535 IN FLASK CULTURE. IT WAS FOUND THAT THE OPTIMUM CULTURE TEMPERATURE WAS 25 OC. THE OPTIMUM MEDIA IN THE CULTURE OF 25 OC WERE FOUND TO BE PH 5.0 AND 25 ML. FURTHERMORE, RICE POWDER WAS CONSIDERED TO BE THE BEST CARBON SOURCE IN GIVING THE MAXIMUM YIELD OF MONACOLIN K. THE MAXIMUM YIELD WAS 4.16 ' 10-2 MG/ML IN THE CULTURE OF 25 OC. THE APPROPRIATE ORGANIC NITROGEN SOURCE WAS CHANGED WITH THE CULTURE TEMPERATURE. AMONG THE NITROGEN SOURCES TESTED, YEAST EXTRACT AND PEPTONE WERE FOUND TO BE SUITABLE FOR MONACOLIN K PRODUCTION IN THE CULTURE OF 25 OC AND 30 OC, RESPECTIVELY. THIS RESEARCH DEMONSTRATED THAT THE SOLID-LIQUID CULTURE WAS WORTH IMPROVING THE YIELD OF MONACOLIN K. RESPONSE SURFACE METHODOLOGY WAS USED TO OPTIMITE MONACOLIN K PRODUCTION BY M.RUBER CCRC 31535 IN FLASK CULTURE. WHEN THE CONCENTRATION OF RICE STARCH 34.4 G/L, PEPTONE 10.8 G/L, GLYCERIN 36.4 ML/L, GLUCOSE 12.92 G/L, KNO₃ 8 G/L, MGSO₄ 4G/L, FOUND THE MAXIMUM CONCENTRATION OF MONACOLIN K WAS 0.157 MG/ML.

Keywords : MONASCUS RUBER, MONACOLIN K, RESPONSE SURFACE METHODOLOGY

Table of Contents

第一章 緒論--P1 第二章 文獻回顧--P6 2.1 紅麴菌簡介與起源--P6 2.2 紅麴菌的形態與分類--P6 2.3 紅麴菌的代謝產物--P8 2.4 紅麴的色素--P8 2.5 膽固醇合成抑制劑--P17 2.6 其他紅麴菌的代謝產物--P25 2.7 紅麴菌在機能性食品上的開發與用途--P28 2.8 紅麴菌的培養--P29 2.9 其他有關紅麴菌之研究--P30 2.10 色差儀--P32 2.11 回應曲面實驗設計法--P37 2.12 二水準因子設計--P39 2.13 陡升路徑法--P43 2.14 中心混成設計--P45 2.15 回應曲面模式適切性之統計檢驗--P45 2.16 因子影響效應之分析--P46 第三章 研究步驟--P49 3.1 前言--P49 3.2 材料與方法--P50 3.2.1 試驗材料--P50 3.2.2 試驗之儀器與設備--P50 3.2.3 培養方法--P51 3.2.4 膽固醇合成抑制劑 (monacolin K) 之HPLC定量分析...--P53 3.2.5 紅麴菌的紅色色素之分光光度儀定量分析--P55 3.2.6 紅麴菌的紅色色素之色差儀分析--P59 3.3 回應曲面法之實驗設計--P59 3.3.1 部分因子之設計實驗--P60 3.3.2 陡升路徑之實驗設計--P60 3.3.3 中心混成設計之實驗--P62 3.3.4 回應曲面模式適切性之統計檢驗--P62 3.4 結果與討論--P66 3.4.1 部分因子設計實驗--P66 3.4.2 陡升路徑實驗--P77 3.4.3 中心混成設計實驗--P85 3.4.4 回應曲面模式適切性之統計檢驗--P154 第四章 結論與展望--P162

REFERENCES

- 1.雲萍、張永吉 (1996) 文明產物 - 降血脂劑LOVASTATIN。化工資訊, 10 (4) :53-57。
- 2.李昌憲、洪哲穎、熊光濱 (1992) 利用回應曲面法進行以STREPTOCOCCUS FAECALIS生產酪氨酸脫竣 酵素之培養基最適化研究。中國農業化學會誌, 31:28-34。
- 3.李昭蓉 (1997) 漫談紅麴菌。食品工業月刊, 29 (2) :86-89。
- 4.李琇鈴、周正俊、吳淳美 (1993) 利用回應曲面法尋求STREPTOCOCCUS FAECALIS產生 g-DECALACTO -NE之最適條件。中國農業化學會誌, 31:28-34。
- 5.林俊宏 (1999) 製備含紅麴菌膽固醇合成抑制劑MONACOLIN K健康之研究。國立東華大學生物技術研究所碩士論文, 花蓮縣壽豐鄉。
- 6.林讚峰 (1982) 紅麴菌研究發展之演進。製酒科技專論彙編, 4:66-77。
- 7.林讚峰 (1983 A) 紅麴菌之鑑定及實用分類法。製酒科技專論彙編, 5:104-113。
- 8.林讚峰 (1983 B) 改良紅麴製造方法之探討。酒類試驗所研究71年報, 159-172。
- 9.林讚峰 (1985) 紅麴菌的次級代謝物聚克味代謝。製酒科技專論彙編, 7:170-187。
- 10.林讚峰 (1986) 紅麴菌級代謝物的經濟性評估及增產策略。製酒科技專論彙編, 8:81-99。
- 11.林讚峰 (1987) 利用紅麴菌產生膽固醇合成抑制劑。酒類試驗所研究年報76年度, 157-164。
- 12.林讚峰 (1992 A) 紅麴菌在保健食品上的新用途。食品工業, 24 (10) :41-45。
- 13.林讚峰 (1992 B) 紅麴菌研究發展之演進。科學農業, 40 (3-4) :193-198。
- 14.林讚峰、黃正財 (1983) 紅麴菌釀造性質之研究 (一) 澱粉水解酵素。酒類試驗所研究年報72年度, 157-167。
- 15.邱建人 (1977) 紅麴色素之各種性質及其應用。食品科學文摘, 第五卷, 11:8-14。
- 16.施國琛 (1985) 色差分光分析原理與應用。食品科學文摘, 5 (1) :32-36。
- 17.洪哲穎 (1998) 回應曲面品質工程技術。工業局八十八年度人才培訓計畫研習班, 1998年11月, 私立義守大學, 高雄縣大樹鄉。
- 18.洪哲穎、陳國誠 (1992) 回應

曲面實驗設計法在微生物酵素生產上之應用。中國化學工程學會會刊, 39(2):3-18。19.張耀南(1997)利用紅麴菌以固-液態培養方式產生膽固醇合成抑制劑。八十六年度國科會化學門專題研究計劃成果報告,生化工程(I)專輯,25-28。20.陳昭姿(1996)降低血膽固醇藥再添新兵。當代醫學,23(11):937-939。21.黃顯宗(1985)紅麴菌研究之回顧與展望。真菌學之最近發展(曾聰徹、陳瑞青主編),109-124。國科會生物科學研究中心專刊第十二集,台北。22.劉繼賢、廖啟成(1994)利用回應曲面法尋求以CORYNEBACTERIUM GLUTAMICUM生產苯丙氨酸之培養基之最適化研究。中國農業化學會誌,32(2):149-155。23.蕭明熙(1985)真菌代謝物之最新研究趨勢。真菌學之最近發展(曾聰徹、陳瑞青主編),163-183。國科會生物科學研究中心專刊第十二集,台北。24.蕭明熙(1994)降膽固醇與抗動脈粥狀硬化藥物。中國化學會誌,52(4):442-453。25.謝鳳龍、黃育輝、張耀南、曾耀銘(1998)利用紅麴菌(MONASCUS PILOSUS)生產膽固醇合成抑制劑之固-液態培養條件探討。第三屆生化工程研討會,P133-136,1998年6月27-28日,國立東華大學,花蓮縣壽豐鄉。26.謝鳳龍、黃育輝、陳亮尹、張耀南、曾耀銘(1997)利用紅麴菌(MONASCUS PILOSUS)產生膽固醇合成抑制劑之搖瓶培養條件探討。中國化學會86年年會,NO.P-2-BI-010,P240。27.ALBERT, A. W., C. CHEN, G. KURON, V. HUFF, C. HOFFFMAN, J. ROTHROCK, M. LOPEZ, H. JOSHUA, A. E. HARRIS, A. PATCHETT, R. MONAGHAN, S. CURRIE, E. STAPLEY, G. ALBERTS-SCHONBERG, O. HENSENS, J. HIRSHFIELD, K. HOOGSTEEN, J. LIESCH AND J. SPRINGER (1980) MEVINOLIN: A HIGHLY POTENT COMPETITIVE INHIBITOR OF HYDROXYMETHYL-GLUTARYL-COENZYME A REDUCTASE AND A CHOLESTEROL-LOWERING AGENT. PROC. NATL. ACAD. SCI., USA, 77: 3957-3961。28.BOX, G. E. P. AND WILSON, K. B. (1951) ON THE EXPERIMENTAL ATTAINMENT OF OPTIMUM CONDITION -S. J. ROY. STANT. SOC., B13:1-45。29.BROWN, M. S. AND J. L., GOLDSTEIN (1984) HOW LDL RECEPTORS INFLUENCE CHOLESTEROL AND ATHEROSCLEROSIS. SCIENTIFIC AMERICAN, 251(5): 52-60。30.BUCHANAN, R. L. AND J. G. PHILIPS (1990) RESPONSE SURFACE MODEL FOR PREDICTING THE EFFECTS OF TEMPERATURE, PH, SODIUM CHLORIDE CONTENT, SODIUM NITRITE CONCENTRATION AND ATMOSPHERE ON THE GROWTH OF LISTERIA MONOCYTOGENES. J. FOOD PROTECT., 53: 370-376。31.CHAN, J. K., R. N. MOORE, T. T. NAKASHIMA AND J. C. VEDERAS (1983) BIOSYNTHESIS OF MEVINOLIN (SPECTRAL ASSIGNMENT BY DOUBLE-QUANTUM COHERENCE NMR AFTER HIGH CARBON-13 INCORPORATION). J. AM. CHEM. SOC., 105:3334-3335。32.DOUGLAS C. MONTGOMER (1997) DESIGN AND ANALYSIS OF EXPERIMENTS. JOHN WILEY AND SONS, INC.,575-641。33.ENDO, A. (1979) MONACOLIN K, A NEW HYPOCHOLESTEROLEMIC AGENT PRODUCED BY MONASCUS SPECIES. THE J. ANTIBIOTICS, 32: 852-854。34.ENDO, A., K. HASUMI AND S. NEGISHI (1985) MONACOLINS J AND L, NEW INHIBITORS OF CHOLESTEROL BIOSYNTHESIS PRODUCED BY MONASCUS RUBER. THE J. ANTIBIOTICS, 38: 420-422。35.ENDO, A., D. KOMAGATA AND H. SHIMADA (1986) MONACOLIN M, A NEW INHIBITOR OF CHOLESTEROL BIOSYNTHESIS. THE J. ANTIBIOTICS, 39: 1670-1673。36.FEARS, R. (1983) PHARMACOLOGICAL CONTROL OF 3-HYDROXY-3-METHYLGLUTARYL COENZYME A REDUCTASE. IN 3-HYDROXY-3-METHYLGLUTARYL COENZYME A REDUCTASE, SABINE, J. R., ED, 189-208, CRC PRESS, INC., BOCA RATON。37.HALTRICH, D., M. PRESS AND W. STEINER (1993) OPTIMIZATION OF A CULTURE MEDIUM FOR INCREASED XYLANASE PRODUCTION BY A WILD STRAIN OF SCHIZOPHYLLUM COMMUNE. ENZYME MICROB. TECHNOL., 15: 854-860。38.HAWKSWORTH, D. L. AND J. I. PITT (1983) A NEW TAXONOMY FOR MONASCUS SPECIES BASED ON CULTURAL AND MICROSCOPICAL CHARACTERS. AUST. J. BOT., 31: 51-61。39.HEBER D., L. YIP, J. M. ASHELY, ELASHOFF DA, ELASHOFF RM, GO VLW. (1998) CHOLESTEROL-LOWERING EFFECTS OF PROPRIETARY CHINESE RED YEAST DIETARY SUPPLEMENT. FASEB JOURNAL, 12(4): 206。40.JOSEPH, L. GOLDSTEIN AND MICHAEL S. BROWN (1990) REGULATION OF THE MEVALONATE PATHWAY, NATURE, 343:425-430。41.JUZLOVA, P., L. GOLDSTEIN AND MICHAEL S. BROWN (1990) REGULATION OF THE MEVALONATE PATHWAY. NATURE, 343:425-430。42.JUZLOVA, P., L. MARTINKOVA AND V. KREN (1996) SECONDARY METABOLITES OF THE FUNGUS MONASCUS: A REVIEW. J. IND. MICROBIOLOGY, 16:163-170。43.JOHN, M. D. M. (1976) COLOR. PRINCIPLES OF FOOD CHEMISTRY, WESTPORT, CONN., 203-241。44.KAUTOLA, H. AND Y. Y. LINKO (1989) FUMARIC ACID PRODUCTION FROM XYLOSE BY IMMOBILIZED RHIZOPUS ARRHIZUS CELLS. APPL. MICROBIOL. BIOTECHNOL., 31: 448-452。45.KIMURA, KOMAGATA, MURAKAWA AND ENDO (1990) BIOSYNTHESIS OF MONACOLINS: CONVERSION OF MONACOLIN J TO MONACOLIN K (MEVINOLIN). J. ANTIBIOTICS, 43(12):1621-1622。46.LIN, T. F., K. YAKUSHIJIN, G. H. BUCHI AND A. L. DEMAIN (1992) FORMATION OF WATER-SOLUBLE MONASCUS PIGMENTS BY BIOLOGICAL AND SEMI-SYNTHETIC PROCESSES. J. IND. MICROBIOLOGY, 9:173-179。47.LIN, T. F., A. L. DEMAIN (1994) LEUCINE INTERFERENCE IN THE PRODUCTION OF WATER-SOLUBLE RED MONASCUS PIGMENTS ARCH MICROBIOL, 162:114-119。48.MADDOX, I. S. AND S. H. RICHERT (1977) PRODUCTION OF GIBBERELIC ACID USING A DAIRY WASTE AS THE BASAL MEDIUM. APPL. ENVIRON. MICROBIOL., 33: 201-202。49.MUDAHAR, S., R. T. TOLEDO, J. D. FLORES AND J. J. JEN, (1989) OPTIMIZATION OF CARROT DEHYDRATION PROCESS USING RESPONSE SURFACE METHODOLOGY. J. FOOD SCI., 54: 714-719。50.NIL (1995 A) SSRI: UNPRECEDENTED US GROWTH, SCRIP, 2024: 23。51.NIL (1995 B) YEN EFFECT ON JAPAN'S PHARMA MARKET, SCRIP, 2023: 22。52.NIL (1996) TOP 10 DRUGS IN EUROPE, SCRIP, 2120: 23。53.PRAPULLA, S. G., S. JACOB, N. CHAND, D. RAJALAKSHMI AND N. G. KARANTH (1992) MAXIMIZATION OF LIPID PRODUCTION BY RHODOTROULA GRACILIS CFR-A USING RESPONSE SURFACE METHODOLOGY. BIOTECH. BIOENG., 40: 965-969。54.SHIAO, M. S. AND H. S. DON, (1987) BIOSYNTHESIS OF MEVINOLIN, A HYPOCHOLESTEROLEMIC FUNGAL METABOLITE,

IN ASPERGILLUS TERRUES. PROC. NATL. SCI. COUNC. B. ROC., 11 (3): 223-231. 55.SU, Y. C. (1978) FEREMENATIVE PRODUCTION OF ANKA-PIGMENT (MONASCUS-PIGMENT) . PROCEED -INGS OF THE ORIENTAL FERMENTED FOODS. FOOD INST. RES. DEVEL., HSINCHU, TAIWAN, R. O. C. 56.SWEENY, J. G., H. C. ESTRADA-VALDES, G. A. IIACOBUCCI, H. SATO, AND S. SAKAMURA (1981) PHOTOPROTECTION OF THE RED PIGMENTS OF MONASCUS ANKA IN AQUEOUS MEDIA BY 1,4,6-TRIHYD -ROXYNAPHTHALENE. J. AGRIC. FOOD CHEM., 29 : 1189-1193. 57.THOMSON, D. (1982) RESPONSE SURFACE EXPERIMENTATION. J. FOOD PROCESSING PRESERVATION, 6:155-188. 58.YONGSMITH, B., S. KRAIRAK AND R. BAVAVODA (1994) PRODUCTION OF YELLOW PIGMENTS IN SUBM -ERGED CULTURE OF A MUTANT OF MONASCUS SPP. J. FERMENTANTION AND BIOENGINEERING.,78(3) :223-228.