

# Studies on Production Conditions of Monacolin K and Pigment from Red Fermented Rice

戴坤良、柯文慶；謝昌衛

E-mail: 9607833@mail.dyu.edu.tw

## ABSTRACT

The monascus spp. could product the intracellular secondary metabolites (ex:red pigment and monacolin K)which advances high commercial value of the monacus fermentation. In the first stage, the objectives of this research were to study different coditions addition water, 4% fructose,0.5% ethanol and 1% peptone during the solid culture. In the second stage, using RSM for discussion optimum additive and concentration during koji making procedure.The derived results were discussed as follows: 1. In the procedure, the different additional results showed that the titratable acidity in the highest approximately 0.09% with adding 4% fructose and the darkness to compare enhance or improved, as for protease activity (0.18 Unit/g), amylase activity (117 glucose  $\mu$  mole/ml), reducing sugar(13.8 mg/ml) and red pigment yield is also to the highest, but the highest approximately 95 mg/kg of monacolin K yield as the with 0.5% ethanol cultures. 2. According to superimposed plots finds optimum produced high amylase activity with approximately is 144.89  $\mu$  mole/ml during fructose, 0.3% ethanol and 1.2% peptone. The highest of protease activity was approximately 0.28 Unit/g in 2.5% fructose, 0.7% ethanol and 0.9% peptone. The highest red pigment yield (45 mg/ml) which including 4.6% fructose, 0.4% ethanol and 1.4% peptone. The sections of monacolin K, which optimum concentration added 4.0% fructose, 0.7% ethanol and 0.9% peptone and then the ultimate yield could achieve 102 mg/kg. In conclusion, chosen different goal product division into culture, as a result close to the different production of optimum addition before, therefore demonstrated that could use different additional condition for advance there general and value.

Keywords : Monascus spp., monacolin K, red pigment, response surface methodology(RSM)

## Table of Contents

目錄 封面內頁 簽名頁 授權書.....	iii	中文摘要.....	iv	英文摘要.....	vi
誌謝.....	viii	目錄.....	ix	圖目錄.....	xiii
表目.....	xviii	1.緒言.....	1	2.文獻回顧.....	5
2.1紅麴的起源與使用歷史.....	5	2.2紅麴菌形態分類.....	5	2.3紅麴之代謝產物.....	7
2.3.1紅麴色素.....	7	2.3.2色素的穩定性.....	14	2.3.2.1碳、氮源的影響.....	15
2.3.2.2酸鹼值的影響.....	15	2.3.2.3培養基組成份的影響.....	16	2.3.2.4溫度的影響.....	16
2.3.3膽固醇合成抑制劑 ( monacolin K ) .....	17	2.3.3.1Monacolin K之發現.....	20	2.3.3.2Monacolin K之作用機.....	21
2.3.3.3Monacolin K之合成機.....	22	2.3.3.4培養條件對monacolin K生成之影響.....	27	2.3.4紅麴二次代謝物.....	29
2.3.4.1降血壓物質.....	29	2.3.4.2降血糖.....	29	2.3.4.3抗氧化能力.....	30
2.3.4.4抑菌功效.....	30	2.3.4.5抗疲勞功效.....	30	2.3.4.6防癌功效.....	31
2.3.4.7不飽和脂肪酸.....	31	2.4反應曲面法之簡介.....	32	2.4.1反應曲面法之原理.....	32
2.4.2二水準因子設計.....	37	2.4.3反應曲面模式適切性之統計檢驗.....	39	3.材料與方法.....	41
3.1實驗材料.....	41	3.2儀器設備.....	41	3.3試驗藥品.....	43
3.4實驗設計與方法.....	43	3.4.1實驗流程.....	43	3.4.1.1紅麴製麴試驗流程圖.....	43
3.4.1.2紅麴製麴中最適添加條件之試驗流程圖....	43	3.4.2實驗設計.....	43	3.5分析方法.....	47
3.5.1紅麴粗酵素液萃取.....	47	3.5.2紅麴色素萃取.....	47	3.5.3酸鹼值測定.....	48
3.5.4水分測定.....	48	3.5.5酸度測定.....	48	3.5.6色澤測定.....	49
3.5.7還原糖含量測定.....	49	3.5.8澱粉?活性測定.....	50	3.5.9蛋白?活性測定.....	50
3.5.10色素產量測定.....	51	3.5.11monacolin K之分析方法.....	51	3.5.11.1固態培養monacilin K 之萃取.....	51
3.5.11.2monacilin K濃度之測定.....	52	4.結果與討論.....	58	4.1紅麴成品相關成份分析.....	58
4.1.1發酵期間中水分含量及溫度之變化.....	58	4.1.2發酵期間中pH值及可滴定酸度之變化.....	61	4.1.3發酵期間中紅麴萃取液之L、a值與色差之變化.....	64
4.1.4發酵期間中澱粉?活性與還原糖產量之變化... ..	68	4.1.5發酵期間中蛋白?活性之變化.....	71	4.1.6發酵期間中色素產量之變化.....	73
4.1.7發酵期間中monacolin K之變化.....	75	4.2反應曲面模式分析.....	77	4.2.1添加物條件對紅麴米中澱粉?活性之影響.....	77
4.2.2添加物條件對紅麴米中還原糖含量之影響....	82	4.2.3添加物條件對紅麴米中酸度之影響.....	85	4.2.4添加物條件對紅麴米中蛋白?活性之影響.....	88
4.2.5添加物條件對紅麴米萃取液中L值之影響.....	91	4.2.6添加物條件對紅麴米萃取液中a值之影響.....	96	4.2.7添	

## REFERENCES

- 1.中台忠信。1977。?油麴菌?自己消化(第4報)?油麴菌?培養?件(II)培地水分。?研(日文)。3:16-19。2.王雲萍、張永吉。1996。文明產物-降血脂劑 Lovastatin。化工資訊, 10(4):53-57。3.玉田英明。1988。紅麴各種調味料之應用。食品科學, July:96-99。4.李琇鈴、周正俊、吳淳美, 1993, 利用回應曲面法尋求Streptococcus faecalis產生 $\gamma$ -decalactone之最適條件。中國農業化學會誌, 31:28-34。5.李時珍。1590。本草綱目, 穀部第二十五卷。6.李昭蓉。1997。漫談紅麴菌。食品工業月刊, 29(2):33-39。7.李秀、賴滋漢、柯文慶。2000。食品分析與檢驗(二增定版)。富林出版社。台中, 台灣。8.李俊霖。2003。提高紅麴中 monacolin K、GABA 與降低citrinin生成量之研究。台灣大學農業化學研究所碩士論文。台北。9.宋應星。1637。天工開物, 紅麴第十七卷。10.宋祖瑩。1994。番石榴果漿中混濁物之特性及其安定性之改進。中興大學食品科學研究所碩士論文。台中。11.杜姿瑩。2000。具調節血脂功能的機能性食品漫談。食品工業月刊, 32(2):22-32。12.沈明來。1999。試驗設計學。九州圖書文物有限公司。台北, 台灣。13.沈明來。2000。生物檢定統計法。第31-219頁。九州圖書文物有限公司。台北, 台灣。14.林讚峰。1983。紅麴菌之鑑定及實用分類法。製酒科技專論彙編, 第五期, 104-113。15.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。16.林讚峰。1986。紅麴菌二級代謝產物的經濟性評估及增產策略。製酒科技專論彙編, 第八期, 81-99。17.林讚峰。1992。紅麴菌在保健食品上的新用途。食品工業, 24(10):41-45。18.林讚峰。1992b。紅麴菌研究發展之演進。科學農業, 40(3-4):193-198。19.林讚峰。1995。製酒科技專論彙編。17:156-168。20.林秦璋。2005。探討培養基與培養條件對固態培養紅麴菌生產Monacolin K、Citrinin及色素的影響。大同大學生物工程研究所碩士論文。台北。21.林麗雲。1998。蔴油製造的研究。台灣大學農業化學研究所博士論文。台北。22.邱建人。1977。紅麴色素之各種性質及其應用。食品科學文摘, 5(11):8-14。23.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。24.洪哲穎。1998。回應曲面品質工程技術。第64-269頁。義守大學化學工程學系。高雄, 台灣。25.施麟碩。2005。紅麴山藥豆腐乳色澤分析之研判。大葉大學生物產業科技學系碩士班。彰化。26.郭錦富。1986。醬油釀造過程中香味之變化及不同成品之比較。台灣大學農業化學研究所碩士論文。台北。27.凌美月、周正俊。1995。Aspergillus oryzae在不同擠壓醬油發酵基質上之生長及酵素生產。中國農業化學會誌, 33:521-532 28.許紅峰、毛寧、黃諺諺、馬宏。1999。紅曲霉菌絲體及發酵濾液抗疲勞作用之研究。中國體育科技, 35(11):50-52。29.陳彥霖、李昭蓉、陳建州、袁國芳。1998。紅麴菌種的研究開發與應用。食品工業月刊, 30(7):1-10。30.陳彥霖。1999。紅麴與高血壓。科學與技術, 32(12):54-59。31.陳運中。2003a。功能性紅麴色素發酵工藝研究。工藝技術食品科學, 24(7):83-87。32.陳威銘。2003b。利用紅麴菌發酵生產機能性魚肉產品之新技術。台灣海洋大學食品科學系碩士論文。基隆。33.陳美琪。2005。溫度效應對紅麴菌生產色素暨monacolin K之影響。朝陽科技大學應用化學系碩士論文。台中。34.曾貽湧。2005。以反應曲面法探討蜂蜜酒糟醋發酵較適條件之研究。中興大學食品科學系碩士論文。台中。35.黃顯宗。1985。紅麴菌研究之回顧與展望。真菌學會之最近發展, 109-124。國科會生物科學研究中心專刊第十二集。台北, 台灣。36.黃育輝。2000。紅麴菌二級代謝物中紅麴色素與膽固醇合成抑制劑共存性之探討。大葉大學食品工程研究所碩士論文。彰化。37.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。38.劉春敏。2004。利用酵素法提昇胡蘿蔔濃縮汁收率及品質之研究。大葉大學生物產業科技研究所碩士論文。彰化。39.廖玉萍。2003。利用不同發酵槽培養紅麴菌(Monascus ruber)生產monacolin K和紅麴色素之研究。東海大學食品科學研究所碩士論文。台灣。40.鄭顏昆。2002。甲硫胺酸與乙酸钠對紅麴生成膽固醇合成抑制劑產量影響之研究。大葉大學食品工程研究所碩士論文。彰化。41.鄧化瑜。2003。以米為基質固態培養紅麴菌生產色素、Monacolin K及Citrinin產量變化之研究。大同大學生物工程研究所碩士論文。台北。42.謝鳳龍。1998。利用紅麴菌以固-液態培養方式產生膽固醇合成抑制劑。大葉大學食品工程研究所碩士論文。彰化。43.簡可欣。2004。固態培養Monascus spp.生產monacolin K及色素。台灣大學食品科技研究所碩士論文。台北。44.羅李?。2004。紅麴發酵製品之開發, 農政與農情, 農會出版品。第143期。45.蘇遠志、黃健雄。1976。紅麴色素之生產研究。中國農業化學會誌, 14:45-58。46.Alberts, A. W., J. Chem, G. Kuron, V. Hunt, J. Huff, C. Hoffman, J. Rothrock, M. Lopez, H. Joshua, E. Harris, A. Patcrllett, R. Monachan, S. Currie, E. Stapley, G. Albers. Schonberc, O. Hensens, J. Hirshfield, K. Hoogsteen, and J. Liesch., 1980, Mevinolin: a highly potent competitive inhibitor of hydroxymethylglutaryl-coenzyme a reductase and a cholesterol-lowe ring agent. Proc. Natl. Acad. Sci. 77 : 3957-3961. 47.A.O.A.C., 1984, " Official Method of Analysis ". 14th ed. Association of Official Analytical Chemists, Washington, D. C., U.S.A. 48.Alberts, A. W., 1988, Discovery, biochemistry and biology of lovastatin. Am. J. Cardiol. 62 : 10J-15J. 49.Aniya, Y., T. Yokomakura, M. Yonamime, K. Shimada, T. Nagamine, M. Shimabukuro, and H. Gibo., 1999, Screening of antioxidant action of various molds and protection of Monascus anka against experimentally induced liver injuries of rats. Gen Pharmacol. 32 : 225-231. 50.Aniya, Y., I.I. Ohtani, T. Higa, C. Miyagi, H. Gibo, M. Shimabukuro, H. Nakanish, and J. Taira., 2000, Dimerumic acid as an antioxidant of the mold, Monascus anka. Free Radi Boil Medic. 28 : 999-1004. 51.Alison, D., and P. Collins., 2000, Colouring our foods in the last and next millennium. Int. J. Food Sci. 35 : 5-22. 52.Allok. 2004, www.Allok-e.mandt.de/etoxi.htm. 53.Box, G. E. P., and Wilson, K. B., 1951, On the experimental attainment optimum conditions. J. Roy. Statist. Soc. 13 : 1-45. 54.Box, G. E. P., and Behnken, D. W., 1960, Some new three level design for the study of quantitative variables. Technometrics 2 : 455-475. 55.Brown, A. G., and T. C. Smale., 1976, Crystal and molecular structure of compactin, a new antifungal metabolite from Penicillium brevicompactum. J. Chem Soc. I. 1165-1170. 56.Brown, M. S., and J. L. Goldstein., 1984, How LDL receptors influence cholesterol and atherosclerosis. Scientific American, 251(5) : 52-60. 57.Budavari, S., J. O. Maryadele., A. Smith., and P. E. Heckelman.,

1989, The Merck Index. 11 : 2330-2331 and 6042-6043. 58. 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. 59. Blanc, P. J., Loret, M. O., and Santerre, A. L., 1994, Pigments of *Monascus*. J. Food Sci. 59 : 862-5. 60. Buxbaum, J.D., G. Thinakaran, V. Koliatsos, J. O' Callahan, H.H. Slunt, D.L. Price, and S.S. Sisodia. 1998. Alzheimer amyloid protein precursor in the rat hippocampus : transport and processing through the perforant path. J. Neurosci. December 1. 18 : 9629-9637. 61. Chiu, S. W., Poon, Y. K., 1993, Submerged production of *Monascus* pigment. Mycologia 85:214-218. 62. Chen, M. H., and Johns M. R., 1994, Effect of carbon source on ethanol: A pigment production by *Monascus purpureus*. Enz. Microb. Technol. 16 : 584-590. 63. Chang, Y.N., J.C. Huang, C.C. Lee, I.L. Shih, and Y.M. Tzeng. 2002. Use of response surface methodology to optimize culture medium for production of lovastatin by *Monascus ruber*. Enzyme Microb. Technol. 30 : 889-894. 64. Chen, F. S. and Hu, X. Q., 2005, Study on red fermented rice with high concentration of monacolin K and low concentration of citrinin. Int. J. Food Sci. 103 : 331-337. 65. Endo, A., M. Kuroda, and Y. Tsujita, 1976, ML-236A, ML-236B, ML-236C, new inhibitors of cholesterol synthesis produced by *Penicillium citrinum*. The J. Antibiot. 29 : 1345-1348. 66. Endo, A., 1979, Monacolin K, a new hypocholesterolemic agent produced by *Monascus* species. The J. Antibiotics 32 : 852-854. 67. Endo, A., 1980. Biological and biochemical aspects of ML-236B ( compactin ) and monacolin K, specific competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase. The J. Atherosclerosis 35 : 152-155. 68. Endo, A., Hasumi, K., Negishi, S., 1985, Monacolin J and L, new inhibitors of cholesterol biosynthesis produced by *Monascus ruber*. J. Antibiot. 38 : 420-422. 69. Endo, A., Komagata, D., Shimada, H., Murkawa, S., 1989, Biosynthesis of monacolin L to monacolin J by a monooxygenase of *Monascus ruber*. J. Antibiot. 42 : 407-412. 70. Elibol, M., and Muvituna, F., 1997, Characteristics of antibiotic production in a multiphase system. Proc. Biochem. 32 : 417-422. 71. Fabre, C. E., Santerre, A. L., Loret, M. O., Baberian, R., Pareilleux, A., Goma, G., Blanc, P. J., 1993, Production and food applications of the red pigments of *Monascus ruber*. J. Food. Sci. 58: 1099-1110. 72. Griffin, D. H., 1981, Fungal physiology, New York: John Wiley & Sons. pp.219-239. 73. Hawksworth, D. L., and Pitt, J. L., 1983, A new taxonomy for *Monascus* species based on culture and microscopical character. Aust. J. Bot. 31 : 51-61. 74. Henika, R. G., 1972, Simple and effective system for use with response surface methodology. Cereal Sci. 17 : 309-312. 75. Hu, J. Q., 1997, Production and application of red fermentation rice (Chinese). Light Industry Press, Beijing, PR China, pp.1-40. 76. Hu, X. Q., Chen, F. S., 2004, Double direction thin layer chromatogram for Monacolin K in red fermented rice (Chinese). J. Chin. Brew. 2, 45-48. 77. Juzlova, P., Martinkova, L., Kren, V., 1996, Secondary metabolites of the fungus *Monascus*: A review. J. Ind. Microbiol. 16, 163-170. 78. Jick, H., G. L. Zornberg, S. S. Jick, S. Seshadri, and D. A. Drachman., 2000, Statins and the risk of dementia. The Lancet. 356 : 1627-1631. 80. Kumasakim, S. Nakanishi, and Nishikawa., 1962, Structure of monascorubrin. Tetrahedron. 18 : 1171-1184. 81. Kroon, P. A., Hand K. M., Huff J. W., Albert, A. W., 1982, The effect of Mevinolin on serum cholesterol levels of rabbits with endogenous hypercholesterolemia. Atherosclerosis. 44 : 41-48. 82. Kautola, H. and Linko, Y. Y., 1989, Fumaric acid production from xylose by immobilized *Rhizopus arrhizus* cells. Appl. Microbiol. Biotechnol. 31 : 448-452. 83. Kimura, K., Komagata, D., S. Murakawa, and Endo, A., 1990, Biosynthesis of monacolins: conversion of monacolin J to monacolin K ( mevinolin ) . J. Antibiot. 43 : 1621-1622. 84. Lin, T. F., and Demain, A. L., 1991, Effect of nutrition of *Monascus* sp. on formation of red pigment. Appl. Microb. Biotechnol. 36 : 70-75. 85. Lin, T. F., Yakushijin K, Buchi, G. H., 1992, Formation of water-soluble monascus red pigment by biological and semi-synthetic processes. J. Ind. Microbiol. 9 : 173-9. 86. Li, C., Zhu, Y., Wang, Y., Zhu, J. S., Chang, J., Kritchevsky, D., 1998, *Monascus purpureus* fermented rice ( red yeast rice ) : a natural food product that lowers blood cholesterol in animal models of hypercholesterolemia. J. Food. Res. 18 : 71-78. 87. Mukker, G. L., 1965, Use of dinitrosalicylic acid reagent for determination of reducing sugar. J. Food. Sci. 47 : 1983-1986. 88. Montgomery, D. C., 1984, Response Surface Methods and Designs. " Design and analysis of Experiments " , John Wiley. New York. pp.521. 89. Mudahar, S., R. T. Toledo, J. D. Floros and J. J. Jen., 1989, Optimization of carrot dehydration Process using response surface methodology. J. Food Sci. 54 : 714-719. 90. Maddox, I. S. and S. H. Richert., 1997, Production of gibberellic acid using a dairy waste as the basal medium. Appl. Environ. Microbiol. 33 : 201-202. 91. Nil., 1995a, SSRI: unprecedented US Growth, Scrip, 2024 : 23. 92. Nil., 1995b, Yen Effect on Japan ' s Pharma Market, Scrip, 2023 : 22. 93. Narahara, H., Koyama, Y., Yoshida, T., Pichangkura, S., Ueda, R., and Taguchi, H., 1982. Growth and enzyme production in a solid state culture of *Aspergillus oryzae*. J. Ferment. Technol. 60 : 311-319. 94. Prapulla, S. G., Jacob, S., Chand, N., Rajalakshmi, D., and Karanth, N. G., 1992, Maximization of lipid production by *Rhodotroula gracilis* CFR-A using response surface methodology. Biotech. Bioeng. 40 : 965-969. 95. Pandey, A., Soccol, C.R., Rodriguez-Leon, J.A., Nigam, P., 2001, Solid-state Fermentation in Biotechnology. Asiatech Publishers, Inc., New Delhi. pp. 221. 96. Pandey, A., 2003, Solid-state fermentation. Biochem. Eng. J 14, 81-84. 97. Sung, Y. H., 1966, Yeasts in " T ' ien-kung K ' ai-Wu " (transl.). Sun, E.T., Sun, Z. (Eds.), Chinese Technology in the Seventeenth Century. Pennsylvania State University Press, University Park, PA, pp. 292-294. 98. Su, Y. C., 1978, Fermentative production of anka-pigment ( *Monascus*-pigment ) . Proceedings of the oriental fermented foods. Food. Inst. Res. Devel., Hsinchu, Taiwan, R.O.C. 99. Sweeny, J. G., Estrada-Valdes, H. C., Iacobucci, G. A., Sato, H., and Sakamura, S., 1981, Photoprotection of the red pigments of *Monascus anka* in aqueous media by 1,4,6-trihydroxynaphthalene. J. Agric. Food Chem. 29 : 1189-1193. 100. Sato, K., 1992, Novel natural colorants from *Monascus anka*. U-1 Heterocycles 34, 2057-2060. 101. Sharmila, R., D.C. Porter, X. Chen, T. Herliczek, M. Lowe, and K. Keyomarsi, 1999, Lovastatin-mediated G1 arrest through inhibition of the proteasome, independent of hydroxymethyl glutaryl-CoA reductase. Proc. Natl. Acad. USA. 96 : 7797-7802. 102. Shindia, A. A., 2000, Studies on mevinolin production by some fungi. Microbios. 102 : 53-61. 103. Su, Y.C., Wang, J.J., Lin, T.T., and Pan, T.M., 2003, Production of the secondary metabolites -aminobutyric acid monacolin K by *Monascus*. J Ind Microbiol Biotechnol. 30 : 41-46. 104. Sumathy, B., Carlos, R. S., Ashok, P., 2007, Solid-state fermentation for the production of *Monascus* pigments from jackfruit seed. Bio. Technol. 98 : 1554-1560. 105. Tsujita, Y.,

Kuroda, M., Tanzawa, K., Kitano, N., and Endo, A., 1979, Hypolipidemic effects in dogs of ML-236B, a competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme a reductase. *Atherosclerosis* 32 : 307-313.

106.Thomson, D., 1982, Response surface experimentation. *J. Food Process. Pres.* 6 : 155-188.

107.Tsuji, K., Ichikawa, T., Tanabe, N., Abe, S., Tarui, S., Nakagawa, Y., 1992, Effect of two kinds of Koji on blood pressure in spontaneously hypertensive rats. *Nippon Nogeikagaku Kaishi* 66 : 1241-1246.

108.Taira J, Miyagi C, Aniya Y., 2002, Dimerumic acid as an antioxidant from the mold, *Monascus anka*: the inhibition mechanisms against lipid peroxidation and heme protein mediated oxidation. *Biochem. Pharmacol.* 63 : 1019-1026.

109.Van Tieghem, P., 1884, *Monascus*, genre nouveau de 1<sup>er</sup> ordre des Ascomycetes. *Bulletin Societe botanique de France.* 31 : 226-231.

110.Wong, H, C., Koehler, P, E., 1983, Production of red water-soluble *Monascus* pigments. *J. Food Sci.* 48 : 1200-1203.

111.Watanbe, T., Yamamoto, A., Nagai, S., Terabe, S., 1997, Separation and determination of *Monascus* yellow pigment for food by micellar electrokinetic chromatography. *Anal. Sci.* 13 : 571-575.

112.Winston, B., 2000, National colors as Functional ingredients in healthy foods. *Vol.45, No.5.* pp.221-222.

113.Wang, J.J. and T.M. Pam, 2003, Effect of red rice supplements on serum and egg yolk cholesterol levels of laying hens. *J. Agric. Food Chem.* 51 : 4824-4839.

114.Xijin, L., 2004, Study on photostability of monascus pigments. Doctoral thesis, Tianjin University of Science and Technology, China.

115.Yasuda, M., Uechi, G., Miyazato, K., 1983, Production of koji with *Monascus* sp. for tofuyo-manufacturing. *Nippon Shokuhu Kogyo Gakkaishi* 30(2) : 63-67.

116.Yongsmith, B., Tabloka, W., Yongmanitchai, W., Bavavoda, R., 1993, Culture condition for yellow pigment formation by *Monascus* sp. KB10 grown on cassava medium. *World J Microbiol Biotechnol.* 9 : 85-90.

117.Yasukawa, K. M., Takahashi, S., Natori, M., Yamazaki, M., Takeuchi, M. Takido., 1994, Azaphilones inhibit tumor promotion by 12-o-tetradecanoylphorbol-13-acetate, *Oncology*, 45 : 108-112.

118.Yang, S. L., Zhang, H., Li, Y. Q., Qian, J. Q., Wang, W., 2005, The ultrasonic effect on biological characteristics of *Monascus* sp. *Enz. Microb. Technol.* 37 : 139-144.