STUDIES ON THE EXTRACTION OF CORDYCEPS SP. MYCELIUM USING SUPERCRITICAL CARBON DIOXIDE FLUID AND THE ANTIOXIDANT PROPER

林聖智、張基郁,洪淑嫻,林麗雲,楊明華

E-mail: 9017518@mail.dyu.edu.tw

ABSTRACT

"DONGCHONGXIACHAO" IS A RARE AND EXPENSIVE DRUG IN CHINESE MEDICINE, WHICH IS PRODUCED IN THE LARVA OF HEPIALIDAE INFECTING MAINLY BY THE PARASITE FUNGUS CORDYCEPS SINENSIS. DUE TO THE YIELD OF CORDYCEPS SINENSIS IS LIMITED, ITS PRICE IS VERY HIGH, AND THEREFORE THE MANUFACTURERS TRY TO USE FERMENTATION TECHNIQUES TO MASS-PRODUCE CORDYCEPS SINENSIS MYCELIUM TO DECREASE ITS PRICE. HOWEVER, IT REMAIN OBSCURE WHETHER THE CHEMICAL COMPONENTS OBTAINED FROM CORDYCEPS SINENSIS MYCELIUM ARE THE SAME AS THOSE FROM CORDYCEPS SINENSIS AND WHETHER THE ANTIOXIDANT PROPERTIES AND ANTI-TUMOR ACTIVITY ARE AFFECTED BY THE EXTRACTION METHOD AND THE SOLVENT USED. IN THIS RESEARCH, CORDYCEPS SINENSIS MYCELIUM WAS EXTRACTED USING SUPERCRITICAL CO2 FLUID AND RESPONSE SURFACE METHODOLOGY WAS USED TO ANALYZE THE EXTRACTION CONDITIONS. THE EXTRACT OBTAINED FROM SUPERCRITICAL CO2 FLUID EXTRACTION WAS ALSO COMPARED WITH THOSE EXTRACTED BY METHANOL, ETHANOL, AND WATER. FURTHERMORE, THE METHANOL EXTRACT OF CORDYCEPS SINENSIS MYCELIUM WAS FRACTIONATED USING SILICA GEL COLUMN CHROMATOGRAPHY AND THEN THE FRACTIONS WERE ANALYZED FOR THEIR ANTIOXIDANT PROPERTIES AND ANTI-TUMOR ACTIVITY. RESULTS SHOWED THAT THE EXTRACTION OF CORDYCEPS SINENSIS MYCELIUM WITH SUPERCRITICAL CO2 FLUID AT 4500PSI AND 60℃ FOR 3 HOURS GAVE THE HIGHEST YIELD OF 58.47MG/G MYCELIUM. THE RESULTS OF ANTIOXIDATIVE ASSAYS SHOWED THAT ALL SOLVENT EXTRACTS INHIBITED THE DECOMPOSITION OF DEOXYRIBOSE, AND THE HYDROXYL RADICAL SCAVENGING ACTIVITY OF ALL EXTRACTS INCREASED WITH THE INCREASING CONCENTRATION OF ALL EXTRACTS. THE ORDER OF RELATIVE HYDROXYL RADICAL SCAVENGING ACTIVITY OF VARIOUS EXTRACTS IS BHT > METHANOL EXTRACT > ETHANOL EXTRACT > WATER EXTRACT > SUPERCRITICAL CO2 FLUID EXTRACT. THE CS-A, B, C, D, AND E FRACTIONS OBTAINED FROM THE METHANOL EXTRACT OF CORDYCEPS SINENSIS MYCELIUM USING A SILICA GEL COLUMN CHROMATOGRAPHY ALSO INHIBITED THE DECOMPOSITION OF DEOXYRIBOSE. THE CS-B FRACTION HAD THE HIGHEST HYDROXYL RADICAL SCAVENGING ACTIVITY, WHICH IS HIGHER THAN THAT OF BHT. THE CS-A FRACTION HAD THE SECOND HIGHER ACTIVITY, WHICH IS HIGHER THAN THAT OF BHT IN THE CONCENTRATION RANGE FROM 400 TO 800 μG/ML. IN THE EXAMINATION OF REDUCING POWER, EXCEPT BHT HAD A STRONG REDUCING POWER, ALL THE EXTRACTS FROM CORDYCEPS SINENSIS MYCELIUM SHOWED VERY LOW REDUCING POWER, WHEREAS THE REDUCING POWER OF VARIOUS EXTRACTS STILL INCREASED WITH THE INCREASING CONCENTRATION. IN THE RESULTS OF DPPH RADICAL SCAVENGING ACTIVITY ASSAY, THE ETHANOL EXTRACT HAD THE HIGHEST VALUE OF 91.5% AND THE SUPERCRITICAL CO2 FLUID EXTRACT HAD THE LOWEST. THE ORDER OF DPPH RADICAL SCAVENGING ACTIVITY OF THE FRACTIONS IS BHT = CS-B > CS-C > CS-D > CS-A > CS-E. THE ETHANOL EXTRACT SHOWED THE HIGHEST ABILITY TO CHELATE FERROUS IONS AND THE SUPERCRITICAL CO2 FLUID EXTRACT OPPOSITELY HAD THE LOWEST. THE CS-B FRACTION OF METHANOL EXTRACT CHELATED 43.8% OF FE(II), WHICH WAS THE HIGHEST CHELATING POWER AMONG ALL THE FRACTIONS. WHEN THE CONCENTRATION OF ALL FRACTIONS WAS 10000 μG/ML, THE FRACTIONS HAD A RELATIVE FERROUS ION CHELATING POWER AS CS-B > CS-A > CS-E > CS-D > CS-C >BHT. IN THE ANTI-TUMOR ACTIVITY TEST, THE INHIBITORY EFFECTS OF CORDYCEPS SINENSIS MYCELIUM ON C6 AND MG-63 TUMOR CELL LINES WERE STUDIED USING MTT TEST. THE RESULTS SHOWED THAT METHANOL EXTRACT HAD THE HIGHEST INHIBITORY ACTIVITY (53.7%INHIBITION FOR C6 CELL LINE AND 70.6%FOR MG-63 CELL LINE). SUPERCRITICAL CO2 FLUID EXTRACT HAD THE NEXT VALUE (55.5 %INHIBITION FOR C6 CELL LINE AND 55.2%FOR MG-63 CELL LINE). AMONG FIVE FRACTIONS OF METHANOL EXTRACT, CS-A FRACTION SHOWED THE HIGHEST ANTI-TUMOR ACTIVITY, WHICH WAS 87.4 %INHIBITION FOR C6 CELL LINE AND 73.6%FOR MG-63 CELL LINE.

Keywords : CORDYCEPS SINENSIS MYCELIUM, SUPERCRITICAL CO2 FLUID, ANTIOXIDANT PROPERTIES, ANTI-TUMOR ACTIVITY, MTT TEST

Table of Contents

REFERENCES

1.王西華、陳志昇、黃雅惠、許瑞祥。1999。傳統保健食品－冬蟲夏草。生物產業10(1):19-27。 2.王化遠、唐心曜。1996。川產野生冬蟲夏草不同時期生長子座、蟲體中甘露醇含量比較。華西藥學 雜誌11(1):58-59。 3.王伯徹。1990。藥用真菌系列報導（二）冬蟲夏草。食品工業22(2):36-40。 4.王伯徹、邱世浩、黃仁彰。1998。食用菇保健食品專輯。30(5):1-35。 5.王文獻 編著。1995。藥理精義。合記圖書出版社。台北。PP280。 6.王國棟、晉天春。1994。冬蟲夏草對免疫功能的影響。中成藥。16(11):43-44。 7.王青牡、孫姝媛。1997。我國液態培養藥用蟲草菌絲體的研究進展。食用菌19(3):2-3。 8.王國棟。1995。冬蟲夏草類防治腎臟病研究進展。遼寧中醫雜誌22(2):93-95。 9.汪寶琪、廣志功。1995。西藏冬蟲夏草中D-甘露醇的薄層掃描分析。中藥草。26(4):189-191。 10.李喬治。1990。動物細胞培養。食品工業。22(3):38-43。 11.沈曉雲、李兆蘭、田軍。1998。冬蟲夏草與蟲草菌絲有效成分分析比較。山西大學學報（自然科學 版）21(1):81-85。 12.沈穎、劉華、張金黎及王堅。1996。冬蟲夏草應用於急性腎功能衰竭31例的臨床對照研究。雲南中 醫中藥雜誌。17(3):36-37。 13.林新發、廖俊雄、陳健忠、凌勇健。1995A。超臨界流體萃取和潔淨技術(上)。科儀新知。27(2): 50-58。 14.林新發、廖俊雄、陳健忠、凌勇健。1995A。超臨界流體萃取和潔淨技術(下)。科儀新知。27(3): 82-91。 15.林桂英。2000。不同冬蟲夏草菌株醱酵產程中機能性指標成分之探討。大葉大學食品工程研究所碩 士論文。彰化，台灣。 16.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。化工，39（2）:3-17。 17.徐文豪、薛智、馬建民。1988。冬蟲夏草的水溶性成分-核?類化合物的研究。中藥通報13(4):34- 36。 18.徐泰浩、曾耀銘。1992。利用發酵技術開發機能性食物-冬蟲夏草。科學發展月刊:388-392。 19.桂椿雄。1990。超臨界流體簡介。科儀新知。11(4):44-48。 20.陳召南。1992。細腳擬青霉(固培物)與冬蟲夏草化學成分的初步比較。中成藥14(2):35-37。 21.陳宗融。1995。。冬蟲夏草的抗癌療效研究。明通醫藥P34-35。 22.陳明、張榮。1995。冬蟲夏草中核?及其鹼基含量測定方法之研究。中成藥。17(4):40-41。 23.陳琮融。1995.4.10。「冬蟲夏草」的抗癌療效研究。明通醫藥。34-36。 24.陳萬群、陳古榮。1994。冬蟲夏草代用品研究進展。中草藥。25(5):269-271。 25.施益民、呂鋒州。1989。自由基與各種疾病。當代醫學。16(5):54-62。 26.馮頤、傅蓮瑛、袁淑蘭。1996。天然冬蟲夏草與蟲草菌提取液薄層對比試驗。天津藥學。8(4):93- 94。 27.馮玉環、高鳳儀。1994。冬蟲夏草的藥理及臨床研究近況。實用醫學雜誌。10(4):413-414。 28.黃天福、陳仕江、傅善全、羅慶明。1996。康定冬蟲夏草菌憂勢寄主昆蟲的生態型的研究。時珍國 藥研究。7(3):178-179。 29.張毅生。1996。善用冬蟲夏草可提升免疫機能。常春月刊。85年3月號:96-102。 30.蕭麗華。1997。冬蟲夏草藥材真偽品與發酵培養製備物之結構特徵與成份分析比較。大葉工學院食 品工程研究所碩士論文。彰化，台灣。 31.解軍、郭欣、李培毅。1994。冬蟲夏草及人工菌絲體中蟲草菌素的定性定量研究。山西中醫。10(4) :36-38。 32.郭育綺、陳建志。1999。冬蟲夏草腫瘤細胞生長抑制因子之純化。產業科技發展學術合作研討會。 321-328。 33.葉佳聖。1993。補骨脂抗氧化成分之研究。食品科學。 20(6):574-585。 34.張士善、張丹參、朱桐、陳醒言。1991。冬蟲夏草氨機酸成分的藥理分析。藥學學報。26(5):326- 330。 35.張明慧、吳天賞。1996。茵陳蒿抗氧化成分之研究。食甲、品科學。23(4):594-607。 36.蘇正德。1992。果實種子類中藥之抗氧化性及生育醇含甲、量之調查研究。食品科學，19(1):12- 24。 37.蘇正德。1991。茶湯與茶渣之兒茶酚含量及抗氧化性之甲、調查研究。食品科學，18(3):234-248。 38.張毅偉。1998。百香果主要花青素及其抗氧化性之研甲、究。食品科學，25(5):651-656。 39.劉伯康、陳惠英。1999。數種傳統食用植物甲醇萃取物甲、抗氧化性之研究。中國農業化學會誌， 37(1):105-116。 40.翁瑞光。1998。蘿蔔嬰萃取物於模式系統之抗氧化性。甲、食品科學。25(3):268-280。 41.翁瑞光、顏國欽。1997。綠豆芽、黃豆芽及蘿蔔嬰抗氧甲、化性之研究。中國

農業化學會誌。35(6) :661-670。 42.蔡琇萱、胡淼琳。1995。茶抽出物的抗氧化性及添加維生素C於茶抽出液中的穩定性。中國農業化學會誌。33(5):561-569。 43.廖怡禎。1997。超臨界流體技術在台灣食品工業之發展與未來應用的展望。食品工業。29(8):38-47。 44.褚西寧、白玉明、江如琴、羅建穎及程巧梅。1997。蟲生真菌超氧歧化梅同功梅的研究。中國蟲生 真菌研究與應用。中國農業科技出版社。北京。PP82-86。 45.ANON. 1997A. 茸類之機能研究與素材之研究。食品與開發(日本)。32(7):48-51。 46.BHATTANYA, M., HANNA, M. A. AND MUDIGO, R. A. 1988. LIPID OXIDATION IN GROUND BEEF PATT -IES AS EFFECTED BY TIME- TEMPERATURE AND PRODUCT PACKAGING PARAMETERS. J. FOOD SCI. 53 : 714- 717. 47.BOX, G. E. P. AND WILSON, K. B. 1951. ON THE EXPERIMENTAL 甲、ATTRAINMENT OF OPTIMUM CONDITIONS. J. ROY. STATIST. SOC., B13: 1-45. 48.CROSS, C. E., HALLIWELL, B., BORISH, E. T., PRYOR, W. A., AMES, B. N., SAUL, R. L., MCCORD, M. J. AND HARMAN, D. 1987. OXYGEN RADICALS AND HUMAN DIAEASES. ANN. INT. MED., 107:526-545. 49.CUNINGHAM, K. G., HUTCHINSON, S. A., MANSON, W. AND SPRING, F. S. 1950. CORDYCEPIN, A METABOLIC PRODUCT FROM CULTURES OF CORDYCEPS MILITARIS LINK. NATURAL (LONDON) 166: 949 -951. 50.CUNNING, K. G., HUTCHISON, S. A., MANSON, W. AND SPRING, F. S. 1951. CORDYCEPIN, A META -BOLIC PRODUCT FROM CULTURES OF CORDYCEPS MILITARIS (LINN.) LINK. PART Ⅰ. ISOLATION AND CHARACTERIZATION. J. CHEM. SOC. 2299. 51.CHEN, Y. J., SHIAO, M. S., LEE, S. S. AND WANG, S. Y. 1997. EFFECT OF CORDYCEPS SINENSI -S ON THE PROLIFERATION AND DIFFERENTITATION OF HUMAN LEUKEMIC U937 CELL. LIFE SCI. 60: 2349-2359. 52.CHRISTIANSON, D. D., FRIEDRICH, J. P., LIST, G. R., WARNER, K., BAGLEY, E. B., STRINGFE -LLOW, A. C. AND INGLETT, G. E. 1984. SUPERCRITICAL FLUID EXTRACTION OF DRY-MILLED CORN GERM WITH CARBON DIOXIDE. J. FOOD SCI. 49:229-232. 53.DECKER, E. A. AND WELCH, B. 1990. ROLE OF FERRITIN AS A 甲、LIPID OXIDATION CATALYST IN MUSCLE FOOD. J. AGRIC. FOOD 乙、CHEM. 38:674-677. 54.DU, D. J. 1986. ANTITUMOR ACTIVITY OF CORDYCEPS SINENSIS AND CULTURED CORDYCEPS MYCELIA. CHUNG YAO TUNG PAO. 11:51. 55.DECKER, E. A. AND WELCH, B. 1990. ROLE OF FERRITIN AS A LIPID OXIDATION CATALYST IN MUS -CLE FOOD. J. AGRIC. FOOD CHEM. 38:674-677. 56.ERDMAN, J. W. JR. 1979. OILSEED PHYTATE: NUTRITIONAL IMPLICATIONS. J. AM. OIL CHEM. SOC. 56: 736. 57.EMPSON, K. L., LABUZA, T. P. AND GRAF, E. 1991. PHYTIC ACID AS A FOOD ANTIOXIDANT. J. FOOD SCI., 56(2): 560-563. 58.FARKVAM, D. O., NELSON, T. S., KIRBY, L. K., JOHN SON, Z. B. AND STAMPS, A. T. 1989. CALCIUM AND PHYTIC ACID IN CHICK NUTRITION. NUTR. REP. INT., 40(1): 33-42. 59.FENG, M. G., ZHOU, O. G. AND FENG, G. H. 1987. VASODILATING EFFECT OF CULTURED CORDYCEP -S SINENSIS (BERK) SACC. MYCELIA IN ANESTHETIZED DOGS. CHUNG YAO TUNG PAO. 12(12):41-45. 60.FLOROS, J. D. AND CHINNAN, M. S. 1988. SEVEN FACTOR RESPONSE SURFACE OPTIMIZATION OF A DOUBLE-STAGE LYE (NAOH) PEELING PROCESS FOR PIMIENTO PEPPERS. J. FOOD SCI. 53: 631. 61.FREDERIKSEN, S. AND RASMUSSEN, A. H. 1967. ANTINEOPLASTIC ACTIVITY OF CORDYCEPIN, IN EHRILICH ASCITES CARCINOMA IN MOUSE. CANCER RES. 27:385. 62.GIOVANNI, M.1983. RESPONSE SURFACE METHODOLOGY AND PRODUCT OPTIMIZATION. FOOD TECHNOL. 37(11): 41-45. 63.GUTTERIDGE J. M. C. 1981. THIOBARBITURIC ACID-REACTIVITY FOLLOWING IRON-DEPENDENT FREE- RADICAL DAMAGE TO AMINO ACIDS AND CARBOHYDRATES. BIOCHEM. 128:343-346. 64.HANNAY, J. B. AND HOGARTH, J. 1879. ON THE SOLUBILITY OF SOLIDS IN GASES. PROC. ROY. SOC. (LONDON) 29: 324. 65.HALLIWELL, B., GUTTERIDGE J. M. C. AND ARUOMA, O. I. 1987. THE DEOXYRIBOSE METHOD: A SIMPLE "TEST TUBE" ASSAY FOR DETERMINATION OF RATE CONSTANTS FOR REACTIONS OF HYDROXYL RADICALS. BIOCHEM. 165:215-219. 66.HALLIWELL, B. AND GUTTERIDGE J. M. C. 1981. FORMATION OF A THIOBARBITURIC-ACID-REACTIVE SUBSTANCE FROM DEOXYRIBOSE IN THE PRESENCE OF IRON SALTS. BIOCHEM. 128:347-352. 67.HALLIWELL, B. ANTIOXIDANTS SENSE OR SPECULATION. 1994. NUTR. TODAY, 29(6):15-19. 68.HYBELL, H. B., PEQUIGNOT, E. C., WILLIS, D. H. AND LEE, C. 1985. DIFFERENTIAL AUTOPROLI -FERATIVE ACTIONS OF 2'-5'-OLIGO A TRIMER CORE AND ITS CORDYCEPIN ANALOGUE ON HUMAN TU -MOR CELLS. INT. J. CANCER 36:389. 69.ITO, N., FUKUSHIMA S. AND TSUDA H. 1985. CARCINOGENICITY AND MODIFICATION OF THE CARCIN -OGENIC RESPONSE BY BHA, BHT, AND OTHER ANTIOXIDANTS. CRC CRIT. REV. TOXICOL., 15:109- 150. 70.KOBAYASI, Y. 1941. THE GENUS CORDYCEPS AND ITS ALLIES. SCI. REP. TOKYO. BUN. DQIGAKU. 5, 53-260. 71.KIHO, T., HUI, J. I., YAMANE, A. AND UKAI, S. 1993. POLYSACCHARIDES IN FUNGI. XXXⅡ. HYPOGLYCEMIC ACTIVITY AND CHEMICAL PROPERTIES OF A POLYSACCHARIDES FROM THE CULTURAL MYCELIUM OF CORDYCEPS SINENSIS. BIOL. PHARM. BULL. 16(12):1291-1293. 72.KIHO, T. AND UKAI, S. 1995. TOCHUKASO (SPMITAKE AND OTHERS CORDYCEPS SPECIES). FOOD RE VIEWS INTERNATIONAL. 11(1): 231-234. 73.KIHO, T., YAMANE, A., HUI, J., USUI, S., UKAI, S. 1996. POLYSACCHARIDES IN FUNGI. XXXVI. HYPOGLYCEMIC ACTIVITY OF A POLYSACCHARIDE (CS-F30) FROM THE CULTURAL MYCELIUM OF CORDYC -EPS SINENSIS AND ITS EFFECT ON GLUCOSE METABOLISM IN MOUSE LIVER. BIOL. PHARM. BULL. 19(2):294-296. 74.KIHO, T., OOKUBO, K., USUI, S., UKAI, S., HIRANO, K. 1999. STRUCTURAL FEATURES AND HYP -OGLYCEMIC ACTIVITY OF A POLYSACCHARIDE (CF-F10) FROM THE CULTURED MYCELIUM OF CORDYCEP -S SINENSIS. 1999. BIOL. PHARM. BULL. 22(9):966-970. 75.KUO, Y. C., TSAI, W. J., SHIAO, M. S., CHEN, C. F., LIN, C. Y. 1996. CORDYCEPS SINENSIS AS AN IMMUNOMODULATORY AGENT. AM. J. CHIN. MED. 24(2):111-125. 76.KUO, Y. C., LIN, C. Y., TSAI, W. J., WU, C. L., CHEN, C. F. AND SHIAO, M. S. 1994. GROW -TH INHIBITORS AGAINST TUMOR CELL IN CORDYDEPS SINENSIS OTHER THAN CORDYCEPIN AND POLYS -ACCHARIDES. CANER INVESTIGATION. 12:611-615. 77.LI, L. S., ZHENG, F., LIU, Z. H. 1996.

EXPERIMENTAL STUDY ON EFFECT OF CORDYCEPS SINEN -SIS IN AMELIORATING AMINOGLYCOSIDE INDUCED NEPHROTOXICITY. CHUNG KUO CHUNG HSI I CHIEH HO TSA CHIH. 16(12):733-737. 78.LI, Y., CHEN, G. Z., JIANG D. Z. 1993. EFFECT OF CORDYCEPS SINENSIS ON ERYTHROPOIESIS IN MOUSE BONE MARROW. CHINESE MEDICAL JOURNAL-PEKING. 106:313. 79.LIU, P., ZHU, J., HUANG, Y., LIU, C. 1996. INFLUENCE OF CORDYCEPS SINENSIS (BERK.) SACC . AND RAT SERUM CONTAINING SAME MEDICINE ON IL-1, IFN AND TNF PRODUCED BY RAT KUFFER CELLS. CHUNG KUO CHUNG HSI I CHIEH HO TSA CHIH. 21(6):367-384. 80.MCHUGH, M. A. AND KRUKNOIS, V. J. 1986. SUPERCRITICAL FLUID EXTRACTION: PRINCIPLES AND PRACTICE. BUTTERWORTHS, STONEHAM, MA. USA. 81.NAKAMURA, K., YAMAGUCHI, Y., KAGOTA, S., KWON, Y. M.,甲、SHINOZUKA, K., KUNITOMO, M. 1999. INHIBITORY EFFECT OF CORDYCEPS SINENSIS ON SPONTANEOUS LIVER METASTASIS OF LEWIS LUNG CARCINOMA AND B16 MELANOMA CELLS IN SYNGENEIC MICE. JPN. J. PHARMACOL. 79(3):335- 341. 82.OYAIZU, M. 1986. ANTIOXIDATIVE ACTIVITIES OF PRODUCTS OF 甲、BROWNING REACTION PREPARED FROM GLUCOSAMINE. JPN. J. 乙、 NUTR., 44: 307-315 83.RAPOPORT, S. 1940. PHYTIC ACID IN AVIAN ERYTHROCYTES. J.甲、BIOL. CHEM., 135, 403-406. 84.RIZVI, S. S. H., BENADO. A. L., ZOLLWEG. J. A. AND DANIELS, J. A. 1986A. SUPERCRITICAL FLUID EXTRACTION: FUNDAMENTAL PRINCIPLES AND MODELLING METHODS. FOOD TECHNOL., 40(6): 55-65. 85.RIZVI, S. S. H., DANIELS, J. A., BENADO. A. L. AND ZOLLWEG, J. A. 1986B. SUPERCRITICAL FLUID EXTRACTION: OPERATING PRINCIPLES AND FOOD APPLICATIONS. FOOD TECHNOL., 40(7): 57- 64. 86.ROSOWSKY, A., LAZAURS, H. AND YAMASHITA, A. 1976. NUCLEOSIDES. 1. 9-(3-ALKYL-3DEOXY-BE -TA-D-甲、RIBOFURANOSYL) ADENINE AS LIPOPHILICANALOQUES OF CORDYCEPIN. SYNTHESIS AND PRELIMINARY BIOLOGICAL STUDIES. J. MED. CHEM. 19(11):1265-1279. 87.SHIAO, M. S., WANG, Z. N., LIN, L. J., LIEN, J. Y. AND WANG, J. J. 1994. PROFILES OF NUCLEOSIDES AND NITROGEN BASES IN CHINESE MEDICINAL FUNGUS CORDYCEPS SINENSIS AND RELA -TED SPECIES. BOT. BULL. ACAD. SIN. 35:261-267. 88.SHIMADA, K., FUJIKAWA, K., YAHARA, K. AND NAKAMURA, T. 1992. ANTIOXIDATIVE PROPERTIES OF XANTHAN ON THE AUTOXIDATION OF SOYBEAN OIL IN CYCLODEXTRIN EMULSION. J. AGRIC. FOOD CHEM. 40:945-948. 89.THOMSON, D. 1982. RESPONSE SURFACE EXPERIMENTATION. J. FOOD PROCESSING PRESERVATION. 6: 155-188. 90.WANG, S. M., LEE, L. J., LIN, W. W., CHANG, C. M. 1998. EFFECT OF A WATER-SOLUBLE EXTR -ACT OF CORDYCEPS SINENSIS ON STEROIDOGENESIS AND CAPSULAR MORPHOLOGY OF LIPID DROPLETS IN CULTURED RAT ADRENOCORTICAL. J. CELL BIOCHEM. 69(4):483-489. 91.XU, R. H., PENG, X. E., CHEN, G. Z., CHEN, G. L. 1992. EFFECT OF CORDYCEPS SINENSIS ON NATURAL KILLER ACTIVITY AND COLONY FORMATION OF B16 MELANOMA. CHINESE MEDICAL JOURNAL- PEKING. 105:97. 92.YAMAGUCHI, N. AND OKADA, Y. 1986. BROWNING REACTION PRODUCTS PRODUCED BY THE REACTION BETWEEN SUGARS AND AMINO ACIDS. VⅡ. DECOMPOSITION OF LIPID HYDROPEROXIDE BY THE BROWN -ING PRODUCTS. NIPPON SHOKUHIN KOGYO GAKKAISHI. 15:187-191. 93.YIN, D., TANG, X. 1995. ADVANCES IN THE STUDY ON ARTIFICIAL CULTIVATION OF CORDYCEPS SINENSIS. CHUNG KUO CHUNG HSI I CHIEH HO TSA CHIH. 20(12):707-709. 94.YOSHIDA, J., TAKAMURA, S., YAMAGUCHI, N., REN, L. J., CHEN, H. 1989. ANTITUMOR ACTIVITY OF AN EXTERACT OF CRODYCEPS SINENSIS(BREK) SACC. AGAINST MURINE TUMOR CELL LINES JAPANE -SE JOURNAL OF EXPERIMENTAL MEDICINE. 59:157. 95.ZUE, J. S., HALPERN, G. M., JONES, K. 1998. THE SCIENTIFIC REDISCOVERY OF AN ANCIENT CHINESE HERBAL MEDICINE: CORDYCEPS SINENSIS: PART I. J ALTERN COMPLEMENT MED. 4(3):289 -303.