

## 參考資料

1. Knekt P, Kumpulainen J, Jarvinen R, Rissanen H, Heliövaara M, Reunanen A, Hakulinen T, Aromaa A. Flavonoid intake and risk of chronic diseases. *Am J Clin Nutr.* 2002; 76(3):560-8.
2. Kim JY, Jung KJ, Choi JS, Chung HY. Hesperetin: a potent antioxidant against peroxynitrite. *Free Radic Res.* 2004; 38(7): 761-9.
3. Wei BL, Weng JR, Chiu PH, Hung CF, Wang JP, Lin CN. Antiinflammatory Flavonoids from *Artocarpus heterophyllus* and *Artocarpus communis*. *J Agric Food Chem.* 2005; 53(10): 3867-71.
4. Guglielmone HA, Agnese AM, Nunez Montoya SC, Cabrera JL. Inhibitory effects of sulphated flavonoids isolated from *Flaveria bidentis* on platelet aggregation. *Thromb Res.* 2005; 115(6): 495-502.
5. Orallo F, Alvarez E, Basaran H, Lugnier C. Comparative study of the vasorelaxant activity, superoxide-scavenging ability and cyclic nucleotide phosphodiesterase-inhibitory effects of hesperetin and hesperidin. *Naunyn Schmiedebergs Arch Pharmacol.* 2004; 370 (6): 452-63.
6. Kim HK, Jeon WK, Ko BS. Flavanone glycosides from *Citrus junos* and their anti-influenza virus activity. *Planta Med.* 2001; 67(6): 548-9.
7. Chen D, Daniel KG, Chen MS, Kuhn DJ, Landis-Piowar KR, Dou QP. Dietary flavonoids as proteasome inhibitors and apoptosis inducers in human leukemia cells. *Biochem Pharmacol.* 2005; 69(10): 1421-32.
8. Chao PDL, Hsiu SL, Hou YC. Flavonoids in herbs: Biological fates and potential interactions with xenobiotics. *Journal of Food and Drug*

- Analysis*. 2002; 10: 219-28.
9. Crespo ME, Galvez J, Cruz T, Ocete MA, and Zarzuelo A. Anti-inflammatory activity of diosmin and hesperidin in rat colitis induced by TNBS. *Planta Med*. 1999; 65 (7): 651-3.
  10. Lee NK, Choi SH, Park SH, Park EK, Kim DH. Antiallergic activity of hesperidin is activated by intestinal microflora. *Pharmacology*. 2004; 71(4): 174-80.
  11. Kawanguchi K, Kikuchi S, Takayanagi K, Yoshikawa T, and Kumazawa Y. Colony stimulating factor-inducing activity of hesperidin. *Planta Med*. 1999; 65 (4): 365-6.
  12. Monforte MT, Trovato A, Kirjavainen S, Forestieri AM, Galati EM, and Lo Curo RB. Biological effects of hesperidin, a Citrus flavonoid. (note II): hypolipidemic activity on experimental hypercholesterolemia in rat. *Farmaco*. 1996; 51(3): 219-21.
  13. Kurowska EM, Borradaile N, Meade M, Spence JD, and Carroll KK. Cholesterol-lowering effects of dietary citrus juices and their flavonoids. Studies in rats, mice and rabbits. *Farmaco*. 1995; 50 (9): 595-9.
  14. Jeong TS, Kim EE, Lee CH, Oh JH, Moon SS, Lee WS, Oh GT, Lee S, Bok SH. Hypocholesterolemic activity of hesperetin derivatives. *Clin Chim Acta*. 2003; 327(1-2): 129-37.
  15. Kim HK, Jeong TS, Lee MK, Park YB, Choi MS. Lipid-lowering efficacy of hesperetin metabolites in high-cholesterol fed rats. *Bioorg Med Chem Lett*. 2003; 13(16): 2663-5.
  16. Manach C, Morand C, Gil-Izquierdo A, Bouteloup-Demange C, Remesy C. Bioavailability in humans of the flavanones hesperidin

- and narirutin after the ingestion of two doses of orange juice. *Eur J Clin Nutr.* 2003; 57(2): 235-42.
17. Shi YQ, Fukai T, Sakagami H, Kuroda J, Miyaoka R, Tamura M, Yoshida N, Nomura T. Cytotoxic and DNA damage-inducing activities of low molecular weight phenols from rhubarb. *Anticancer Res.* 2001; 21: 2847-53.
  18. Kuo PL, Lin TC, Lin CC. The antiproliferative activity of aloe-emodin is through p53-dependent and p21-dependent apoptotic pathway in human hepatoma cell lines. *Life Sci.* 2002; 71: 1879-92.
  19. Suzuki T, Nishio K, Tanabe S. The MRP Family and Anticancer Drug Metabolism. *Current Drug Metabolism.* 2001; (2):pp. 367-77.
  20. Garg A, Garg S, Zaneveld LJ, Singla AK. Chemistry and pharmacology of the *Citrus* bioflavonoid hesperidin. *Phytother Res.* 2001; 15(8): 655-69.
  21. Radtke J, Linseisen J, Wolfram G. Fasting plasma concentrations of selected flavonoids as markers of their ordinary dietary intake. *Eur J Nutr.* 2002; 41(5): 203-9.
  22. Lin YT, Hsiu SL, Hou YC, Chen HY, Chao PD. Degradation of flavonoid aglycones by rabbit, rat and human fecal flora. *Biol Pharm Bull.* 2003; 26(5): 747-51.
  23. Matsumoto H, Ikoma Y, Sugiura M, Yano M, Hasegawa Y. Identification and quantification of the conjugated metabolites derived from orally administered hesperidin in rat plasma. *J Agric Food Chem.* 2004; 52(21): 6653-9.

24. Fujisaw S, Ishihara M, Kadoma Y. Kinetic evaluation of the reactivity of flavonoids as radical scavengers. *SAR QSAR Environ Res.* 2002 ; 13(6):617-27.
25. Olszanecki R, Gebaska A, Kozlovski VI, Gryglewski RJ. Flavonoids and nitric oxide synthase. *J Physiol Pharmacol.* 2002; 53(4 1): 571-84.
26. Mohammad Howlader, Coleridge Smith PD. CHRONIC VENOUS DISEASE AND VENOUS ULCER: PHARMACOLOGICAL APPROACH. *J Cardiovasc Dis.* 2004; 2(1): 33-41.
27. Bae EA, Han MJ, Kim DH. In vitro anti-Helicobacter pylori activity of some flavonoids and their metabolites. *Planta Med.* 1999; 65(5): 442-3.
28. Guthrie N, Carroll KK. Inhibition of mammary cancer by citrus flavonoids. *Adv Exp Med Biol.* 1998; 439: 227-36.
29. So FV, Guthrie N, Chambers AF, Moussa M, and Carroll KK. Inhibition of human breast cancer cell proliferation and delay of mammary tumorigenesis by flavonoids and citrus juices. *Nutrition & Cancer.* 1996; 26 (2): 167-81.
30. Lee SH, Jeong TS, Park YB, Kwon. YK, Choi MS, and Bok SH. Hypocholesterolemic effect of hesperetin mediated by inhibition of 3-hydroxy-3-methylglutaryl coenzyme a reductase and acyl coenzyme A: cholesterol acyltransferase in rats fed high-cholesterol diet. *Nutrition Reserch,* 1999; 19 (8): 1245-58.
31. Doostdar H, Burke MD, and Mayer RT. Bioflavonoids: selective substrates and inhibitors for cytochrome P450 CYP1A and CYP1B1. *Toxicology.* 2000; 144 (1- 3): 31-8.

32. Cha JY, Cho YS, Kim I, Anno T, Rahman SM, Yanagita T. Effect of hesperetin, a citrus flavonoid, on the liver triacylglycerol content and phosphatidate phosphohydrolase activity in orotic acid-fed rats. *Plant Foods Hum Nutr.* 2001; 56(4): 349-58.
33. 陳建仁等編修小組，中華中藥典，2004，大黃：P 7；黃芩：P163。
34. 焦東海、杜上鑒：大黃研究，上海科學技術出版社，pp.94-8, 136-7,144-7, 2000。
35. 鄭虎占、董澤宏、余靖：中藥現代研究與應用 第一卷，北京學苑出版社，1996。
36. 徐珞珊、徐國鈞、金蓉鸞、何宏賢：中國藥材學(上)，中國醫藥科技出版社，1996，pp130-5。
37. Tang W, Eisenbrand G. Chinese Drugs of Plant Origin. *Berlin*, 1992;pp.919-29.
38. Ishimaru K, Nishikawa K, Omoto T, Asai I, Yosshihira K, Shimomura K. Two flavone 2'-glucosides from *Scutellaria baicalensis*. *Phytochemistry* 1995;40:279-81.
39. 國家中醫藥管理編委局：中華本草 (7)，上海科學技術出版社，上海，1999; 7: pp.200-10.
40. Gabrielska J, Oszmianski J, Zylka R, Komorowska M. Antioxidant activity of flavones from *Scutellaria baicalensis* in lecithin liposomes. *J Biosci* 1997; 52: 817-23.
41. Nan JX, Park EJ, Kim YC, Ko G, Sohn DH. *Scutellaria baicalensis* inhibits liver fibrosis induced by bile duct ligation or carbon

- tetrachloride in rats. *J Pharm Pharmacol*. 2002; 54: 555-63.
42. Ikemoto S, Sugimura K, Yoshida N, Yasumoto R, Wada S, Yamamoto K, Kishimoto T. Antitumor effects of *Scutellariae radix* and its components baicalein, baicalin, and wogonin on bladder cancer cell lines. *Urology*. 2000; 55: 951-5.
43. Ranganathan P, Eisen S, Yokoyama WM, McLeod HL, Will pharmacogenetics allow better prediction of methotrexate toxicity and efficacy in patients with rheumatoid arthritis? *Ann Rheum Dis*. 2003; 62: 4-9.
44. Postovsky S, Ben Arush MW. Acral erythema caused by high-dose methotrexate therapy in patients with osteogenic sarcoma. *Pediatr Hematol Oncol*. 2005; 22(2): 167-73.
45. Crews KR, Liu T, Rodriguez GC, Tan M, Meyer WH, Panetta JC, Link MP, Daw NC. High-dose methotrexate pharmacokinetics and outcome of children and young adults with osteosarcoma. *Cancer*. 2004; 100(8):1724-33.
46. Aquerreta I, Aldaz A, Giraldez J, Sierrasesumaga L. Methotrexate pharmacokinetics and survival in osteosarcoma. *Pediatr Blood Cancer*. 2004; 42(1): 52-8.
47. Fernandez Megia MJ, Alos Alminana M, Esquer Borrás J. Pharmacokinetic monitoring of 24-hour infusion of methotrexate in an adult population with non-Hodgkin lymphoma. *Farm Hosp*. 2004; 28(6): 433-9.
48. Chladek J, Grim J, Martinkova J, Simkova M, Vaneckova J. Low-dose methotrexate pharmacokinetics and pharmacodynamics in the therapy of severe psoriasis. *Basic Clin Pharmacol*. 2005; 96(3):

- 247-8.
49. Chladek J, Grim J, Martinkova J, Simkova M, Vaniekova J, Koudelkova V, Noiekova M. Pharmacokinetics and pharmacodynamics of low-dose methotrexate in the treatment of psoriasis. *Br J Clin Pharmacol*. 2002; 54(2): 147-56.
  50. Zhou H, Mayer PR, Wajdula J, Fatenejad S. Unaltered etanercept pharmacokinetics with concurrent methotrexate in patients with rheumatoid arthritis. *J Clin Pharmacol*. 2004; 44(11): 1235-43.
  51. Ranganathan P, McLeod HL. Methotrexate and long-term treatment of rheumatic disease: comment on the article by Kremer. *Arthritis Rheum*. 2005; 52(2): 670-2.
  52. Godfrey C, Sweeney K, Miller K, Hamilton R, Kremer J. The population pharmacokinetics of long-term methotrexate in rheumatoid arthritis. *Br J Clin Pharmacol*. 1998; 46(4): 369-76.
  53. Ehab S. El Desoky, MD. Pharmacotherapy of Rheumatoid Arthritis: An Overview. *Current Therapeutic Research*. 2001; 62 (2).
  54. Puchta J, Hattenbach LO, Baatz H. Intraocular levels of methotrexate after oral low-dose treatment in chronic uveitis. *Ophthalmologica*. 2005; 219(1): 54-5.
  55. Grim J, Chladek J, Martinkova J. Pharmacokinetics and pharmacodynamics of methotrexate in non-neoplastic diseases. *Clin Pharmacokinet*. 2003; 42(2): 139-51.
  56. Egan LJ, Sandborn WJ, Mays DC, Tremaine WJ, Fauq AH, Lipsky JJ. Systemic and intestinal pharmacokinetics of methotrexate in patients with inflammatory bowel disease. *Clin Pharmacol Ther*. 1999; 65(1): 29-39.

57. Borst P, Evers R, Kool M, Wijnholds J. A family of drug transporters: the multidrug resistance-associated proteins. *J Natl Cancer Inst.* 2000; 16; 92(16): 1295-302.
58. Carson CW, Cannon GW, Egger MJ, Ward JR, Clegg DO. Pulmonary disease during the treatment of rheumatoid arthritis with low dose pulse methotrexate. *Semin Arthritis Rheum.* 1987; 16: 186-95.
59. Ameen M, Taylor DA, Williams IP, Wells AU, JNWN Barker. Pneumonitis complicating methotrexate therapy for pustular psoriasis. *Journal of the European Academy of Dermatology & Venereology.* 2001; 15(3): 247.
60. Wheeler DL, Vander Griend RA, Wronski TJ, Miller GJ, Keith EE, Graves JE. The short- and long-term effects of methotrexate on the rat skeleton. *Bone.* 1995; 16(2): 215-21.
61. Jones WK, Patel SR. A Family Physician's Guide to Monitoring methotrexate. *American Family Physician.* 2000; 62(7)
62. Buchbinder R, Hall S, Sambrook PN, Champion GD, Harkness A, Lewis D, et al. Methotrexate therapy in rheumatoid arthritis: a life table review of 587 patients treated in community practice. *J Rheumatol.* 1993; 20: 639-44.
63. McKendry RJ, Dale P. Adverse effects of low dose methotrexate therapy in rheumatoid arthritis. *J Rheumatol.* 1993; 20: 1850-6.
64. West SG. Methotrexate hepatotoxicity. *Rheum Dis Clin North Am.* 1997; 23: 883-915.
65. Kremer JM, Galivan J, Streckfuss A, Kamen B. Methotrexate metabolism analysis in blood and liver of rheumatoid arthritis patients. association with hepatic folate deficiency and formation of



- polyglutamates. *Arthritis Rheum.* 1986; 29: 832-5.
66. Gutierrez-Urena S, Molina JF, Garcia CO, Cuellar ML, Espinoza LR. Pancytopenia secondary to methotrexate therapy in rheumatoid arthritis. *Arthritis Rheum.* 1996; 39: 272-6.
67. Bertram G. Katzung. Basic & Clinical Pharmacology. *LANGE*. Eight Edition; 932-3.
68. Jansen, G., and Pieters, R. The role of impaired transport in (pre)clinical resistance to methotrexate: insights on new antifolates. *Drug Resistance Updates*, 1998; 1: 211-8.
69. Cole SPC, Bhardwaj G, Gerlach JH, Mackie, JE, Grant CE, Almquist, KC, Stewart AJ, Kurz EU, Duncan AMV, Deeley RG. Overexpression of a transporter gene in a multidrug-resistant human lung cancer cell line. *Science.* 1992; 258, 1650-4.
70. Yabuuchi H, Takayanagi S, Yoshinaga K, Taniguchi N, Aburatani H and Ishikawa T. ABCC13, an unusual truncated ABC transporter, is highly expressed in fetal human liver. *Biochem. Biophys. Res. Commun.* 2002; 299, 410-7.
71. Jorg K, Mark H, Anne T N, Marc E. M, Junchao G, Markus W, Helmut F and Dietrich K. Expression and localization of human multidrug resistance protein (ABCC). *Int. J. Cancer.* 2005; 115, 359-67.
72. Laurretta MSC, Simon L, Barry HHb. The ABCs of drug transport in intestine and liver: efflux proteins limiting drug absorption and bioavailability. *European Journal of Pharmaceutical Sciences.* 2004; 21, 25-51.
73. Litmana T, Druleyb TE, Steinc WD and Batesd SE. From MDR to

- MXR: new understanding of multidrug resistance systems, their properties and clinical significance. *Life Sci.* 2001; 58, 931-59.
74. Peng, KC, Cluzeaud, F, Bens, M, Van Huyen, JP, Wioland, MA, Lacave, R, Vandewalle, A. Tissue and cell distribution of the multidrug resistance-associated protein (MRP) in mouse intestine and kidney. *J. Histochem. Cytochem.* 1999; 47, 757-68.
75. Schaub, TP, Kartenbeck, J, König, J, Vogel, O, Witzgall, R, Kriz, W, Keppler, D. Expression of the conjugate export pump encoded by the *mrp2* gene in the apical membrane of kidney proximal tubules. *J. Am. Soc. Nephrol.* 1997; 8, 1213-21
76. Fromm MF, Kauffman HM, Fritz P, Burk O, Kroemer HK, Warzok RW, Eichelbaum M, Siegmund W, Schrenk D. The effect of rifampin treatment on intestinal expression of human MRP transporters. *Am. J. Pathol.* 2000; 157, 1575-80.
77. Büchler M, König J, Brom M, Kartenbeck J, Spring H, Horie T, Keppler D. cDNA cloning of the hepatocyte canalicular isoform of the multidrug resistance protein, cMrp, reveals a novel conjugate export pump deficient in hyperbilirubinemic mutant rats. *J. Biol. Chem.* 1996; 271: 15091-8.
78. Gary DK, and Martin GB. The MRP family of drug efflux pumps. *Oncogen.* 2003; 7537- 52.
79. Cherrington NJ, Hartley DP, Li N, Johnson DR, Klaassen CD. Organ distribution of multidrug resistance proteins 1, 2, and 3 (Mrp1, 2, and 3) mRNA and hepatic induction of Mrp3 by constitutive androstane receptor activators in rats. *J. Pharmacol. Exp. Ther.* 2002; 300,97- 104.

80. Flens MJ, Zaman GJ, Van Der Valk P, Izquierdo MA, Schroeijers AB, Scheffer GL, Van Der Groep P, De Haas M, Meijer CJ, Scheper RJ. Tissue distribution of the multidrug resistance protein. *Am. J. Pathol.* 1996, 148, 1237-47.
81. Zhang Y, Han H, Elmquist WF, Miller DW. Expression of various multidrug resistance-associated protein (MRP) homologues in brain microvessel endothelial cells. *Brain Res.* 2000; 876, 148-53.
82. Mayer R, Kartenbeck J, Büchler M, Jedlitschky G, Leier I, Keppler D. Expression of the MRP gene-encoded conjugate export pump in liver and its selective absence from the canalicular membrane in transport-deficient mutant hepatocytes. *J. Cell. Biol.* 1995; 131, 137-50.
83. Scheffer GL, Kool M, De Haas M, De Vree JM, Pijnenborg AC, Bosman DK, Elferink RP, Van Der Valk P, Borst P, Scheper RJ. Tissue distribution and induction of human multidrug resistant protein 3. *Lab. Invest.* 2002; 82, 193-201.
84. Kool M, De Haas M, Scheffer GL, Scheper RJ, Van Eijk MJ, Juijn JA, Baas F, Borst P. Analysis of expression of cMOAT (MRP2), MRP3, MRP4, and MRP5, homologues of the multidrug resistance-associated protein gene (MRP1), in human cancer cell lines. *Cancer Res.* 1997; 57, 3537-47.
85. Kiuchi Y, Suzuki H, Hirohashi T, Tyson CA, Sugiyama Y. cDNA cloning and inducible expression of human multidrug resistance associated protein 3 (MRP3). *FEBS Lett.* 1998; 433, 149-52.
86. Taipalensuu J, Tornblom H, Lindberg G, Einarsson C, Sjöqvist F, Melhus H, Garberg P, Sjöström B, Lundgren B, Artursson P.

- Correlation of gene expression of ten drug efflux proteins of the ATP-binding cassette transporter family in normal human jejunum and in human intestinal epithelial Caco-2 cell monolayers. *J. Pharmacol. Exp. Ther.* 2001; 299, 164- 70.
87. Van Aubel RA, Smeets PH, Peters JG, Bindels RJ, Russel FG. The MRP4/ABCC4 gene encodes a novel apical organic anion transporter in human kidney proximal tubules: putative efflux pump for urinary cAMP and cGMP. *J. Am. Soc. Nephrol.* 2002; 13, 595 - 603.
88. McAleer MA, Breen MA, White NL, Matthews N. pABC11 (also known as MOAT-C and MRP5), a member of the ABC family of proteins, has anion transporter activity but does not confer multidrug resistance when overexpressed in human embryonic kidney 293 cells. *J. Biol. Chem.* 1999; 274, 23541- 8.
89. Hopper E, Belinsky MG, Zeng H, Tosolini A, Testa JR, Kruh GD. Analysis of the structure and expression pattern of MRP7 (ABCC10), a new member of the MRP subfamily. *Cancer Lett.* 2001; 162, 181-91.
90. Bera TK, Lee S, Salvatore G, Lee B, Pastan I. MRP8, a new member of ABC transporter superfamily, identified by EST database mining and gene prediction program, is highly expressed in breast cancer. *Mol. Cell Biol.* 2001; 21, 6997-7002. ed. 2002; 7, 509-16.
91. Chen, ZS, Hopper-Borge, E, Belinsky, MG, Shchaveleva, I, Kotova, E, Kruh, GD. Characterization of the transport properties of human

- multidrug resistance protein 7 (MRP7, ABCC10). *Mol. Pharmacol.* 2003; 63, 351-8.
92. Guo Y, Kotova E, Chen ZS, Lee K, Hopper-Borge, E, Belinsky MG, Kruh GD. MRP8, ATP-binding cassette C11 (ABCC11), is a cyclic nucleotide efflux pump and a resistance factor for fluoropyrimidines 2\_3\_-dideoxycytidine and 9-(2-phosphonylmethoxyethyl)-adenine. *J. Biol. Chem.* 2003; 278, 29509-14.
93. Haimeur A, Conseil G, Deeley RG, Cole SP. The MRP-related and BCRP/ABCG2 multidrug resistance proteins: biology, substrate specificity and regulation. *Curr Drug Metab.* 2004, 5(1): 21-53.
94. Barnes MJ, Estlin EJ, Taylor GA, Aherne GW, Hardcastle A, McGuire JJ, et al. Impact of polyglutamation on sensitivity to raltitrexed and methotrexate in relation to drug-induced inhibition of de novo thymidylate and purine biosynthesis in CCRF-CEM cell lines. *Clin Cancer Res.* 1999; 5: 2548-58.
95. Hooijberg JH, Broxterman HJ, Kool M, Assaraf YG, Peters GJ, Noordhuis P. Antifolate resistance mediated by the multidrug resistance proteins MRP1 and MRP2. *Cancer Res.* 1999, 59: 2532-5.
96. Kool M, van der Linden M, de Haas M, Scheffer GL, de Vree JM, Smith AJ, et al. MRP3, an organic anion transporter able to transport anti-cancer drugs. *Proc Natl Acad Sci.* 1999, 96:6914-9.
97. Victor D, Winter J. Hydrolysis of dietary flavonoid glycosides by strains of intestinal bacteroides from humans. *Biochem. J.* 1987, 248: 953-6.
98. 楊啟裕，橙皮苷之動力學及其溶離度改善之研究，中國藥學研究

所碩士論文，2001。

99. Iris Erlund, Esa Meririnne, Georg Alfthan and Antti Aro. Plasma Kinetics and Urinary Excretion of the Flavanones Naringenin and Hesperetin in Humans after Ingestion of Orange Juice and Grapefruit Juice. *American Society for Nutritional Sciences* 131. 2001; 235-41.
100. Kurowska EM, Spence JD, Jordan J, Wetmore S, Freeman DJ, Piche LA, Serratore P. HDL-cholesterol-raising effect of orange juice in subjects with hypercholesterolemia. *Am J Clin Nutr.* 2000; 72(5): 1095-100.
101. Chabner BA and MJ Collins. Cancer chemotherapy: principles and practice. *Cancer Res.* 1990, 110-53.
102. Chello PL, Sirotnak FM, Dorick DM. Alterations in the kinetics of methotrexate transport during growth of L1210 murine leukemia cells in culture. *Mol. Pharmacol.* 1980; 18: 274-78.
103. Fry DW, Anderson LA, Borst M. Analysis of the role of membrane transport and polyglutamation of methotrexate in gut and Ehrlich tumor in vivo as factors in drug sensitivity and selectivity. *Cancer Res.* 1983, 43:1087-92.
104. Wachsman M, Hamzeh FM, Saito H, Lietman PS. Anticytomegaloviral activity of methotrexate associated with preferential accumulation of drug by cytomegalovirus-infected cells. *Antimicrob Agents Chemother.* 1996, 40(2): 433-6.
105. Funk M, Baker D. Effect of soy products on methotrexate toxicity in rats. *J Nutr.* 1991; 121(10):1684-92.

106. Graciela S. Alarcon. Methotrexate use in Rheumatoid arthritis. A clinician's perspective. *Immunopharmacology*. 2000; 47: 259-71.
107. Hou YC, Hsiu SL, Huang TY, Yang CY, Tsai SY, Chao LPD. Effect of Honey and Sugars on the Metabolism and Disposition of Naringin in Rabbits. *Planta med*. 2001; 67: 538-41.

## 附 錄

### 非室體模式 ( Noncompartment model )

$AUC_{0-t}$  : 血中濃度對時間之曲線下面積 ; 血藥面積

$T_{max}$  : 達到最高血中濃度之時間

$C_{max}$  : 藥物在血中之最高濃度 ; 血峰濃度

$AUMC_{0-t}$  : 第一動差時間對時間曲線下從 0 到 t 之面積

MRT : 藥物之平均滯留時間

$t_{1/2}$  : 藥物之半衰期

V/F : 藥物之分佈體積/生可用率

Cl : 藥物之全身清除率