抗生素在畜牧業之應用

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摘 要

本研究之目的主要針對抗生素之一般特性，包括結構及物化性質、作用機制、抗藥性、藥物動力學、毒性與副作用、抗生素之殘留及檢測、抗生素之市場概況、畜牧產業之現況及抗生素在畜牧產業之應用作一完整之探討。 研究結果顯示台灣畜牧生產一直佔農業生產中相當重要的地位，在2001年台灣畜牧產業之總產值佔農業生產總值的28.7%，高達新台幣1,012億元。其中毛豬462.5億元，肉雞270.6億元，分居畜牧產業一、二名。 抗生素（Antibiotics）是抗感染用藥中最重要的一種，根據2000年全球各類抗感染用藥比率，抗生素在市場佔有率為59%。人類陸續發現的抗生素種類約有一千多種，根據美國疾病防治中心（CDC）指出，目前臨床使用之抗生素約有一百五十種。抗生素依化學結構之不同可分為： β-內醯胺類抗生素、四環素類抗生素、巨環類抗生素、氨基醣?類抗生素、奎諾酮類抗生素及其他類抗生素。其作用機制因其特性之不同而有抑制細菌細胞壁形成（β-內醯胺類）及抑制蛋白質（四環素類、巨環類、氨基醣?類、氯黴素）和核酸（奎諾酮類）之合成等。此外依其抗菌範圍又可分為廣效性及窄效性抗生素等。 目前抗生素在畜牧產業之使用，除了動物的疾病治療及預防外，通常添加低劑量之抗生素於飼料中以期促進動物生長及提高飼料利用率。由於抗生素被廣泛使用於動物上，因此應正確合理的使用以避免抗生素在畜禽產品中殘留及細菌抗藥性的產生。 關鍵字：抗生素、畜牧產業、抗藥性、殘留、抗感染用藥。

關鍵詞 : 抗生素 ; 畜牧產業 ; 抗藥性 ; 殘留 ; 抗感染用藥

目錄

參考文獻

1.小野淨治，工藤力，小此木成夫 (1987) 乳酸菌?代謝?增殖收率。 New Food Industry，29(5):59-76。 2.中華民國獸醫學會 (1996) 臨床豬病

學。華香園出版社，台北。 3.王三郎 (2002) 應用微生物學。高立圖書有限公司，台北。 4.王玉寶 (2003) 腸球菌對大環內酯類抗生素的耐藥機制。國外醫藥抗生 素分冊，24(1):5,6,17。 5.王渭賢、鄧晶瑩、劉正義 (1993) Quinolone類藥物在魚類細菌性疾病 治療之應用探討。台灣畜牧獸醫學會會報，62:37-46。 6.尹宗寧、韋鳳華 (2001) 恩諾沙星緩釋片釋藥性質研究。中國抗生素雜 誌，26(3):232-233。 7.台灣省政府農林廳（1998）台灣農業年報。南投。 8.行政院農業委員會動植物防疫檢疫局 (2001) 含藥物飼料添加物使用規 範。行政院農業委員會90.1.2 (90)農防字第891553026號公告。 9.行政院農業委員會動植物防疫檢疫局 (2000) 動物用藥品使用手冊。 10.行政院衛生署 (1995) 中華藥典。行政院衛生署 84.6.30. 衛署藥字 第 84041544 號令。 11.曲芬、姜素椿、李瑞霞、張維國、王力娜 (1998) 孕婦血漿、羊水及 胎兒血漿、軟骨中環丙沙星濃度的測定。中國抗生素雜誌，23（2）: 151-153。 12.曲芬 (1998) 奎諾酮類藥物的軟骨毒性。國外醫藥抗生素分冊，19 （1）:61-64。 13.何曼德、L. C. McDonald、楊采菱、葉梁蘭蘭、陳珮琛、蕭溢茹 (2000) 1998年台灣地區之抗生素抗藥性監測。院內感染控制雜誌，10 (4):277-293。 14.肖永紅、王其南、彭明利 (2000) 傷寒桿菌耐奎諾酮類機理研究。中 國抗生素雜誌，25(6):462-466。 15.呂車鳳、方麗香 (1993) 以高效液相層析法及光二極體陣列式檢測器 偵測台灣南部市售豬肉中chloramphenicol之殘留。屏東技術學院學報 2:75-81。 16.呂車鳳、陳瑞雄、杜杰憲、邱鴻英、方文祥、戴東發、趙長勝、李宏 智 (1998) 獸醫藥理與治療學。藝軒圖書出版社，台北。 17.巫文玲 (1994) 抗微生物用藥抗生素市場調查。財團法人生物技術開 發中心，台北。 18.李新進、鄭秀蓮、劉雅方、楊喜金 (1996) 泰妙素於豬肉組織中殘留 檢驗之探討。台灣省畜衛所研報 32:29-36。 19.吳孟謙 (2002) 無抗生素添加劑飼料應用於豬隻生產的未來策略。現 代養豬，23(11)：87-93。 20.吳移謀、向斌、張文波、尹節國、余敏君、武濟民 (2001) 人型枝原 體對奎諾酮類藥物的耐藥性機理研究。中國抗生素雜誌，26(3):211- 213。 21.吳繼芳 (2001) 飼料中添加微生物製劑取代抗生素之未來趨勢。畜牧 半月刊，67 (3):85-90。 22.余自成 (1998) 大環內酯類抗生素的正確選用。國外醫藥-合成藥、生 化藥製劑分冊，19(3):160-163。 23.沈定霞、崔岩、趙麗萍、吳堅 (1998) 對環丙沙星耐藥的肺炎克雷伯 氏菌外膜蛋白圖譜分析。中國抗生素雜誌，23(5):380-381。 24.林志勳 (2000) 生菌劑之原理與應用。畜牧半月刊，64 (2):18-23。 25.周榮章 (2003) 台灣養豬產業發展情形與收益分析。農牧旬刊，116 (9):61-65。 26.金毓芳 (1998) 奎諾酮類抗菌劑和耐藥。國外醫藥抗生素分冊，19 (3):221-227。 27.柯錫津、林旭陽、陳陸宏 (1994) 以薄層色層層析法與生物自析法探 討市售牛肉、雞肉中孟寧素之殘留情形。中國農業化學會誌，32(5): 497-506。 28.高清澤 (2000) 養豬飼料中含菲汀酵素與變酸劑功能之研究報導。畜 牧半月刊，64(1):9-14。 29.財團法人生物技術開發中心 (1996) 製藥產業現況與趨勢專題研究。 台北。 30.財團法人生物技術開發中心 (2001) 製藥產業年鑑2001。台北。 31.馬恩龍、王澈、王敏偉 (2003) 大環內酯類抗生素免疫調節作用的研 究進展。國外醫藥抗生素分冊，24(1):1-4。 32.馬紀平 (1997) 依據細菌藥敏試驗結果合理使用抗生素。中華醫學檢 驗雜誌，20(5):309-310。 33.陳石松、蔡佳芬、胡美珍、楊仕喜、周薰修 (1997) 牛肉、豬肉暨雞 肉中甲磺氯黴素之殘留分析。食品科學，24(4):448-457。 34.陳保基 (2001) 新的挑戰－加入世界貿易組織 (WTO) 後的家禽產業策 略(一)。畜牧半月刊，67(3):15-20。 35.許桂森、林明忠、蕭哲志 (2002) 簡明圖解藥理學。藝軒出版社，台 北。 36.許順堯 (1996) 加工方法對雞蛋中殘留氯四環素之影響。食品科學， 23(4):503-508。 37.許應哲 (1997) 口蹄疫衝擊對本省毛豬產業未來展望之探 討。台灣農 業，33(4):196-208。 38.曾誠齊 (1979) 基礎藥物化學。正川出版社，台灣。 39.程中江 (2001) 台灣畜牧產業之展望。畜牧半月刊，65(8):16-19。 40.程書權 (1999) 大環內酯類抗生素的臨床拓寬應用研究。國外醫藥-合 成藥，生化藥製劑分冊，20(4):226-232。 41.張上淳、方啟泰 (1998) 抗生素的合理使用。當代醫學，25(6):460- 468。 42.張上淳、謝維銓 (1996) 目前台灣地區抗藥性菌株流行概 況。中華感 染醫誌，7:83-88。 43.張菊香、戴東發、李素萍 (2000a) 評估以改良式四種培養基檢測法篩 檢豬肉抗生物質殘留之可行性。藥物食品分析，8(1): 25-34。 44.張德銘、黃勤鎮、林鉅鋃 (2000b) 「抗生素濫用影響國人健康」專案 調查報告。凱侖出版社，台北。 45.張霞光、李天云 (2003) 奎諾酮類抗菌藥在臨床使用中的不良反應。 國外醫藥抗生素分冊，24（1）:30-33。 46.郭蓓寧、張菁、張嬰元 (1996) Azithromycin 臨床藥物動力學研究。 中國抗生素雜誌，21(5):376-378。 47.森地敏樹 (1986) 乳酸菌?特性?利用。New Food Industry， 28 (2):1-6。 48.鈴木一郎 (1986) 有用乳酸菌????。乳技協資料，36(2):14-28。 49.黃文徹（2002）動物用藥品管理及使用應注意事項。畜牧半月刊，67 (10):22-24。 50.廖俊凱、周慈怡 (2001) Wilson and Gisvold ’ s藥物化學。合記圖書 出版社，台北。 51.劉昌宇 (2001a) 品種、抗生素添加策略及生長肥育期管理對瘦肉生長 速率與屠體性狀的影響。畜牧半月刊，65(7):9-14。 52.劉朝鑫 (2001b) 抗生素飼料添加物之使用:功能與風險及對策。中化 藥訊，48(1):1-12。 53.劉朝鑫 (2002) 動物用藥品之使用與畜產品中之藥物殘留。現代養 豬，23(12):19-23。 54.劉榮標 (1986) 獸醫微生物學。藝軒圖書出版社，台北。 55.劉曉岩、孫曼琴、候杰 (2000) 環丙沙星對幼齡大鼠軟骨的影響。中 國抗生素雜誌，25(6):457-461。 56.劉錦志 (2000) 抗生素做為飼料添加物之認知。畜牧半月刊，64(4): 69-72。 57.鄧日青 (1999) 丹麥肉豬飼料中不用抗生素的經驗。畜牧半月刊，61 (9):59-60。 58.鄭長義 (1999) 飼料配方技術大全。華香園出版社，台北。 59.蔡英傑 (1998) 乳酸菌與益生菌。生物產業，9(2):98-104。 60.戴東發 (1994) 十年來豬肉藥物殘留檢驗工作之檢討。飼料營養雜 誌，12:19-32。 61.戴卓見 (2000) 豬腸道微生物與促長抗生素。現代養豬， 39-48。 62.謝豪晃 (2002) 生物技術應用於飼料工業。中國畜牧雜誌，34(2):33- 36。 63.鍾利、范昕建 (1998) 大腸桿菌膜孔蛋白研究進展。國外醫藥抗生素 分冊，19(3):208-210。 64.譚艷、方治平、宋曉紅、張海軍、沈月華 (2003) 耐氟奎諾酮類銅綠 假單胞菌的gyr A基因突變研究。中國抗生素雜誌，28(1):48-51。 65.Abdennebi, E. H., N. Khales, R. J. Sawchuk and C. M. Stowe (1994) Thiamphenicol pharmacokinetics in sheep. J. Vet. Pharmacol. & Ther. 17:12-16. 66.Adams, P. E., K. J. Varma, T. E. Powers and J. F. Lamendola (1987) Tissue concentrations and pharmacokinetics of florfenicol in male veal calves given repeated doses. Am. J. Vet. Res. 48:1725-1732. 67.Ahamad, N. and E. H. Marth (1989) Behavior of Listeria monocytogenes at 7,13,21 and 35°C in tryptose broth acidified with acetic, citric or lactic acid. J. Food Prot. 52(10)：688-695. 68.Ahamad, N. and E. H. Marth (1990) Acid-injuring of Listeria monocytogenes. J. Food Prot. 53(1):26-29. 69.Amsden, G. W. (2001) Advanced-generation macrolides: tissue-directed antibiotics. Int. J. Antimicrob. Agents 18: S11-S15. 70.Anadon, A. and M. R. Martonez-Larranaga (1999) Residues of antimicrobial drugs and feed additives in animal products: regulatory aspects. Livestock Prod. Sci. 59:183-198. 71.Aronson, L. (1980) Pharmacotherapeutics of the newer tetracyclines. J. Am. Vet. Med. Assoc. 176:1061-1068. 72.Axelsson, L. T., T. C. Chung, W. J. Dobrogosz and S. E. Lindgren (1989) Production of a broad-spectrum antimicrobial substance by Lactobacillus reuteri. Micro. Ecol. Health Dis. 2:131-136. 73.Bable, F. J. (1976)

Antibiosis by lactic culture bacteria. J. Dairy Sci. 60(5):815-821. 74.Baird-Parker, A. C. (1980) Organic acids. In:Microbial Ecology of Food（Silliker, J. H., Ed.）, pp. 126-135. Academic Press, New York. 75.Barefoot, S. F. and C. G. Nettles (1993) Antibiosis revisited:bacteriocins produced by dairy starter cultures. J. Dairy Sci. 76(8):2366-2379. 76.Bassit, N., C-Y. Boquien, D. Picque and G. Corrieu (1993) Effect of initial oxygen concentration on diacetyl and acetoin production by Lactococcus lactis subsp. lactis biovar. diacetylactis. Appl. Environ. Microbiol. 59(6):1893- 1897. 77.Beauchamp, D., P. Gourde, G. Theriauly and G. Bergeron (1992) Age-dependent gentamicin experimental nephrotoxicity. J. Phamacol. Exp. Ther. 260:444-449. 78.Benno, Y., K. Sawada and T. Mitsuoka (1984) The intestinal microflora of infants: composition of fecal flora in breast- fed and bottle-fed infantis. Microbiol. Immunol. 28:975-986. 79.Boatto, G., R. Cerri, A. Pau, M. Palomba, G. Pintore and M. G. Denti（1998）Monitoring of benzylpenicillin in ovine milk by HPLC. J. Pharm. Biomed. Analysis 17:733-738. 80.Booker, C. W., G. K. Jim, P. T. Guichon, O. C. Schunicht, B. E. Thorlakson and P. W. Lockwood（1997）Evaluation of florfenicol for the treatment of undifferentiated fever in feedlot calves in western Canada. Canada Vet. J. 38:555-560. 81.Budavari S. (1989) The Merck Index, 11th edition, Merck & Co., Inc., New Jersey. 82.Burrows, G. E. (1980) Pharmacotherapeutics of Macrolides, Lincomycins and Spectinomycin. J. Am. Vet. Med. Assoc. 176:1072-1077. 83.Bush, L. M., J. Calmon and C. C. Johnson (1995) Newer penicillins and beta-lactamase inhibitiors. Infect Dis. Clin. North Am. 9:653-686. 84.Chu, D. T. W. and P. B. Fernandes (1991) Recent developments in the field of Quinolone antibacterial agents. Adv. Drug Res. 21:39-144. 85.Conway, P. L., S. L. Gorbach and B. R. Goldin（1987）ival of lactic acid bacteria in the human stomach and adhesion to intestinal cells. J. Dairy Sci. 70:1-12. 86.Cullen, M. E., A. W. Wyke, R. Kuroda and L. M. Fisher (1989) Cloning and characterization of a DNA Gyrase A gene from Escherichia coli that confers clinical resistance to 4- quinolones. Antimicrob. Agent. Chemother. 33:886-894. 87.Daeschel, M. A. (1989) Antimicrobial substances from lactic acid bacteria for use as food preservatives. Food Technol. 17(1):164-167. 88.Dahiya, R. S. and L. Speak (1968) Hydrogen peroxide formation by lactobacilli and its effect on Staphylococcus aureus. J. Dairy Sci. 51:1568-1572. 89.Daigneault，J.，L. W. George and J. D. Baggot（1990）Ocular and Serum disposition kinetics of cloxacillin after topical administration of benzathine cloxacillin and intravenous administration of sodiuim cloxacillin to calves. Am. J. Vet. Res. 51:381-385. 90.Darmadji, P., M. Izumino, T. Miyamoto and K. Katoaka (1990) Lactic fermentation effects on preservative qualities of dendeny giling. J. Food Sci. 55(6):1523-1527. 91.Datamonitor Pharmaceutical/Healthcare (1993) World Anti-Infectives:Competitive Analysis and Forecasts. 92.Dax, S. L. (1997) Antibacterial Chemotherapeutic Agents. Chapman & Hall, London. 93.Davis, W. T., D. C. Maplesden, R. P. Natzke, W. N. Philpot, P. Garrett and C. S. Card（1975）Benzathine cloxacillin intramammary infusion for treatment of mastitis in dry cows. Vet. Med. Small Anim. Clin. 70:287-289. 94.Dobrogosz, W. J., N. C. Raleigh and S.E. Lindgren (1995) Antibiotic reuterin. U. S. Patent No. 5413960. 95.Edel, W.（1994）Salmonella enteritidis eradication programme in poultry breeder flocks in the Netherlands. Int. J. Food Microbiol. 21:171-178. 96.Engvall, E. and P. Perlmann (1971) Enzyme-linked immunosorbent assay of immunoglobulin G. Immunochemistry. 8:871-879. 97.Eliopoulos, G. M. (1995) In vitro activity of fluoroquinolones against gram-positive bacteria. Drugs. 49 (Suppl.2):48-57. 98.Ellis, J., C. R. Bagshaw and W. V. Shaw (1995) Kinetic mechanism of chloramphenicol acetyltransferase:the role of ternary complex interconversion in rate determination. Biochem. 34:16852-16859. 99.Fedeniuk, R. W. and P. J. Shand (1998) Theory and methodology of antibiotic extraction from biomatrices (review). J. Chromatogr. A 812:3-15. 100.Frazier, W. C. and D. C. Westhoff (1978) Food Microbiology. McGraw-Hill, New York. 101.Fthenakis, G. G.（1998）Susceptibility to antibiotics of Staphylococcal isolates from cases of ovine or bovine mastitis in Greece. Small Rumin. Res. 28:9-13. 102.Fuller, R. and B. E. Brooker (1973) Ecological studies on the Lactobacillus flora associated with the crop epithelium of the fowl. Am. J. Clin. Nutr. 27:1305-1312. 103.Giles, G. J., W. T. R. Grimshaw, D. J. Shanks and D. G. Smith（1990）The efficacy of danofloxacin in the therapy of acute bacterial pneumonia in housed beef cattle. In: Danofloxacin in the Therapy of Respiratory Disease. Scientific papers presented at the XVI world buiatrics congress, Salvador, Bahia, Brazil, August 14. p. 19-22. 104.Gilliland，S. E. and D. K. Walker（1990）Factors to consider when selecting a dietary adjunct to produce a hypocholesteroleric effect in humans. J. Dairy Sci. 73:905- 911. 105.Giroux, D., G. Sirois and G. P. Martineau（1995）Gentamicin pharmacokinetics in newborn and 42-day-old male piglets. J. Vet. Pharmacol. Ther. 18:407-412. 106.Glazer, A. N. and H. Nikaido (1998) Microbial biotechnology:fundamentals of applied microbiology. W. H. Freeman and Company, New York. 107.Goldberg, I. (1994) Functional Foods:Designer Foods, Pharmafoods, Nutraceuticals. Chapman & Hall, Inc., New York. 108.Gonzalez, L. S. and J. P. Spencer（1998）Aminoglycoside:A practice review. Am. Fam. Physician. 58:1811-1821. 109.Gude, T., A. Preiss and K. Rubach (1995) Determination of chloramphenicol in muscle, liver, kidney and urine of pigs by means of immunoaffinity chromatography and gas chromatography with electron-capture detection. J. Chromatogr. B. 673:197-204. 110.Haasnoot, W., P. Stouten, G. Cazemier, A. L. Jacques, F. M. Nouws and H. J. Keuken (1999) Immunochemical detection of aminoglycosides in milk and kidney. Analyst 124:301-305. 111.Haesebrouck, F., M. Vanrobaeys, P. D. Herdt and R. Ducatelle （1995）Effect of antimicrobial treatment on the course of an experimental Yersinia pseudotuberculosis infection in canaries. Avian Pathol. 24:273-283. 112.Hardman, J. G., L. E. Limbird and A. G. Gilman（2001） Goodman and Gilman ’ s The Pharmacological Basis of Therapeutics 10th ed. McGraw-Hill Companies, Inc., New York. 113.Hayes, J. D. and C. R. Wolf (1990) Molecular mechanisms of drug resistance. Biochem. J. 272:281-295. 114.Hayes, D. J., H. H. Jensen and J. Fabiosa (2002) Technology choice and the economic effects of a ban on the use of antimicrobial feed additives in swine rations. Food Control 13:97-101. 115.Heisig, P., H. Schedletzky and H. Falkenstein-Paul.（1993） Mutations in the gyr A gene of a highly fluoroquinolone- resistant clinical isolate of Escherichia coli. Antimicrob. Agent. Chemother. 37:696-701. 116.Hemme, D., M. Nardi and D. Jette (1980) β-galactosidase et phospho- β-galactosidases de Streptococcus thermophilus. Le. Lait. 60:595-618. 117.Hinz, K. H. and S. Rottmann (1990) Studies in vivo on the efficacy of enrofloxacin against Mycoplasma gallisepticum. Avian Pathol. 19:511-522. 118.Hooper, D. C. and J. S. Wolfson（1987）Mechanisms of action and resistance to ciprofloxacin. Am.

J. Med.（Suppl 4A）: 12-20. 119.Howard, D. and T. Cowen（1982）Determination of tiamulin hydrogen fumarate in animal feeds using high-performance liquid chromatography. Analyst 107:319-323. 120.Jay, J. M. (1982) Antimicrobial properties of diacetyl. Appl. Environ. Microbiol. 44(3):525-532. 121.Jordan, F. T. W., B. K. Horrocks and R. Froyman （1993）A model for testing the efficacy of enrofloxacin（baytril ） administered to turkey hens in the control of Mycoplasma iowae infection in eggs and embryos. Avian Dis. 37:1057- 1061. 122.Juven, B. J. and M. D. Pierson (1996) Antibacterial effects of hydrogen peroxide and methods for its detection and quantitation. J. Food Prot. 59(11):1233-1241. 123.Klevan, L. and J. C. Wang （1980） DNA gyrase-DNA complex containing 140 bp of DNA and an a2 s2 protein core. Biochemi. 19:5229-5234. 124.Korsrud, G.O. and J. O. Boison (1998) Bacterial inhibition tests used to screen for antimicrobial veterinary drug residues in slaughtered animals. J. Assoc. Off. Anal. Chem. 81:21-24. 125.Korsrud, G. O., M. G. Papich, A. C. E. Fesser, C. D. C. Salisbury and J. D. Macneil (1995) Laboratory testing of the Charm Test II receptor assays and the Charm Farm Test with tissues and fluids from hogs fed sulfamethazine, chlortetracycline and penicillin G. J. Food Prot. 59:161-166. 126.Krueger, S., G. Zaccai, A. Wlodawer, J. Langowski, M. Odea, A. Maxwell and M. Gellert （1990）Neutron and light- scattering studies of DNA gyrase and its complex with DNA. J. Mol. Biol. 211:211-220. 127.Kuhne, M., S. Wegmann, A. Kobe and R. Fries (2000) Tetracycline residues in bones of slaughtered animals. Food Control 11:175-180. 128.Lesher, G. Y., E. D. Forelich, M. D. Gruet, J. H. Bailey and R. P. Brumdage (1962) 1,8-Naphthyridine dervatines. A new class of chemotherapeutic agents. J. Med. Pharm. Chem. 5:1063-1068. 129.Li, Y. M. A., V. Schepdael, E. Roets and J. Hoogmartens (1997) Optimized methods for capillary electrophoresis of tetracyclines. J. Pharm. and Biomed. Analysis 15:1063-1069. 130.Lilly, D. M. and R. H. Stillwell (1965) Probiotics:growth promoting factors produced by microorganisms. Science 147: 747-748. 131.Luo, W., C. Y. W. Ang and H. C. Thompson (1997) Rapid method for the determination of ampicillin residues in animal muscle tissues by high-performance liquid chromatography with fluorescence detection. J. Chromatogr. B 694:401-407. 132.Mann, D. D and G. M. Frame（1992）Pharmacokinetic study of danofloxacin in cattle and swine. Am. J. Vet. Res. 53:1022-1026. 133.Marche, P., S. Koutouzov and A. Girard (1983) Impairment of membrane phosphoinositide metabolism by aminoglycoside antibiotics:streptomycin，amikacin，kanamycin，dibekacin，gentamicin and neomycin. J. Pharmacol. Exp. Ther. 227: 415-420. 134.Marzo, A. and D. B. Lorenzo (1998) Chromatography as an analytical tool for selected antibiotic classes:a reappraisal addressed to pharmacokinetic applications. J. Chromatogr. A 812:17-34. 135.Mevius, D. J., M. J. M. Sprenger and H. C. Wegener（1999） EU conference ‘ The Microbial Threat ’ . Int. J. Antimicro. Agents 11:101-105. 136.Miller, D. J. S., J. J. O ’ Connor and N. L. Roberts（1986） Tiamulin/salinomycin interactions in pigs. Veterinary Record 118:73-75. 137.Miller, T. E., S. Burnham and J. D. K. North（1976） Immunological enhancement in the pathogenesis of pyelonephritis. Clin. and Experi. Immunol. 24:336-345. 138.Mitscher, L. A. (1995) Antibiotics and antimicrobial agent. In:Medicinal Chemistry. 4th ed. U.S.A., Williams and Wilkins. pp. 759-802. 139.Nettles, C. G. and S. F. Barefoot (1993) Biochemical and genetic characteristics of bacteriocins of food-associated lactic acid bacteria. J. Food Prot. 56(4):338-356. 140.Neu, H. C. (1992) The crisis in antibiotic resistance. Science 257:1064-1073. 141.Nikaido, H. (1994) Prevention of drug access to bacterial targets:permeability barriers and active efflux. Science 264:382-388. 142.Nozaki, M., K. Tannka, N. Takeda, M. Niwa, K. Kohno, M. Kobayashi and K. Tsurumi (1991) Neuro excitability of spafloxacin, a novel quinolone antibacterial drug,in combination with non-steroidal anti-inflammatory drugs. Chemotherapy 39:167-174. 143.Oku, T. (1996) Oligosaccharides with beneficial health effects:a Japanese perspective. Nutr. Rev. 54(11):59-66. 144.O ’ sullivan, M. G., G. Thornton, G. C. O ’ sullivan and J. K. Co ’ llins (1992) Probiotic bacteria:myth or reality? Trends Food Sci. Technol. 3:309-314. 145.Pedersen, K. and G. W. Tannock (1989) Colonization of the porcine gastrointestinal tract by lactobacilli. Appl. Environ. Microbiol. 55:279-283. 146.Piddock, L. J. V.（1995）Quinolone resistance and Campylobacter spp. J. Antimicrob. Chemother. 36:891-898. 147.Prescott, J. F. and J. D. Baggot (1988) Antimicrobial therapy in veterinary medicine. Yearbook Medical Publishers, Boston. U.S.A. 148.Preu，M.，D. Guyot and M. Petz（1998）Development of a gas chromatography-mass spectrometry method for the analysis for aminoglycoside antibiotics using experimental design for the optimization of the derivatisation reactions. J. Chromatogr. A 818:95-108. 149.Rambaud, J. C., Y. Bouhnik, P. Marteau and P. Pochart (1993) Manipulation of the human gut microflora. Proc. Nutr. Soc. 52:357-366. 150.Reiter, B. and G. Harnulv (1984) Lactoperoxidase antibacterial system:natural occurrence, biological functions and practical applications. J. Food Prot. 47(9): 724-732. 151.Riond, J. L. and J. E. Riviere（1988 ）Multiple intravenous dose pharmacokinetics and residue depletion profile of gentamicin in pigs. J. Vet. Pharmacol. Ther. 11:210-214. 152.Riviere, J. E. and J. W. Spoo (1995) Tetracycline、Aminoglycoside、Chloramphenicol、Macrolides、Licosamides、Fluoroquinolones and miscellaneous antibiotics. In Veterinary pharmacology and therapeutics. Adams, H. R. 7th ed. Iowa State University Press. Iowa. U.S.A. pp. 784-854. 153.Robillard, N. J. and A. L. Scarpa（1988）Genetic and physiological characterization of ciprofloxacin resistance in Pseudomonas aeruginosa PAO. Antimicrob. Agents Chemother. 32:535-539. 154.Rubin, H. E. and F. Vaughan (1979) Elucidation of the inhibitory factory of yogurt against Salmonella tyhiwurium. J. Dairy Sci. 62(12):1873-1879. 155.Schneider, M. J. and D. J. Donoghue（2002）Multiresidue analysis of fluoroquinolone antibiotics in chicken tissue using liquid chromatography-fluorescence-multiple mass spectrometry. J. Chromatogr. B 780:83-92. 156.Scott, V. N. and S. L. Taylor (1981) Effect of nisin on the outgrowth of Clostridium botulinum. J. Food Sci. 46:117- 121. 157.Setlow, J. K., E. Cabrera-Juarez, W. L. Albritton, D. Spikes and A. Muschler（1985）Mutations affecting gyrase in Haemophilus influenzae. J. Bacteriol. 164:525-534. 158.Shalit, I. and M. I. Marks (1984) Chloramphenicol in the 1980s. Drugs 28:281-291. 159.Sharpnack, D. D., J. P. Mastin, C. P. Childress and G. M. Henningsen（1994）Quinolone arthropathy in juvenile New Zealand white rabbits. Lab. Anim. Sci. 44:436-442. 160.Shen, L. L., J. Baranowski and A. G. Pernet (1989) Mechanism of inhibition of DNA gyrase by quinolone antibacterial agents:specificity and cooperativity of drug binding. Biochem. 28:3879. 161.Stehly, G. U. and W. H. Gingerich (1999) A bridging study for oxytetracycline in edible fillet of rainbow trout:analysis by a liquid chromatographic method and the official microbial inhibition assay. J. Assoc. Off. Anal. Chem. 82:866-870. 162.Tagg, T.

R., A. S. Dajani and L.W. Wannamaker (1976) Bacteriocins of Gram-positive bacteria. Bacteriol. Rev. 40: 722-756. 163.Takayama, S., M. Hirohashi, M. Kato and H. Shimada（1995） Toxicity of quinolone antimicrobial agents. J. Toxicol. Environ. Health 45:1-45. 164.Talarico, T. L., I. A. Casas, T. C. Chung and W. J. Dobrogosz (1988) Production and isolation of reuterin, a growth inhibitor produced by Lactobacillus reuteri. Antimicrob. Agents Chemother. 32(12):1854-1858. 165.Talarico, T. L. and W. J. Dobrogosz (1989) Chemical characterization of an antimicrobial substance produced by Lactobacillus reuteri. Antimicrob. Agents Chemother. 33(5): 674-679. 166.Tanner, A. C., A. P. Avakian, H. J. Barnes, D. H. Ley, T. T. Migaki and R. A. Magonigle（1993）A comparison of danofloxacin and tylosin in the control of induced Mycoplasma gallisepticum infection in broiler chicks. Avian Dis. 37:515-522. 167.Teske, R. H., L. D. Rollins, R. J. Condon and G. G. Carter (1973) Serum oxytetracycline concentrations after intravenous and intramuscular administration in horses. J. Am. Vet. Med. Assoc. 162:119-120. 168.Theodorides, V. J., C. J. DiCuollo, J. R. Guarini and J. F. Pagano (1968) Serum concentrations of chloramphenicol after intraruminal and intra-abomasal administration in sheep. Am. J. Vet. Res. 29:643-645. 169.Thomas, E. P. and C. G. Ramesh （1980）Pharmacotherapeutics of newer penicillins and cephalosporins. J. Am. Vet. Med. Assoc. 176:1054-1060. 170.Ueda, Y. and I. Suenaga（1995）In vitro antibacterial activity of florfenicol against Actinobacillus pleuropneumoniae. J. Vet. Med. and Sci. 57:363-364. 171.Vaden, S. L. and J. E. Riviere（1995）Penicillins and related β-lactam antibiotics. In Veterinary pharmacology and therapeutics. Adams, H. R. 7th ed. Iowa State University Press. Iowa. U.S.A. pp. 774-783. 172.Verdon, E., R. Fuselier, D. Hurtaud-Pessel, P. Couedor, N. Cadieu and M. Laurentie (2000) Stability of penicillin antibiotic residues in meat during storage. J. Chromatogr. A 882:135-143. 173.Wan, Q. H. and X. C. Le（1999）Capillary electrophoretic immunoassays for digoxin and gentamicin with laser-induced fluorescence polarization detection. J. Chromatogr. B 734: 31-38. 174.Weinberg, J. M., C. F. Jr. Simmons and H. D. Humes（1980） Alterations of mitochondrial respiration induced by aminoglycoside antibiotics. Res. Commum. Chem. Pathol. Pharmacol. 27:521-531. 175.Wilson, R. C., S. H. Duran, C. R. Jr. Horton and L. C. Wright (1989) Bioavailability of gentamicin in dogs after intramuscular or subcutaneous injections. Am. J. Vet. Res. 50:1748-1750. 176.Witte, W. (2000) Selective pressure by antibiotics use in livestock. Int. J. Antimicrob. Agents 16:S19-S24. 177.Wu, C. J. and G. R. Janssen (1997) Expression of a Streptomycete leaderless mRNA encoding chloramphenicol acetyltransferase in Escherichia coli. J. Bacteriol. 179: 6824-6830. 178.Yunis, A. A., A. M. Miller, Z. Salem, M. D. Corbett and G. K. Arimura (1980) Nitroso-chloramphenicol:possible mediator in chloramphenicol-induced aplastic anemia. J. Lab. & Clin. Med. 96:36-46.