

REFERENCES

1. Oda R. P. and Landers J. KP. (1997) Introduction to capillary electrophoresis. In: *Handbook of Capillary Electrophoresis*. pp.1-47, Landers J. P. (ed.), CRC Press, Boca Raton, Floreda
2. Grossman, P. D. (1992) Factors affecting the performance of capillary electrophoresis separations: joule heating, electroosmosis, and zone dispersion. In: *Capillary Electrophoresis: Theory and Practice*, pp. 3-34, Grossman P. D. and Colburn J. C. (eds.), Academic Press, San Diego, California.
3. Karger B. L., Chu Y.-H. and Foret F. (1995) Capillary electrophoresis of proteins and nucleic acids. *Annu. Rev. Biophys. Biomol. Struct.* 24, 579-610.
4. Bergquist J., Tarkowski A., Ekman R. and Ewing A. (1994) Discovery of endogenous catecholamines in lymphocytes and evidence for catecholamine regulation of lymphocyte function via an autocrine loop. *Proc. Natl. Acad. Sci.*, USA. 91, 12912-12916.
5. Bay S., Starke H., Zhang J. Z., Elliott J. F., Coulson L. D and Dovichi N. J. (1994) Capillary gel electrophoresis for DNA sequencing of a template from the malaria genome by use of 4% T, 5% C polyacryamide and two-color peak-height encoded fluorescence detection. *J. Cap. Electrophor.* 1, 121-126.
6. Lee K. J., Heo G. S., Kim N. J. and Moon D. C. (1992) Analysis of antiepileptic drugs in human plasma using micellar electrokinetic capillary chromatography. *J. Chromatogr.* 608, 243-250.
7. Thormann W., Meier P., Marcolli C. and Binder F. (1991) Analysis of barbiturates in human serum and urine by high-performance capillary electrophoresis-micellar

- electrokinetic capillary chromatography with on-column multi-wavelength detection. *J. Chromatogr.* 545, 445-460.
8. Evenson M. A. and Wiktorowicz J. E. (1992) Automated capillary electrophoresis applied to therapeutic monitoring. *Clin. Chem.* 38, 1847-1852.
 9. Thormann W., Minger A., Molteni S., Caslavska J. and Gebauer P. (1992) Determination of substituted purines in body fluids by micellar electrokinetic capillary chromatography with direct sample injection. *J. Chromatogr.* 593, 275-288.
 10. Shihabi Z. K. (1993) Serum pentobarbital assay by capillary electrophoresis. *J. Lip. Chromatogr.* 16, 2059-2068.
 11. Shihabi Z. and Hinsdale M. E. (1996) Analysis of ibuprofen in serum by capillary electrophoresis. *J. Chromatogr. B* 683, 115-118.
 12. Salomon K., Burgi D. S. and Helmer J. C. (1991) Separation of seven tricyclic antidepressants using capillary electrophoresis. *J. Chromatogr.* 549, 375-385.
 13. Johansson I. M., Pavelka R. and Henion J. D. (1991) Determination of small drug molecules by capillary electrophoresis-atmospheric pressure ionization mass spectrometry. *J. Chromatogr.* 559, 515-528.
 14. Roach M., Gozel p. and zare R. N. (1988) Determination of methotrexate and its major metabolite, 7-hydroxy-methotrexate using capillary zone electrophoresis and laser induced fluorescence detection. *J. Chromatogr.* 426, 129-140.
 15. Reinhoud N. J., Tjaden U. R., Irth H. and van der Greef J. (1992) Bioanalysis of some anthracyclines in human plasma by capillary electrophoresis with laser-induced fluorescence detection. *J. Chromatogr.* 574, 327-334.
 16. Lloyd D. K., Cypess A. M. and Wainer I. W. (1991) Determination of cytosine-(D-arabinoside in plasma using capillary electrophoresis. *J. Chromatogr.*

- 568, 117-124.
17. Schmalzing D., Nashabeh W., Yao X. W., Mhatre R., Regenier F. E., Afeyan N. B. *et al.* (1995) Capillary electrophoresis-based immunoassay for cortisol in serum. *Anal. Chem.* 67, 606-612.
 18. Schmalzing D., Nashabeh W. and Fuchs M. (1995) Solution-phase immunoassay for determination of cortisolin serum involving capillary electrophoresis. *Clin. Chem.* 41, 1403-1406.
 19. Chen F. T. and Evangelista R. A. (1994) Feasibility studies for simultaneous immunochemical multianalyte drug assay by capillary electrophoresis with laser-induced fluorescence. *Clin. Chem.* 40, 1819-1822.
 20. Chen F. T. and Pentoney S. L. (1994) Characterization of digoxigenin-labeled B-phycoerythrin by capillary electrophoresis with laser-induced fluorescence, application to homogenous digoxin immunoassay. *J. Chromatogr. A* 680, 425-430.
 21. Blais B. W., Cunningham A. and Yamazaki H. (1994) A Novel immunofluorescence capillary electrophoresis assay system for the determination of chloramphenicol in milk. *Food Agric. Immunol.* 6, 409-417.
 22. Pritchett T. J., Evangelista R. A. and Chen F. T. A. (1995) Peptide immunoassay using capillary electrophoresis with laser-induced fluorescence detection. *J. Cap. Elec.* 2, 145-149.
 23. Ganzler k., Greve K. S., Cohen A. S., Karger B. L., Guttman A. and Cooke N. C. (1992) High-performance capillary electrophoresis of SDS-protein complexes using UV-transparent polymer networks. *Anal. Chem.* 64, 2665-2671.
 24. Grossman p. D. and Soane D. S. (1991) Capillary electrophoresis of DNA in entangled polymer solutions. *J. Chromatogr.* 559, 257-266.
 25. Grossman P. D., Colburn J. C. and Lauer H. H. (1989) A semiempirical model for

- the electrophoretic mobilities of peptides in free-solution capillary electrophoresis. *Anal. Biochem.* 179, 28-33.
26. Yao X. W., Wu D. and Regnier F. E. (1993) Manipulation of electroosmotic flow in capillary electrophoresis. *J. Chromatogr.* 636, 21-29.
27. Bao J. and Regnier F. E. (1992) Ultramicro enzyme assays in a capillary electrophoretic system. *J. Chromatogr.* 608, 217-224.
28. Novotny M. V. and Sudor J. (1993) High-performance capillary electrophoresis of glycoconjugates. *Electrophoresis* 14, 373-389.
29. Cobb K. A. and Novotny M. V. (1992) Peptide mapping of complex proteins at the low picomole level with capillary electrophoretic separations. *Anal. Chem.* 64, 879-886.
30. Lemmo A. V. and Jorgenson J. W. (1993) Transverse flow gating interface for the coupling of microcolumn LC with CZE in a comprehensive two-dimensional system. *Anal. Chem.* 65, 1576-1581.
31. Moseley M. A., Jorgenson J. W., Shabanowitz J., Hunt D. F. and Tomer K. B. (1992) Optimization of capillary zone electrophoresis/electrospray ionization parameters for the mass spectrometry and tandem mass spectrometry analysis of peptides. *J. Am. Soc. Mass Spectrom.* 3, 289-300.
32. Foret F., Demi M., Kahle V. and Bocek P. (1986) On-line fiber optic UV detection cell and conductivity cell for capillary zone electrophoresis. *Electrophoresis* 7, 430-432.
33. Bruno A. E., Gassmann E., Pericles N. and Anton K. (1989) On-line capillary flow cell utilizing optical waveguides for chromatographic applications. *Anal. Chem.* 61, 876-883.

34. Ludi H., Gassmann E., Grossenbacher H. and Marki W. (1988) Analysis of peptides synthesized by recombinant DNA-technology using capillary zone electrophoresis. *Anal. Chem. Acta.* 213, 215-219.
35. Shera E. B., Seitzinger N. K., Davis L. M., Keller R. A. and Soper S. A. (1990) Detection of single fluorescent molecules. *Chem. Phys. Lett.* 174, 553-557.
36. Soper S. A., Shera E. B., Martin J. C., Jett J. H., Hahn J. H., Nutter H. L. *et al.* (1991) Single-molecule detection of rhodamine-6G in ethanolic solutions using continuous wave laser excitation. *Anal. Chem.* 63, 432-437.
37. Soper S. A., Mattingly Q. L. and Vegunta P. (1995) Photon burst detection of single nearinfrared fluorescent molecules. *Anal. Chem.* 65, 740-747.
38. Peck K., Stryer L., Glazer A and Mathies R. A. (1989) Single-molecule fluorescence detection: autocorrelation criterion and experimental realization with phycoerythrin. *Proc. Natl. Acad. Sci. U. S. A.* 86, 4087-4091.
39. Hirschfeld T. (1976) Quantum efficiency independence of the time integrated emission from a fluorescent molecule. *Applied Optics* 15, 3135-3139.
40. Lee Y. H., Maus R. G., Smith B. W. and Winefordner J. D. (1994) Laser-induced fluorescence detection of a single molecule in a capillary. *Anal. Chem.* 66, 4142-4149.
41. Severs J. C. and Games D. E. (1994) CZE and Transient CITP-ES-MS using H₂O and D₂O based electrolyte systems. *Proc. 42nd ASMS Conf. Mass Spectrometry and Allied Topics*, 787.
42. Perkins J. R., Parker C. E. and Tomer K. B. (1992) Nanoscale separations combined with electrospray ionization mass spectrometry: sulfonamide determination. *J. Am. Soc. Mass Spectrom.* 3, 139-149.
43. Hsieh Y. L., Cai J., Li Y. T., Henion J. D. and Ganem B. (1995) Detection of

- noncovalent FKBP-FK506 and FKBP-Rapamycin complexes by capillary electrophoresis-tandem mass spectrometry. *J. Am. Soc. Mass Spectrom.* 6, 85-90.
44. Tetler L. W., Cooper P. A. and Carr C. M. (1994) The application of capillary electrophoresis/mass spectrometry using negative-ion electrospray ionization to areas of importance in the textile industry. *Rapid Commun. Mass Spectrom.* 8, 179-182.
45. Lu W., Wang G. and Cole R. B. (1995) Determination of amino acids by on-line capillary electrophoresis-electrospray ionization mass spectrometry. *Electrophoresis* 16, 487-492.
46. Varghese J. and Cole R. B. (1993) Optimization of capillary zone electrophoresis electrospray mass spectrometry for cationic and anionic laser dye analysis employing opposite polarities at the injector and interface. *J. Chromatogr.* 639, 303-316.
47. Huggins T. G. and Henion J. D. (1993) Capillary electrophoresis/mass spectrometry determination of inorganic ions using an ion-spray-sheath flow interface. *Electrophoresis* 14, 531-539.
48. Chu Y. H., Avila L. Z., Biebuyck H. A. and Whitesides G. M. (1992) Use of affinity capillary electrophoresis to measure binding constants of ligands to proteins. *J. Med. Chem.* 35, 2915-2917.
49. Chu Y. H. and Whitesides G. M. (1992) Affinity capillary electrophoresis can simultaneously measure binding constants of multiple peptides to vancomycin. *J. Org. Chem.* 57, 3524-3525.
50. Gomez F. A., Avila L. z., Chu Y. H. and Whitesides G. M. (1994) Determination of binding constants of ligands to proteins by affinity capillary electrophoresis: compensation for electroosmotic flow. *Anal. Chem.* 66, 1785-1791.

51. Avila L. Z., Chu Y. H., Blossey E. C. and Whitesides G. M. (1993) Use of affinity capillary electrophoresis to determine kinetic and equilibrium constants for binding of arylsulfonamides to bovine carbonic anhydrase. *J. Med. Chem.* 36, 126-133.
52. Chu Y. H., Lees W. J., Stassinopoulos A. and Walsh C. T. (1994) Using affinity capillary electrophoresis to determine binding stoichiometries of protein-ligand interactions. *Biochemistry* 33, 10616-10621.
53. Chu Y. H., Avila L. Z., Biebuyck H. A. and Whitesides G. M. (1993) Using affinity capillary electrophoresis to identify the peptide in a peptide library that binds most tightly to vancomycin. *J. Org. Chem.* 58, 648-652.
54. Chu Y. H., Kirby D. P. and Karger b. L. (1995) Free solution identification of candidate peptides from combinatorial libraries by affinity capillary electrophoresis/mass spectrometry. *J. Am. Chem. Soc.* 117, 5419-5420.
55. Chu Y. H., Dunayevskiy Y. M., Kirby D. P., Vouros P and Karger B. L. (1996) Affinity capillary electrophoresis-mass spectrometry for screening combinatorial libraries. *J. Am. Chem. Soc.* 118, 7827-7835.
56. Towns J. K. and Regnier F. E. (1991) Capillary electrophoretic separation of proteins using nonionic surfactant coatings. *Anal. Chem.* 63, 1126-1132.
57. Bushey M. M. and Jorgenson J. W. (1989) Capillary electrophoresis of proteins in buffers containing high concentrations of zwitterionic salts. *J. Chromatogr.* 480, 301-310.
58. Updike S. J. and Hicks G. P. (1967) The enzyme electrode. *Nature.* 214(92), 986-998.
59. Fatibello-Filho, O., Suleiman A. A., Guilbault G. G. and Lubrano, G. J. (1988) Bienzymatic electrode for the determination of aspartame in dietary products. *Anal. Chem.* 60, 2397-2399.

60. Giaever I. (1973) The antibody-antigen reaction: a visual observation. *J. Immunol.* 110(5), 1424-1426
61. Sugao N., Sugawara M., Minami H., Uto M. and Umezawa Y. (1993) Na+/D-glucose cotransporter based bilayer lipid membrane sensor for D-glucose. *Anal. Chem.* 65(4), 363-369.
62. Rogers K. R., Valdes J. J. and Eldefrawi M. E. (1989) Acetylcholine receptor fiber-optic evanescent fluorosensor. *Anal. Biochem.* 182(2), 353-359.
63. Parce JW, Owicki JC, Kercso KM, Sigal GB, Wada HG, Muir VC, Bousse LJ, Ross KL, Sikic BI, McConnell HM. (1989) Detection of cell-affecting agents with a silicon biosensor. *Science* 246(4927), 243-247.
64. Suzuki M., Tamiya E., Kataoka, T., Tokunaga, T. and Karube I. (1987) Rapid detection of leukemia cells by use of a complement-mediated cytolytic reaction and an imaging sensor system. *Clin. Chem.* 33, 558-561.
65. Gandhi C. R., Behal R. H., Harvey S. A. K., Nouchi T. A. and Olson M. S. (1992) Hepatic effects of endothelin. Receptor characterization and endothelin-induced signal transduction in hepatocytes. *J. Biochem.* 287, 897-904.
66. Monnig C. A. and Kennedy R. T. (1994) Capillary electrophoresis. *Anal. Chem.* 66(12), 280R-314R.
67. Olefirowicz T. M. and Ewing A. G. (1990) Capillary electrophoresis in 2 and 5 microns diameter capillaries: application to cytoplasmic analysis. *Anal. Chem.* 62(17), 1872-1876.
68. Rounds M. A. and Nielsen S. S. (1993) Anion-exchange high-performance liquid chromatography with post-column detection for the analysis of phytic acid and other inositol phosphates. *J. Chromatogr.* 653(1), 148-152.
69. Commors K. A. (1987) Binding Constants: The Measurements of Molecular

Complex Stability. *John Wiley and Sons, New York, New York*, 350 pp.

70. Yu H. M., Tseng M. J., Fang J. M., Phutrakul S. and Chen S. T. (2004) Capillary electrophoresis using immobilized whole cells with overexpressed endothelin receptor for specific ligand screening. *Electrophoresis*, 25, 1034-1041.
71. Yanagisawa, M., Kurihara, H., Kimura, S., Tomobe, Y., Kobayashi, M., Mitsui, Y., Yazaki, Y., Goto, K. and Masaki, T. (1988) A novel potent vasoconstrictor peptide produced by vascular endothelial cells. *Nature* 332, 411-415
72. Doherty, A. M. (1992) Endothelin: a new challenge. *J. Med. Chem.* 35, 1493-1508
73. Schiffrin, E. L. and Touyz, R. M. (1998) Vascular biology of endothelin. *J. Cardiovasc Pharmacol.*, Suppl 3, S2-S13.
74. Sakurai, T., Yanagisawa, M. and Masaki, T. (1992) Molecular characterization of endothelin receptors. *Trends Pharmacol Sci.* 13, 103-108.
75. Lerman, A., (2001) New insight and therapeutic strategies in cardiovascular disease and focus on endothelial target: endothelin-1 and angina. *J. Cardiovasc Pharmacol.*, 38, S27-S30.
76. Elliott, J. D., Lago, M. A. and Peishoff, C. E. (1996) Endothelin Receptors: from the Gene to the Human, *Ruffolo, R. R., Ed., CRC, Boca Raton, Florida*, 79-107.
77. Webb, M. L. and Meek, T. D. (1997) Inhibitors of endothelin. *Med. Res. Rev.* 17, 17-67.
78. Fishman, H. A., Orwar, O., Scheller, R. H. and Zare, R. N. (1995) Identification of receptor ligands and receptor subtypes using antagonists in a capillary electrophoresis single-cell biosensor separation system. *Proc. Natl. Acad. Sci. U.S.A.* 92, 7877-7881.

79. Landers, J. P., Ed. (1997) *Handbook of Capillary Electrophoresis*, 2nd ed., CRC, Boca Raton, Florida, 591-609.
80. Chu, Y. H. and Cheng, C. C. (1998) Affinity capillary electrophoresis in biomolecular recognition. *Cell Mol. Life Sci.* 54, 663-683.
81. Yeung, E. S. (1999) Study of single cells by using capillary electrophoresis and native fluorescence detection. *J. Chromatogr A.* 830, 243-262.
82. Smetana, K. Jr, Lukáš, J., Palečková, V., Bartůňková, J., Liu, F.-T., Vacík, J. and Gabius, H.-J. (1997) Effect of chemical structure of hydrogels on the adhesion and phenotypic characteristics of human monocytes such as expression of galectins and other carbohydrate binding sites. *Biomaterials* 18, 1009-1014.
83. Colton, I. J., Carbeck, J. D., Rao, J. and Whitesides, G. M. (1998) Affinity capillary electrophoresis: a physical-organic tool for studying interactions in biomolecular recognition. *Electrophoresis* 19, 367-382.
84. Zang, X., Yu, Z. and Chu, Y.-H. (1998) Tight-binding streptavidin ligands from a cyclic peptide library. *Bioorg. Med. Chem. Lett.*, 17, 2327-2332.
85. Mito, E., Zhang, Y., Esquivel, S. and Gomez, F. A. (2000) Estimation of receptor-ligand interactions by the use of a two-marker system in affinity capillary electrophoresis. *Anal Biochem.* 280, 209-215..
86. Kaddis, J., Mito, E., Heintz, J., Plazas, A. and Gomez, F. A. (2003) Flow-through partial-filling affinity capillary electrophoresis can estimate binding constants of neutral ligands to receptors via a competitive assay technique. *Electrophoresis* 24, 1105-1110.
87. Fishman, H. A., Orwar, O., Scheller, R. H. and Zare, R. N. (1995) Identification of receptor ligands and receptor subtypes using antagonists in a capillary electrophoresis single-cell biosensor separation system. *Proc. Natl. Acad. Sci.*

- U.S.A.* 92, 7877-7881.
88. Landers, J. P., Ed., *Handbook of Capillary Electrophoresis*, 2nd ed., CRC, Boca Raton, Florida, 1997, 591-609..
89. Chu, Y. H. and Cheng, C. C.(1998) Affinity capillary electrophoresis in biomolecular recognition. *Cell Mol. Life Sci.* 54, 663-683.
90. Wang Q., Luo G., Ou J. and Yeung, W. S. (1999) Noncompetitive immunoassays using protein G affinity capillary chromatography and capillary electrophoresis with laserinduced fluorescence detection. *J. Chromatogr. A* 848, 139-148.
91. Kaufman, S. E.; Brown, S. and Stauber, G. B. (1993) Characterization of ligand binding to immobilized biotinylated extracellular domains of three growth factor receptors. *Anal. Biochem.* 211, 261-266.
92. Oda, Y., Owa, T., Sato, T., Boucher, B., Daniels, S., Yamanaka, H., Shinohara, Y., Yokoi, A., Kuromitsu, J. and Nagasu, T. (2003) Quantitative chemical proteomics for identifying candidate drug targets. *Anal. Chem.*, 75, 2159-2165.
93. Fishman, H. A., Orwar, O., Allbritton, N. L., Modi, B. P., Shear, J. B., Scheller, R. H. and Zare, R. N. (1996) Cell-to-cell scanning in capillary electrophoresis. *Anal. Chem.* 68, 1181-1186.
94. Miller, K. J. and Lytle, F. E. (1994) Enzymatic profiling of immobilized cells using CZE. *Anal. Chem.*, 66, 2420-2423.
95. (a) Stewart, J. M and Young, J. D. (1983) Solid Phase Peptide Synthesis. Handbook.
 (b) Rich, D. H. and Singh, J. (1979) In *The Peptides: Analysis, Synthesis and Biology*; Gross, E., Meienhofer, J., Eds., Academic Press: New York, 1, 241-261.
 (c) Bodanszky, M. and Bednarek, M. A. (1989) Active esters in solid-phase peptide synthesis. *J. Protein Chem.* 8, 461-469.
96. Fukuroda, T., Ozaki, S., Ihara, M., Ishikawa, K., Yano, M., Miyauchi, T., Ishikawa,

- S., Onizuka, M., Goto, K. and Nishikibe, K. (1996) Necessity of dual blockade of endothelin ETA and ETB receptor subtypes for antagonism of endothelin-1-induced contraction in human bronchi. *Br. J. Pharmacol.* 117, 995-999.
97. Berryman, K. A., Edmunds, J. J., Bunker, A. M., Haleen, S., Belch, K. M. and Doherty, A. M. (1998) Endothelin receptor antagonists: synthesis and structure-activity relationships of substituted benzothiazine-1,1-dioxides. *Bioorg. Med. Chem.* 6, 1447-1456.
98. Babu C., Yu, H. M., Yang, S. M. and Fang, J. M. (2004) Carbazolothiophene-2-carboxylic acid derivatives: synthesis and bioactivity. *Bioorg. Med. Chem. Lett.* 14, 1129-1132.
99. Elliott, J. D., Lago, M. A., Cousins, R. D., Gao, A., Leber, J. D., Erhard, K. F., Nambe, P., Elshourbagy, N. A., Kumar, C. and Lee, J. A. (1994) 1,3-Diarylindan-2-carboxylic acids, potent and selective non-peptide endothelin receptor antagonists. *J. Med. Chem.* 37, 1553-1557.
100. Wu, C., Chan, M. F., Stavros, F., Raju, B., Okun, I., Mong, S., Keller, K. M., Brock, T. P. and Dixon, R. A. (1997) Discovery of TBC11251, a potent, long acting, orally active endothelin receptor-A selective antagonist. *J. Med. Chem.* 40, 1690-1697.
101. Yang, S. M., Shie, J. J., Fang, J. M., Nandy, S. K., Chang, H. Y., Lu, S. H. and Wang, G. (2002) Synthesis of polysubstituted benzothiophenes and sulfur-containing polycyclic aromatic compounds via samarium diiodide promoted three-component coupling reactions of thiophene-2-carboxylate. *J. Org. Chem.* 67, 5208-5215.
102. Osman, A. N., el-Gendy, A. A., Omar, R. H., Wagdy, L. and Omar, A. H. (2002) Synthesis and pharmacological activity of 1,4-benzodiazepine derivatives. *Boll.*

Chim. Farm. 141, 8-14,

103. Cheng, M. F. and Fang, J. M. (2004) Liquid-phase combinatorial synthesis of 1,4-benzodiazepine-2,5-diones as the candidates of endothelin receptor antagonism. *J. Comb. Chem.*, 6, 99-104.
104. Kennedy, A. L., Fryer, A. M. and Josey, J. A. (2002) A new resin-bound universal isonitrile for the Ugi 4CC reaction: preparation and applications to the synthesis of 2,5-diketopiperazines and 1,4-benzodiazepine-2,5-diones. *Org. Lett.* 4, 1167-1170.
105. Rubanyi, G. M. (1993) The role of endothelium in cardiovascular homeostasis and diseases. *J. Cardiovasc Pharmacol.* 22, S1-14.
106. Sakurai, T. and Goto, K. (1993) Endothelins. Vascular actions and clinical implications. *Drugs* 46, 798-804.
107. Marsdin, P. A., Danthuluri, N. R., Brenner, B. M., Ballermann, B. J. and Brock, T. A. (1989) Endothelin action on vascular smooth muscle involves inositol trisphosphate and calcium mobilization. *Biochem. Biophys. Res. Commun.* 158, 86-93.
108. Danthuluri, N. R. and Brock, T. A. (1990) Endothelin receptor-coupling mechanisms in vascular smooth muscle: a role for protein kinase C. *J. Pharmacol Exp. Ther.* 254, 393-399.
109. Chueh, S. H. and Kao, L. S. (1993) Extracellular ATP stimulates calcium influx in neuroblastoma x glioma hybrid NG108-15 cells. *J. Neurochem.* 61, 1782-1788.
110. Nilius, B., Hess, P., Lansman, J. B. and Tsien, R. W. (1985) A novel type of cardiac calcium channel in ventricular cells. *Nature* 316, 443-446.
111. Blachier, F. and Malaisse, W. J. (1988) Effect of exogenous ATP upon inositol

- phosphate production, cationic fluxes and insulin release in pancreatic islet cells. *Biochim. Biophys. Acta.* 970, 222-229.
112. Miyamoto, T., Restrepo, D., Cragoe, E. J. and Teeter, J. H. (1992) IP₃-and cATP-induced responses in isolated olfactory receptor neurons from the channel catfish. *J. Membr. Biol.* 127, 173-183.
113. Hoth, M. and Penner, R. (1992) Depletion of intracellular calcium stores activates a calcium current in mast cells. *Nature* 355, 353-356.
114. Tsien, R. W. and Tsien, R. Y. (1990) Calcium channels, stores, and oscillations. *Annu. Rev. Cell Biol.* 6, 715-760.
115. Ueda, T., Chueh, S. H., Noel, M. W. and Gill, D. L. (1986) Influence of inositol 1,4,5-trisphosphate and guanine nucleotides on intracellular calcium release within the N1E-115 neuronal cell line. *J. Biol. Chem.* 261, 3184-3192.
116. Tseng, M. J., Detjen, K., Struk, V. and Logsdon, C. D. (1995) Carboxyl-terminal domains determine internalization and recycling characteristics of bombesin receptor chimeras. *J. Biol. Chem.* 270, 18858-18864.
117. Leif, R. C., Ingram, D., Clay, C., Bobbitt, D., Gaddis, R., Leif, S. B. and Nordqvist S. (1977) Optimization of the binding of dissociated exfoliated cervico-vaginal cells to glass microscope slides. *J. Histochem. Cytochem.* 25, 538-543.
118. Vieklind, U. and Swierenga, S. H. (1989) A simple fixation procedure for immunofluorescent detection of different cytoskeletal components within the same cell. *Histochemistry*, 91, 81-88.
119. Kimura, S., Kasuya, Y., Sawamura, T., Shinmi, O., Sugita, Y., Yanagisawa, M., Goto, K. and Masaki, T. (1988) Structure-activity relationships of endothelin: importance of the C-terminal moiety. *Biochem. Biophys. Res. Commun.*, 156, 1182-1186.

120. Hashido, K., Gamou, T., Adachi, M., Tabuchi, H., Watanabe, T., Furuichi, Y. and Miyamoto, C. (1992) Truncation of N-terminal extracellular or C-terminal intracellular domains of human ETA receptor abrogated the binding activity to ET-1. *Biochem. Biophys. Res. Commun.* 187, 1241-1248.
121. Miyata, S., Hashimoto, M., Fujie, K., Nishikawa, M., Kiyoto, S., Okuhara, M. and Kohsaka, M. (1992) WS-7338, new endothelin receptor antagonists isolated from Streptomyces sp. No. 7338. II. Biological characterization and pharmacological characterization of WS-7338 B. *J. Antibiot. (Tokyo)* 45, 83-87.
122. Elliott, J. D., Lago, M. A., Cousins, R. D., Gao, A., Leber, J. D., Erhard, K. F., Nambi, P., Elshourbagy, N. A., Kumar, C., Lee, J. A., Bean, J. W., DeBrosse, C. W., Eggleston, D. S., Brooks, D. P., Feuerstein, G., Ruffolo, R. R., Weinstock, J., Gleason, J. G., Peishoff, C. E. and Ohlstein, E. H. (1994) 1,3-Diarylindan-2-carboxylic acids, potent and selective non-peptide endothelin receptor antagonists. *J. Med. Chem.* 37, 1553-1557.
123. Representative procedure for the SmI₂ promoted three-component coupling reactions: Under an atmosphere of argon, a deep blue SmI₂ solution (0.1 M) was prepared by treatment of Sm (661 mg, 4.4 mmol) with 1,2-diiodoethane (1.01 g, 3.6 mmol) in HMPA¹⁰ (2.8 mL, 16 mmol) and anhydrous THF (32 mL) for 1.5 h at room temperature. To the SmI₂ solution (cooled in an ice bath) were added a THF solution (3 mL) of methyl thiophene-2-carboxylate (142 mg, 1 mmol) and *N*-methylindole-2-carbaldehyde (159 mg, 1 mmol). The reaction mixture was stirred at 0 °C for 45 min, and then at room temperature (27 °C) for 45 min. A THF solution (2 mL) of 4-methoxyacetophenone (180 mg, 1.2 mmol) was added at 0 °C, and the mixture was stirred at 27 °C for additional 10 h. The reaction was quenched by addition of saturated aqueous NH₄Cl solution (0.1 mL). The mixture

was passed through a short silica gel column by rinse with EtOAc/hexane (1:1). The filtrate was concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexane (3:7) to give the desired three-component coupling product 4 (349 mg, 77%) as a mixture of isomers as shown by the ¹H NMR analysis.

124. Gill, D L., Ueda, T., Chueh, S. H. and Noel, M. W. (1986) Ca²⁺ release from endoplasmic reticulum is mediated by a guanine nucleotide regulatory mechanism. *Nature* 320, 461-464.
125. Arai, H., Hori, H., Aramori, I., Ohkubo, H., Nakanishi, S. (1990) Cloning and expression of a cDNA encoding an endothelin receptor. *Nature* 348, 730-732.
126. Sakurai, T., Yanagisawa, M., Takuwa, Y., Miyazaki, H., Kimura, S., Goto, K. and Masaki, T. (1990) Cloning of a cDNA encoding a non-isopeptide-selective subtype of the endothelin receptor. *Nature* 348, 732-735.
127. Sakamoto, A., Yanagisawa, M., Tsujimoto, G., Nakao, K., Toyo-oka, T. and Masaki, T. (1994) Pseudo-noncompetitive antagonism by BQ-123 of intracellular calcium transients mediated by human ETA endothelin receptor. *Biochem. Biophys. Res. Commun.* 200, 679-686.
128. Fischli, W., Clozel, M. and Guilly, C. (1989) Specific receptors for endothelin on membranes from human placenta. Characterization and use in a binding assay. *Life Sci.* 44, 1429-1436.
129. Waeber, C., Hoyer, D. and Palacios J. M. (1991) Similar distribution of [¹²⁵I]endithelin-1, 2,3 binding sites in the human kidney. *Eur. J. Pharm.* 176, 233-236.
130. Kimura, S., Kasuya, Y., Sawamura, T., Shinmi, O., Sugita, Y., Yanagisawa, M., Goto, K. and Masaki, T. (1988) Structure-activity relationships of endothelin:

- importance of the C-terminal moiety. *Biochem. Biophys. Res. Commun.* 156, 1182-1186.
131. Hashido, K., Gamou, T., Adachi, M., Tabuchi, H., Watanabe, T., Furuichi, Y. and Miyamoto, C. (1992) Truncation of N-terminal extracellular or C-terminal intracellular domains of human ETA receptor abrogated the binding activity to ET-1. *Biochem. Biophys. Res. Commun.* 187, 1241-1248.
132. Ishikawa, K., Fukami, T., Nagase, T., Fujita, K., Hayama, T., Niyama, K., Mase, T., Ihara, M. and Yano, M. (1992) Cyclic pentapeptide endothelin antagonists with high ETA selectivity. Potency-and solubility-enhancing modifications. *J. Med. Chem.* 35, 2139-2142.
133. Miyata, S., Hashimoto, M., Fujie, K., Nishikawa, M., Kiyoto, S., Okuhara, M. and Kohsaka, M. (1992) WS-7338, new endothelin receptor antagonists isolated from Streptomyces sp. No. 7338. II. Biological characterization and pharmacological characterization of WS-7338 B. *J. Antibiot(Tokyo)*. 45, 83-87.
134. Miyata, S., Fukami, N., Neya, M., Takase, S. and Kiyoto, S. (1992) WS-7338, new endothelin receptor antagonists isolated from Streptomyces sp. No. 7338. III. Structures of WS-7338 A, B, C, and D and total synthesis of WS-7338 B. *J. Antibiot (Tokyo)*. 45, 788-791.
135. Grynkiewicz, G., Poenie, M. and Tsien, R.Y. (1985) A new generationof Ca²⁺ indicators with greatly improved fluorescence properties. *J. Biol. Chem.* 260, 3440-3450.
136. Hamasaki, Y., Kobayashi, I., Zaitu, M., Tsuji, K., Kita, M., Hayasaki, R., Muro, E., Yamamoto, S., Matsuo, M., Ichimaru, T. and Miyazaki, S. (1999) Magnolol inhibits leukotriene synthesis in rat basophilic lerkemia-2H3 cells. *Planta Med.* 65, 222-226.

137. Chen, Y. H., Lin, S. J., Chen, J. W., Ku, H. H. and Chen, Y. L. (2001) Salvianolic acid B attenuates VCAM-1 and ICAM-1 expression in TNF-alpha-treated human aortic endothelial cells. *J. Cell Biochem.* 82, 512-521.
138. Park, E. J., Zhao, Y. Z., Na, M. K., Bae, K. H., Kim, Y. H., Lee, B. H. and Sohn, D. H. (2003) Protective effects of honokiol and magnolol on tertiary butyhydroperoxide-or D-galactosamine-induced toxicity in rat primary hepatocytes. *Planta Med.* 69, 33-37.
139. Yamazaki, M., Chiba, K. and Mohri, T. (1996) Neuritogenic effect of natural iridoid compounds on PC12h cells and its possible relation to signaling protein kinases. *Biol. Pharm. Bull.* 19, 791-795.