JEP> Vol.3 No.7, July 2012

OPEN ACCESS

Development of Immunochemical Methods for Purification and Detection of the Steroid Drug Medroxyprogesterone Acetate

PDF (Size:404KB) PP. 624-639 DOI: 10.4236/jep.2012.37076

Author(s)

Alisa Bronshtein, Alex Krol, Haim Schlesinger, Miriam Altstein

ABSTRACT

An immunochemical sol-gel-based immunoaffinity purification (IAP) method for purification and detection of the progestin drug medroxyprogesterone acetate (MPA) was developed. A polyclonal antibody (Ab) for MPA was generated, and two competitive (indirect and direct) sensitive enzyme-linked immunosorbent assays (ELISAs) for its detection were developed and implemented to determine the recovery and efficiency of the sol-gel based IAP method. The detection limits of the assays were 1.4 ± 0.2 ng · mL^{-1} (n = 4) and 4.0 ± 0.4 ng · mL^{-1} (n = 25) for the indirect and direct ELISAs, respectively. The Abs did not exhibit cross-reactivity with any other progestin or steroid hormone, with the exception of megestrol acetate, with which the Ab exhibited 76% cross-reactivity. The sol-gel IAP method successfully eliminated serum interference to a degree that enabled ELISA analysis of spiked serum samples. This method was also found fully compatible with subsequent chemical analytical methods, such as liquid chromatography followed by mass spectrometry (LC-MS/MS). The approaches developed in this study form a basis for analysis of MPA in biological samples and may be further used to study population exposure to MPA and to monitor MPA contamination in water samples.

KEYWORDS

Medroxyprogesterone Acetate; ELISA; Immunoaffinity Chromatography; Sol-Gel; Pharmaceutical Residues; Residue Monitoring

Cite this paper

A. Bronshtein, A. Krol, H. Schlesinger and M. Altstein, "Development of Immunochemical Methods for Purification and Detection of the Steroid Drug Medroxyprogesterone Acetate," *Journal of Environmental Protection*, Vol. 3 No. 7, 2012, pp. 624-639. doi: 10.4236/jep.2012.37076.

References

[1] M. Crane, C. Watts and T. Boucard, "Chronic Aquatic Environmental Risks from Exposure to Human Pharmaceuticals," Science of the Total Environment, Vol. 367, No. 1, 2006, pp. 23-41. doi:10.1016/j.scitotenv.2006.04.010

[2] K. Fent, A. A. Weston and D. Caminada, "Ecotoxicology of Human Pharmaceuticals," Aquatic Toxicology, Vol. 76, No. 2, 2006, pp. 122-159. doi:10.1016/j.aquatox.2005.09.009

[3] I. Figa-Talamanca, M. E. Traina and E. Urbani, "Occupational Exposures to Metals, Solvents and Pesticides: Recent Evidence on Male Reproductive Effects and Biological Markers," Occupational Medicine, Vol. 51, No. 3, 2001, pp. 174-188. doi:10.1093/occmed/51.3.174

[4] M. Yang, M. S. Park and H. S. Lee, "Endocrine Disrupting Chemicals: Human Exposure and Health Risks," Journal of Environmental Science and Health, Vol. 24, No. 2, 2006, pp. 183-224. doi:10.1080/10590500600936474

[5] P. K. Jjemba, "Excretion and Ecotoxicity of Pharmaceutical and Personal Care Products in the Environment," Ecotoxicology and Environmental Safety, Vol. 63, No. 1, 2006, pp. 113-130. doi:10.1016/j.ecoenv.2004.11.011

[6] O. A. H. Jones, N. Voulvoulis and J. N. Lester, "Human Pharmaceuticals in Wastewater Treatment

• Open Special Issues
• Published Special Issues
• Special Issues Guideline

JEP Subscription

Most popular papers in JEP

About JEP News

Frequently Asked Questions

Recommend to Peers

Recommend to Library

Contact Us

Processes," Critical Reviews in Environmental Science and Technology, Vol. 35, No. 4, 2005, pp. 401-427. doi:10.1080/10643380590956966

[7] A. Nikolaou, S. Meric and D. Fatta, "Occurrence Patterns of Pharmaceuticals in Water and Wastewater Environments," Analytical and Bioanalytical Chemistry, Vol. 387, No. 4, 2007, pp. 1225-1234. doi:10.1007/s00216-006-1035-8

[8] A. H. Piersma, M. Luijten, V. Popov, V. Tomenk, M. Altstein, F. Kagampang and H. Schlesinger, "Pharmaceuticals," In: I. Shaw, Ed., Endocrine-Disrupting Chemicals in Food, Woodhead Publishing Limited, Cambridge, 2009, pp. 459-518. doi:10.1533/9781845695743.4.459

[9] L. Sun, W. Yong, X. Chu and J. M. Lin, "Simultaneous Determination of 15 Steroidal Oral Contraceptives in Water Using Solid-Phase Disk Extraction Followed by High Performance Liquid Chromatography-Tandem Mass Spectrometry," Journal of Chromatography A, Vol. 1216, No. 28, 2009, pp. 5416-5423. doi:10.1016/j.chroma.2009.05.041

[10] M. Velicu and R. Suri, "Presence of Steroid Hormones and Antibiotics in Surface Water of Agricultural, Suburban and Mixed-Use Areas," Environmental Monitoring and Assessment, Vol. 154, No. 1-4, 2009, pp. 349-359. doi:10.1007/s10661-008-0402-7

[11] M. Shalev, M. Bardugo, A. Nudelman, A. Krol, H. Schlesinger, A. Bronshtein and M. Altstein, "Monitoring of Progestins: Development of Immunochemical Methods for Purification and Detection of Levonorgestrel," Analytica Chimica Acta, Vol. 665, No. 2, 2010, pp. 176-184. doi:10.1016/j.aca.2010.03.029

[12] M. Shalev and M. Altstein, "Sol-Gel Entrapped Levonorgestrel Antibodies: Activity and Structural Changes as a Function of Different Polymer Formats," Materials, Vol. 4, No. 3, 2011, pp. 469-486.

[13] N. Skalka, A. Krol, H. Schlesinger and M. Altstein, "Monitoring of the Non-Steroid Anti-Inflammatory Drug Indomethacin: Development of Immunochemical Methods for Its Purification and Detection," Analytical and Bioanalytical Chemistry, Vol. 400, No. 10, 2011, pp. 3491-3504. doi:10.1007/s00216-011-5027-y

[14] A. Black, D. Francoeur, T. Rowe, J. Collins, D. Miller, T. Brown, M. David, S. Dunn, W. A. Fisher, N. Fleming, C. A. Fortin, E. Guilbert, L. Hanvey, A. Lalonde, R. Miller, M. Morris, T. O'Grady, H. Pymar, T. Smith and E. Henneberg, "Canadian Contraception Consensus," Journal of Obstetrics and Gynaecology Canada, Vol. 26, No. 2, 2004, pp. 347-436.

[15] A. M. Kaunitz, "Long-Acting Injectable Contraception with Depot Medroxyprogesterone Acetate," American Journal of Obstetrics and Gynecology, Vol. 170, No. 5, 1994, pp. 1543-1549.

[16] S. Kennedy, A. Bergqvist, C. Chapron, T. D'Hooghe, G. Dunselman, R. Greb, L. Hummelshoj, A. Prentice and E. Saridogan, "ESHRE Guideline for the Diagnosis and Treatment of Endometriosis," Human Reproduction, Vol. 20, No. 10, 2005, pp. 2698-2704. doi:10.1093/humrep/dei135

[17] E. R. Guilbert, J. P. Brown, A. M. Kaunitz, M. S. Wagner, J. Berube, L. Charbonneau, D. Francoeur, A. Gilbert, F. Gilbert, G. Roy, V. Senikas, R. Jacob and R. Morin, "The Use of Depot-Medroxyprogesterone Acetate in Contraception and Its Potential Impact on Skeletal Health," Contraception, Vol. 79, No. 3, 2009, pp. 167-177. doi:10.1016/j.contraception.2008.10.016

[18] C. Choksuchat, S. Zhao, T. D. Deutch, T. D. Kimble and D. F. Archer," Effects of Progesterone, Levonorgestrel and Medroxyprogesterone Acetate on Apoptosis in Human Endometrial Endothelial Cells," Contraception, Vol. 79, No. 2, 2009, pp. 139-145. doi:10.1016/j.contraception.2008.08.008

[19] C. Lanari, C. A. Lamb, V. T. Fabris, L. A. Helguero, R. Soldati, M. C. Bottino, S. Giulianelli, J. P. Cerliani, V. Wargon and A. Molinolo, "The MPA Mouse Breast Cancer Model: Evidence for a Role of Progesterone Receptors in Breast Cancer," Endocrine-Related Cancer, Vol. 16, 2009, pp. 333-350. doi:10.1677/ERC-08-0244

[20] H. Chang, S. Wu, J. Hu, M. Asami and S. Kunikane, "Trace Analysis of Androgens and Progestogens in Environmental Waters by Ultra-Performance Liquid Chromatography-Electrospray Tandem Mass Spectrometry," Journal of Chromatography A, Vol. 1195, No. 1-2, 2008, pp. 44-51. doi:10.1016/j.chroma.2008.04.055

[21] G. Kaklamanos, G. Theodoridis and T. Dabalis, "Gel Permeation Chromatography Clean-up for the Determination of Gestagens in Kidney Fat by Liquid Chromatography-Tandem Mass Spectrometry and Validation According to 2002/657/EC," Journal of Chromatography A, Vol. 1216, No. 46, 2009, pp. 8067-8071. doi:10.1016/j.chroma.2009.04.050

[22] G. Kaklamanos, G. Theodoridis and T. Dabalis, "Determination of Anabolic Steroids in Muscle Tissue by Liquid Chromatography-Tandem Mass Spectrometry," Journal of Chromatography A, Vol. 1216, No. 46, 2009, pp. 8072-8079. doi:10.1016/j.chroma.2009.04.051

[23] J. C. Cornette, K. T. Kirton and G. W. Duncan, "Measurement of Medroxyprogesterone Acetate (Provera) by Radioimmunoassay," Journal of Clinical Endocrinology & Metabolism, Vol. 33, No. 3, 1971, pp. 459-466. doi:10.1210/jcem-33-3-459

[24] M. Hiroi, F. Z. Stanczyk, U. Goebelsmann, P. F. Brenner, M. E. Lumkin and D. R. Mishell, "Radioimmunoassay of Serum Medroxyprogesterone Acetate (Provera) in Women Following Oral and Intravaginal Administration," Steroids, Vol. 26, No. 3, 1975, pp. 373-386. doi:10.1016/0039-128X(75)90082-3

[25] G. Cui, H. Q. Chu, Y. M. Hu and C. L. Xu, "Ultrasensitive Signal Amplified Immunoassay of Medroxyprogesterone Acetate (MPA) Using the Atomic Absorption of Silver Deposited on the Surface of Gold Nanoparticles," Food and Agricultural Immunology, Vol. 21, No. 2, 2010, pp. 165-173. doi:10.1080/09540100903556021

[26] L. K. Lewis, P. A. Elder and G. K. Barrell, "An Enzyme-Linked-Immunosorbent-Assay (Elisa) for Plasma Medroxyprogesterone Acetate (Mpa)," Journal of Steroid Biochemistry and Molecular Biology, Vol. 42, No. 2, 1992, pp. 179-183. doi:10.1016/0960-0760(92)90026-F

[27] C. F. Peng, Y. W. Chen, W. Chen, C. L. Xu, J. M. Kim and Z. Y. Jin, "Development of a Sensitive Heterologous Elisa Method for Analysis of Acetylgestagen Residues in Animal Fat," Food Chemistry, Vol. 109, No. 3, 2008, pp. 647-653. doi:10.1016/j.foodchem.2007.12.072

[28] H. L. Qi, R. R. Wang, G. Yang and J. L. Liu, "An Enzyme-Linked Immunoassay for the Detection of Medroxyprogesterone Acetate in Intestines Based on Monoclonal Antibody," Food and Agricultural Immunology, Vol. 22, c2011, pp. 125-134. doi:10.1080/09540105.2010.549208

[29] H. Tieming, P. Chifang, C. Xiaogang and X. Chuanlai, "Rapid Determination of Time-Resolved Fluoroimmunoassay for Medroxyprogesterone Acetate Residues in Pork Tissues and Comparison with Liquid Chromatography and Tandem Mass Spectrometry," Journal of Fluorescence, Vol. 16, No. 6, 2006, pp. 743-747. doi:10.1007/s10895-006-0132-6

[30] C. F. Peng, T. M. Huo, L. Q. Liu, X. G. Chu and C. L. Xu, "Determination of Medroxyprogesterone Acetate Residues by Ce Immunoassay with Chemiluminescence Detection," Electrophoresis, Vol. 28, No. 6, 2007, pp. 970-974. doi:10.1002/elps.200600290

[31] C. Peng, Z. Li, Y. Zhu, W. Chen, Y. Yuan, L. Liu, Q. Li, D. Xu, R. Qiao, L. Wang, S. Zhu, Z. Jin and C. Xu, "Simultaneous and Sensitive Determination of Multiplex Chemical Residues Based on Multicolor Quantum Dot Probes," Biosensors and Bioelectronics, Vol. 24, No. 12, 2009, pp. 3657-3662. doi:10.1016/j.bios.2009.05.031

[32] M. Altstein and A. Bronshtein, "Sol Gel Immunoassays and Immunoaffinity Chromatography," In: J. M. Van Emon, Ed., Immunoassay and Other Bioanalytical Techniques, CRC Press, 2007, pp. 357-383.

[33] D. Avnir, T. Coradin, O. Lev and J. Livage, "Recent Bio-Applications of Sol-Gel Materials," Journal of Materials Chemistry, Vol. 16, 2006, pp. 1013-1030. doi:10.1039/b512706h

[34] M. Cichna-Markl, "Selective Sample Preparation with Bioaffinity Columns Prepared by the Sol-Gel Method," Journal of Chromatography A, Vol. 1124, No. 1-2, 2006, pp. 167-180. doi:10.1016/j.chroma.2006.06.077

[35] V. B. Kandimalla, V. S. Tripathi and H. X. Ju, "Immobilization of Biomolecules in Sol-Gels: Biological AND Analytical Applications," Critical Reviews in Analytical Chemistry, Vol. 36, No. 2, 2006, pp. 73-106. doi:10.1080/10408340600713652

[36] M. Alstein, O. Ben-Aziz, N. Skalka, A. Bronshtein, J. C. Chuang and J. M. Van Emon, "Development of an Immunoassay and a Sol Gel Based Imuunoaffinity Cleanup Method for Coplanar Pcb ' s from Soil and Sediment Samples," Analytica Chimica Acta, Vol. 675, No. 2, 2010, pp. 138-147.

[37] P. Degelmann, S. Egger, H. Jurling, J. Muller, R. Niessner and D. Knopp, "Determination of Sulfonylurea Herbicides in Water and Food Samples Using Sol-Gel Glass-Based Immunoaffinity Extraction and Liquid Chromatography-Ultraviolet/Diode Array Detection or Liquid Chromatography-Tandem Mass Spectrometry," Journal of Agricultural and Food Chemistry, Vol. 54, No. 6, 2006, pp. 2003-2011. doi:10.1021/jf052718+

[38] R. J. Hodgson, M. A. Brook and J. D. Brennan, "Capillary-Scale Monolithic Immunoaffinity Columns for

Immunoextraction with in-Line Laser-Induced Fluorescence Detection," Analytical Chemistry, Vol. 77, No. 14, 2005, pp. 4404-4412. doi:10.1021/ac048142p

[39] M. Kaware, A. Bronshtein, J. Safi, J. M. Van Emon, J. C. Chuang, B. Hock, K. Kramer and M. Altstein, "Enzyme-Linked Immunosorbent Assay (ELISA) and SolGel-Based Immunoaffinity Purification (IAP) of the Pyrethroid Bioallethrin in Food and Environmental Samples," Journal of Agricultural and Food Chemistry, Vol. 54, No. 18, 2006, pp. 6482-6492. doi:10.1021/jf0607415

[40] P. Pulido-Tofino, J. M. Barrero-Moreno and M. C. Perez-Conde, "Analysis of Isoproturon at Trace Level by Solid Phase Competitive Fluoroimmunosensing after Enrichment in a Sol-Gel Immunosorbent," Analytica Chimica Acta, Vol. 562, No. 1, 2006, pp. 122-127. doi:10.1016/j.aca.2005.12.072

[41] F. Tsagkogeorgas, M. Ochsenkuhn-Petropoulou, R. Niessner and D. Knopp, "Encapsulation of Biomolecules for Bioanalytical Purposes: Preparation of Diclofenac Antibody-Doped Nanometer-Sized Silica Particles by Reverse Micelle and Sol-Gel Processing," Analytica Chimica Acta, Vol. 573-574, 2006, pp. 133-137. doi:10.1016/j.aca.2006.03.006

[42] L. E. Vera-Avila, J. C. Vazquez-Lira, L. M. Garcia and R. Covarrubias, "Sol-Gel Immunosorbents Doped with Polyclonal Antibodies for the Selective Extraction of Malathion and Triazines from Aqueous Samples," Environmental Science & Technology, Vol. 39, No. 14, 2005, pp. 5421-5426. doi:10.1021/es048000c

[43] X. Zhang, D. Martens, P. M. Kramer, A. A. Kettrup and X. Liang, "Development and Application of a Sol-Gel Immunosorbent-Based Method for the Determination of Isoproturon in Surface Water," Journal of Chromatography A, Vol. 1102, No. 1-2, 2006, pp. 84-90. doi:10.1016/j.chroma.2005.10.072

[44] X. Zhang, D. Martens, P. M. Kramer, A. A. Kettrup and X. Liang, "On-Line Immunoaffinity Column-Liquid Chromatography-Tandem Mass Spectrometry Method for Trace Analysis of Diuron in Wastewater Treatment Plant Effluent Sample," Journal of Chromatography A, Vol. 1133, No. 1-2, 2006, pp. 112-118. doi:10.1016/j.chroma.2006.08.007

[45] R. R. Sokal and J. F. Rohlf, "Biometry," W.H. Freeman and Co., New York, 1995.

[46] M. Altstein, A. Bronshtein, B. Glattstein, A. Zeichner, T. Tamiri and J. Almog, "Immunochemical Approaches for Purification and Detection of TNT Traces by Antibodies Entrapped in a Sol-Gel Matrix," Analytical Chemistry, Vol. 73, No. 11, 2001, pp. 2461-2467. doi:10.1021/ac001376y

[47] J. C. Chuang, J. M. Van Emon, R. Jones, J. Durnford and R. A. Lordo, "Development and Application of Immunoaffinity Column Chromatography for Atrazine in Complex Sample Media," Analytica Chimica Acta, Vol. 583, No. 1, 2007, pp. 32-39. doi:10.1016/j.aca.2006.09.060

[48] J. D. Groopman and A. Zarba, "Immunoassays for Trace Chemical Analysis." In: M. Vanderlan, L. H. Stanker, B. E. Watkins, D. W. Roberts, Eds., ACS Symposium Series, American Chemical Society, Washington DC, 1991, pp. 207-214.

[49] J. F. Lawrence, C. Menard, M. C. Hennion, V. Pichon, F. Le Goffic and N. Durand, "Use of Immunoaffinity Chromatography as a Simplified Cleanup Technique for the Liquid Chromatographic Determination of Phenylurea Herbicides in Plant Material," Journal of Chromatography A, Vol. 732, No. 2, 1996, pp. 277-281. doi:10.1016/0021-9673(95)01274-5