

CURRICULUM VITAE

Name: KEITH ROGER BRAIN
Date of birth: 250545
Nationality: British
Qualifications: BPharm (Nottingham) 1966 PhD (Bath) 1969

Employment : **CEO**
An-eX analytical services ltd
Cardiff, UK
(1988-date)
and
Honorary Senior Research Fellow
School of Pharmacy and Pharmaceutical Sciences
Cardiff University, UK
(2011-date)
Reader in Dermatopharmaceutics
School of Pharmacy and Pharmaceutical Sciences
Cardiff University, UK
(1969-2011)

For past 28 years CEO of An-eX analytical Services ltd, an independent contract R&D company based in Cardiff that is globally recognised for expertise in development and evaluation, particularly in the dermal field.

Also member of the academic staff of the School of Pharmacy and Pharmaceutical Sciences, Cardiff University for 42 years.

Expert Witness in Patent Litigation:

I have acted as an Expert Witness in the following three patent litigation cases in the dermal area in the past four years.

- 1) FOUGERA v TOLMAR Civil Action No 10-2635 (KSH) (PS) - Declaration (settled)
- 2) NOVEN V WATSON Civil Action No 2: 11-cv-5997 (DMC) (MF) - Expert Reports, Deposition, Trial Preparation (settled)
- 3) ENDO v MYLAN Civil Action No 1:11-cv-00220-GMS - Expert Reports (settled)

I have also provided expert advice on other matters.

Selected external participation/esteem measures

Expert Panel Member, Workshop on Dermal Absorption for Pesticide Risk Assessment: Harmonization of an In Vitro Protocol for Regulatory Use, IIVS, Gaithersburg, MD, May 1-2, 2012

Member of HIPODERM consortium (An-eX, Cardiff University, Eirgen Pharma and Waterford Institute) awarded 836,000 euros through EU Marie Curie IAPP scheme (2011-2015)

Member of the Planning Committee for the FDA/DIA meeting on Improved Development and Regulation of Transdermal Systems, Arlington VA, Sep 15-16, 2011

Invited Speaker on TDDS: Past, Present and Future, at the FDA/DIA meeting on Improved Development and Regulation of Transdermal Systems, Arlington VA, Sep 15-16, 2011

Invited Speaker on An Integrated Data-Driven Approach to Development and Evaluation of Improved Formulations for Dermal Protection, DTRA Dermal Toxicity Workshop, St Petersburg, FL, Jan 11-14, 2010

One of two academic members on the ECETOC Selection Team - HETRA A2.3 International workshop on dermal exposure modelling meeting (part of the CEFIC Long-range Research Initiative) in Brussels, Belgium, August 2003

Invited participant in CEFIC expert workshop on methods to determine dermal permeation for human risk assessment, Utrecht, Netherlands, July 2004

Invited member of Expert Workshop on Percutaneous Absorption, Institute for In Vitro Sciences, Gaithersburg, Md, USA, July 2005

Frequent presentations at major national/international meetings

Invited participant in Gordon Research Conference on Barrier Function of Mammalian Skin in Pisa, Italy, 1999, Bristol, RI, USA, 2001 and Mount Holyoake, MA, USA, 2005 and 2007. Member of the Debating Team on each occasion. Invited Debate Moderator in 2009.

Invited to join the Scientific Board, Society for Molecular Imprinting, September, 2006

Invited Speaker, American Association of Pharmaceutical Scientists Annual Meeting, Salt Lake City, USA, November, 2003

Invited Speaker, American Association of Pharmaceutical Scientists, Pharmaceuticals and Drug Delivery Meeting, Philadelphia, USA, July, 2004

Invited Speaker, Perspectives in Percutaneous Conference, La Grande Motte, France, April, 2004

Invited Speaker, AgChemForum Meeting, Amsterdam, Netherlands, September, 2004

Invited Speaker, MIP2004 Workshop, Cardiff, September, 2004

Invited Speaker, Perspectives in Percutaneous Conference, La Grande Motte, France, April, 2006

Invited Speaker, Perspectives in Percutaneous Conference, Southampton, April, 1999

Conference Organisation

Organiser of biennial international Perspectives in Percutaneous Penetration conference and Introductory Course on Percutaneous Penetration from 1993-date ((93, 95, 97, 98, 00, 02, 04, 06, 08, 10, 12, 14, 16)).

Organiser of biennial international Molecularly Imprinted Polymers Workshop from 2000-date (00, 02, 04, 06, 08, 10).

Both of these meetings are recognised as major global events.

Reviewing

Regular reviewer for:

Analytical and Bioanalytical Chemistry
Analytica Chimica Acta
Bioorganic and Medicinal Chemistry
Drug Metabolism and Disposition
International Journal of Pharmaceutics
Journal of Controlled Release
Journal of Drug Targeting
Journal of Investigative Dermatology
Journal of Pharmacy and Pharmacology
Nature Biotechnology
Pharmaceutical Research

Publications

The data contained in the publication list below is divided into peer-reviewed publications, invited book chapters, authored books, edited books, peer reviewed papers in conference proceedings and conference abstracts.

Publications in peer reviewed journals

1. Martin CJ, Allender CJ, Brain KR, Morrissey, A, Birchall, JC, Low temperature fabrication of biodegradable sugar glass microneedles for transdermal drug delivery applications, *J Contr Rel*, 2012, 158, 93-101
2. Green DM, Jones AC, Brain KR, Content variability of active drug substance in compounded oral 3,4-diaminopyridine products. *J Clin Pharm Ther.* 2012, 37, 53-57
3. Hillberg AL, Brain KR, Allender CJ, Design and evaluation of thin and flexible theophylline imprinted polymer membrane materials, *J Mol Recognit.* 2009, 22, 223-31
4. Morris AP, Brain KR, Heard CM, Skin permeation and ex vivo skin metabolism of O-acyl haloperidol ester prodrugs. *Int J Pharm.* 2009, 367, 44-50
5. Morris AP, Brain KR, Heard CM, Synthesis of haloperidol prodrugs and their hydrolysis by porcine liver esterase, *Drug Metab Lett.* 2008, 2, 275-9
6. Pearton M, Allender C, Brain K, Anstey A, Gateley C, Wilke N, Morrissey A, Birchall J, Gene delivery to the epidermal cells of human skin explants using microfabricated microneedles and hydrogel formulations, *Pharm Res.* 2008, 25, 407-16
7. Brain KR, Green DM, Api AM and Lalko J, In-vitro human skin penetration of the fragrance material geranyl nitrile, *Toxicol. In Vitro*, 2007, 2, 133-138
8. Turner NW, Jeans CW, Brain KR, Allender CJ, Hlady V, and Britt DW, From 3D to 2D: A Review of the Molecular Imprinting of Proteins, *Biotechnol. Prog.*, 22, 1474-1489
9. Lavignac N, Brain KR, Allender CJ, Concentration dependent atrazine-atrazine complex formation promotes selectivity in atrazine imprinted polymers, *Biosens Bioelectron*, 2006, 22, 138-44
10. Coulman SA, Barrow D, Anstey A, Gateley C, Morrissey A, Wilke N, Allender C, Brain K, Birchall JC, Minimally invasive cutaneous delivery of macromolecules and plasmid DNA via microneedles, *Curr Drug Deliv*, 2006, 3, 65-75
11. Brain KR, Green DM, Dykes PJ, Marks R, Bola TS, The role of menthol in skin penetration from topical formulations of ibuprofen 5% in vivo, *Skin Pharmacol. Physiol.*, 2006, 19,17-21
12. Hillberg AL, Brain KR, Allender CJ, Molecular imprinted polymer sensors: Implications for therapeutics, *Adv. Drug Del. Rev.*, 2005, 57, 1875-1889
13. Birchall J, Coulman S, Pearton M, Allender C, Brain K, Anstey A, Gateley C, N Wilke, A Morrissey, Cutaneous DNA delivery and gene expression in ex vivo human skin explants via wet-etch microfabricated microneedles, *J. Drug Targeting*, 2005, 13, 415-421

14. Pearton M, Barrow D, Anstey A, Gateley C, Morrissey A, Wilke N, Allender C, Brain K, Birchall JC, Disruption of stratum corneum by microfabricated microneedles for gene delivery from hydrogels, *Br.J.Dermatol.*, 2005, 152, 842-842
15. Brain KR, Walters KA, Green DM, Brain S, Loretz LJ, Sharma RK, Dressler WE, Percutaneous penetration of diethanolamine through human skin in vitro: Application from cosmetic vehicles, *Fd.Chem.Toxicol.*, 2005, 43, 681-690
16. Chabri F, Bouris K, Jones T, Barrow D, Hann A, Allender C, Brain K, Birchall J, Microfabricated silicon microneedles for nonviral cutaneous gene delivery, *Br.J.Dermatol.*, 2004, 150, 869-877
17. Lavignac N, Allender CJ, Brain KR, 4-(3-aminopropyl)-7-nitrobenzofurazan: a new polymerisable monomer for use in homogeneous molecularly imprinted sorbent fluoroassays, *Tet.Lett.*, 2004, 45, 3625-3627
18. Lavignac N, Allender CJ, Brain KR, Current status of molecularly imprinted polymers as alternatives to antibodies in sorbent assays, *Anal.Chim.Acta*, 2004, 510, 139-145
19. Watkinson AC, Brain KR, Basic mathematical principles in skin permeation, *J.Tox.Cutan.Ocular Tox.*, 2002, 21, 371-402
20. Allender CJ, Brain KR, Ballatore C, Cahard D, Siddiqui A, McGuigan C, Separation of individual antiviral nucleotide prodrugs from synthetic mixtures using cross-reactivity of a molecularly imprinted stationary phase, *Anal.Chim.Acta*, 435, 2001, 107-113
21. CJ Allender, C Richardson, B Woodhouse, CM Heard and KR Brain, Pharmaceutical applications for molecularly imprinted polymers, *Int.J.Pharm.*, 195, 2000, 39-43
22. R Suedee, KR Brain and CM Heard, Differential permeation of propranolol enantiomers across human skin in vitro from formulations containing an enantioselective excipient, *Chirality*, 11, 680-683
23. KA Walters, AC Watkinson and KR Brain, In vitro skin permeation evaluation: the only realistic option, *Int.J.Cosm.Sci.* 20, 1998, 307-316
24. KA Walters, KR Brain, DM Green, VJ James, AC Watkinson and RH Sands, Comparison of the transdermal delivery of estradiol from two gel formulations, *Maturitas*, 29, 1998, 189-195
25. AC Watkinson and KR Brain, Ceramides and fatty acids; Boosting the skin's barrier function, *Soap, Perfumery and Cosmetics*, 6, 1998, 49-54
26. KA Walters, KR Brain, WE Dressler, DM Green, D Howes, VJ James, CK Kelling, AC Watkinson, SD Gettings, Percutaneous penetration of N-nitroso-N-methyl dodecylamine through human skin in vitro: Application from cosmetic vehicles, *Fd Chem.Toxicol.* 35 (1997) 705-712
27. MA Pellett, AC Watkinson, J Hadgraft and KR Brain, Comparison of permeability data from traditional diffusion cells and ATR-FTIR spectroscopy Part II. Determination of diffusional pathlengths in synthetic membranes and human stratum corneum, *Int.J.Pharm.* 154 (1997) 217-227
28. MA Pellett, AC Watkinson, J Hadgraft and KR Brain, Comparison of permeability data from traditional diffusion cells and ATR-FTIR spectroscopy Part I. Synthetic membranes, *Int.J.Pharm.* 154 (1997) 205-215
29. MA Pellett, AC Watkinson, KR Brain and J Hadgraft, Evaluation of diffusion coefficients in silicone membranes using ATR-FTIR spectroscopy and concentration-depth profiles, *Pharm.Res.*, 14 (1997) S36
30. KA Walters, KR Brain, D Howes, VJ James, AL Kraus, NM Teetsel, M Toulon, AC Watkinson and SD Gettings Percutaneous penetration of octyl salicylate from representative sunscreen formulations through human skin in vitro, *Fd.Chem. Toxicol.*, 35 (1997) 1219-1225
31. R Suedee, KR Brain and CM Heard, Stereoselective release of propranolol enantiomers from matrices containing cellulose derivatives. *Chirality* 9 (1997) 307-312
32. CJ Allender, CM Heard and KR Brain, Mobile phase effects on enantiomer resolution using molecularly imprinted polymers, *Chirality* 9 (1997) 238-242
33. CJ Allender, KR Brain and CM Heard, Binding cross-reactivity of boc-phenylalanine enantiomers on molecularly imprinted polymers, *Chirality* 9 (1997) 233-237
34. CM Heard, KR Brain and R Suedee, Differential penetration of propranolol across human skin in vitro caused by stereoselective sorption in vehicle, *J.Pharm.Pharmacol.*, 49 (1997) S41
35. WJ Kee, KR Brain and CM Heard, Towards malaria prophylaxis by transdermal delivery of some anti-malarial drugs, *J.Pharm.Pharmacol.*, 49 (1997) S142
36. CJ Allender, MAE Bowman, KR Brain and CM Heard, Evaluation of molecularly imprinted polymers as selective sorbents for the preliminary screening of combinatorial libraries, *J.Pharm.Pharmacol.*, 49 (1997) S173
37. CJ Allender, MAE Bowman, KR Brain and CM Heard, Molecularly imprinted polymers as novel excipients in controlled release systems, *J.Pharm.Pharmacol.*, 49 (1997) S119

38. JE Harrison, PW Groundwater, KR Brain and J Hadgraft, Azone® induced fluidity in human stratum corneum. A fourier transform infrared spectroscopy investigation using the perdeuterated analogue. *J.Contr.Rel.* 41 (1996) 283-290
39. C M Heard, K R Brain and K A Walters, Chiral Delivery, *Brit Pat Appl* 9526478.4 (1996)
40. GC Ebi, , KR Brain and OK Udeala, Mannich reaction of 1-n-butyl-3-p-tosylurea .1. syntheses of 3-n-butyl-2-oxo-1,5-di-p-tosyl-perhydro-1,3,5-triazine and 3,5-di-n-butyl-2-oxo-1-p-tosyl-perhydro-1,3,5-triazine, *Chem.Pharm. Bull.* 44 (1996) 639-641
41. K R Brain, M A Shatalebi, A Abdel-Aziz and A Carabot Cuervo, Relacion estructura-actividad de saponinas con efecto molusquicida, *Revista Latinoamericana de Quimica*, 24 (1996) 25-32
42. A C Watkinson, J Harrison, DM Green, K R Brain and J Hadgraft, The relative effect of Azone® and Transcutol® on diffusivity and solubility in human stratum corneum. *Pharm. Res.* (1996)13, 542-546
43. A C Watkinson, H Joubin, D M Green, K R Brain and J Hadgraft, The influence of vehicle on permeation from saturated solutions, *Int.J.Pharm.*, 121 (1995) 27-37
44. C M Heard and K R Brain, Does solute stereo-chemistry influence percutaneous penetration? *Chirality* 7 (1995) 305-309
45. A M L Tralhaõ, A C Watkinson, K R Brain, J Hadgraft and N A Armstrong, Use of ATR-FTIR spectroscopy to study the diffusion of ethanol through glycerogelatin films, *Pharm. Res.* 12 (1995) 572-575
46. A M Trailhao, A C Watkinson, K R Brain, J Hadgraft and N A Armstrong, Measurement of diffusion of ethanol through glycerogelatin films by ATR-FTIR spectroscopy, *Eur J Pharm Sci* 2 (1994) 155
47. K R Brain, K A Walters, V J James, W E Dressler, D Howes, C K Kelling, S J Moloney and S D Gettings, Percutaneous Penetration of dimethylnitrosamine through human skin in vitro : Application from cosmetic vehicles, *Fd Chem Toxic* 33 (1995) 315-322
48. A C Watkinson, J Hadgraft, K A Walters and K R Brain, Measurement of diffusional parameters in membranes using ATR-FTIR spectroscopy, *Int J Cosmet Sci* 16 (1994) 199-210
49. C M Heard, K R Brain and J Hadgraft, Enantiomer enrichment and differential facilitated transport of propranolol and bupranolol enantiomers across a solid-supported liquid membrane, *Bioseparation*, 4 (1994) 111-116
50. K R Brain and A. Abdel-Aziz, Cromatografia de gases-espectrometria de masas de captura de iones de espirostenos y sapogeninas 22,25-epoxifurostenos hidroxilados en el anillo F, *Rev Fac Farm* 29 (1994) 31-38
51. J Hadgraft and K.R. Brain, Comments on 'A new approach towards the development of a transdermal terbutaline releasing system', *J Contr Rel* 27 (1993) 175-176
52. AC. Watkinson , K. R. Brain, K. A. Walters and J. Hadgraft, Investigation of relative rates of solvent and solute penetration through protective glove materials. *Pesticide Sci*, 39, 251-256 (1993)
53. CM Heard, A.C. Watkinson, K.R. Brain and J. Hadgraft, In vitro skin penetration of propranolol enantiomers, *Int.J.Pharm*, 90 (1993) R5-R8
54. KR Brain, The implications of developments in pharmaceutical analysis and new medicines on pharmaceutical education, *J.Pharm.Pharmacol.* 45S (1993) 381-383
55. AC Watkinson, K.R. Brain, K.A. Walters and J. Hadgraft, Prediction of the percutaneous penetration of ultra-violet filters used in sunscreen preparations, *Int.J. Cosmet.Sci.* 14 (1992) 265-275
56. P Ashton, K.A. Walters, K.R. Brain and J. Hadgraft, Surfactant effects in percutaneous absorption II. Effects on protein and lipid structure of the stratum corneum, *Int. J. Pharm* 87 (1992) 261-264
57. P Ashton, K.A. Walters, K.R. Brain and J. Hadgraft, Surfactant effects in percutaneous absorption I. Effects on the transdermal flux of methyl nicotinate, *Int. J. Pharm* 87 (1992) 261-264
58. KR Brain, J. Hadgraft, D. Lewis and G. Allan, The Influence of Azone® on the Percutaneous Absorption of Methotrexate, *Int. J. Pharm* 71 (1991) R9-11
59. KR Brain, Representing Pharmaceutical Scientists, *Pharm.J.* 245 (1990) 619
60. Ming-He Yang, G.Blunden, A. Patel, T.A. Crabb, K. Brain and W. J. Griffin, Two Furostane Sapogenins From *Cordyline Rubra*, *Phytochemistry* 29 (1990) 1332 - 1334
61. KR Brain, J. Hadgraft and M. Al-Shatalebi, Membrane Modification in Activity of Plant Molluscicides, *Planta Medica* 56 (1990) 663
62. J.Hadgraft and K. R. Brain, Predicting Pesticide Percutaneous Penetration, *Pestic.Sci* 30 (1990) 81-89
63. J Daly, D.K. Nicholls, K.R. Brain, P.F. Grassby and D.J. Temple, A Novel Approach to Computer-assisted Learning for Pharmacists, *Pharm.J.* 245 (1990) E1-3
64. A.Abdel-Aziz, K. Brain, M. A. Shatalebi, G. Blunden, A. Patel, T. A. Crabb and A. K. Bashir, A B-Ring Contracted Spirostane From *Tacca leontopetaloides*, *Phytochemistry* 29 (1990) 2623 - 2627

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