

M.D. Coleman

The Biochemical Pharmacology and Toxicology of Anti-parasitic Agents:

Published Work:

KEY: Publications marked with * denote national collaborations:

Publications marked with ** denote international collaborations.

(i) Disposition and Analysis of Antimalarial Agents in The Rat.

1. **M.D. Coleman**, A.J. Thompson, G. Edwards, I.M. Braithwaite and A.M. Breckenridge. The pharmacokinetics of pyrimethamine in the rat: effect of mefloquine. *J. Pharm. Pharmacol.* 38: 840-842 (1986).
2. **M.D. Coleman** and K.K. Adjepon-Yamoah. The disposition of suramin in the isolated perfused rat liver. *Biochem. Pharmacol.* 35: 3389-3392 (1986).
3. **M.D. Coleman** and K.K. Adjepon-Yamoah. The disposition of pyrimethamine in the isolated perfused rat liver: effect of suramin. *J. Pharm. Pharmacol.* 38: 531-533 (1986).
4. **M.D. Coleman**, G. Edwards, I.M. Braithwaite and A.M. Breckenridge. A high performance liquid chromatographic method for the determination of ampyroquine in biological fluids. *J. Chromatogr.* 414: 242-247 (1987).
5. **M.D. Coleman**, L. Fleckenstein, L.A. Shipley and M.H. Heiffer. The disposition of mefloquine in the isolated perfused rat liver: *Biochem. Pharmacol.* 37: 235-239 (1988).
6. **M.D. Coleman**, L. Fleckenstein, L.A. Shipley and M.H. Heiffer. Primaquine disposition in the isolated perfused rat liver: effect of mefloquine induced bile flow reduction. *Biopharm. Drug Disp.* 10, 153-164 (1989).
7. **M.D. Coleman**, L. Fleckenstein, R.S. Geary, D.J Mangold, T.G. Brewer and M.H. Heiffer. The pharmacokinetics of WR 2721 in the isolated perfused rat liver. *Radiation Research* 117, 334-341 (1989).
8. **M.D. Coleman**, G. Timony and L. Fleckenstein. The disposition of quinine in the rat isolated perfused rat liver: effect of dose size. *J. Pharm. Pharmacol.* 42, 26-29 (1990).
9. L.A. Shipley, **M.D. Coleman**, T.G. Brewer, R.W. Ashmore and A.D. Theoharides. The disposition of the antileishmanial 9-aminoquinoline WR 6026

in the isolated perfused rat liver: thermospray liquid chromatography -mass spectrometry. Identification of metabolites. *Xenobiotica* 20 31-44 (1990).

(ii) *Basic Dapsone Toxicity and its Amelioration in the Rat*

10. **M.D. Coleman**, M.J. Winn, A.M. Breckenridge and B.K. Park. Inhibition of dapsone-induced methaemoglobinaemia in the rat. *Biochem. Pharmac.* 39, 802-805 (1990).
11. **M.D. Coleman**, M.J. Winn, A.M. Breckenridge and B.K. Park. Sex-dependent sensitivity to dapsone-induced methaemoglobinaemia in the rat. *Biochem. Pharmac.* 39, 805-809 (1990).
12. **M.D. Coleman**, P.E. Hoaksey, A.M. Breckenridge and B.K. Park. Inhibition of dapsone-induced methaemoglobinaemia in the rat isolated perfused liver. *J. Pharm. Pharmacol.* 42 302-307 (1990).
13. **M.D. Coleman**, M.D. Tingle, M.J. Winn and B.K. Park. The effect of gonadal influence on the metabolism and haemotoxicity of dapsone in the rat. *J. Pharm. Pharmacol.* 42 698-703 (1990).
14. **M.D. Coleman**, M.D. Tingle and B.K. Park. Inhibition of dapsone-induced methaemoglobinaemia by cimetidine in the rat during chronic dapsone administration. *J. Pharm. Pharmacol.* 43 186-190 (1991).
15. **M.D. Coleman**, R.M. Russell, M.D. Tingle and B.K. Park. Inhibition of dapsone-induced methaemoglobinaemia by cimetidine in the rat in the presence of trimethoprim during chronic dapsone administration. *J. Pharm. Pharmacol.* 44 114-118 (1992).

(iii) *Toxicity of Sulphones and Sulphonamides in Human Tissues*

16. **M.D. Coleman**, A.M. Breckenridge and B.K. Park. Bioactivation of dapsone to a cytotoxic metabolite by human hepatic microsomal enzymes. *Brit. J. clin. Pharm.* 28, 389-395 (1989).
17. R.J. Riley, P. Roberts, **M.D. Coleman**, N.R. Kitteringham and B.K. Park. Bioactivation of dapsone to a cytotoxic metabolite: in vitro use of a novel two compartment system which contains human tissues. *Brit. J. Clin. Pharm.* 30 417-426 (1990).
18. M.D. Tingle, **M.D. Coleman** and B.K. Park. Investigation into the role of metabolism in dapsone-induced methaemoglobinaemia using a two-compartment *in vitro* test system. *Brit. J. Clin. Pharmac.* 30 829-838 (1990).
19. *M. Pirmohamed **M.D. Coleman**, F. Hussain, A.M. Breckenridge and B.K. Park. Direct and Indirect toxicity of sulphasalazine and its principle metabolites

towards human leucocytes and erythrocytes. *Brit. J. Clin Pharmac.* 32 303-311 (1991)

20. M.D. Tingle, **M.D. Coleman** and B.K. Park. Effects of pre-incubation with cimetidine on the N-hydroxylation of dapsone by human liver microsomes. *Brit. J. Clin Pharmac.* 32 120-124 (1991).

21. ***M.D. Coleman** and C. Kohl. A comparison of the *in vitro* toxicities of sulphametrole and sulphamethoxazole. *Pharm. Sci.* 1 479-481 (1995).

(iv) *Clinical Amelioration of Sulphone and Sulphonamide Toxicity.*

22. **M.D. Coleman**, A.K. Scott, A.M. Breckenridge and B.K. Park. The use of cimetidine as a selective inhibitor of dapsone N-hydroxylation in man. *Brit. J. Clin. Pharmac.* 30 761-767 (1990).

23. **M.D. Coleman**, L.A. Rhodes, A.K. Scott, J. Verbov P. Friedmann A.M. Breckenridge and B.K. Park. The use of cimetidine to reduce dapsone-dependent methaemoglobinaemia in dermatitis herpetiformis patients. *Brit. J. Clin Pharmac.* 34 244-249 (1992)

24. M. Pirmohamed, **M.D. Coleman**, D. Galvani, R.C. Bucknall, A.M. Breckenridge and B.K. Park. Lack of interaction between sulphasalazine and cimetidine in patients with rheumatoid arthritis. *Brit. J. Rheumatol.* 32 222-226 (1993)

(v) *Dapsone-Dependent Methaemoglobin Formation.*

25. ****M.D. Coleman** and D.P. Jacobus. Reduction of dapsone hydroxylamine to dapsone during methaemoglobin formation in human erythrocytes *in vitro*. *Biochem. Pharmacol.* 45 1027-1033 (1993).

26. ****M.D. Coleman** and D.P. Jacobus. Reduction of dapsone hydroxylamine to dapsone during methaemoglobin formation in human erythrocytes *in vitro* II Movement of dapsone across a semipermeable membrane into erythrocytes and plasma. *Biochem. Pharmacol.* 46 1363-1368 (1993)

27. **M.D. Coleman** and M.S. Ogg. Effect of diethyldithiocarbamate on dapsone hydroxylamine-dependent methaemoglobin formation in human erythrocytes in static and rotating systems *in vitro* *Pharmaceutical Sciences* 1 15-17, (1995).

28. **M.D. Coleman**, K.K. Pahal and J.M. Gardiner. Reduction of dapsone hydroxylamine to dapsone during methaemoglobin formation in human erythrocytes *in vitro*: effect of acetylation and deacetylation. *J. Pharm. Pharmacol.* 48 403-408 (1996)

29. **M.D. Coleman** and N.A. Coleman. Drug-Induced Methaemoglobinaemia *Drug Safety* 14 394-405 (1996)
30. **M.D. Coleman** and C.H. Taylor. Bioactivation of Benzocaine in rat and human microsomal systems in vitro. *Env. Tox. Pharmacol.* 3 47-52, (1997)
31. **M.D. Coleman** and M.K. Kuhns. Methaemoglobin formation by 4-aminopropiophenone in single and dual compartmental systems. *Env. Tox. Pharmacol.* 7 75-80 (1999)
32. **M.D. Coleman** and C.T. Taylor. Effects of Dihydrolipoic acid (DHLA), α -Lipoic acid. N-Acetyl Cysteine and Ascorbate on Xenobiotic-Mediated Methaemoglobin Formation in Human Erythrocytes In-vitro. *Env. Tox. Pharmacol* 14 121-127 (2003).

(vi) *Studies on the Replacement of Dapsone with Sulphone Analogues.*

33. **M.D. Coleman**, M.D. Tingle F. Hussain, R.C. Storr and B.K. Park. An investigation into the haematological toxicity of structural analogues of dapsone *in vivo* and *in vitro*. *J. Pharm. Pharmacol* 43 779-784 (1991)
34. ****M.D. Coleman**, S.N. Smith, D.E. Kelly, S. L. Kelly and J.K. Seydel. Studies on the toxicity of novel analogues of dapsone *in vitro* using rat, human and heterologous metabolising systems. *J.Pharm. Pharmacol*, 48 945-950 (1996)
35. ****M.D. Coleman**, S. Thorpe, S. Lewis, N.S. Buck , A.D. Perris and J.K. Seydel. Preliminary evaluation of the toxicity and efficacy of novel 2,4 diamino 5-benzyl pyrimidine-sulphone derivatives using rat and human tissues in vitro. *Env. Tox. Pharmacol.* 2 389-395 (1996)
36. ****M.D. Coleman**, J.K. Smith, A.D. Perris, N.S. Buck and J.K. Seydel, (1996). Patentanmeldung P19654445.9. Verwendung von substituierten 4-aminodiphenylsulfonen.
37. ****M.D. Coleman**, J.K. Smith, N.S. Buck, A.D. Perris and J.K. Seydel. Studies on the anti-inflammatory effects of novel analogues of dapsone *in vitro* *J. Pharm. Pharmacol.* 49 53-57 (1997).
38. ***M.D. Tingle**, R. Mahmud, J.L. Maggs, **M.D. Coleman**, S.A. Ward and B.K. Park. The effect of 2,2'-substitution on the metabolism and toxicity of dapsone *in vitro* and *in vivo*. *Env. Tox. Pharmacol.* 5 145-153 (1998).
39. ****J.K. Seydel**, H. Burger, A.N. Saxena, **M.D. Coleman**, S. N. Smith, A.D. Perris. Quantitative structure-activity and structure-toxicity relationships of 4-

amino-diphenyl sulphone derivatives with anti-inflammatory activity. *J. Q.S.A.R.* 18 43-51 (1999)

40. ****M.D. Coleman**, S. Hadley, A.D. Perris, K. Jorga and J.K. Seydel. Studies on the toxicity and efficacy of some ester analogues of dapsone in vitro using rat and human studies. *Env. Tox. Pharm.* 12 7-13, (2002).
41. ****M.D. Coleman**, J.K. Smith, A.D. Perris, N.S. Buck and J.K. Seydel, (2003). International Patent (WO03097030A1) 4-(4'-aminophenylsulphonyl)-benzoic acid and esters thereof as anti-inflammatory agents.

(vii) Development of Amidrazone Anti-mycobacterial Agents

42. D.C. Billington, **M.D. Coleman**, J. Ibiabuo, P.A. Lambert, D.L. Rathbone and K.J. Timms. Synthesis and antimycobacterial activity of some heteroarylcarboxyamidrazone derivatives. *Drug Design Des* 15, 269-275, (1998)
43. **M.D. Coleman**, L. Abberley, D.L. Rathbone, P.A. Lambert and D.C. Billington. Preliminary toxicological testing of candidate amidrazone anti-mycobacterial compounds. *Env. Tox. Pharmacol.* 7 59-65 (1999)
44. **M.D. Coleman**, C. Endersby, M.C. Hovey, D.L. Rathbone, P.A. Lambert and D.C. Billington. Preliminary toxicological testing of candidate amidrazone anti-mycobacterial compounds II. *Env. Tox. Pharmacol.* 8 167-172, (2000).
45. **M.D. Coleman**, D.L. Rathbone, R. Chima, P.A. Lambert and D.C. Billington. Preliminary toxicological testing of candidate amidrazone anti-mycobacterial compounds III. *Env. Tox. Pharmacol.* 9 99-102, (2001).
46. **M.D. Coleman** K. Tims and D.L. Rathbone. The use of computational QSAR analysis in the toxicological evaluation of a series of 2-pyridyl-carboxamidrazone-candidate anti-tuberculosis. *Env. Tox. Pharmacol.* 14 69-75 (2003).

47. **M. D. Coleman**, N. Khan, G. Welton, P. A. Lambert, K. J. Tims D. L. Rathbone, Effects of Glutathione, N-acetyl-cysteine, α -lipoic acid and dihydrolipoic acid on the cytotoxicity of a 2-pyridylcarboxamidrazone antimycobacterial agent in human mononuclear leucocytes in vitro. *Env. Tox. Pharmacol* 17 143-148 (2004).

(viii) Studies on the Mechanisms of Idiosyncratic Toxicity

48. ****M.D. Coleman**, J. Simpson and D.P. Jacobus. Reduction of dapsone hydroxylamine to dapsone during methaemoglobin formation in human erythrocytes *in vitro* IV: the role of the erythrocyte in the development of

dapsone-dependent agranulocytosis. *Biochem. Pharmacol.* 48 1349-1354 (1994).

49. **M.D. Coleman.** Dapsone Toxicity: some current perspectives. *Gen. Pharmacol.* 26 1461-1467 (1995).
50. L.E. Rhodes, **M.D. Coleman** and M.S. Lewis-Jones. Dapsone-induced motor peripheral neuropathy in pemphigus foliaceus. *Clin. Exper. Derm.* 20 155-156 (1995).
51. **M.D. Coleman.** Dapsone mediated agranulocytosis: risks, possible mechanisms and prevention. *Toxicology* 162 53-60, (2001).
52. ***M.D. Coleman**, L.F. Khalaf and P.J. Nicholls. Further development of a model for the induction of drug-induced agranulocytosis: effects of aminoglutethimide. *Env. Tox. Pharmacol Pharmacol* 15 27-32 (2003).

(ix) *The Use of Dapsone Metabolites in Diabetic Erythrocytic Toxicology*

53. ****M.D. Coleman.** J. Simpson and D.P. Jacobus. Reduction of dapsone hydroxylamine to dapsone during methaemoglobin formation in human erythrocytes *in vitro*.III: effect of type I diabetes. *Biochem. Pharmacol.* 48 1341-1347 (1994).
54. ****M.D. Coleman**, M.S. Ogg, J.L. Holmes, J.M. Gardiner and D.P. Jacobus. Studies on the differential sensitivity between diabetic and non-diabetic human erythrocytes to monoacetyl dapsone hydroxylamine-mediated methaemoglobin formation *in vitro*. *Env. Tox. Pharmacol.* 1 97-102 (1996)
55. ****M.D.Coleman**, P.J. Hayes.and D.G. Jacobus. Methaemoglobin formation due to nitrite, disulfiram, 4-aminophenol and monoacetyldapsone hydroxylamine in diabetic and non-diabetic human erythrocytes *in vitro*. *Env. Tox. Pharmacol.* 5 61-67 (1998)
56. **M.D. Coleman** and C.H. Rustioni. Differences between diabetic and non-diabetic human intraerythrocytic glutathione pools. *J. Pharm. Pharmacol.* 51 23-27 (1999)
57. **M.D. Coleman**, and L. J. Holden, The Methaemoglobin Forming and GSH depleting effects of dapsone and monoacetyl dapsone hydroxylamines in human diabetic and non-diabetic erythrocytes *in vitro*. *Env. Tox. Pharmacol* 17 55-59 (2004)

(x) *The Use of Dapsone Metabolites in Antioxidant-Mediated Amelioration of Diabetic Erythrocytic Toxicity*

58. **M.D. Coleman**, 'Commentary' The use of *in vitro* methaemoglobin generation to study antioxidant status in the diabetic erythrocyte. *Biochem. Pharmacol.* 60 1409-1416 (2000)
59. **M.D Coleman** and Charlotte L. Walker. Effects of the antioxidants α -lipoic acid and α -tocopherol on xenobiotic-mediated methaemoglobin formation in human diabetic and non-diabetic erythrocytes *in vitro* *Env. Tox. Pharmacol.* 8 127-132, (2000).
60. **M.D Coleman** and Claire D. Baker. Effects of the antioxidants dihydrolipoic acid (DHLA) and probucol on xenobiotic-mediated methaemoglobin formation in human diabetic and non-diabetic erythrocytes *in vitro* *Env. Tox. Pharmacol.* 9 161-167, (2001).
61. **M.D Coleman**, H.L. Tolley and A.K. Desai. Monitoring antioxidant effects using methaemoglobin formation in diabetic erythrocytes. *Brit. J.. Diab. Vas. Dis.* 1 88-92, (2001).
62. **M.D. Coleman**. Editorial: 'Antioxidants: unlocking their potential' *Env. Tox. Pharm.* 10 139-140, (2001).
63. **M.D. Coleman**, C. Gaskin, S. Fernandez, L. Khanderia. The use of xenobiotic-mediated methaemoglobin formation to assess the effects of tri-iodothyronine (T3) on diabetic and non-diabetic human erythrocytic oxidant defence mechanisms *in vitro*. *Env. Tox. Pharm.* 13 15-19, (2003).
64. **M.D. Coleman**, S. Fernandez, L. Khanderia. A novel clinical monitoring method to evaluate a triple antioxidant combination (vitamins E, C and α -lipoic acid) in diabetic volunteers using *in vitro* methaemoglobin formation. *Env. Tox. Pharmacol.* 14 33-42 (2003).

I carried out the dapsone HPLC assays, assisted in the design of the study, evaluation of the results and the drafting of the paper.

Publication No. 19

Dr M. Parvathani, M.D. Coleman, P. Hussian, A.M. Breckenridge and B.K. Park. Dapsone and induced toxicity of sulphasalazine and its principle metabolites towards human leucocytes and erythrocytes. *Brit. J. Clin. Pharmacol.* 12 303-311 (1991)

I carried out mononuclear cell isolations and H₂O₂ assays, as well as assisting in the design and data interpretation.

Publication No. 20

M.D. Coleman

A statement of the candidate's contribution to publications arising from Collaborative projects.

Publication No. 9

L.A. Shipley, **M.D. Coleman**, T.G. Brewer, R.W. Ashmore and A.D. Theoharides. The disposition of the antileishmanial 9-aminoquinoline WR 6026 in the isolated perfused rat liver: thermospray liquid chromatography -mass spectrometry. Identification of metabolites. *Xenobiotica* 20 31-44 (1990).

In this study, I supplied the expertise in the technique of isolated rat liver perfusion, carrying out all the perfusion procedures and analysing some of the data on HPLC. I also contributed the drafting of the paper and supplied constructive criticism of the final draft.

Publication No. 17

R.J. Riley, P. Roberts, **M.D. Coleman**, N.R. Kitteringham and B.K. Park. Bioactivation of dapsone to a cytotoxic metabolite: in vitro use of a novel two compartment system which contains human tissues. *Brit. J. Clin. Pharm.* 30 417-426 (1990)

In this work, I suggested the use of cellulose membranes to prevent cell adherence to the two-compartment membranes and carried out some of the HPLC dapsone assays, as I had developed this assay several months previously. I also supplied constructive criticism of the final draft.

Publication No. 18

M.D. Tingle, **M.D. Coleman** and B.K. Park. Investigation into the role of metabolism in dapsone-induced methaemoglobinaemia using a two-compartment *in vitro* test system. *Brit. J. Clin. Pharmac.* 30 829-838 (1990).

I carried out the dapsone HPLC assays assisted in the design of the study, evaluation of the results and the drafting of the paper.

Publication No. 19

*M. Pirmohamed **M.D. Coleman**, F. Hussain, A.M. Breckenridge and B.K. Park. Direct and Indirect toxicity of sulphasalazine and its principle metabolites towards human leucocytes and erythrocytes. *Brit. J. Clin Pharmac.* 32 303-311 (1991)

I carried out monoleucocyte isolations and HPLC assays, as well as assisting in study design and data interpretation.

Publication No. 20

M.D. Tingle, **M.D. Coleman** and B.K. Park. Effects of pre-incubation with cimetidine on the N-hydroxylation of dapsone by human liver microsomes. *Brit. J. Clin Pharmac.* 32 120-124 (1991).

I performed the HPLC analysis of the samples from the two-compartment system and assisted in study design, execution and data evaluation. I also assisted in drafting the manuscript.

Publication No. 24

M. Pirmohamed, **M.D. Coleman**, D. Galvani, R.C. Bucknall, A.M. Breckenridge and B.K. Park. Lack of interaction between sulphasalazine and cimetidine in patients with rheumatoid arthritis. *Brit. J. Rheumatol.* 32 222-226 (1993)

I developed and validated a HPLC assay for sulphapyridine (one of the active components of sulphasalazine) and performed the assays. I also assisted in criticism and preparation of the manuscript.

Publication No. 38

*M.D. Tingle, R. Mahmud, J.L. Maggs, **M.D. Coleman**, S.A. Ward and B.K. Park. The effect of 2,2'-substitution on the metabolism and toxicity of dapsone *in vitro* and *in vivo*. *Env. Tox. Pharmacol.* 5 145-153 (1998).

I performed mononuclear leucocyte toxicity assays on novel compounds supplied by Prof. Park's group and supplied suggestions for study design and manuscript criticism.

Publication No. 39

J.K. Seydel, H. Burger, A.N. Saxena, **M.D. Coleman, S. N. Smith, A.D. Perris. Quantitative structure-activity and structure-toxicity relationships of 4-amino-diphenyl sulphone derivatives with anti-inflammatory activity. *J. Q.S.A.R.* 18 43-51 (1999)

I supplied data on sulphone metabolism in human erythrocytes that was used to derive predictive equations on the toxicity of these drugs. I also assisted in checking calculations and made constructive criticisms of the manuscript.

Publication No. 42

D.C. Billington, **M.D. Coleman**, I. Ibiabuo, P.A. Lambert, D.L. Rathbone and K.J. Timms. Synthesis and antimycobacterial activity of some heteroarylcarboxyamidrazone derivatives. *Drug Design Des* 15, 269-275, (1998)

I supplied information necessary for the design of the study and carried out toxicological evaluation of the finished molecules. I also assisted in the drafting of the paper and supplied constructive criticism.

L.E. Rhodes, **M.D. Coleman** and M.S. Lewis-Jones. Dapsone-induced motor peripheral neuropathy in pemphigus foliaceus. *Clin. Exper. Derm.* 20 155-156 (1995).

I supplied background information on the mechanisms of dapsone toxicity and provided some interpretation of the general toxicological clinical effects of the drug. I assisted in manuscript drafting and constructive criticism of the final draft.