

CONTENTS

How it all Began: A Brief History of the Pteridine Symposia	
A. Albert	1
The Gowland Hopkins Lecture:	
The Mechanisms of Action of Folate and Pterin Requiring Enzymes	
S.J. Benkovic, L.J. Slieker, S.C. Daubner, L.F. Courtney, T.A. Dix, S.O. Pember, L.M. Bloom, C.A. Fierke, R.J. Mayer, J.-T. Chen, K. Taira	13

SECTION A: CHEMISTRY OF PTERINS AND FOLATES

Side-Chain Chemistry of Pteridines	
W. Pfeleiderer, Y. Kang, R. Soyka, W. Hutzenlaub, M. Wiesenfeldt, W. Leskopf	31
A General Method for the Synthesis of 10-Substituted-10-Deaza Folate Analogues	
M.G. Nair, T.R. Toghiyani, B. Ramamurthy, R.L. Kisliuk, Y. Gaumont	45
Synthesis and Properties of Pyrimidodiazepines as Ring-Strained Probes of Pterin Utilizing Enzymes	
S.W. Bailey, D.C. Pike, J.E. Ayling	51
Summary: Pterin and Folate Chemistry	
E. Taylor	55
A Facile Method for Preparing 2,4-Diamino-5,8-Dideazapterins	
J.B. Hynes, A. Pathak, C.H. Panos, C.C. Okeke	57
Synthesis of 5,10-Dideaza-5,6,7,8-Tetrahydrofolic Acid (DDATHF) and Analogues	
E.C. Taylor, G.S.K. Wong, S.R. Fletcher, P.J. Harrington, G.P. Beardsley, C.J. Shih	61
Synthetic Routes to Methotrexate- and Folic Acid-Polyglutamates of High Chemical and Enantiomeric Purity	
M. Przybylski, R. Renkel, P. Fonrobert	65

In Vivo and In Vitro Evaluations of 5-[4-(Substituted Aryl)-1-Piperaziny]-6-Alkyl-2,4-Pyrimidinediamines as Antitumor Agents L.M. Werbel, J. Hung, J.A. Besserer, T.J. Boritzki, W.R. Leopold, D.W. Fry	69
The Electrochemical Oxidation of Tetrahydropterin Derivatives S. Kwee	73
A Practical Synthesis of (6R)- and (6S)-5,6,7,8-Tetrahydrobiopterins S. Matsuura, T. Sugimoto, S. Murata	77
Chemical Synthesis and Properties of Quinonoid (6R)-Dihydrobiopterin S. Matsuura, S. Murata, T. Sugimoto	81
Pyrazine-Ring Conformations of Tetrahydropterins and Quinonoid-Dihydropterins J.E. Gready	85
Hydrogenation of Silylated Pterins in Benzene Solution P.H. Boyle, M.F. Kelly	91
N(5)-Alkylation of Polyacetylated 5,6,7,8-Tetrahydroneopterins S. Antoulas, M. Viscontini	95
Oxidations Photosensitized by Pterins and Diaminopteridines M. Aubailly, R. Santus	99
Structure of the Riboflavin Synthase/Lumazine Synthase Complex. Arrangement and Chain Folding of Subunits in the Icosahedral Capsid R. Ladenstein, H.D. Bartunik, M. Schneider, R. Huber, K. Schott, A. Bacher	103
Use of C18 Silica Cartridges to Purify and Characterize Pterins K.B. Jacobson, J. Ferre	107
Synthesis and Structure-Activity Relationships of Tetrahydrobiopterin Cofactor Analogues E.C. Bigham, G.K. Smith, J.F. Reinhard, Jr.	111

Synthesis, Purification and Properties of a New Class of Pteridine Derivatives

J. Ferre, J.J. Yim, W. Pfeleiderer, K.B. Jacobson 115

Summary: Chemistry of Pterins

J.B. Hynes 121

SECTION B: BIOSYNTHESIS AND BIOCHEMISTRY OF PTERINS

Biosynthesis of Tetrahydrobiopterin and Related Compounds in Drosophila melanogaster

G.M. Brown, J.P. Primus, A.C. Switchenko 125

Tetrahydrobiopterin Biosynthesis in Man

H.-C. Curtius, S. Takikawa, A. Niederwieser 141

The Biosynthesis of Tetrahydrobiopterin in the Bovine Adrenal Medulla

G.K. Smith, D.S. Duch, C.A. Nichol 151

The Biosynthesis of Tetrahydrobiopterin in Rat Brain

S. Milstien, S. Kaufman 169

Summary: Biosynthesis of Tetrahydrobiopterin

G.M. Brown 183

The Metabolic Role of Tetrahydrobiopterin

S. Kaufman 185

Spectroscopic Studies on Tyrosine 3-Monooxygenase from Bovine Adrenal Medulla: A Blue Iron Protein

J. Haavik, K.K. Andersson, L. Petersson, T. Flatmark 201

Queuine-Lacking tNRAs in Relation to the Grade of Malignancy of Specific Tumors, Possible Role of Pteridines

W. Kersten, E. Zubrod, B. Emmerich, P. Maubach 205

Pteridine Synthesis During Interaction of Interleukin 2 with T Lymphocytes - Modulator Function in IL-2 Signal Transmission

I. Ziegler, J. Ellwart, U. Schwulera 209

SECTION C: BIOLOGY OF PTERINS

Dopamine Neurons in Culture: A Model System for Examination of Neuronal Biopterin Metabolism

G. Kapatos, L.A. Chiodo 215

Role of the Pituitary in the Regulation of Tetrahydrobiopterin Biosynthesis in the Non-Neuronal Tissues

D.S. Duch, S.W. Bowers, C.A. Nichol 219

Distribution of GTP Cyclohydrolase-I, Neopterin, and Biopterin in the Human Brain

T. Nagatsu, M. Sawada, M. Akino, M. Masada, T. Sugimoto, S. Matsuura 223

Enzymatic Synthesis of 6,7-Dimethyl-8-Ribityllumazine

A. Bacher, G. Neuberger, R. Volk 227

A Model for Hyperphenylalaninaemia Due to Tetrahydrobiopterin Deficiency

R.G.H. Cotton 231

The Effect of Biopterin and its Reduced Derivatives on Cultured Human Lymphocytes

S. Webber, D.L. Jaye 235

Developmental Aspects of Biopterin Metabolism in Human

J.L. Dhondt, J.M. Hayte, G. Forzy, M. Delcroix, J.P. Farriaux, C. Largilliere 239

Screening for Biopterin Defects Among Hyperphenylalaninemic Patients: Report of a Canadian Program After 3 Years

F. Mohyuddin, C.A. Rupar, M.C. Evers 243

Need for Therapy in utero of Fetuses with Tetrahydrobiopterin Deficiency

Y. Sawada, H. Shintaku, I. Suyama, G. Isshiki, Y. Hase, Y. Okano, H. Yamamoto, T. Tsuruhara, T. Oura 247

Pteridine Metabolism in Patients Suffering from Amyotrophic Lateral Sclerosis	
H.-J. Zeitler, B. Andondonskaja-Renz, G. Küther, A. Struppler	251
Urinary Neopterin in Cocaine-Abusing Individuals	
R.W. Guynn, K. Biehl, D.K. Merrill, K.J. Krajewski	257
Features of Neopterin Determination in Clinical Use	
E.R. Werner, D. Fuchs, A. Hausen, G. Reibnegger, H. Wachter, J.F.K. Huber .	263
Diurnal Variation in Urinary Pterin Excretion in Man	
A.E. Pheasant	267
The Relationship between Pteridines and Colour Dimorphism in the Scorpion Fly	
M. Tsusuë, M. Nakagoshi	271
Pteridine Biosynthesis and Manifestation of Pigment Phenotypes in Normal and Neoplastic Cells of Goldfish in Vitro	
M. Masada, J. Matsumoto, M. Akino	275
Light Depending Regulations of Pteridines in the Retina	
G. Cremer-Bartels, K. Krause	279
Differences in the Regulation of Tetrahydrobiopterin Biosynthesis in Neuronal Cells in Culture	
J.H. Woolf, C.A. Nichol, D.S. Duch	283
NADPH- and NADH-Specific Dihydropteridine Reductase in Teratocarcinoma Cells in Culture: Effect of Nerve Growth Factor Treatment of the Cells on the Enzyme Activities	
N. Nakanishi, K. Ozawa, S. Yamada, K. Akiba, N. Sato	287
Reversibility of α -Diketo Reductase Activity by Sepiapterin Reductase	
S. Katoh, T. Sueoka, S. Yamada	291
Non-Enzymatic Synthesis of "Drosopterins" from Dihydropterin and 2-Amino-4-Oxo-6-Acetyl-3H, 9H-7,8-Dihydropyrimido [4,5b] [1,4]Diazepine	
D.R. Paton, G.M. Brown	295

BH ₄ Biosynthesis: ¹ H-NMR Evidence for the Pyruvoyl-Tetrahydropterin-Synthase Catalyzed Formation of 6-Pyruvoyl-Tetrahydropterin from Dihydroneopterin Triphosphate	
S. Ghisla, S. Takikawa, P. Steinerstauch, T. Hasler, H.-C. Curtius	299
Catabolism of Tetrahydrobiopterin in Man	
A. Niederwieser, A. Matasović, T. Kuster, W. Staudenmann, W. Pfleiderer, S. Scheibenreiter	305
Pteridine Biosynthesis in Human Amniocytes and Chorionic Villi	
J. Ferré, E.W. Naylor	309
The Role of the Kidney in Biopterin Metabolism	
J.-L. Dhondt, J.M. Hayte, C. Noël, M. Dracon, G. Lelievre, A. Tacquet	315
Tetrahydrobiopterin-Producing Enzyme Activities in Liver of Animals and Man	
T. Hasler, A. Niederwieser	319
Effect of 3-Hydroxykynurenine on GTP Cyclohydrolase Activity and on the Pteridine Pattern in <u>Drosophila melanogaster</u>	
F.J. Silva, J.L. Mènesua	323
Tetrahydrobiopterin Metabolism in Normal Brain, Senile Dementia of the Alzheimer Type and Down's Syndrome	
J.M. Anderson, C.G.B. Hamon, R.A. Armstrong, J.A. Blair	327
Summary: Biology of Pteridines	
M.A. Parniak	331
Biosynthesis of Pteridines and Metabolism of Aromatic Amino Acids in <u>Drosophila melanogaster</u>	
Y. Bel, J. Ferré	335
The Inhibition of tRNA Transglycosylases by Pteridines as a Mean for Metabolic Control of Gene Expression	
H. Kersten, H.J. Aschhoff, P. Böhm, E. Zubrod	339
Modulation of Dopamine Synthesis by Nerve Terminal Autoreceptors: A Role for Tetrahydrobiopterin?	
M.P. Galloway, R.A. Levine	347

A Monoclonal Antibody Reacting with All Three Aromatic Amino Acid Hydroxylases	
R.G.H. Cotton, I.G. Jennings, R. Kuskinsky, C.W. Chow, E. Haan, W.J. McAdam, C. Bell, F. Morgan, H. Nakata, A.C. Cuellar	351
Alterations in Cofactor-Dependent Activity of Phenylalanine Hydroxylase as a Function of pH	
M.A. Parniak, S. Kaufman	355
Interaction of a Monoclonal Antibody with Rat Liver Phenylalanine Hydroxylase	
M.A. Parniak, I.G. Jennings, R.G.H. Cotton	359
The Effect of Dietary Iron on the Activity of Rat Liver Phenylalanine Hydroxylase	
M.D. Davis, S. Kaufman	363
Strict Requirement of Fe^{2+} for Tryptophan 5-Monooxygenase from Mouse Mastocytoma, P-815	
H. Hasegawa, A. Ichiyama	369
Tetrahydrobiopterin and the Regulation of Catecholamine Synthesis in Bovine Adrenal Medullary Chromaffin Cells	
R.A. Levine, K.L. Kelner	373
Cofactor Activity of Tetrahydropterins for Tyrosine Hydroxylation in PC12 Pheochromocytoma Cells	
D.S. Duch, J.F. Reinhard, M.P. Edelstein, J.Y. Chao, C.A. Nichol	377
Summary: Pterin-Dependent Biological Reactions	
R.A. Levine	381
Tetrahydrobiopterin Deficiency. Analysis from an International Survey	
J.L. Dhondt	385
Cofactor Specificity of 6,6-Disubstituted Tetrahydropterins, and their Potential in the Treatment of Neurological Disorders	
J.E. Ayling, S.W. Bailey, S.B. Dillard	391
Normal Concentrations of Tetrahydrobiopterin in the Cerebrospinal Fluid of Patients with Dihydropteridine Reductase Deficiency	
K. Hyland, I. Smith, D.W. Howells	395

Prenatal Diagnosis of Tetrahydrobiopterin Deficiency

- A. Niederwieser, H. Shintaku, T. Hasler, H.-C. Curtius, H. Lehmann,
D. Leupold, O. Guardamagna, A. Ponzone, H. Schmidt 399

Defective Biopterin Biosynthesis in a Chinese Infant

- C.R. Scriver, C.L. Clow, P. Kaplan, G.V. Watters, C. Laberge,
F. Mohyuddin, S. Milstien 403

Correlation of Dihydropterine Reductase Cross Reacting Material with
Non-Responsiveness to a Tetrahydrobiopterin Load

- R.G.H. Cotton, I.G. Jennings, G. Bracco, A. Ponzone, O. Guardamagna 407

Neopterin and Dihydroneopterins in Serum of Controls and Patients with
Various Diseases. Circadian Rhythm of Neopterin. Influence of Cortisol?

- H. Rokos, H. Frisius, R. Kunze 411

Neopterin Content and GTP-Cyclohydrolase Activity of Blood Cells of
Controls and Patients Positive for LAV/HTLV-III Antibodies

- K. Rokos, R. Kunze, W. Lange, M.A. Koch 415

Neopterin in Bone Marrow Transplant Monitoring: An Improvement in its
Use for GVHD Diagnosis

- P. Mura, A. Piriou, D. Reiss, F. Guilhot, E. Benz-Lemoine, J. Tanzer 419

Importance of Neopterin Determination in Individuals at Risk for AIDS

- D. Fuchs, A. Hausen, G. Reibnegger, E.R. Werner, H. Wachter, H.G. Blecha,
H. Roessler, B. Unterweger, H. Hinterhuber, P. Hengster, T. Schulz,
M.P. Dierich, D. Renner 427

Biochemical Aspects of Pteridines During Interaction Between Activated
T-Lymphocytes and Monocytes/Macrophages in Patients

- B. Andondonskaja-Renz, H.J. Zeitler 431

Summary: Pterins and Human Illness

- D. Fuchs, H. Wachter 443

SECTION D: FOLATES AND PTERINS IN MAMMALIAN TISSUES

Folates in Tissues and Cells. Support for a "Two-Tier" Hypothesis of Regulation of One-Carbon Metabolism C.L. Krumdieck, I. Eto	447
Elevation in the Rate of Cellular Folate Catabolism in Mid-Pregnancy in the Rat J.M. Scott, E. Wilson, D.G. Weir	467
The Red Blood Cell as a Storage Site for Folic Acid S.E. Steinberg	471
Methotrexate and Biopterin Levels in Blood Following Low Dose Administration for Psoriasis R.J. Leeming, R.M. Conlon, A. Pollock, J. Kumari	475
Summary: Folates in Tissue and Cells D.G. Priest	479
Folate Rescue of N_2O -Induced Inhibition in Murine Lymphocytes J.G. Hilton, B.A. Cooper, W. Lapp	481
Folate Absorption and Metabolism in Alcohol Fed Rats J.M. Noronha, V. Kesavan	485
Chronic and Acute Effects of Ethanol on Renal Clearance and Urinary Excretion of Folate in Rats K.E. McMartin, B.H. Eisenga, T.D. Collins, L. Bairnsfather	489
Effect of Chronic Anticonvulsant Treatment on Folate Concentrations in the Rat G.F. Carl	495
Alcohol Induced Methyl Group Wastage as a Possible Cause of Fatty Liver A.M. Molloy, J.M. Scott, D.G. Weir	505
Folate Catabolism in the Syrian Golden Hamster D. Al-Haddad, A.E. Pheasant, J.A. Blair, C.G.B. Hamon	509

The Level of Folate Catabolism in Normal Human Populations, Suggesting that the Current Level of RDA for Folate is Excessive	
J.M. McPartlin, D.G. Weir, G. Courtney, H. McNulty, J.M. Scott	513
Microdetermination of Folate Monoglutamates in Serum by High-Performance Liquid Chromatography with Electrochemical Detection	
K. Iwai, K. Inoue, M. Kohashi	517
Folate Status in Psychiatric Patients: Relationship with CSF Neurotransmitter Metabolites	
T. Bottiglieri, M. Laundry, M.W.P. Carney, T.K.N. Chary, B.K. Toone, E.H. Reynolds	523
Folate, Thiamine and Vitamin B ₁₂ Levels in Outpatient Epileptics	
M.I. Botez	527
Effect of Aspirin Ingestion on Folate Bioavailability Evaluated by Rat Liver Bioassay	
K. Hoppner, B. Lampi	531
Brush Border Pteroylpolyglutamate Hydrolase in Pig Jejunum	
C.J. Chandler, T.T.Y. Wang, C.H. Halsted	539
Use of CI-920 in the Characterization of the Methotrexate Transport Defect in a Resistant Human Leukemic CCRF-CEM Cell Line	
G. Jansen, J.H. Schornagel, G. Rijksen, J. de Gier	543
The Effect of Oxidative Stress on Methotrexate (MTX) Transport by Rat Hepatocytes	
M.S. Rhee, A. Pupons, Z. Nimec, J. Galivan	547
Folate Transport by Pig Intestinal Brush Border Vesicles	
A.M. Reisenauer	551
Depressed Folate Transfer Across the Mammary Gland Secondary to Iron Deficiency in the Rat	
D.L. O'Connor, M.F. Picciano, A.R. Sherman, S.L. Burgert	555
Studies on the Mechanism of Folate Transport in Isolated Hepatocytes	
D.W. Horne	559

Analysis of the pH and Na ⁺ Dependence of Intestinal Folate Transport I.H. Rosenberg, J. Zimmermann, J. Selhub	563
Intestinal Transport of Folate. Characterization of the Transport Events at the Brush Border and the Basolateral Membranes H.M. Said, W.B. Strum	567
The Synthesis of Some Novel Probes of Folate Transport and Binding R.J. Kempton, L.A. Sams, K.M. Harpring, A.G. Smith, F. Kohrs, E. Price, J.H. Freisheim	571
Photoaffinity Probes of Dihydrofolate Reductase and of the Membrane Carrier for Folate Analogues E.M. Price, P.L. Smith, J.H. Freisheim	575
The Use of Biosynthetic Radioactive Folylpolyglutamates to Study Intestinal Digestion and Absorption of Folate B. Darcy-Vrillon, J. Selhub, I.H. Rosenberg	579
Selective Inhibition of Bacterial Carboxypeptidase G and Pancreatic Conjugase by 2-Mercaptomethylglutaric Acid T.I. Kalman, V.K. Nayak, A.R.V. Reddy	583
Summary: Folate Absorption and Transport I.H. Rosenberg	587
Studies on Glycine-N-Methyltransferase C. Wagner, R.J. Cook	593
Folate Binding Protein from <i>Pediococcus Cerevisiae</i> Strains Possessing Active Transport Systems for Folates F. Mandelbaum-Shavit	597
Immobilized Folate Binding Protein from Cow's Milk Used for Quantitation of Folate S.I. Hansen, E. Nexø, J. Holm	603
Characterization of Rabbit Antibodies Against the Folate Binding Protein from Cow's Milk M. Hoier-Madsen, S.I. Hansen, J. Holm	607

SECTION E: ENZYMOLOGY OF FOLATES

1. Thymidylate Synthase

Genetic and Chemical Studies on Thymidylate Synthase

F. Maley, F.K. Chu, D.K. West, G.F. Maley 613

Active Site Probes of Thymidylate Synthetase

A.D. Broom, I.Y. Yang 631

Resonance-Raman Spectroscopic Identification of the Transient Intermediates Formed in the Native Ternary Complex with Thymidylate Synthase

A.L. Fitzhugh, S. Kaufman, S. Fodor, T.G. Spiro 639

The Reversal of the Cytotoxicity of Folate-Based Thymidylate Synthase Inhibitors in Cultures L1210 Cells

A.L. Jackman, A.H. Calvert, R.G. Moran 645

Thymidylate Synthase Activity in the Tapeworm, Hymenolepis diminuta

J. Cieřla, Z. Zieliński, W. Rode, B. Machnicka 651

Identification of Poly G Bound to Thymidylate Synthase

J. Thorndike, R.L. Kisliuk 655

Methotrexate Derivates of Deoxyuridylate Showing Inhibitory Properties for Thymidylate Synthetase from Lactobacillus casei

S. Webber, R. Nazarbaghi, J.M. Whiteley 659

Comparison of Thymidylate Synthase Isolated from Mouse Normal and Tumour Tissues

Z. Zieliński, J. Cieřla, B. Kedzierska, W. Rode 663

Thymidylate Synthase Interaction with Analogues of dUMP and 5-Fluorid-2'-Deoxyuridine-5'-Phosphate with Modified Phosphate Groups

W. Rode, B. Kedzierska, T. Kulikowski, D. Shugar 667

An In Vitro System for Studies on Inhibition of the Thymidylate Cycle

H. Rebandel, Y. Gaumont, R.L. Kisliuk 671

N ¹⁰ -Propargyl-5,8-Dideazafolic Acid Polyglutamates as Inhibitors of Thymidylate Synthase and their Intracellular Formation E. Sikora, A.L. Jackman, D.R. Newell, K.R. Harrap, A.H. Calvert, T.R. Jones, K. Pawelczak, B. Rzeszutarska	675
Sequential CMF in Metastatic Breast Cancer: An Attempt to Increase Effectiveness by Means of Biochemical Modulation P. Pronzato, L. Repetto, D. Amoroso, A. Ardizzoni, G. Bertelli, P.F. Conte, V. Fusco, M. Gulisano, R. Rosso	681
Model Studies of Thymidylate Synthase Reaction P.F.C. Van der Meij, E. Hilhorst, T.B.R.A. Chen, E.R. de Waard, U.K. Pandit	687
Synergistic Interaction Between Folinic Acid and the Fluoropyrimidines K. Keyomarsi, R.G. Moran	691
2. Methionine Biosynthesis	
Methionine Biosynthesis R.G. Matthews, D.A. Jencks, V. Frasca, K.D. Matthews	697
Impaired Formylation and Uptake of Tetrahydrofolate by Rat Small Gut Following Cobalamin Inactivation J. Perry, R. Deacon, M. Lumb, I. Chanarin	709
Heterogeneity in Functional Methionine Synthase Deficiency D. Watkins, D.S. Rosenblatt	713
Summary: Methionine Biosynthesis E.L.R. Stokstad	717
3. Folyl Polyglutamate Synthetase	
Folylpoly- γ -glutamate Synthetase B. Shane	719
Cytotoxic Effects and Inhibition of Folylpolyglutamate Synthetase by Folate Analogs Containing 2, Omega-Diaminoalkanoic Acids J.J. McGuire, J.R. Piper	729

An Upstream Gene Regulates the Expression of Folylpolylglutamate Synthetase-Dihydrofolate Synthetase in <u>Escherichia coli</u>	
A. Bogнар, C. Osborne, B. Shane	733
Occurence and Synthesis of Pteroyl- γ -glutamyl- γ -glutamyl-poly- α -glutamates in <u>Escherichia coli</u>	
R. Ferone, M. Hanlon, S. Singer, D. Hunt	737
Summary: Folylpolylglutamate Synthesis	
E. Cossins	741
The Metabolism of Pteroylpolylglutamates	
R.L. Kisliuk	743
Dihydropteroyl Hexaglutamate and T4 Phage Baseplate Assembly	
B. Szewczyk, K. Szewczyk, L.M. Kozloff	757
Effects of Polyglutamylation on Folate Cofactor and Antifolate Activity in the Thymidylate Synthase Cycle of Permeabilized Murine Leukemia L 1210 Cells	
T.I. Kalman	763
Summary: Pteroylpolylglutamate metabolism	
R.E. Mackenzie	767
4. Dihydrofolate Reductase	
Recent Advances in the Study of Dihydrofolate Reductase	
R.L. Blakley, J.R. Appleman	769
The 2.8 Å Structure of a Type II Plasmid Encoded Dihydrofolate Reductase	
D.A. Matthews, S.L. Smith, D.P. Bacanari, J.J. Burchall, S.J. Oatley, J. Kraut	789
Mutations in the Human Dihydrofolate Reductase	
B.I. Schweitzer, S. Srimatkandada, S.K. Dube, J.R. Bertino	793
Theoretical Studies of the Structure, Conformational and Electronic Properties of Anticancer Folate Inhibitors	
W.J. Welsh, V. Cody	799

Binding of Inhibitors with Spin-Labeled Side Chains to Dihydrofolate Reductase (DHFR) from Several Species

R.L. Blakley, R.L. Kulinski, J.R. Appleman, J.R. Piper 803

Affinity Labeling of Dihydrofolate Reductase with an Iodoacetyl Lysine Analogue of Methotrexate

T.J. Delcamp, A. Rosowsky, P.L. Smith, J.E. Wright, J.H. Freisheim 807

Escherichia coli Dihydrofolate Reductase Isolated as a Folate Complex

S.S. Joyner, D.P. Baccanari 811

Dihydrofolate Reductase from Soybean Seedlings

S. Ratnam, T.J. Delcamp, J.H. Freisheim 815

Use of Antibodies as Structural Probes of Dihydrofolate Reductases and Enzyme-Ligand Complexes

M. Ratnam, T.J. Delcamp, J.H. Freisheim 819

Cooperativity in Inhibitor Binding to Neisseria gonorrhoeae Dihydrofolate Reductase

R.L. Tansik, D.P. Baccanari 823

pH Studies of the Reaction Catalyzed by Dihydrofolate Reductase from E. coli

J.F. Morrison, S.R. Stone 827

Effects of pH on Reactions Catalyzed by Dihydrofolate Reductase from Chicken Liver

J.F. Morrison, S.R. Stone 831

Unconjugated Dihydropterin Substrates for Bovine Liver Dihydrofolate Reductase

G.K. Smith, S.D. Banks, E.C. Bigham, C.A. Nichol 835

Enzymatic Characterization of Recombinant Human Dihydrofolate Reductase Produced in E. coli

D. Stüber, H. Bujard, E. Hochuli, H.P. Kocher, I. Kompis, K. Talmadge, E.K. Weibel, F. Winkler, R.L. Then 839

Levels of Folates and Methotrexate Polyglutamate Formation in Chinese Hamster Ovary Cells Lacking Dihydrofolate Reductase

P. Joannon, H. Goldberg, V.M. Whitehead, D.S. Rosenblatt, M.J. Vuchich, D. Beaulieu 843

Methotrexate in Adjuvant Arthritis	
J. Galivan, M.C. Rehder, S. Kerwar	847
Computer Graphic Modeling in Drug Design: Conformational Analysis and Active-Site Modeling of Lipophilic Diaminopyrimidines	
V. Cody	851
Effect of Antifolates 10-Methyl- and 10-Ethyl-10-Deaza-Aminopterin on a Human Breast Cancer Cell Line	
F. Mandelbaum-Shavit	855
Biochemical and Cytotoxic Effects of the Erythro- and Threo-Isomers of Gamma-Fluoro-Methotrexate	
J.J. McGuire, J. Galivan, J.K. Coward	861
5. Other Folate Enzymes	
C ₁ -Tetrahydrofolate-Synthase, a Multifunctional Enzyme Involved in Purine Metabolism, and its Related Monofunctional Enzymes	
K.W. Shannon, T.R. Whitehead, C. Staben, J.C. Rabinowitz	865
The Interaction of Tetrahydropteroylpolyglutamates with 10-Formyltetra- Hydrofolate Synthetase	
V. Schirch, B. Strong, G. Joshi, R. Lura, T. Dennis	887
Summary: Folates in C ₁ Metabolism	
V. Schirch	891
Chemical Aspects of Dimethylglycine Dehydrogenase and Sarcosine Dehydrogenase	
R.J.Cook, P.Gettins, C. Wagner	893
Folate Normalizes Elevated PRPP Levels of Folate-Deficient HL-60 Cells	
J. Ghitis, C. Schreiber, S. Waxman	897
Stereochemistry of Hydride Transfer to NADP ⁺ by Methylene Tetrahydro- folate Dehydrogenase from Pig Liver	
J. Green, R.G. Matthews, R.E. MacKenzie	901

The Effects of Thyroxine Status on Hepatic Levels of 10-Formyl-tetrahydrofolic Acid: NADP Oxidoreductase	
J.M. Keating, H. Choe, E.L.R. Stokstad	905
Interaction of Homocysteine with Methionine Synthetase	
G.P. Lewis	909
Minor Form of Human Hepatic Betaine: Homocysteine S-Methyltransferase	
W.E. Skiba, M.S. Wells, J.H. Mangum, W.M. Awad	913
Studies of Cobalamin-Dependent Methionine Synthase from <u>Escherichia coli</u> B	
V. Frasca, W.R. Dunham, R.H. Sands, B.S. Riazzi, R.G. Matthews	917
Inhibition of Methylenetetrahydrofolate Reductase by Adenosyl Methionine	
D.A. Jencks, R.G. Matthews	921
Regulation of Folate Homeostasis	
C. Osborne, K. Lowe, B. Shane, D.J. Cichowicz, D. Sussman, G. Milman	925
An Endogenous Inhibitor of Neurospora Folylpolylglutamate Synthetase	
E.A. Cossins, P.Y. Chan	929
Folylpolylglutamate Hydrolase from Beef Liver	
P.J. Vickers, R. Di Cecco, Z.B. Pristupa, K.G. Scrimgeour	933
Use of Mammalian Cell Transformation to Isolate Genomic Sequences Encoding Human Folylpolylglutamate Synthetase (FPGS) and Dihydrofolate Reductase (DHFR)	
S.M. Taylor, N. Davidson, R.G. Moran	937

SECTION F: METHOTREXATE AND OTHER ANTI-FOLATES

Antifolates: Expanding Horizons in 1986	
B.A. Chabner, C.J. Allegra, J. Baram	945

Deaza Derivatives of Tetrahydrofolic Acid. A New Class of Folate Antimetabolite	
G.P. Beardsley, E.C. Taylor, G.B. Grindey, R.G. Moran	953
Structure Activity Relationships of Novel Triazine Antifolates	
C. Dias-Selassie, Y.C. Zheng, H. Zhu, C. Hansch, T. Khwaja, J.H. Freisheim, T.J. Delcamp	959
The Effect of 7-Hydroxymethotrexate on the Antitumor Activity and Host Toxicity of Methotrexate <i>In Vivo</i>	
P.A. Newton, R.A. Finch, T.L. Avery	963
Summary: The Biology of Antifolates	
J. Gallivan	967
Crystal Structure of Methotrexate and its Conformational Comparison with Related Structures	
P.A. Sutton, V. Cody	969
Effect of Methotrexate on Reduced Folates and Thymidylate Synthesis During Growth of L1210 Cells	
D.G. Priest, V. Kesavan, M.T. Doig	973
Dihydrofolate Reductase from Human Osteosarcoma Cells Resistant to Methotrexate	
J.K. Sato, T.J. DeFrank	977
Evidence for Direct Inhibition of Metabolic Pathways as a Mechanism of Action of Methotrexate	
C.J. Allegra, J. Baram, B.A. Chabner	981
Inhibition of Dihydrofolate Reductase and Thymidylate Synthase by Methotrexate Polyglutamate Analogues Lacking "Internal" α -Carboxyl Groups	
A. Rosowsky, R.A. Forsch, M.M. Wick, J.H. Freisheim, P.V. Danenberg, T.I. Kalman	985
The Antifolate Activity of Poly- γ -Glutamyl Derivatives of Methotrexate, 10-Deazaaminopterin and 10-Ethyl-10-Deazaaminopterin	
R.L. Kisliuk, Y. Gaumont, P. Kumar, M.G. Nair, B.T. Kaufman	989

Polyglutamation of the Thymidylate Synthase Inhibitor, N ¹⁰ -Propargyl-5,8-Dideazafolic Acid (CB 3717), in Organs of Ehrlich Ascites Carcinoma-Bearing Mice	
M. Manteuffel-Cymborowska, B. Kamińska, B. Grzelakowska-Sztabert	993
5,8-Dideazafolates as Substrates for Polypoly- γ -Glutamate Synthetase from Pig Liver	
J.B. Hynes, D.J. Cichowicz, B. Shane	997
5-Substituted-5-Deaza Analogues of Classical Antifolates	
J.R. Piper, G.S. McCaleb, J.A. Montgomery, F.M. Sirotnak	1001
Azido-Substituted Antifolate Drugs: Synthesis, Structure, and Activity	
P.K. Bryant, K.P. Wong, J. Colby, C.H. Schwalbe, M.F.G. Stevens, R.J. Griffin, E.A. Bliss	1005
Summary: Novel Antifolates	
R. Jackson	1009
AUTHOR INDEX	1011
SUBJECT INDEX	1017
LIST OF PARTICIPANTS	1033