Progress in Tryptophan and Serotonin Research

Proceedings
Fourth Meeting of the
International Study Group for
Tryptophan Research ISTRY
Martinsried, Federal Republic of Germany
April 19 – 22, 1983

Editors
H. G. Schlossberger · W. Kochen
B. Linzen · H. Steinhart

Walter de Gruyter · Berlin · New York 1984
CONTENTS

OPENING SESSION

E. Biekert
Adolf Butenandt's Work on the Metabolism of Tryptophan 3

Th. Wieland
Tryptophan, the Heart of the Toxic Peptides from Amanita Mushrooms 13

B. Witkop
Forty Years of Trypto-Fun 21

O. Hayaishi, R. Yoshida, O. Takikawa, H. Yasui
Indoleamine Dioxygenase - a Possible Biological Function 33

QUALITATIVE AND QUANTITATIVE ANALYSIS OF TRYPTOPHAN AND ITS METABOLITES

P.T. Kissinger
Liquid Chromatography/Electrochemistry Determination of Biogenic Amines: Improved Performance Using Low Dead Volume Multiple Electrode Transducers 45

M.H. Joseph
GLC and HPLC Analysis of Tryptophan, Kynurenine and Related Metabolites 55

A. Bettero, C. Costa, G. Allegri
Monitoring of Tryptophan Levels in Biological Fluids by HPLC: An Improved Method 63

C. Costa, A. Bettero, G. Allegri
Rapid Determination of Tryptophan and its Metabolites along the Kynurenine Pathway by HPLC 67

J. Schrijver, F. van Schaik, J. van der Greef, K.D. Bos, W.H.P. Schreurs
HPLC-Analysis of Xanthurenic Acid and its 8-Methyl-Ether 71
J.-C. Bigot, M.-P. Moineau, J.-F. Ménez, L.-G. Bardou
Free and Total Tryptophan Microdetermination by an
Automated Fluorometric Method 77

E. Martinez, A. Adell, C. Suñol, F. Artigas,
J.M. Tusell, E. Gelpí
Comparison of HPLC and GC-MS Methods for the
Determination of Tryptophan and its Indole
Metabolites in Biological Samples 83

S.N. Young, G.M. Anderson
Pineal Indoles: Their Determination by High
Performance Liquid Chromatography and the
Influence of Diurnal Variation and Tryptophan
Administration on their Level in the Rat 91

G. Talsky, S. Tichy
Higher-Order Derivative Spectrophotometry for the
Quantitative Determination of Tryptophan, Tyrosine
and Phenylalanine in Two- and Three-Component
Mixtures, Peptides and Proteins 95

H. Steinhart, P. Stützle
The Application of a Spectrofluorometer-Optical-
Multichannel Analyzer System to the Determination
of Tryptophan 103

K. Takai, S. Inoue
Picomole Determination of Tryptophan by Derivati-
zation to 9-Hydroxymethyl-β-Carboline 107

H.K. Nielsen, R.F. Hurrell
Determination of Tryptophan in Food after Alkaline
Hydrolysis: An Evaluation 111

E. Votisky
Colorimetric Determination of Tryptophan in Corn-Cob
Mix (CCM) 115

M. Friedman, C.E. Levin, A.T. Noma, W.C. Montague, Jr.,
J.C. Zahnley
Comparison of Tryptophan Assays for Food Proteins 119

WORKSHOP: ANALYSIS OF TRYPTOPHAN

M. Friedman
Discussion at the Workshop on "Analysis of Tryptophan" 127
<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tryptophan Transport to the Brain: Newer Findings and Older Ones Reconsidered</td>
<td>145</td>
</tr>
<tr>
<td>Tryptophan Availability and Serotonin Synthesis in Rat Brain: Effects of Experimental Diabetes</td>
<td>161</td>
</tr>
<tr>
<td>Anatomy and Function of Central Serotoninergic Neurons</td>
<td>173</td>
</tr>
<tr>
<td>Serotonin Receptor Binding Sites: Localization and Role in the Brain and Peripheral Tissues</td>
<td>189</td>
</tr>
<tr>
<td>Involvement of 5-HT2 (S2)-Receptor Sites in the Serotonin-Induced Activation of Cat Platelets</td>
<td>197</td>
</tr>
<tr>
<td>The Regulation of 5-Hydroxytryptamine Release from Superfused Synaptosomes by Tryptophan</td>
<td>201</td>
</tr>
<tr>
<td>Selective Increases in High Affinity Tryptophan Transport in Synaptosomes from Different Brain Areas Incubated in Sodium-Free Media</td>
<td>205</td>
</tr>
<tr>
<td>Formation and Function of Tetrahydro-B-Carbolines with Special Reference to their Action on 3H-Tryptamine Binding Sites</td>
<td>209</td>
</tr>
<tr>
<td>Regulations of Serotonergic Neurons Innervating the Basal Ganglia: In vivo Release Studies</td>
<td>217</td>
</tr>
<tr>
<td>Blood Platelets as Models for Neurons: Similarities of the 5-Hydroxytryptamine Systems</td>
<td>231</td>
</tr>
<tr>
<td>In vivo Metabolism of 14C-5-HT, 14C-5,6-DHT and 14C-5,7-DHT by MAO/COMT/Aldehyde Dehydrogenase in Rat Brain</td>
<td>241</td>
</tr>
<tr>
<td>Tryptophan Metabolism in the Pineal Gland</td>
<td>251</td>
</tr>
</tbody>
</table>
J. Arendt
Some Physiological Responses and Effects of the Pineal Indoleamine Melatonin 259

G.M. Brown, T.G. Burns, S. Psarakis, L.J. Grota
Pharmacologic Regulation of Serum N-Acetylserotonin 267

J.-P. Garnier, Ch. Escande, B. Bousquet, G. Tran, C. Dreux
N-Acetyltryptophan: Biochemical and Pharmacological Studies 271

N.N. Osborne, S. Patel, D.W. Beaton
Serotonin, a Major Metabolite of Tryptophan in the Rabbit Retina 275

K. Goda, T. Mori, T. Ueda, Y. Kotake
Effect of 5-Hydroxyanthranilic Acid on Arachidonate Metabolites Function in Platelet Aggregation System 285

WORKSHOP: CLINICAL AND BEHAVIOURAL EFFECTS OF TRYPTOPHAN

E. Hartmann
Introduction to Workshop 291

E. Hartmann, D. Greenwald
Tryptophan and Human Sleep: An Analysis of 43 Studies 297

N. Nedopil, K. Einhäupl, E. Rüther, R. Steinberg
L-Tryptophan in Chronic Insomnia 305

P. Leathwood, P. Pollet:
Tryptophan (500 mg) Decreases Subjectively Perceived Sleep Latency and Increases Sleep Depth in Man 311

H. R. Lieberman, S. Corkin, R.J. Wurtman
Further Evidence of the Hypnotic Properties of Tryptophan 315

S.N. Young, G. Chouinard, L. Annable, C. Morand, F.R. Ervin
The Therapeutic Action of Tryptophan in Depression, Mania, and Aggression 321

S. Seltzer, R.L. Pollack, D. Dewart, and E. Jackson
The Effects of Dietary Tryptophan on Chronic Maxillofacial Pain Tolerance 325
PATHOLOGY, CLINICAL ASPECTS

E. Kienzl, P. Riederer, K. Jellinger, E. Roth, P. Ferenci
Modulation of Serotonin Receptors by L-Valine in Hepatic Encephalopathy 333

L.V. Hankes, C.R. Jansen, E.P. DeBruin, M. Schmaeler
Effect of a B-Vitamin on Tryptophan Metabolism in South African Bantu with Pellagra 339

M. Hattori, Yazo Kotake, Yahito Kotake, H. Otsuka, Y. Shibata
Studies on the Urinary Excretion of Xanthurenic Acid in Diabetics 347

S. Ikeda, Y. Kotake
Urinary Excretion of Xanthurenic Acid and Zinc in Diabetes 355

A. Knapp, U. Grimm
Studies of the Clinical Importance and Molecular Defect of Hereditary Vitamin B₆ Dependent Xanthurenic Aciduria 359

V. Rudzite, G. Sileniece, J. Jirgensons
Tryptophan - Nicotinic Acid Pathway in Cardiovascular Diseases 365

M.H. Joseph, G.A. Kennett
The Dependence of Stress Induced Increases in Functional 5HT Activity on Increased Tryptophan Availability: Evidence that in vivo Electrochemistry Monitors 5-Hydroxyindole Release 383

M.H. Joseph, J.A. Johnson, G.A. Kennett
Increased Availability of Tryptophan to the Brain in Stress is not Mediated via Changes in Competing Amino Acids 387

Free and Bound Plasma Tryptophan Levels in Psychiatric Disorders 391

C.M. Banki, M. Arató, Z. Papp, M. Kurcz
Cerebrospinal Fluid 5HIAA and Tryptophan in Depression and Suicide 397
M. Raba, P. Riederer, W. Danielczyk, D. Seemann
The Influence of L5-Hydroxytryptophan (L5-HTP) on Clinical and Biochemical Parameters in Depressive Patients 401

J. Weil-Fugazza, F. Godefroy, M. Bineau-Thurotte, J.-M. Besson
Plasma Tryptophan Levels and 5-Hydroxytryptamine Synthesis in the Brain and the Spinal Cord in "Arthritic" Rats 405

F. Godefroy, J. Weil-Fugazza, J.-M. Besson, S.H. Butler
Effects of Antirheumatic Drugs and Tricyclic Antidepressants on Total and Free Serum Tryptophan Levels in Arthritic Rats 409

C. Costa, F. Ceccherelli, A. Bettero, G. Marin, L. Mancusi, G. Allegrì
Tryptophan, Serotonin and 5-Hydroxyindoleacetic Acid Levels in Human CSF in Relation to Pain 413

S. Salmon, P. Del Re, D. Caleri, M. Fanciullacci, F. Sicuteri
Dynamics of Plasma Tryptophan Following Antimigraine Drugs 417

M. Evans, A.A.-B. Badawy, A. Dacey
Comparison of Morphine and Meptazinol Effects on Rat Tryptophan Disposition and Metabolism 425

G. Huether, K. Schott, V. Neuhoff
Decreased Concentrations of Tryptophan and Serotonin in the Brain of Developing Hyperphenylalaninemiac Rats - A Contribution to the Understanding of the Metabolic Effects in Phenylketonuria 429

Cofactor Dependency of Serotonin and Catecholamine Biosynthesis in Patients with Atypical Phenylketonuria and Endogenous Depression 437

D.J. Byrd, M. Arslan, H. Meuter, G. Bodammer, D. Hunneman
Tryptophan, 5-Hydroxytryptophan and Dopa Metabolism in the Rat with Experimental Phenylketonuria 443
S. Zigman
The Role of Tryptophan Oxidation in Ocular Tissue Damage 449

G. Allegri, M.R. Angi, C. Costa, A. Bettero
Tryptophan and Kynurenine in Senile Cataract 469

D. Milovanović, B. Stanković, Lj. Milovanović, Z. Koritšanac, D. Trpković
Urinary 5-Hydroxyindoleacetic Acid and Serum Phenobarbital of Children Suffering from Epilepsy 473

J. Pratt, P. Jenner, E.H. Reynolds, S.D. Shorvon
Anticonvulsant Drugs Produce Different Effects on Plasma Tryptophan Concentrations in Epileptic Patients 479

J.R. Carlson, M.R. Nocerini, R.G. Breeze
The Role of Metabolism in 3-Methylindole-Induced Acute Lung Injury 483

P. Baumann, L. Koeb, L. Rivier
Beta-Carboline Levels in Blood of Smokers and Non-Smokers 491

H. Wolf
The Relationship between Tryptophan, Tryptophan Metabolites and Bladder Cancer 503

R. Yoshida, O. Takikawa, H. Yasui, O. Hayaishi, K. Yasuhira
Role of Indoleamine 2,3-Dioxygenase in the Defence Mechanism against Tumor Growth 513

O. Takikawa, R. Yoshida, H. Yasui, O. Hayaishi
The Relationship between Plasma Kynurenine and Indoleamine 2,3-Dioxygenase Activity in the Extrahepatic Tissues 517

L-Tryptophan Metabolism along the Kynurenine Pathway in Human Malignant Melanoma 521

NUTRITIONAL ASPECTS

H.K. Nielsen, R.F. Hurrell
Content and Stability of Tryptophan in Foods 527
H. Takahashi
Increased Aromatic Amine (Kynurenine) in Dried Fish Meat under Sunlight

H. Steinhart
Tryptophan Requirement of Farm Animals

P.-A. Finot, E. Magnenat
Pattern of Radioactivity from Endogenous 3H-Tryptophan Excreted in the Urine of Fasted or Rats Fed Diets Containing Different Levels of Casein

L. Arimanana, D. Ashley, D. Furniss, P. Leathwood
Protein/Carbohydrate Selection in Rats Following Administration of Tryptophan, Glucose or a Mixture of Amino Acids

A.P.N. Majumdar
Influence of Tryptophan on Gastric Mucosal Protein Synthesis

H.J. Cooke
Tryptophan and Intestinal Secretion

S. Kalyanasundaram, P.S.V. Ramanamurthy
Tryptophan Metabolism in Undernourished Developing Rat Brain

K.-H. Menke, F. Gruber
Effect of Tryptophan on Protein Utilization and Energy Intake of Pigs

D.V. Ashley, P.D. Leathwood,
A High Carbohydrate, Protein-Free Meal, either at Breakfast or in the Evening Does not Alter Plasma Tryptophan to Large Neutral Amino Acid Ratios in Healthy Men

D.V. Ashley, M. Fleury, S. Hardwick, P.D. Leathwood, D. Moennoz
Effects of Large Neutral Amino Acids on Tryptophan Transport into the Brain during Development

D.V. Ashley, P.A. Finot, R. Liagdon
Contribution of Exogenous N^15-Tryptophan to Plasma and Red Blood Cell Tryptophan and Kynurenine in Healthy Humans
D.V. Ashley, P.D. Leathwood, D. Moennoz
Carbohydrate Meal Increases Brain
5-Hydroxytryptamine Synthesis in the
Adult Rat only after Prolonged Fasting 591

D. Ghosh, I.U. Affiah, J. Guilford, L.L. Henderson
Exogenous Tryptophan: A Study of its Effects
on the Levels of Aromatic Amine(s) in Cerebral
and Hepatic Tissues in Mice 595

T. Suzuki, S. Yuyama, A. Sasaki, M. Yamada, R. Kumagai
Influence of Excess Leucine Intake on the Conversion
of Tryptophan to NAD in Rats Fed Low Protein Diet 599

D.A. Bender, B.I. Magboul
The Pellagragenic Action of a Dietary Excess of
Leucine: Effects of a High-Leucine Diet on
Tryptophan Metabolism 603

S. Yuyama, A. Sasaki, T. Suzuki
Effect of Cadmium on some Key Enzymes of
Tryptophan - NAD Pathway in Rats in vivo 607

G. Huether
The Influence of Increased Availability of
Tryptophan on the Formation of Tryptamine and
Serotonin during Early Ontogenesis 613

TRYPTOPHAN METABOLISM IN MAMMALS

Ch.I. Pogson, R.A. Munoz-Clares, J.S. Cook, S.A. Smith
Tryptophan Metabolism and its Control in Mammalian
Liver 625

H. Otsuka, S. Nomura, F. Takeuchi, R. Yokomine,
H. Fujimoto, M. Ugata, Y. Shibata
Tryptophan Metabolism by the Isolated, Perfused
Liver and Kidney of Rat (Quantification of the
Metabolism by the Compartmental Analysis) 633

D.A. Bender
Effects of Oestrogens on the Metabolism of Tryptophan:
Implications for the Interpretation of the Tryptophan
Load Test for Vitamin B<sub>6</sub> Nutritional Status 637

A.A.-B. Badawy
The Functions and Regulation of Tryptophan Pyrrolase 641
R. Kido
Kynurenine Aminotransferase Activity in Human and other Mammalian Tissues 651

J. Inada, M. Kimura, E. Okuno, R. Kido
Intracellular Localization and Characterization of 3-Hydroxykynureninase in Human Liver 657

V. Politi, G. De Luca, G. Di Stazio, G. Palamara, M. Materazzi
Time-Course of 5-HTP Metabolism in Rabbits: Relevance of Transaminating Pathway 661

J. Stanley, A. Nicholas, I. Thompson, Ch. Pogson
Tryptophan Aminotransferase Activity in Rat Liver 665

E. Balogh-Hergovich, G. Speier
The Oxygenation of Tryptophan and Indoles with Superoxide Ion and Dioxygen in the Presence of Copper and Ruthenium Catalysts 669

T. Uemura, K. Kadota
Serotonin- and Melatonin-Dependent Light Emission Induced by Xanthine Oxidase 673

F. Geeraerts, L. Schimpfessel, R. Crokaert
The in vivo Effect of Sodium Fluoride on the Key Enzymes of Tryptophan Metabolism 677

Y. Ohta, R. Shinohara, J. Naito, I. Ishiguro
Roles of Active Oxygen and Superoxide Dismutase in Anthranilamide Hydroxylation and its Derived Phenoxazinone-Like Pigment Formation by Rat Liver Microsomal Monooxygenase System 681

H. Kröger, R. Grätz, H. Grahn
Protective Effect of Tryptophan upon the Influence of N-Methylformamide on the Development, the NAD Synthesis, and the Activity of the Adenosine Diphosphate Ribosyl Transferase of Rat Embryos 685

H. Kröger, R. Grätz
Induction of Tyrosine Aminotransferase by Tryptophan in Rat Liver 689

TRYPTOPHAN METABOLISM IN INSECTS

D.T. Sullivan
Tryptophan Metabolism in Drosophila 697
H. Ogawa, Y. Nagamura, I. Ishiguro  
Roles of Active Oxygen and Catalase in the Formation of Phenoxazinone Pigments Catalysed by Manganese Ion  

A.E. Bouthier  
Ommochrome-Potassium Urate Complex as Pigment of Red Faeces of Locusta migratoria (Insecta, Orthoptera, Acrididae)  

S. Yagi  
Changes in Fluorescence and Size of the Cytoplasmic Granules in the Malpighian Tubules of Drosophila melanogaster Linked with Tryptophan Metabolism  

L.M. Riddiford, K. Hiruma  
Hormonal Control of Pigmentation in Manduca sexta  

D. Bückmann  
Tryptophan Metabolism and Morphological Color Change in Insects  

H. Rembold, Y. Umebachi  
The Structure of Papiliochrome II, the Yellow Wing Pigment of the Papilionid Butterflies  

Y. Umebachi  
Some Chemical Properties of Papiliochrome R  

TRYPTOPHAN METABOLISM IN PLANTS AND MICROORGANISMS  

K.-H. van Péé, F. Lingens  
Metabolism of Tryptophan in Pseudomonas aureofaciens  

W. van der Graaff, J.A. Duine, J. Frank, Jzn and J.A. Jongejan  
Does Tryptophan Side Chain Oxidase from Pseudomonas ATCC 29574 Contain a Quinoprotein?  

K. Takai, S. Inoue, F. Zavala, R. Müller, T. Hamasaki, Y. Sasai  
Tryptophan Side Chain Oxidase (TSO) - Structure and Reaction Mechanism  

R. Bode, D. Birnbaum  
Characterization of three Tryptophan Aminotransferases from Candida maltosa
H.-H. Schott, K. Zinke, D. Langenbach-Schmidt
Anthranilate Hydroxylase and the Short-Cut-Pathway for the Biosynthesis of Nicotinamide Nucleotides in Aspergillus niger

J. Stöckigt
Biosynthesis of Tryptophan Derived Alkaloids in Higher Plants: Enzymatic Formation of the Sarpagine-Ajmaline Group

D. Gröger, A. Baumert
Acridone Alkaloid Biosynthesis in Tissue Cultures of Ruta graveolens

A. Marston, E. Hecker
Isolation and Biological Activities of Diterpene Anthraniloyl and 3-Hydroxyanthraniloyl Peptide Esters from Euphorbia milii

New Biological Significance of Indole-Containing Compounds as Initiators or Tumor Promoters in Chemical Carcinogenesis

W. Große
Biosynthesis of Serotonin and Auxin in Seeds of Juglans regia

A. Miyake
Blepharismone: a Conjugation-Inducing Tryptophan Derivative in the Ciliate Blepharisma

L. Jaenicke
Biological Activity of Blepharismone Derivatives - An Approach Towards Biogenesis of the Hormone

TRYPTOPHAN IN PROTEINS AND PEPTIDES

A. Fontana
Advances in the Chemical Modification of Tryptophan in Peptides and Proteins

A. Fontana, C. Grandi, D. Dalzoppo, M. Zambonin
Peptide Bond Cleavage at Tryptophan with Cyanogen Bromide - Mechanism of the Reaction

L. Moroder, E. Wünsch
Tryptophan, a Pitfall for the Peptide Chemist
J.-J. Toulmé
Photochemical and Radiochemical Reactions of Tryptophan: Modification of a Single-Strand Binding Protein from Bacteriophage T4 853

A. Gieren, V. Lamm, M. Sturm
X-Ray Structure Analyses of Tryptophan Derivatives as Models for Stereochemical Aspects of the Toxic Peptides from Amanita Mushrooms 861

AUTHOR INDEX 865

SUBJECT INDEX 869