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Professor Hideaki Yamada and his Scientific Career

Professor Hideaki Yamada

Hideaki Yamada was born on 11 March 1929 in Toyama, Japan, in a family of a brewer of a Japanese Sake. He attended the Faculty of Agriculture, Kyoto University where, in 1953, he received a B.Sci. degree. Hideaki then took up graduate studies in applied microbiology at the same university under supervision of Professor Hideo Katagiri, a distinguished microbial biochemist. The degree of Doctor of Agriculture was conferred to him in 1960 through the thesis entitled 'Enzymatic studies on group transfer'. In 1959, he got married to Kyoko Kanaoka. He and his wife raised two children: one son and one daughter.

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Hideaki Yamada's first academic appointment was Research Associate at the Department of Agricultural Chemistry of Kyoto University in 1953. He was promoted to Lecturer in 1963 at the Research Institute for Food Science, Kyoto University, to Associate Professor in 1964, and finally to full Professor in 1971. He then moved to his original Laboratory of Applied Microbiology at the Faculty of Agriculture as a Professor in 1977, upon the sudden death of the former Professor Koichi Ogata.

After his retirement from Kyoto University in 1992 as a Professor Emeritus of Kyoto University, he served as a Professor at the Department of Biotechnology of Kansai University. He then led the newly established Biotechnology Research Center of Toyama Prefectural University from 1994. He spent two years in 1960 at the University of Hawaii, USA to study the enzymology of bovine amine oxidase, through collaboration with Professor Kerry T. Yasunobu. His scientific career is summarized in Table 1.

Table 1
Scientific career of Professor Hideaki Yamada

Education:
Graduated the Department of Agricultural Chemistry, Faculty of Agriculture, Kyoto University (March, 1953)
Conferred the degree of Doctor of Agriculture (Kyoto University), (September, 1960)

Career:
Research Associate of the Department of Agricultural Chemistry, Kyoto University (April, 1953)
Lecturer of the Research Institute for Food Science, Kyoto University (July, 1963)
Associate Professor of the Research Institute for Food Science, Kyoto University (April, 1964)
Professor of the Research Institute for Food Science, Kyoto University (December, 1971)
Professor of the Department of Agricultural Chemistry, Faculty of Agriculture, Kyoto University (January, 1977)
Professor Emeritus of Kyoto University (April, 1992)
Professor of the Department of Biotechnology, Faculty of Engineering, Kansai University (April, 1992)
Professor and Director of the Biotechnology Research Center, Faculty of Engineering, Toyama Prefectural University (April, 1994)

Awards:
the Vitamin Society of Japan (1978)
the Chemical Society of Japan (Technical Award) (1982)
the Japan Society for Bioscience, Biotechnology, and Agrochemistry (formerly the Agricultural Chemical Society of Japan) (1986)
Fellow of the International Institute of Biotechnology, London (1989 ~)
the Society for Fermentation and Bioengineering, Japan (1991)
the Purple Ribbon Medal (the Japanese Emperor) (1991)
Distinguished Biochemical Engineer Award (Asia Pacific Biochemical Engineering Conference) (1994)
Fellow of the American Academy of Microbiology (1997 ~)
the Japan Academy Prize (1998)

Academic Activities:
Titular Member of the Biotechnology Commission, IUPAC (1984–1988)
Member of the Science Council of Japan (1987–1990)
Scientific Adviser of the Ministry of Education, Science and Culture, Japan (1988–1990)
Vice Chairman of the Steering Committee, Japan Bioindustry Association (1989–1997)
President of the Japan Society of Bioscience, Biotechnology, and Agrochemistry (1993–1995)
Honorary member of the Japan Society for Bioscience, Biotechnology, and Agrochemistry (1995 ~)
Vice President of Japan Bioindustry Association (1997 ~)

Research Fields:
Applied Microbiology, Applied Enzymology, Biotransformation, Biocatalysis

Publications:
Original Papers, 443
Review Articles, 226

During his academic career, he studied a wide area from stand points of basic to applied aspects, including fermentation physiology, applied microbiology, and applied enzymology. His study focused on the microbial physiology concerning on the biosynthesis and biodegradation by microorganisms and characterized a number of enzymatic reactions, and he applied them in the enzymatic syntheses of optically active amino acids, amines, nucleosides, vitamins, coenzymes, pyrogallol, amides, and bioactive fats, etc. He established new enzymatic methods for analysis of several biochemicals such as fatty acids, amino acids and polyamines.

(i) Synthesis of Amino Acids by Multifunctional Pyridoxal Phosphate-dependent Enzymes

He and coworkers found that a pyridoxal phosphate-dependent enzyme, β-tyrosinase, is a multifunctional enzyme catalyzing not only the degradation of L-tyrosine (α,β-elimination reaction), but also the β-replacement reaction and the reverse of α,β-elimination reaction to form L-amino acid. A reaction mechanism was presented to show that the amino-acrylic acid intermediate was a common intermediate of the enzymatic reaction with crystalline enzyme. Similar multi-function was confirmed also with tryptophanase and cysteine desulfhydrase. Next, intact microbial cells containing much amount of the enzyme were prepared and used as a catalyst of the reaction to industrially synthesize L-dihydroxyphenylalanine (L-DOPA). Furthermore, many pyridoxal enzymes of microbial origin were used for the synthesis of various natural and unnatural amino acids in high amounts and yields.

(ii) New Process of D-Amino Acid Synthesis Utilizing Hydantoinase

Some microorganisms were found to produce hydantoinases which catalyze D-stereospecific hydrolysis of chemically synthesized DL-5-substituted hydantoin forming *N*-carbamoyl D-amino acid. The enzyme was purified, crystallized and its properties were clarified. The enzyme showed a wide substrate specificity, acting on 5-substituted hydantoin to produce *N*-carbamoyl amino acid. When the enzyme reaction was carried out in an alkaline condition, the remaining L-5-substituted hydantoin is nonenzymatically racemized, finally all of the substrates are converted to *N*-carbamoyl D-amino acid. The resulting *N*-carbamoyl D-amino acid was easily decarbamylated in the presence of $NaNO_2$, thus a new process of enzymatic synthesis of D-amino acid using the microbial hydantoinase was established. Based on this process, *p*-hydroxy-D-phenylglycine is industrially synthesized in the largest scale worldwide, together with D-phenylglycine and D-valine.

(iii) Enzymatic Syntheses of Vitamins and Coenzymes

A novel lactonase catalyzing the stereospecific hydrolysis of D-pantoyl lactone, an intermediate to synthesize D-pantothenic acid in a racemic mixture of pantoyl lactone, was discovered. A new enzymatic method of D-pantothenic acid synthesis was proposed using the enzyme. Furthermore, basis of the industrial production of coenzyme A, *S*-adenosylmethionine, *S*-adenosylhomocysteine were established.

(iv) Production of Amides by Nitrile Hydratase

In his laboratory, a new enzyme 'nitrile hydratase' was discovered during studies on microbial degradation of nitrile compounds, including polyacrylonitrile oligomers, dinitriles, and low molecular weight nitriles. The enzyme was characterized from several soil microorganisms to be completely different from the previously known nitrilase. Next, the microbial production of acrylamide using the enzyme was attempted with microbial producers *Pseudomonas chlororaphis* B23 and *Rhodococcus rhodocurous* J1, and conditions to prepare cells with high activity were optimized. It attracted much attention by stoichiometrically accumulating more than 600 g/l of acrylamide in a short time. This method is known to be the first microbial method of the industrial production of commodity chemicals in the world.

R. rhodochrous J1 nitrile hydratase exhibits very broad substrate specificity. Using *R. rhodochrous* J1 cells and 3-cyanopyridine as the substrate, the highest yield achieved was almost 1.5 kg of nicotinamide/l of reaction mixture without formation of nicotinic acid. Due to the high yields of this process, the use of this enzymatic hydration is promising for the industrial production of various aliphatic, aromatic and heterocyclic amides.

(v) Development of New Clinical Methods of Microdetermination of Metabolites

During the course of the studies on the microbial physiology, new enzymes, sarcosine oxidase, long chain and medium chain fatty acyl-CoA synthetases, acyl-CoA oxidase, *S*-adeno-

Table 2
Enzymatic production of useful compounds

Product	Enzyme (source)	Yield g/liter (mol %)
Amino acids		
p-Hydroxy-D-phenylglydne	Dihydropyrimidinase (*Bacillus* sp.)	5 (74)
D-Phenylglycine	Dihydropyrimidinase (*Bacillus* sp.)	6 (91)
L-Tyrosine	β-Tyrosinase (*Erwinia herbicola*)	61
L-DOPA	β-Tyrosinase (*E. herbicola*)	53
L-Tryptophan	Tryptophanase (*Proteus rettgeri*)	10 (95)
L-Cysteine	Cysteine desulfhydrase (*Enterobacter cloacae*)	50 (86)
L-Cysteine	Cysteine synthase (*Bacillus sphaericus*)	70 (82)
D-Cysteine	β-Chloro-D-alanine chloride-lyase (*Pseudomonas putida*)	22 (88)
L-Cystathionine	Cystathionine γ-synthase (*B. sphaericus*)	42 (92)
L-Serine	Serine hydroxymethyltransferase (*Hyphomicrobium* sp.)	52
Ethyl (*R*)-4-chloro-3-hydroxybutanoate	Aldehyde reductase (*Sporobolomyces salmonicolor*)	88 (95)
Amides and acids		
Acrylamide	Nitrile hydratase (*Pseudomonas chlororaphis*)	400 (100)
Acrylamide	Nitrile hydratase (*Rhodococcus rhodochrous*)	650 (100)
Methacrylamide	Nitrile hydratase (*Pseudomonas chlororaphis*)	200
Crotonamide	Nitrile hydratase (*P. chlororaphis*)	200
Nicotinamide	Nitrile hydratase (*R. rhodochrous*)	1465 (100)
Acrylic acid	Nitrilase (*R. rhodochrous*)	380 (100)
Nicotinic acid	Nitrilase (*R. rhodochrous*)	172 (100)
6-Hydroxynicotinic acid	Hydroxylase (*Comamonas acidovorans*)	120 (96)
6-Hydroxypicolinic acid	Hydroxylase (*Alcaligenes faecalis*)	116 (97)
D-Malic acid	Maleate hydratase (*Arthrobacter* sp.)	87 (72)
Pyrogallol	Gallic acid decarboxylase (*Citrobacter* sp.)	23 (100)
Theobromine	Oxygenase (*Pseudomonas putida*)	20 (92)
D-Pantoyl lactone	Carbonyl reductase (*Caudvia parapsilosis*)	100 (83)
D-Pantoic acid	Aldonolactonase (*Fusarium oxysporum*)	700 (95)
Coenzymes		
5′-IMP	Nucleoside phosphotransferase (*Pseudomonas trifolli*)	5.6 (80)
Coenzyme A	Multi-step enzyme system (*Brevibacterium ammoniagenes*)	115 (95)
Adenosylmethionine	AdoMet synthetase (*Saccharomyces sake*)	12 (45)
Adenosylhomocysteine	AdoHcy hydrolase (*Alcaligenes faecalis*)	74 (97)
FAD	FAD pyrophosphorylase (*Arthrobacter grobiformis*)	18 (28)
Pyridoxal 5′-phosphate	Pyridoxamine 5′-phosphate oxidase (*Pseudomonas fluorescens*)	0.15 (98)
NADH	Formate dehydrogenase (*Arthrobacter* sp.)	30 (90)
NADPH	Glucose dehydrogenase (*Gluconobacter suboxydans*)	3 (100)

sylhomosysteine hydrolase, putrescine oxidase, spermine and spermidine oxidases were crystallized or highly purified and characterized, followed by the development of new clinical analytical methods using these enzymes. Especially, long chain fatty acyl-CoA synthetase and acyl-CoA oxidase are actually used in a kit for the microdetermination of free fatty acids in serum.

This special issue of *Journal of Molecular Catalysis B: Enzymatic* is dedicated to Professor Hideaki Yamada on the occasion of his 70th birthday. It consists of 26 papers on 'Enzymatic synthesis of useful compounds', contributed by collaborators and friends to show their appreciation for him. The theme title is closely related to his lifework and the phrase 'Enzyme catalysis'. Table 2 summarizes the results of the enzymatic synthesis of various chemicals studied in his laboratory.

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