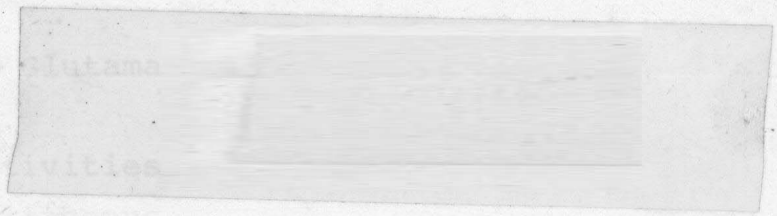

FERMENTATION DEVELOPMENTS IN JAPAN, 1976-77

Report No. 781

Information Services Group
Compo Center Bldg.
Westport, Conn. 06880

FERMENTATION DEVELOPMENTS IN JAPAN, 1976-77

CONTENTS

Report No. 781

CONTENTS (Contd)

CONTENTS (Contd)

CONTENTS (Contd)

CONTENTS (Contd)

CONTENTS (Contd)

LIST OF TABLES

INTRODUCTION

Amino acids are the most developed area in the Japanese fermentation industry. Monosodium glutamate (MSG) was discovered in Japan around the beginning of the twentieth century. Later inosinic acid and guanylic acid were produced on a commercial scale and used as food flavor enhancers and for food additives.

L-lysine and DL-methionine have become important as additives for feedstuffs and food. These are prepared by the fermentation process.

Nucleic acid was initially developed for use as a flavor enhancer. However, it is now of worldwide interest as a medicinal material. Carcinostats and various pharmaceuticals based on nucleic acids are coming on the market.

Developments to the end of the first quarter of 1977 are reported in this survey. Other developments through the first quarter of 1978 are also reported but more briefly.

This report has been translated from the Japanese language into English. Because of this, there are some inevitable misspellings of chemical names in the Patent Lists. We have corrected the worst of them, but have not altered most terminology which is comprehensible.

AMINO ACID INDUSTRY

BACKGROUND

The amino acid industry in Japan started in Japan with the production of L-sodium glutamate (MSG). MSG is used as a flavor enhancer. Since the initial production of MSG, many other amino acids have come on the market and many new applications for amino acids were developed.

The flavor enhancer industry has changed and is still changing. Not only MSG but ribonucleic acids and other amino acids have successively come on the market. Now "delicious flavor enhancer" is a new name for a sophisticated food additive. The Agriculture and Forestry Ministry published in September, 1975, a Japan Agricultural Standard regulating the quality of this new kind of flavor enhancer.

The method for production of amino acids was initially by hydrolysis of natural protein sources followed by extraction of the amino acid from the decomposed product. But now synthetic processes (as for producing methionine) and fermentation or microorganism processes are used.

There are many amino acids produced at present and they are used in many applications. The major amino acids listed are in Table I . The market prices of the leading amino acids are shown (December, 1976).

DL-methionine (feedstuff grade)	620 yen/kg
L-lysine HCl	2,000 yen/kg
Glycine	730 yen/kg
DL-alanine	1,000 yen/kg
MSG	700 yen/kg

TABLE I

MAJOR AMINO ACIDS, PRODUCERS, PROCESS SYSTEM

Amino Acid	Process System	Producers
L-alanine	Fermentation and Synthesis	Ajinomoto, Kyowa Hakko Kogyo, Tanabe Pharmaceutical, Musashino Chemical
D-alanine	Fermentation and Synthesis	Ajinomoto, Tanabe Pharmaceutical, Nippon Kayaku, Musashino Chemical
L-arginine	Extraction, Fermentation and Synthesis	Ajinomoto, Kyowa Hakko Kogyo
L-arginine HCl salt		Tanabe Pharmaceutical, Ajinomoto
L-asparagine	Synthesis	Ajinomoto, Tanabe Pharmaceutical
L-sodium asparaginate	Fermentation	Ajinomoto, Kyowa Hakko Kogyo, Dainippon Pharmaceutical, Tanabe Pharmaceutical
L-cystine HCl salt	Extraction	Ajinomoto, Tanabe Pharmaceutical, Nippon Rikagaku
L-cystine	Extraction	Ajinomoto, Tanabe Pharmaceutical, Nippon Rikagaku
L-glutamic acid	Fermentation	Ajinomoto, Kyowa Hakko Kogyo
L-glutamine	Fermentation	Ajinomoto, Kyowa Hakko Kogyo
Glycine	Synthesis	Ajinomoto, Yukigosei Yakuhin, Kyowa Hakko Kogyo, Tanabe Pharmaceutical, Nippon Kayaku
L-histidine HCl salt	Fermentation	Ajinomoto, Tanabe Pharmaceutical
L-oxyproline	Extraction	Ajinomoto

TABLE I (Contd)

Amino Acid	Process System	Producers
L-isoleucine	Fermentation	Ajinomoto, Kyowa Hakko Kogyo, Tanabe Pharmaceutical
L-leucine	Extraction	Ajinomoto, Kyowa Hakko Kogyo, Tanabe Pharmaceutical
L-lysine HCl salt	Fermentation	Ajinomoto, Kyowa Hakko Kogyo, Tanabe Pharmaceutical
L-methionine	Separation	Ajinomoto, Tanabe Pharmaceutical, Nippon Kayaku
DL-methionine	Synthesis	Nippon Soda, Sumitomo Chemical, Nippon Kayaku, Tanabe Pharmaceutical, Ajinomoto
L-phenyl alanine	Synthesis and Separation	Ajinomoto, Tanabe Pharmaceutical
DL-phenyl alanine	Synthesis	Tanabe Pharmaceutical
D-phenyl alanine		Tanabe Pharmaceutical
L-proline	Fermentation	Ajinomoto, Tanabe Pharmaceutical
L-serine	Separation	Tanabe Pharmaceutical
DL-serine	Synthesis	Tanabe Pharmaceutical
L-oxyproline		Tanabe Pharmaceutical
L-threonine	Fermentation and Synthesis	Ajinomoto, Kyowa Hakko Kogyo, Tanabe Pharmaceutical, Nippon Kayaku
DL-threonine	Synthesis	Tanabe Pharmaceutical, Ajinomoto
D-threonine		Tanabe Pharmaceutical
L-tryptophan	Separation	Ajinomoto, Tanabe Pharmaceutical
DL-tryptophan	Synthesis	Tanabe Pharmaceutical

TABLE I (Contd)

Amino Acid	Process System	Producers
D-tryptophan		Tanabe Pharmaceutical
L-tyrosine	Extraction	Ajinomoto, Kyowa Hakko Kogyo, Tanabe Pharmaceutical
L-valine	Fermentation	Ajinomoto, Tanabe Pharmaceutical, Musashino Chemical
DL-valine	Synthesis	Tanabe Pharmaceutical, Musashino Chemical
D-valine		Tanabe Pharmaceutical
Glutathione	Extraction and Synthesis	Ajinomoto, Tanabe Pharmaceutical
D-phenyl glycine		Tanabe Pharmaceutical, Nippon Kayaku
DL-phenyl glycine		Nippon Kayaku
Various AOC, BOC, 2-amino acid		Ajinomoto, Tanabe Pharmaceutical
DL-amino lactic acid		Musashino Chemical

The estimated 1976 production of the leading amino acids in Japan is shown in Table II . The value of production (including derivatives) was in the order of $300 million during that period.

TABLE II

JAPANESE PRODUCTION OF LEADING AMINO ACIDS (1976)

Amino Acid	Process System	Production tonnes/yr.
L-alanine	E.C.	10-50
DL-alanine	C	150-200
L-arginine	F	200-300
L-aspartic acid	E	500-1,000
L-asparagine	Ex	10-50
L-citrulline	F	10-50
L-cysteine	Ex	100-200
L-cystine	Ex	100-200
L-DOPA	F.C.	80-200
Glycine	C	80,000 (as MSG)
L-glutamic acid	F	100,000
L-histidine	F	100-200
L-homoserine	F	10-50
L-hydroxyproline	Ex	10-50
L-glutamine	F	200-300
L-isoleucine	F. Ex	10-50
L-leucine	F. Ex	50-100
L-lysine	F	15,000
DL-methionine	C	20,000
L-methionine	F.C.	100-200
L-ornithine	F	10-50
L-phenylalanine	F.C.	50-100
L-proline	F	10-50
L-serine	I.C.	10-50
L-threonine	F	50-100
L-tryptophan	E.C.	10-50
DL-tryptophan	C	50-100
L-valine	F	50-100

E - Enzymatic synthesis
C - Chemical synthesis
F - Fermentative production
Ex - Extraction
I - Microbial production from intermediate

Source: Japan Chemical Week and others.

As indicated, L-glutamic acid and its salt is the major amino acid followed by DL-methionine, L-lysine and glycine.

MONOSODIUM GLUTAMATE

The MSG industry had a big shock in 1975 due to the general depression and production decreased by 30% compared to that of 1974. The decrease was due mainly in the drop in domestic consumption, but a decrease also was shown in exports. The domestic consumption was 60/40 in a ratio of business/consumer use. The amount used by consumers directly gradually increased and the ratio became 50/50 in 1975.

TABLE III

EXPORTS OF MSG BY DESTINATION

	1974	1975
	Metric Tons	
U.S.A.	2,448	2,205
Hong Kong	1,287	1,395
Italy	1,120	1,200
Argentina	1,439	798
Venezuela	953	700
Mexico	650	687
Canada	1,911	614
Brazil	1,570	544
Australia	405	373
United Kingdom	166	225
Switzerland	1,190	215
Others	2,281	1,972
Total	15,420	10,928

TABLE IV

PRODUCTION, CONSUMPTION AND EXPORT OF MSG

Year	Production	Domestic	Exports
		Metric Tons	
1971	100,313	80,920	19,397
1972	93,394	74,668	18,726
1973	84,707	69,631	15,076
1974	90,300	78,000	15,420
1975	76,300	63,000	10,928
1976	80,000	64,000	16,000

Exports of MSG are shown in Table III . There was a big drop in recent years to Central America, South America and Europe. This is due to the production of MSG all over the world by Japanese know-how, as shown in Table IV. Consequently, future export of MSG from Japan is very difficult to accomplish. Moreover, Ajinomoto Inter Americana Co. in Brazil is constructing a large 12,000 tons/yr. plant in Sao Paulo. This plant was completed in March, 1977. MSG produced here will be exported to all over the South and North American countries.