GLUTAMIC ACID AS AN INDUSTRIAL CHEMICAL

B. V. RAMACHANDRAN

National Chemical Laboratory, Poona

GLUTAMIC ACID has been known to students of protein chemistry for nearly a century, but it emerged out of the laboratory and became a chemical of commercial importance only in recent times. At present the production of glutamic acid amounts to millions of pounds annually. In 1948, the production in the U.S.A. of sodium glutamate was 6·2 million pounds, while the installed plant capacity was estimated at twice this figure.[1] Before World War II, Japan, which was the chief centre of production, manufactured about 9 million pounds; smaller quantities appear to have been produced in China also. Most of the production goes into the manufacture of processed foods, where it is utilised for its remarkable property of stabilising natural flavours.

Glutamic acid, $HOOC.CH_2.CH_2CH(NH_2).COOH$, was discovered[2] by the German chemist, Ritthausen, in 1866, who isolated it from an acid hydrolysate of gliadin, the alcohol-soluble protein of wheat. The flavour and taste enhancing properties of glutamic acid were discovered by the Japanese chemist, Ikeda, who in 1908, found that the essential constituent of a certain sea-weed, *Laminaria japonica*, extensively used in Japan as a condiment was glutamic acid. Manufacture of the amino acid was begun in Japan under a patent dated 21st April 1909, and under trade names such as "Ajinomoto" (literally, enhancer of taste), glutamic acid became a common household article like salt and sugar.[3] Considerable quantities were imported into America where interest in its production developed in the twenties. Much research and developmental work was found necessary before glutamate manufacture was established in the U.S.A. In addition to the fabrication of new corrosion-resistant materials for use with concentrated hydrochloric acid, this work also resulted in a new process which involved alkaline hydrolysis of beet-sugar molasses.[4]

Occurrence and Physiology

Glutamic acid occurs in combination in practically every protein. The richest sources are given in Table I.

The amino acid occurs in proteins in the form of its acid-amide, glutamine.[5] The raw materials used for manufacture both in the East and in the U.S.A. are wheat and corn gluten from starch factories. Some quantity is also produced in the U.S.A. from beet-sugar molasses. Beet contains 0·06-0·12 per cent. of the amino acid, the entire quantity of which is ultimately found in the de-sugared molasses known as "Steffens waste water".

Table I

Glutamic acid content of some proteins[22]

Source	Protein	Glutamic acid %
Wheat gluten	Gliadin	42·2
,,	Whole	36·0
Corn gluten	Zein	36·0
,,	Whole	24·5
Milk (Cattle)	Casein	22·0
,,	Lactoglobulin	20·0
Peanut	Arachin	21·0
Cottonseed	Globulin	17·2
Hemp-seed	Edestin	17·7
Blood (Cattle)	Albumin	17·0
,,	Fibrin	15·0
Muscle	Myosin	21·0
Soya-bean	Whole meal	18·4

Table II

*Approximate glutamic acid content of some oilcakes**

Oilcake	Glutamic acid %
Groundnut	7·8
Cottonseed	7·5
Hemp	6·4
Sunflower	5·2
Castor	5·6
Cocoanut	5·0
Linseed	3·8

* Values calculated from the protein and glutamic acid content given in (21) and (22) of bibliography.

The mammalian organism is capable of synthesising glutamic acid, and for this reason, it is not one of the "essential" amino acids which have to be supplied by dietary protein. This fact is, however, definitely established only for certain species such as the rat. Chicks and probably humans require an external supply of glutamic acid for growth.[8,9]

Glutamic acid plays a central role in intermediary protein metabolism on account of the many reactions it is capable of undergoing.[10] The fact that most food proteins contain glutamic acid as a major constituent cannot be without significance.

A special function of glutamic acid is that it is the only amino acid which is oxidised in the brain.[11,12] It is not known whether this property has any connection with its therapeutic use in the treatment of mental deficiency. It has been demonstrated by groups of workers headed by Zimmerman and Waelsch that the mental power of retarded children and adolescents is greatly improved by administration of glutamic acid.[13,14]

Use as Food Flavour

The emergence of glutamic acid as an industrial chemical is not due to its biochemical functions or therapeutic action, but to its widespread use as a food flavour. Mono-sodium glutamate is used extensively as a condiment for enhancement of taste and flavour. Due to its balancing and blending effect it is added as an adjuvent in meats, sea-foods, soups and chowdars. The conclusion from the work of more than one taste panel[16,17] is that mono-sodium glutamate not only combines all the four components of taste but gives, in addition, a tingling sensation which has been described as a "feeling of satisfaction". A remarkable property of glutamate is its seasoning and blending effect, rounding off sharp profile and suppressing certain undesirable qualities such as the sharpness of onions, rawness of vegetables, volatile characteristic of boiled rice and bitter tastes in certain other dishes. It is estimated that in the U.S.A. 2 million pounds are used in canned soup, an equal quantity in canned meat products, one million pounds in dry soups and one million pounds directly in restaurants. Some quantity is used in the beer industry also. There are indications that the armed forces are likely to be one of the important users of glutamic acid in the future The monotony of military rations under field conditions is a serious problem and the Food Acceptance Branch of the U.S. Army has been keenly interested in research on glutamic acid with a view to its incorporation in canned rations.

Manufacture

The preparation of glutamic acid in the laboratory is simple A protein rich in the amino acid, usually wheat gluten, is hydrolysed with concentrated hydrochloric acid, the hydrolysate concentrated to a thin syrup and saturated with hydrochloric acid gas in the cold. Crystallisation of glutamic acid as the hydrochloride is almost quantitative after about 48 hours in the cold. In Japan, this process was used on an industrial scale, the high grade chemical stoneware manufactured in the country serving as a suitable corrosion-resistant material for the construction of equipment. The raw materials used were wheat glutten and soya-bean meal.

The major portion of the U.S.A. production of glutamic acid is from corn gluten which is a by-product in the starch industry. A considerable portion is also produced from concentrated Steffens Waste, obtained by lime treatment of beet molasses, in which the amino acid is present to the extent of about 7·5 per cent. of the total solids.[18]

Possibilities of Manufacture in India

Press cakes of oilseeds are generally rich in proteins with a high content of glutamic acid (Table II) and any one of several oilcakes available in India can serve as a cheap raw material for the manufacture of glutamic acid, and incidentally, of other amino acids, as by-products, which have uses in the laboratory and in the pharmaceutical industry. Thus groundnut and cottonseed cake have about the same content of glutamic acid as the soya-bean meal much used in Japan as a raw material of this process.

Recent developments[19] in the field of corrosion-resistant material have removed the chief difficulties in the use of concentrated hydrochloric acid for hydrolysis of oilcake protein and the isolation of glutamic acid as the hydrochloride Specially noteworthy is the fabrication of hydrochloric acid-resistant equipment from carbon or graphite rendered impervious by synthetic resins. The use of these materials sold under such trade names as "Karbate" and "Impervite" have made the handling of concentrated hydrochloric acid easy and its recovery economical. With cheap raw material available, it should be possible to establish a flourishing glutamic acid industry in India which would supply the material not only for consumption in the country but also for export.

The author is indebted to Dr. M. Damodaran for the benefit of discussion and advice.

---

1. *Food Industries*, 1950, **22,** 238. 2. Ritthausen, H., *J. prakt. Chem.*, 1866, **99,** 454. 3. Han, J. E. S., *Industr. Engng. Chem.*, 1929, **21,** 984. 4. *Proceedings of the Symposium on Mono-Sodium Glutamate*, Chicago: Associates, Food & Container Institute, 1948. 5. Damodaran, M., *Biochem. J.*, 1931, **25,** 2123. 6. —, *Ibid.*, 1932, **26,** 1704. 7, Gale, E. F., *Ibid.*, 1945, **39,** 46. 8. Almquist, H. J., and Grau, G. R., *J. Nutri.*, 1944, **28,** 325, 9. Albanese, A. A., *Adv. Protein Chem.*, 1947, **3,** 227. 10. Braunstein, A. E., *Ibid.*, 1947, **3,** 1. 11. Krebs, H. A., *Biochem. J.*, 1935, **29,** 1951. 12. Weil-Malherbe, H., *Ibid.*, 1936, **30,** 665. 13. Zimmerman, F. T., Burgmeister, B. B. and Putnam, T. J., *Arch. Neurol. Psychiat., Chicago.*

1946, **56,** 489. 14. Albert, K., Hoch. P. and Waelsch, H., *J. Nerv. and Ment. Dis.*, 1946, **104,** 263. 15. Ikeda, K., *Original Communications. Eighth International Congress of Applied Chemistry*, 1912, **18,** 147. 16. Howe P. E. and Barbella, N. G., *Food Res.*, 1937, **2,** 197. 17. Crocker, E. C. and Sjostrm, L. B., *Ibid.*, 1948, **6,** 450. 18. Meyer, W. G., *Food Mannf.*, 1950, **25,** 317. 19. Kirkpatrick, S. D. and Callaham, J. R., *Chem. Engng. Novr.*, 1950, **11,** 107. 20. Hatfield, M. R. and Ford, C. E., *Trans. Amer. Inst. Chem. Engrs.*, 1946, **42,** 121. 21. Winton, A. L. and Winton, K. B., *Structure and Composition of Foods*, 1946, **1,** New York, John Wiley & Sons. 22. Block, R. J., and Bolling, D., *Amino-acid Composition of Proteins and Foods*, 1950, Springfield, C. C. Thomas.

NEW TYPE OF PENICILLIN

A SPECIES of Cephalosporium has been found to produce two different kinds of anti-bacterial substances. The first consists of a group of acidic antibiotics which are soluble in common organic solvents, are active mainly against gram-positive organisms, and show similarities to helvotic acid. The second consists of a substance (or group of substances) which is insoluble in most organic solvents, and is active against a number of gram-positive and gram-negative organisms. This has been called 'Cephalosporin N'. Evidence has now been obtained that cephalosporin N is a new type of penicillin.

The reasons for believing that the antibiotic is a penicillin are: (1) It was inactivated by preparations of the enzyme penicillinase in high dilution, and, like benzyl-penicillinase, it stimulated the adaptive production of penicillinase by suspension of *Bacillus cereus*. (2) It was rapidly inactivated at room temperature in aqueous solution below p_H 4 or above p_H 9, and also at p_H 7 in the presence of heavy metal ions such as those of copper, lead and tin (3) Various chemical reactions yielded thiazolidine hydrochloride, penicilline hydrochloride, penicillaminic acid and glyoxal *bis*-2 : 4-dinitrophenyl hydrazone.

Cephalosporin N differs strikingly from the common penicillins in its hydrophillic character and its anti-bacterial activity. It behaves like an acidic substance on ion-exchange resins, and ionophoresis on paper shows that it carries a negative charge at p_H 6-7. Also it appears likely that the activity of pure cephalosporin N against many gram-negative bacteria will be of the same order as that of benzylpenicillin. The relatively low activity of the antibiotic against gram-positive bacteria suggests that it reaches the sensitive parts of these organisations much less readily than the other penicillins.—(*Nature*, 1953, 171, 343.)

'DARAPRIM' IN TREATMENT OF VIVAX MALARIA

THE effects of pyrimethamine ("daraprim") on the clinical symptoms and also on the parasites in 30 cases of vivax malaria attending hospitals in Delhi State are reported by Jaswant Singh and collaborators of the Malaria Institute of India in a recent issue of the *British Medical Journal*. The clearance of symptoms and asexual parasites was more rapid in those who had a previous history of malaria than in those who had not. Though one must withhold judgment until reports on a large-scale and continued observations are available, daraprim seems to be remarkably effective against *P. vivax* in doses as small as 25 mg. The drug in all probability has a future and further work is indicated.

It may be mentioned that more recent reports from the U.S.A. show that the drug has gone through laboratory and field tests and found to be an anti-malarial of unusual scope and potency—perhaps the most effective agent discovered so far for the cure and suppression of malaria. It is claimed that the drug is 10 to 200 times as active as chloroquine, proguanil and mepacrine, the standard drugs in use at present for the treatment of malaria. It is reported that a 50 mg. dose of 'daraprim' is often sufficient to control the fever in acute malarial attacks and render the blood free from most strains of the disease, and that there are no after-effects.

COMMONWEALTH INDEX OF SCIENTIFIC TRANSLATIONS

THE British Commonwealth Scientific Liaison Offices in London are operating a scheme for a Commonwealth Index of Scientific Translations, and have appointed so far seven agencies in the Commonwealth countries. These agencies act in a liaison capacity and are responsible for collecting information about existing translations in that area for advising BCSO, London, of these, for the maintenance of a central index of translation as also for assisting research workers in each area to obtain copies of translations requested by them and already prepared elsewhere. Scientific organisations are invited to participate in the scheme and to get into touch with the Ministry of Natural Resources and Scientific Research, New Delhi, who hold the agency for our country.