Name: Sara Lawyer Danke Date of Degree: May 26, 1963

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Title of Study: HEXAHOMOSERINE AS A COMPETITIVE INHIBITOR FOR THE INCORPORATION OF LYSINE INTO PROTEIN MOLECULES

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Scope and Method of Study: The purpose of this report is to assemble the known information on hexahomoserine from its beginning as the unknown anemia-causing factor in deaminated casein until the present time. In the literature many names for hexahomoserine are used. Other names found are α-amino-ε-hydroxycaproic acid, 2-amino-6-hydroxycaproic acid, α-amino-ε-hydroxyhexanoic acid, ε-hydroxynorleucine and 6-hydroxynorleucine. The materials used in this study are chiefly (1) scientific journal articles and (2) abstracts of articles in foreign languages. An attempt has been made to include all significant references to hexahomoserine.

Findings and Conclusions: The chemical structure of hexahomoserine was proven when it was synthesized from δ-hydroxyvaleraldehyde. Later, by chromatographic methods hexahomoserine was proven to be the same compound as the anemia-causing factor in deaminated casein. The active form is the L-isomer. It has been shown that hexahomoserine is a lysine antagonist in many organisms, preventing growth and causing anemia. Its probable mode of action is to act as a competitive inhibitor to lysine, preventing lysine's normal incorporation into protein molecules. Lysine administered simultaneously will promote growth without affecting the lowered red cell count caused by hexahomoserine. In many cases after hexahomoserine was removed from the diet and replaced with lysine, the animals returned to normal after a period of time. An interesting property of hexahomoserine is that it exhibits chemotherapeutic properties on cancer in rats. It also demonstrates properties which might make it a successful agent for treating polycythemia vera.

ADVISER'S APPROVAL James H. Zant

HEXAHOMOSERINE AS A COMPETITIVE INHIBITOR FOR THE INCORPORATION OF LYSINE INTO PROTEIN MOLECULES

By

SARA LAWYER DANKE

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INTO PROTEIN MOLECULES

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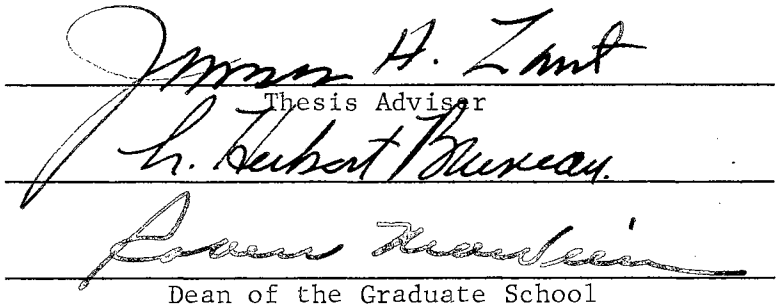

Thesis Adviser

Dean of the Graduate School

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CHAPTER I

INTRODUCTION

The purpose of this report is to assemble the known information on hexahomoserine. Hexahomoserine is an amino acid not found in nature, but closely related in structure to the essential amino acid lysine. Many studies have been made to determine if hexahomoserine could be used as a substitute for lysine in the diet of various organisms. Contrary to expected results, hexahomoserine has been found to be a lysine inhibitor. This compound is of particular interest because it has since been identified as the toxic component of deaminized casein.

Other names found in the literature for hexahomoserine are α-amino-ε-hydroxycaproic acid, 2-amino-6-hydroxycaproic acid, α-amino-ε-hydroxyhexanoic acid, ε-hydroxynorleucine and 6-hydroxynorleucine.

CHAPTER II

HISTORY

As early as 1934, an unidentified anemia-causing factor was discovered in deaminated casein by Hogan and Ritchie (21). The factor was believed to be the deficiency of one or more essential amino acids or the presence of a toxic agent. Albino rats which weighed approximately 75 grams were used as the experimental animals. (Smaller animals were less resistant to the unsatisfactory diet.) The animals were divided into groups and placed on different diets which varied in the amount and kind of protein given. The proteins used were deaminized casein, gelatin, gliadin and casein. The animals on diets that consisted of deaminized casein as the only protein source declined in weight from the beginning. They developed a severe anemia which was confirmed by the presence of abnormally low numbers of red blood cells. None of the animals survived longer than 40 days. The workers believed the anemia was due to a deficiency of lysine. They then fed rats a diet which consisted of deaminized casein and gelatin. (Gelatin was known to contain 5.9 per cent lysine.) The animals survived for a longer period of time on this diet, but soon died and there were no significant weight gains among the animals. The lysine in the gelatin was credited with the improvement. Animals fed a diet of deaminized casein, gelatin and gliadin showed no improvement over the previous diet. Casein alone proved to be a sufficient diet. Gliadin and casein used together were no more satisfactory than casein alone. A

combination of gelatin and gliadin proved to be an adequate source of protein. Other combinations of gelatin, gliadin and casein were unsatisfactory. It was found that when the diet consisted of equal amounts of deaminized casein and casein, the animals did not develop anemia and continued to grow in a normal manner.

In further studies on the anemia, Hogan, Guerrant and Ritchie (19) found that anemic, albino rats on a diet of 10 per cent deaminized casein required an addition to the diet of approximately 5 per cent casein to prevent the anemia. The anemia can be produced by the addition of a minimal amount of deaminized casein, which lies between 5 and 10 per cent of the ration. Substances found ineffective against the anemia at levels from 100 to 400 mg. of dry matter were milk, egg yolk, wheat germ oil, ventriculin, muscle, liver and stomach. Protection against the anemia caused by deaminized casein was conferred by the addition of dry yeast in the amount of 18 per cent to the diet. The attempt to recover the active agent of yeast with water was unsuccessful. Autoclaving casein and yeast inhibits their ability to overcome the anemia produced by deaminized casein. The active agent of deaminized casein could be recovered in the hydrolyzate when it was hydrolyzed with 25 per cent sulfuric acid at atmospheric pressure. The antianemic agent in casein could likewise be recovered.

Smith and Stohlman (45) working with the anemia produced by deaminized casein confirmed the work of Hogan and Ritchie (21). They found that when deaminized casein was fed at a level of 10 per cent in the diet of a white rat, a characteristic macrocytic megaloblastic anemia with many Howell-Jollie bodies was produced. Good quality protein added to the diet would not prevent the anemia, but would lessen its severity.

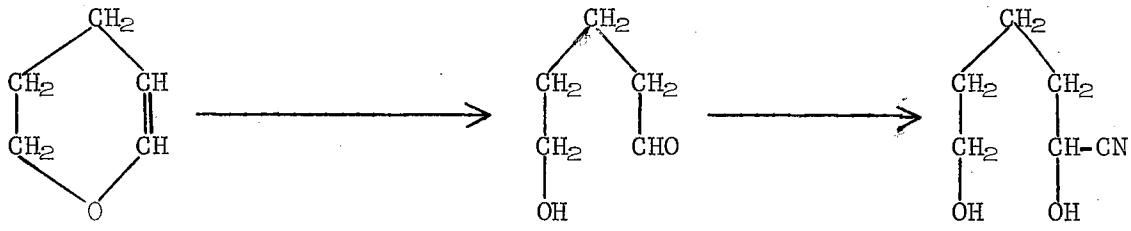
They found that deaminized casein boiled with alcoholic sodium hydroxide or reprecipitated from aqueous alkaline solution lacked the anemia-producing factor for the most part. When animals were injected intraperitoneally with the alcohol soluble fraction of a hydrochloric acid hydrolyzate of deaminized casein, they developed the anemia. This proved that the anemia is an intoxication and not a deficiency disease.

In studies by Hogan, Powell and Guerrant (20) lysine appeared to be the amino acid responsible for recovery when either casein hydrolyzate or that copper-salt fraction which is soluble in water and insoluble in methyl alcohol was administered to anemic rats. It was also shown by biological methods that the only essential amino acid missing in significant amount from deaminized casein is lysine. They showed that lysine added in the amount of approximately 2 per cent was sufficient to permit recovery from the anemia.

CHAPTER III

PROOF OF STRUCTURE AND CHEMICAL PROPERTIES

α-Animo-ε-hydroxycaproic acid was synthesized by Gaudry (8, 9) in 1947. This was the first time that the compound had been synthesized in such a way as to establish its chemical structure. Acid hydrolysis of dihydropyran (I) gives δ-hydroxyvaleraldehyde (II), to which is applied the Bucherer modification of the Strecker synthesis for α-amino acids. The aqueous solution is used to prepare the corresponding cyanohydrin, α,ε-dihydroxycaproic nitrile (III). This compound yields 5-δ-hydroxybutyl-hydantoin (IV) which when hydrolyzed under pressure with barium hydroxide gives a 95 per cent yield of D,L-α-amino-ε-hydroxycaproic acid (V). The name proposed for the compound by Gaudry is "hexahomoserine" because it is a six-carbon compound and a serine homologue.



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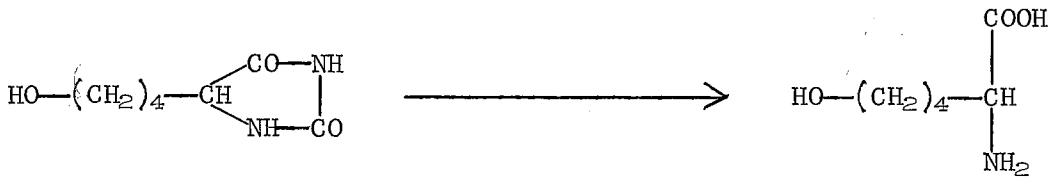


IV V

The melting point varies between 245° and 248°C and 260° and 262°C with

gas evolution varying according to the rate of heating. The nitrogen content calculated for $C_8H_{13}O_3N$ is 9.52 per cent. The amount of nitrogen found (Kjeldahl) is 14.98 per cent. It was suspected that hexahomoserine is the same as the compound in deaminized casein which produced anemia in rats.

The optical rotation of 99.9% optically pure L- and D-isomers and their susceptibility to Crotalus adamanteus L-amino acid oxidase and hog kidney D-amino acid oxidase as determined by Greenstein, Birnbaum and Otey (17) and Greenstein (16) is as follows:

L-Isomers				D-Isomers
$[M]_D$ in			Oxidation by L-amino acid oxidase	Oxidation by D-amino acid oxidase
H_2O	5N HCl	Glacial Acetic Acid		
+5.9	+34.9	+57.4	201	3.2

$[M]_D$ is molar rotation which is $[\alpha]_D$ (rotation) x 147.1 ÷ 100. The "D" stands for the sodium line which is 589mμ. The 147.1 is the molecular weight of hexahomoserine. The rates for oxidation by L- and D-amino acid oxidase is expressed in terms of micromoles of oxygen consumed per mg. of nitrogen.

Berlinquet and Gaudry (4) established the optical rotation for a 2 per cent solution of the D- and L-isomers in 6 N HCl obtained by the asymmetric hydrolysis of chloroacetyl-D,L-α-amino-ϵ-hydroxy-n-caproic acid by an enzyme preparation from hog kidney. The value for L-α-amino-ϵ-hydroxy-n-caproic acid is $[\alpha]_D^{27} = +23.7°$ and for D-α-amino-ϵ-hydroxy-n-caproic acid is $[\alpha]_D^{23} = -23.2°$.

Other rotary dispersion data for the L-isomer of hexahomoserine as determined by Otey et al. (37) is as follows:

H_2O as solvent		5 N HCl as solvent	
$[\alpha]_D$	λ_o	$[\alpha]_D$	λ_o
+3.6	296	+23.5	244

The optical rotations were determined with a photoelectric polarimeter. The values in the table refer to the D or 589 mμ line of sodium. The values of λ_o were determined from the dispersion data by the method of least squares.

In studying lysine biosynthesis in Neurospora Schweet, Holden and Lowy (44) found the chromatographic mobility of hexahomoserine to be 0.42 in butanol-acetic acid, 0.66 in pyridine-water and 0.74 in phenol-water. The values are given as R_F.

Kroegel et al. (22) established the absorption spectrum in the infrared in the 2 to 8μ region to be as follows:

2 – 5μ	5 - 7μ	7 - 8μ
3.06 MS	6.36 SS	6.65 SS
3.40 MB		6.96 MS
3.66 MB		7.14 SS
4.73 WB		7.42 MS
		7.59 MS
		8.05 WB

W=weak intensity, S=sharp band, M=medium intensity, B=broad band and S=strong intensity.

Dent (7) found that hexahomoserine (ninhydrin reactant) is detectable in amounts of 10 μg on phenol-'collidine' filter-paper chromatograms. The characteristic spot gives a purple color. The hydrolyzate of deaminated

casein gives a similar spot in the exact position of the hexahomoserine spot. These results tend to prove that the anemia-producing factor in deaminated casein and hexahomoserine are the same substance.

A compound prepared by MacDonald and Tullock (23) from hexahomoserine is ϵ-acetoxy-D,L-α-aminocaproic acid HCl.

CHAPTER IV

ENZYME AND BACTERIAL STUDIES

Various enzyme studies have been conducted on hexahomoserine with limited results. L-amino oxidase prepared from the hepato-pancreas of Cardium tuberculatum is active on D, L-α-amino-δ-hydroxycaproic acid according to the work of Glahn, Manchon, and Roche (14). The work of Meister (33) shows that the transamination reaction when catalyzed with Lactobacillus arabinosus extracts, is possible with hexahomoserine and ω-N-chloroacetyl derivative of lysine, but not with free lysine. This indicates that the presence of a free ε-amino group inhibits transamination. Roche, Thoai and Verrier (43) noted varying amounts of inhibition on the reaction of purified arginase from beef liver on L-arginine when hexahomoserine was added. Formation of a cobalt-amino acid is thought to be responsible for this inhibition. Yura and Vogel (47, 48) found that α-amino-adipic-δ-semialdehyde is the product formed when hexahomoserine is used as the substrate for the dehydrogenation reaction catalyzed by ω-hydroxy-α-amino acid dehydrogenase. This reaction is DPN- or TPN-dependent and only the L-isomer of hexahomoserine is active. The enzyme which catalyzes this reaction appears to be the same enzyme which catalyzes the pyrroline-5-carboxylate reductase of Neurospora crassa. This probably accounts for the reason that hexahomoserine will satisfy the lysine requirement of certain Neurospora mutants.

Hasse, Homann, and Schuhrer (18) show that the product of the

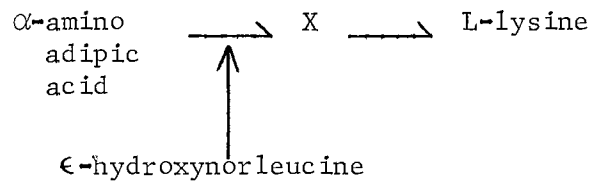
enzymic oxidation of hexahomoserine by a ω-hydroxy-α-amino acid dehydrogenase (from Neurospora crassa) after purification on Dowex 50 is Δ^1-piperideine-6-carboxylic acid. They found that this compound is also the product of the oxidation of lysine by diamine oxidase (from pea seedlings) at pH 6-10.

Davis (5) found that 10 - 300 μgm/ml. of D,L-α-amino-ϵ-hydroxycaproic acid does not inhibit or cause a response from the mutants 173-25, 173-25C3, 26-26, 81-47, 81-83, 81-29, 81-43, 122-64, 39A-21 of Escherichia coli. Meadow, Hoare and Work (31) and Meadow and Work (32) found that hexahomoserine had no effect on lactobacilli or the lysine-requiring E. coli mutants 173-25 and 26-26. It did not replace lysine for growth and did not prevent or cause lysis to occur. They found that it either inhibited growth or replaced lysine in Neurospora mutants. Ravel et al. (42) show that hexahomoserine does not replace lysine in Lactobacillus arabinosus or L. casii.

In studying hexahomoserine as a substitute for lysine for Neurospora, Good et al. (15) found that the mutants 33933 and 4545 could utilize the substance for growth. It was found that when mutant 4545 grown on a given amount of hexahomoserine were reisolated and incubated, their growth responses to hexahomoserine varied considerably. Mutants 37101, 15069 and 39302 utilize lysine like rats and are inhibited by hexahomoserine. They propose the following sequence of substances and mutations:

? $\xrightarrow{33933}$ α-aminoadipic acid $\xrightarrow{4545}$ ϵ-hydroxynorleucine $\xrightarrow{37101,\ 15069,\ 39302}$ lysine

Schweet et al. (44) suggest the following metabolic scheme for lysine biosynthesis in Neurospora:



It is shown by Vogel (46) that the lysine pathway in Euglena is similar to the one in fungi (such as Candida and Neurospora). Using L-[^{14}C] aspartate as tracer and D,L-hexahomoserine as the unlabeled supplement, he finds that the radioactivity in the protein lysine (but not in the protein aspartic acid or threonine) of Euglena is almost completely inhibited.

CHAPTER V

PHYSIOLOGICAL STUDIES

Hexahomoserine added to a complete basal ration or one containing no lysine produces anemia in rats. According to Mertz et al. (36), in young white rats on a diet containing 2 per cent D,L-lysine HCl, the addition of as little as 1 per cent D,L-hexahomoserine will inhibit growth and produce symptoms of anemia. Pagé and Gingras (39) and Pagé, Gingras and Gaudry (41) showed that accompanying the anemia is a marked rise in the blood plasma amino nitrogen. In further studies Pagé, Gaudry and Gingras (38) and Mertz et al. (34) found that hemoglobin, red cell count and red cell volume are lowered. Other blood substances remain normal. Martel (24, 25) and Martel and Gingras (29) found that there is a rise in the blood amino acid without changing urinary excretion. Creatinine excretion increases, while creatine excretion decreases or ceases. The latter pair in further tests found that plasma and muscle creatinine are not altered. In a single study Gaudry (10) showed that plasma ablumin and globulins decrease markedly. A loss of weight always accompanies the anemia. In histological studies Gingras, Pagé and Gaudry (13) found that the kidneys increase in weight, but show no abnormalities. Pagé, Gingras and Gaudry (37) showed that lysine given simultaneously with hexahomoserine prevents the anemia and partially improves growth, but has no effect on the plasma amino nitrogen.

According to Mertz and Golubow (35), when hexahomoserine is resolved

and the isomers fed to weanling rats, it is found that the D-isomer caused no significant reduction in the average red blood cell count and reduces the average weight gain to about one-fourth that of the controls. The L-isomer reduces the average red cell count to about one-third and the average weight gain to about one-half that of the controls. They concluded that the D-isomer acts as a specific growth depressant, while the L-isomer depresses both growth and red cell production.

Gaudry and Martel (11) showed that when hexahomoserine is fed to rats, it is changed to α-keto acids by oxidative deamination and is almost completely discharged in the urine. In a later study Martel (26) showed that in addition to the increase in urinary excretion of ketonic acids, there is also an increased excretion of pyruvic and oxoglutaric acids. DeLong (6) proposes that his data suggests that part of the amino acid is metabolized via α-keto-6-hydroxycaproic acid and part via α-keto-caproic acid, indicating both an oxidative and nonoxidative pathway.

The reduction in growth of Novikoff heptoma in rats when hexahomoserine is administered, as proven by Martel and Berlinquet (27) shows that hexahomoserine possesses chemotherapeutic properties on cancer. Martel and Gingras (28) showed that the addition of 1.5 per cent of hexahomoserine to the diet of rats prevents the polycythemia (high hemoglobin, number of red cells, and total cell volume) induced by the addition of 0.1 per cent cobalt chloride to the ration. For these reasons Gaudry (10) proposes that hexahomoserine might be tried clinically in severe cases of polycythemia vera to try to control a high hemoglobin level, red cell count and cell volume.

Bergeron and Bourbeau (2,3) studied the chronic toxicity of hexahomoserine for the dog. They found that hexahomoserine administered daily

in the diet of dogs produces hyprochromic, microcytic anemia, the severity depending upon the amount of hexahomoserine administered. Evidence, such as anorexia, loss in weight, muscular atropy, skin ulcers, and epilation, shows chronic intoxication by hexahomoserine. Toxi-infectious lesions with centrolobular degeneration and in a few cases a slight fatty metamorphosis were discovered by an autopsy on dogs which had died during the experimental period. There was a decrease in the index and mean diameter of the erythrocytes. There was no change in the blood chemistry. Susceptibility to infection increased among the dogs. In all cases the symptoms were reversible and 10 weeks after hexahomoserine was omitted from the diet, the dogs were normal.

Athens, Cartwright and Wintrobe (1) fed a lysine-deficient diet with hexahomoserine to swine. The swine developed a normocytic, normochromic anemia which was accompanied by hypoalbuminemia and hypocupremia. There was no change in the plasma iron concentration or in bone marrow morphology. The data indicates that lysine is essential for normal erythropoiesis in swine. In other studies with swine Mertz et al. (34) showed that the red cell count is lowered, but all other blood substances remain unchanged.

Gaudry (10) proposes that hexahomoserine is possibly a lysine antagonist in all mammals. Acting as a competitive inhibitor to lysine, it prevents lysine's normal incorporation into protein molecules. The L-isomer appears to be the active form.

CHAPTER VI

SUMMARY

The chemical structure of hexahomoserine was proven when it was synthesized from δ-hydroxyvaleraldehyde. Later, by chromatographic methods hexahomoserine was proven to be the same compound as the anemia-causing factor in deaminated casein. The active form is the L-isomer. It has been shown that hexahomoserine is a lysine antagonist in many organisms, preventing growth and causing anemia. Its probable mode of action is to act as a competitive inhibitor to lysine, preventing lysine's normal incorporation into protein molecules. Lysine administered simultaneously will promote growth without affecting the lowered red cell count caused by hexahomoserine. In many cases after hexahomoserine was removed from the diet and replaced with lysine, the animals returned to normal after a period of time. An interesting property of hexahomoserine is that it exhibits chemotherapeutic properties on cancer in rats. It also demonstrates properties which might make it a successful agent for treating polycythemia vera.

Other names found in the literature for hexahomoserine are α-amino-ε-hydroxycaproic acid, 2-amino-6-hydroxycaproic acid, α-amino-ε-hydroxy-hexanoic acid, ε-hydroxynorleucine and 6-hydroxynorleucine.

BIBLIOGRAPHY

1. Athens, J. W., Cartwright, G. E., and Wintrobe, M. M., Proc. Soc. Exptl. Biol. Med., 97, 909 (1958).

2. Bergeron, G. A., and Bourbeau, G., Rev. can. biol., 10, 272 (1951), via C. A. 45, 9177b (1951).

3. Bergeron, G. A., and Bourbeau, G., Rev. can. biol., 11, 53 (1952), via C. A., 46, 9210g (1952).

4. Berlinquet, L., and Gaudry, R., J. Biol. Chem., 198, 765 (1952).

5. Davis, B. D., Nature, London, 169, 534 (1952).

6. DeLong, D. C., (unpub. Ph. D. dissertation, Purdue University, 1958), via Dissertation Abst., 19, 3110 (1959).

7. Dent, C. E., Biochem. J., 43, 169 (1948).

8. Gaudry, R., Can. J. Research, 26B, 387 (1948).

9. Gaudry, R., Can. J. Chem., 29, 544 (1951).

10. Gaudry, R., Proc. Can. Cancer Research Conf., Honey Harbour, Ontario 1954, 1, 163 (1955).

11. Gaudry, R., and Martel, F., Compt. rend. soc. biol., 148, 472 (1954).

12. Gingras, R., Pagé, E., and Gaudry, R., Rev. can. biol., 6, 801 (1947), via C. A., 42, 3043d (1948).

13. Gingras, R., Pagé, E., and Gaudry, R., Science, 105, 621 (1947).

14. Glahn, P. E., Manchon, P., and Roche, J., Compt. rend. soc. biol., 149, 509 (1955), via C. A., 50, 1218i (1956).

15. Good, N., Heilbronner, R., and Mitchell, H. K., Arch. Biochem., 28, 464 (1950).

16. Greenstein, J. P., Advances in Protein Chemistry, 9, 122 (1954).

17. Greenstein, J. P., Birnbaum, S. M., and Otey, M. C., J. Biol. Chem., 204, 307 (1953).

18. Hasse, K., Homann, P., and Schuhrer, K., Naturwissenschaften, 48, 51 (1961), via C. A., 55, 13520f (1961).

19. Hogan, A. G., Guerrant, R. E., and Ritchie, W. S., J. Biol. Chem., 115, 659 (1936).

20. Hogan, A. G., Powell, E. L., and Guerrant, R. E., J. Biol. Chem., 137, 41 (1941).

21. Hogan, A. G., and Ritchie, W. S., J. Biol. Chem., 107,179 (1934).

22. Koegel, R. J., Greenstein, J. P., Winitz, M., Birnbaum, S. M., and McCallum, R. A., J. Am. Chem. Soc., 77, 5708 (1955).

23. MacDonald, R. N., and Tullock, C. W., U. S. 2,630,423, Mar. 3, 1953, via C. A. 47, P5130h (1953).

24. Martel, F., Laval med., 15, 960 (1950), via C. A., 45, 8116b (1951).

25. Martel, F., Laval med., 15, 1100 (1950), via C. A., 45, 8116b (1951).

26. Martel, F., Laval med., 25, 665 (1958), via C. A., 54, 22896e (1960).

27. Martel, F., and Berlinquet, L., Can. J. Biochem. and Physiol., 37, 433 (1959).

28. Martel, F. and Gingras, R., Rev. can. biol., 9, 199 (1950), via C. A., 44, 7446f (1950).

29. Martel, F. and Gingras, R., Ann. ACFAS, 16, 105 (1950), via C. A., 47, 11570a (1953).

30. Martel, F. and Gingras, R., Ann, ACFAS, 16, 109 (1950), via C. A., 47, 11570a (1953).

31. Meadow, P., Hoare, D. S., and Work, E., Biochem. J., 66, 270 (1957).

32. Meadow, P., and Work, E., Biochem. J., 64, 11P (1956).

33. Meister, A., J. Biol. Chem., 195, 813 (1952).

34. Mertz, E. T., Beeson, W. M., Waltz, Jr., R. H., and Gaudry, R., Proc. Soc. Exptl. Biol. Med., 69, 609 (1948).

35. Mertz, E. T., and Golubow, J., J. Nutrition, 58, 51 (1956).

36. Mertz, E. T., Waltz, Jr., R. H., Shalton, D. C., Doyle, L. P., and Delez, A. L., Proc. Soc. Exptl. Biol. Med., 73, 75 (1950).

37. Otey, M. C., Greenstein, J. P., Winitz, M., and Birnbaum, S. M., J. Am. Chem. Soc., 77, 3112 (1955).

38. Pagé, E., Gaudry, R., and Gingras, R., J. Biol. Chem. 171, 831 (1947).

39. Pagé, E., and Gingras, R., Federation Proc., 8, 122 (1949).

40. Pagé, E., Gingras, R. and Gaudry, R., Ann. ACFAS, 15, 81 (1949), via Biol. Abst., 19778.

41. Pagé, E., Gingras, R., and Gaudry, R., Can. J. Research, 27E, 364 (1949), via C. A. 44, 4556d (1950).

42. Ravel, J. M., Woods, L., Felsing, B., and Shive, W., J. Biol. Chem., 206, 391 (1954).

43. Roche, J., Thoai, N. -V., and Verrier, J., Compt. rend. soc. biol., 148, 782 (1954), via C. A. 49, 1114c (1955).

44. Schweet, R. S., Holden, J. T., and Lowy, P. H., J. Biol. Chem., 211, 517 (1954).

45. Smith, M. I., and Stohlman, W. S., Pub. Health Rep., U.S.P.H.S., 51, 772 (1936).

46. Vogel, H. J., Biochim. and Biophys. Acta., 34, 282 (1959).

47. Yura, T., and Vogel, H. J., Biochim et Biophys. Acta., 24, 648 (1957).

48. Yura, T., and Vogel, H. J., J. Biol. Chem., 234, 339 (1959).

VITA

Sara Lawyer Danke

Candidate for the Degree of

Master of Science

Report: HEXAHOMOSERINE AS A COMPETITIVE INHIBITOR FOR THE INCORPORATION OF LYSINE INTO PROTEIN MOLECULES

Major Field: Natural Science

Biographical:

Personal Data: Born in Ardmore, Oklahoma, March 10, 1940, the daughter of Hugh and Hazel Lawyer.

Education: Attended grade school in Muskogee and Oklahoma City, Oklahoma; graduated from Northwest Classen High School, Oklahoma City, Oklahoma in 1958; received the Bachelor of Arts degree from the Oklahoma State University, with a major in Chemistry, in May, 1962; completed requirements for the Master of Science degree with a major in Natural Science, in May, 1963.

Professional Experience: Laboratory assistant, St. Anthony Hospital, Oklahoma City, Oklahoma, Summer 1959; Part time laboratory assistant, Oklahoma State University, Biochemistry Department, 1961; Participant, National Science Foundation Academic Year Institute in Biology, 1962-1963.

Honorary and Professional Societies: Phi Kappa Phi, Phi Sigma, Kappa Delta Pi.