

G-78-002
(E-108)

EFFECT OF ASPARTAME ON PLASMA AND RED CELL AMINO ACIDS
OF APPARENTLY HEALTHY FEMALE ADULTS AND ON
PRESUMED PHENYLKETONURIC HETEROZYGOTES*

MED-77-06-055

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Revision of April 24, 1978.

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Introduction

Aspartame is a new synthetic sweetener which contains phenylalanine. Since phenylketonuric persons may be on a diet restricted in phenylalanine, it was important to establish what effect ingestion of this sweetener might have upon the dietary control of phenylalanine intake in such persons. On the basis of studies by Searle Laboratories, it was estimated that 34 mg/Kg/day aspartame would be a maximal intake for the average child under normal eating circumstances.¹ This project was designed to complement a study already reported by the senior author on phenylalanine levels following aspartame ingestion in normal PKU heterozygotes receiving aspartame orally over a period of six weeks in varying dosage² and in two homozygotes PKU individuals.³

Material and Methods

Aspartame was accurately weighed on a chemical balance to provide 34 mg/Kg/dose for four normal subjects and four normal obligate PKU heterozygotes. This dose was diluted in 8 oz. of orange juice and administered to subjects in a fasting state. The heterozygotes were selected from a known population of mothers of PKU children. The normal controls consisted of healthy young women varying in age from 20 to 28 years. The PKU heterozygote mothers were selected to match the age of the controls. All subjects were in excellent health at the time of these tests.

Repeat studies on the normal volunteers were performed because the values from the first set of data were notably lower than those from the normal volunteers tested in Iowa City by Drs. Filer and Stegink.⁴ It was thought that perhaps the samples from the first studies were delayed in transit or allowed to stand at room temperature for some time prior to analysis which caused the phenylalanine levels to be lower than those reported by the Iowa group.

Effect of Aspartame on Plasma
and Red Cell Amino Acids

Blood samples for analyses were obtained at 0, 1/4, 1/2, 1, 1 1/2, 2, 3 and 4 hours after ingestion by venipuncture. These blood samples were immediately centrifuged to separate plasma from erythrocytes. The plasma then was deproteinized with a carefully weighed amount of sulfosalicylic acid and prepared for shipment. Specimens were sent from California to the laboratories of Dr. Lloyd Jack Filer and Dr. Lewis D. Stegink in Iowa, where they were tested for the presence of plasma and erythrocyte phenylalanine. They were shipped air express packaged in dry ice. When received in Iowa, they were kept frozen at 0 Centigrade until ready for analysis. The erythrocytes were prepared for analysis by the method of Levy and Barkam.⁵ The amino acid content of plasma and erythrocytes were carried out on Technicon NC-1 or Beckman 121M Amino Acid Analyzers.

Results

Plasma and erythrocyte free amino acid levels in the normal and heterozygote subjects are tabulated in Appendix 1 for the studies carried out by Dr. Koch and Appendix 2 for the studies by Dr. Blaskovics. A comparison of these data with that obtained by Filer and Stegink in Iowa on 12 normal subjects and 5 heterozygote PKU persons is graphed out in Figure 1. Agreement was close with the initial heterozygote data from both Koch and Filer and Stegink; however, the initial Koch data on normals was below that obtained by Filer and Stegink. For this reason, the same 4 normal volunteers were retested by Dr. Blaskovics. Dr. Koch had left Childrens Hospital of Los Angeles and was unavailable to carry out the repeat study. This time the findings by Dr. Blaskovics were comparable to the Iowa data. The data on normals revealed that plasma phenylalanine levels remained within the normal range despite the loading dose of 34 mg. of aspartame/kg. The normally accepted values for blood phenylalanine is between 6.06-18.18 $\mu\text{m}/100\text{ml}$. Even the data obtained on the PKU heterozygotes did not increase above the levels seen in non

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heterozygotic persons. Peak values occurred at the 1 hour level and rapidly returned to near-normal pretest levels; not only was this true for phenylalanine, but for all other amino acids analyzed. During the experiment each woman was seen by a physician every 15 minutes. No clinical changes were noted by observation or by verbal interrogation by each woman.

While it is well documented that generally offspring of the PKU women are mentally retarded, the effect of heterozygosity alone on the subsequent intelligence of offspring has not been studied in detail. This is primarily due to the fact that there are no easy methods to determine heterozygosity with certainty. To the present oral or intravenous phenylalanine tolerance tests have been the only methods used to determine PKU heterozygosity. The oral loading tests are somewhat unreliable because of variation in absorption time among individuals. While intravenous studies avoid the variation due to absorption, they are technically more difficult to perform and more expensive. In our own experience serum phenylalanine levels in heterozygotic PKU women appear to be slightly above the normal range during the entire pregnancy and no elevation has been noted in their non-PKU offspring. Even in the PKU offspring data is scarce and generally shows that the serum phenylalanine levels do not begin to rise until the second day of life. Slightly elevated levels of phenylalanine in known PKU heterozygotes ($6.06-30.30 \mu\text{m}/100 \text{ ml}$)⁶ have been reported, however no abnormalities have been noted in their non-PKU offspring.

Conclusion

Aspartame in a loading dose of 34 mg/Kg did not cause any adverse clinical effects in 4 normal and 4 PKU heterozygote persons and did not cause a rise in blood phenylalanine in either plasma or erythrocytes above normal accepted values of $6.06-18.18 \mu\text{m}/100 \text{ ml}$.

Summary

It would appear from our data that the estimated maximal ingestion of aspartame in normal and PKU heterozygote persons is well-tolerated and does not cause any clinically nor measurably significant rise in plasma or erythrocyte phenylalanine content. One could infer from these data that no harm would come to a fetus carried in-utero due to blood phenylalanine elevation while a prospective normal or heterozygote PKU mother ingested this dosage of aspartame.

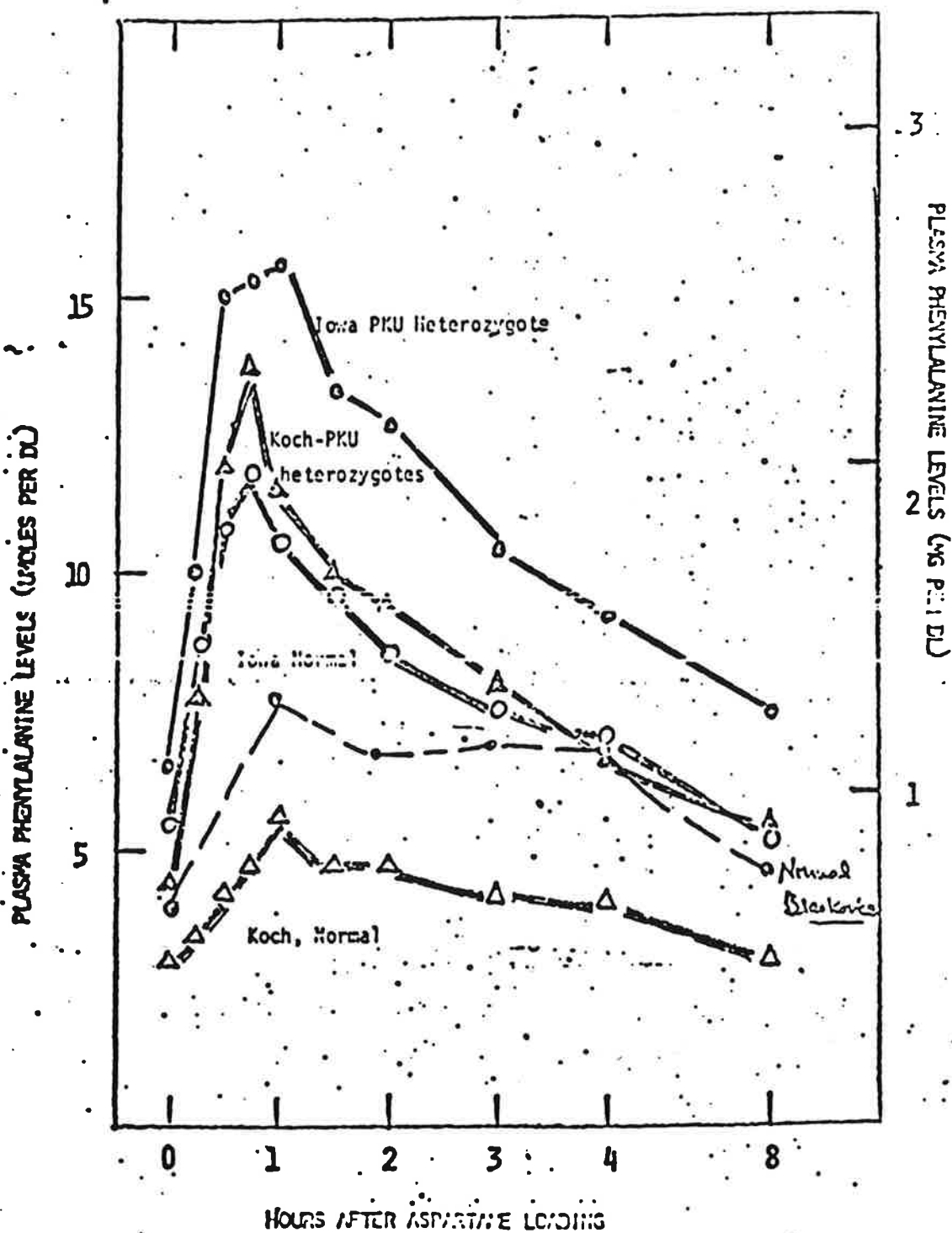
References:

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2. Koch, R., Shaw, K.N.F., Williamson, M. and Haber, M. "Use of Aspartame in Phenylketonuric Heterozygous Adults." J. Tox. Environ. Health. 2:453-457, 1976.
3. Koch, R., Schaeffler, G. and Shaw, K.N.F. "Results of Loading Doses of Aspartame by Two Phenylketonuric (PKU) Children Compared With Two Normal Children." J. Tox. Environ. Health. 2:459-469, 1976.
4. Stegink, L.D., Filer, L.J. and Baker, G.L. Final Report on Aspartame Studies, dated January 19, 1977. Submitted to G. D. Searle & Company, Chicago, Illinois.
5. Levy, H.L. and Barkan, E.J. Lab. Clin. Med., 78:517, 1971.
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FIGURE 1: COMPARISON OF ALL NORMAL SUBJECTS AND PKU HETEROZYGOTE SUBJECTS STUDIED IN BOTH CALIFORNIA AND IN IOWA.

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Appendix I

Koch Study
Plasma and RBC Amino Acid
Levels in Normal and PKU
Heterozygote Volunteers Administered
Aspartame at 34 MPK

KOCH AND STEGINK COLLABORATIVE STUDY ON ASPARTASE

CONTROL SUBJECT X PKU HETEROZYGOTE

PLASMA AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH TIME (μmoles/100 ml)

SUBJECT Chris Koch (CK) DATE _____ TEST MATERIAL ADMINISTERED _____

SUBJECT WEIGHT _____ DOSE ADMINISTERED _____ mg/Kg TOTAL (GM) _____

AMINO ACID	0 time	15 min	30min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
TALRINE	4.57	3.61	2.49	4.12	3.91	3.73	3.45	3.51	3.96	2.77
ASPARTATE	0.089	0.100	0.175	0.108	0.101	0.10	0.103	0.132	0.104	0.122
THREONINE	15.8	13.9	14.2	14.8	14.5	13.0	12.3	12.1	11.7	10.9
SERINE	11.8	11.0	11.9	11.6	11.5	10.1	9.5	10.1	9.10	9.40
ASPARAGINE	7.16	7.47	5.22	6.46	8.15	6.72	7.29	6.63	8.85	7.44
GLUTAMINE	54.51	58.6	59.8	59.00	57.42	58.4	48.1	55.8	52.0	55.70
GLUTAMATE	0.61	0.75	1.88	1.75	2.07	1.81	2.33	1.96	2.04	1.00
PROLINE	26.2	24.3	26.6	27.7	27.9	26.0	23.95	26.2	24.6	20.4
CITRULLINE	2.44	1.56	2.32	1.36	1.31	1.27	1.81	1.21	0.66	0.35
GLYCINE	30.3	37.8	33.8	26.3	26.1	24.6	25.1	27.8	26.5	25.3
ALANINE	41.5	22.2	31.3	47.0	50.1	46.6	44.2	45.9	48.7	35.3
α-AMINOACID.	4.26	2.72	2.13	4.27	4.10	3.85	3.86	3.54	3.36	2.83
VALINE	32.1	23.0	23.9	27.3	21.9	23.2	23.4	21.0	19.5	16.99
β-CYSTINE	2.53	2.77	6.30	7.65	8.10	7.17	9.39	8.00	7.98	9.48
METHIONINE	2.73	2.28	2.22	2.31	2.52	1.83	2.02	1.93	1.89	2.04
ISOLEUCINE	2.60	5.60	5.75	5.86	5.12	4.63	4.13	4.05	3.68	3.90
LEUCINE	14.70	12.6	11.8	11.4	10.8	9.04	8.44	8.61	7.63	9.04
TYROSINE	3.97	3.93	3.03	3.42	3.34	2.93	2.77	2.65	2.47	2.47
P-AMYLALANINE	2.45	4.10	4.64	5.47	5.59	4.83	4.68	4.40	4.00	3.23
C-AMINE	5.66	4.84	4.94	4.69	5.5	5.01	4.69	4.12	4.46	3.40
LYSINE	19.0	18.1	16.0	17.8	16.9	16.5	16.3	17.2	16.5	15.4
METHYLURINE	7.40	7.41	6.73	7.08	7.17	6.35	6.16	6.43	6.45	6.58
ARGININE	10.06	11.10	10.5	11.2	10.6	9.32	8.90	9.75	9.94	10.1

KOCH-PRU HETEROZYGOTE STUDY

ERYTHROCYTE AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH INCREASING TIME (umoles/100 gm RBC)

SUBJECT CHRIS KOCH

DOSE OF ASPARTATE ADMINISTERED 34 mg/kg

AMINO ACID	0 time	15 min	30 min	45 min	60 min	90 min	2 hr	3 hr	4 hr	5 hr
PIDOSP.-SERINE	21.72	26.92	29.66	20.06	19.68	23.01	19.20	14.62	19.45	31.38
TAURINE	20.57	20.05	21.61	30.10	32.07	32.74	24.61	31.83	26.65	16.21
ASPARTATE	28.03	24.96	24.40	24.43	21.23	23.96	24.41	20.74	21.67	23.61
THREONINE	10.36	11.28	11.28	10.97	9.75	9.98	8.98	8.88	11.61	7.71
SERINE	15.74	13.16	12.93	12.59	13.63	11.56	11.17	9.64	10.42	10.61
ASPARAGINE	15.56	13.36	16.89	13.78	13.87	13.33	12.36	14.42	15.97	13.56
GLUTAMINE	43.88	52.42	52.22	54.21	48.42	49.00	50.22	50.21	53.95	50.73
GLUTAMATE	23.65	23.11	24.50	23.51	20.34	23.06	22.60	20.70	23.31	24.40
PROLINE	15.33	17.42	15.56	15.63	18.81	18.21	17.07	17.64	15.43	17.29
GLYCINE	25.17	30.11	31.51	29.97	27.53	28.53	26.76	26.19	23.59	26.17
ALANINE	20.31	20.55	21.71	24.30	24.25	24.82	24.10	22.90	24.86	22.29
α-AMINOBUT.	2.01	2.55	2.49	2.51	2.00	2.13	2.23	2.48	2.61	1.95
VALINE	16.94	21.17	20.80	18.90	15.92	16.04	15.54	15.64	18.64	15.23
β-CYSTEINE	-	-	-	-	-	-	-	-	-	-
METHIONINE	trace	trace	trace	trace	trace	trace	trace	trace	trace	trace
ISOLEUCINE	3.36	4.39	4.16	3.64	2.79	2.47	2.12	2.48	2.52	1.45
LEUCINE	7.86	9.82	9.57	8.25	6.58	6.09	5.62	5.89	5.73	5.33
TYROSINE	3.85	3.82	4.11	3.60	3.21	3.09	2.83	2.58	2.68	4.08
PHENYLALANINE	3.91	4.05	5.37	5.15	4.29	4.29	4.07	3.72	3.77	4.53
ORNITHINE	8.03	7.52	9.85	9.55	9.61	8.98	7.81	10.81	9.94	3.57
LYSINE	10.62	11.16	11.14	10.96	9.52	10.12	9.67	10.22	11.18	14.23
HISTIDINE	6.37	6.15	6.36	6.24	6.05	5.81	5.74	5.45	5.93	7.41
ARGININE	3.39	4.26	4.83	4.63	4.23	4.10	3.56	4.21	3.79	5.03

Stegunke
6/25/82

KUCH AND ST. "K" COLLABORATIVE STUDY ON ASPARTATE

CRITICAL SUBJECT X PKU HETEROZYGOTEPLASMA AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH TIME (μ mles/100 ml)SUBJECT Les Koch

DATE _____

TEST MATERIAL ADMINISTERED _____

SUBJECT WEIGHT _____

DOSE ADMINISTERED _____

mg/Kg _____

TOTAL (GM) _____

AMINO ACID	0 time	15 min	30min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
TAURINE	5.10	5.08	4.99	4.68	4.25	3.75	4.17	4.34	4.51	3.98
ASPARTATE	0.08	.102	0.095	.101	.170	0.08	0.27	0.060	0.057	0.37
THREONINE	6.47	6.92	6.91	7.11	7.26	5.90	5.91	5.79	6.13	6.55
SERINE	6.13	7.51	6.77	6.83	7.08	5.98	6.06	6.34	6.53	7.28
ASPARAGINE	3.45	4.08	3.52	4.51	5.40	4.21	5.31	4.29	5.95	4.14
GLUTAMINE	45.65	46.10	45.1	48.1	41.3	43.6	40.2	42.4	46.5	50.9
GLUTAMATE	0.94	.58	1.27	.93	1.26	1.04	2.09	1.76	1.47	1.82
PROLINE	10.5	12.8	12.3	11.8	10.91	10.2	12.17	14.1	12.43	11.01
CITRULLINE	0.20	.83	0.49	0.67	.67	.37	0.25	0.40	0.24	0.58
GLYCINE	11.5	13.3	11.8	12.2	12.4	11.8	11.27	12.08	13.68	14.13
ALANINE	23.9	28.5	27.0	26.7	25.9	24.6	26.2	29.3	29.6	26.0
α -AMINO BUT.	2.60	3.10	2.99	2.83	2.80	2.28	2.50	2.41	2.31	2.16
VALINE	18.1	19.8	18.1	17.3	16.9	14.7	13.94	13.2	13.03	14.38
L-CYSTINE	7.71	7.61	7.35	6.56	7.98	6.64	7.30	7.27	6.47	8.40
METHIONINE	1.25	1.43	1.18	1.19	1.48	0.80	0.80	0.85	0.49	1.53
ISOLEUCINE	4.40	5.19	4.40	4.05	4.55	3.81	3.71	3.00	3.00	4.45
LEUCINE	10.33	10.30	8.70	8.26	9.00	6.75	6.18	6.10	6.60	9.22
TYROSINE	1.75	1.75	1.73	1.66	1.86	1.86	1.78	1.59	1.55	2.11
PHENYLALANINE	3.12	3.92	4.43	3.98	3.84	3.81	4.77	3.63	3.91	2.78
ORNITHINE	3.127	3.39	3.41	3.16	3.91	2.91	2.14	2.64	2.17	2.11
LYSINE	11.01	12.3	10.46	10.8	11.60	8.41	9.78	10.4	10.33	10.16
HISTIDINE	6.26	6.33	6.14	6.56	6.37	6.01	6.03	6.12	6.66	6.17
ARGININE	5.37	6.46	6.22	6.67	5.67	5.67	5.52	6.10	5.50	6.00

KOCH-PRU HETEROZYGOSE STUDY

ERYTHROCYTE AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH INCREASING TIME (umoles/100 gm RBC)

SUBJECT Les KOCH DOSE OF ASPARTAKE ADMINISTERED 34 mg/kg

AMINO ACID	0 time	15 min	30 min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
PHOSP.-SERINE	14.57	31.51	20.10	20.13	15.26	15.60	19.15	15.68	14.62	19.27
TAURINE	11.22	12.52	15.61	19.47	17.90	18.23	23.08	18.11	12.81	31.81
ASPARTATE	28.02	29.08	29.67	28.99	25.35	24.21	23.39	27.01	27.25	27.70
THREONINE	6.12	11.29	7.97	6.69	4.73	5.99	5.51	5.09	4.20	5.27
SERINE	9.72	11.60	8.59	9.89	1.11	7.25	8.05	8.24	8.36	8.58
ASPARAGINE	12.51	15.82	10.59	13.71	11.18	12.11	11.34	10.59	13.28	12.81
GLUTAMINE	45.64	42.76	45.49	52.32	10.15	51.01	49.93	48.33	46.23	45.99
GLUTAMATE	24.01	22.14	24.88	25.18	22.89	24.59	27.00	25.59	25.41	28.64
PROLINE	7.20	8.05	8.54	8.93	1.85	5.45	6.59	10.11	14.81	7.88
GLYCINE	23.03	22.14	23.45	24.88	24.27	23.98	24.11	24.27	25.51	25.38
ALANINE	24.21	22.10	22.40	25.13	23.89	25.11	24.45	24.28	24.92	26.41
α -AMINO BUT.	1.70	1.37	1.69	1.77	1.85	1.18	0.70	1.22	1.41	1.31
VALINE	17.34	18.64	11.17	12.08	19.05	19.11	10.45	10.69	11.49	9.03
$\frac{1}{2}$ CYSTINE	-	-	-	-	-	-	-	-	-	-
METHIONINE	trace	trace	trace	trace	trace	trace	trace	trace	trace	trace
ISOLEUCINE	2.20	3.02	2.26	2.27	1.88	1.55	1.54	1.51	0.88	1.99
LEUCINE	6.63	7.24	6.15	4.88	4.54	4.23	7.15	4.37	4.67	5.33
TYROSINE	3.46	2.66	2.25	3.33	3.02	2.48	3.31	1.83	2.18	2.84
PHENYLALANINE	3.88	4.14	5.93	5.77	4.99	4.39	5.62	4.69	4.29	3.71
ORNITHINE	6.73	6.84	7.21	6.99	5.08	5.55	5.91	4.64	4.58	4.64
LYSINE	11.33	10.87	9.88	10.58	9.57	9.34	9.21	5.66	6.12	8.05
HISTIDINE	7.81	7.43	7.17	7.48	7.51	7.51	7.14	6.99	5.89	5.74
ARGININE	2.32	1.77	2.32	2.37	2.42	2.40	2.01	1.70	2.30	2.08

Sal Steguik
8/25/75

KUCH AND STEGINK COLLABORATIVE STUDY ON ASPARTATE

CONTROL SUBJECT X PKU HETEROZYGOTEPLASMA AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH TIME (μ moles/100 ml)SUBJECT Jill Tovey (J.T.) DATE _____ TEST MATERIAL ADMINISTERED _____

SUBJECT HEIGHT _____ DOSE ADMINISTERED _____ mg/Kg TOTAL (GM) _____

AMINO ACID	0 time	15 min	30min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
TAURINE	3.98	3.36	3.05	3.56	3.57	3.58	3.60	4.01	3.71	3.63
ASPARTATE	0.118	0.121	0.127	0.140	0.130	0.110	0.160	0.16	0.149	0.204
THREONINE	9.67	8.60	8.60	8.51	9.09	7.53	7.34	7.48	7.77	7.42
SERINE	14.65	13.4	13.5	13.7	14.5	12.6	12.4	12.7	12.3	13.1
ASPARAGINE	3.26	5.73	5.71	5.09	5.76	5.43	4.94	5.02	4.27	5.55
GLUTAMINE	54.7	50.9	51.8	55.0	56.7	51.2	42.5	47.1	47.7	51.1
GLUTAMATE	0.56	0.82	0.73	1.06	1.11	1.26	1.41	1.14	1.19	0.83
PROLINE	11.8	11.0	12.4	13.7	14.9	13.4	12.6	14.3	12.5	10.4
CITRULLINE	1.64	1.26	0.81	0.75	0.75	0.62	0.55	0.63	0.40	1.29
GLYCINE	46.1	42.0	39.4	38.9	40.6	37.7	38.6	40.6	41.4	39.1
ALANINE	29.98	27.3	29.6	32.6	36.0	38.0	33.9	36.3	35.9	25.8
α -AMINOBUT.	1.67	1.81	1.77	1.85	1.72	1.67	1.73	1.89	1.65	1.81
VALINE	13.95	12.5	11.5	11.4	11.7	9.40	9.79	9.65	10.11	12.9
D-CYSTINE	1.63	7.31	6.19	6.44	6.47	6.56	6.58	6.47	6.66	7.19
METHIONINE	1.60	1.55	1.35	1.48	1.31	1.01	1.16	1.19	1.32	1.35
ISOLEUCINE	4.06	3.25	3.27	3.10	3.09	2.07	2.19	2.21	2.60	3.88
LEUCINE	8.54	7.17	7.00	6.73	6.62	4.69	5.14	5.12	5.75	8.75
TYROSINE	3.25	2.72	2.82	2.76	3.20	2.81	2.73	2.75	2.73	2.93
PHENYLALANINE	2.97	3.42	5.17	5.96	7.15	5.55	5.21	4.65	3.95	3.56
ORNITHINE	2.77	2.39	2.41	2.62	2.93	3.35	2.39	2.72	2.39	2.74
LYSINE	11.08	10.7	9.80	10.4	10.8	8.62	9.65	9.91	10.44	10.17
HISTIDINE	6.59	6.57	5.94	6.26	6.63	5.38	5.57	5.76	6.19	6.26
ARGININE	5.75	6.03	6.19	6.56	6.39	5.17	5.47	6.14	5.85	5.88

KCOH-FRU HETEROZYGOSE STUDY

ERYTHROCYTE AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH INCREASING TIME (umoles/100 gm RBC)

SUBJECT JILL TOVEY

DOSE OF ASPARTAME ADMINISTERED 34 mg/kg

AMINO ACID	0 time	15 min	30 min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
PHOSP.-SERINE	14.36	45.07	26.13	16.40	10.95	15.40	18.93	18.72	23.14	35.35
TAURINE	12.77	12.49	16.32	21.63	5.91	18.45	15.21	9.49	10.05	11.06
ASPARTATE	26.70	24.50	24.50	32.10	14.96	24.19	23.88	23.23	22.52	25.95
THREONINE	8.75	6.71	6.06	7.10	6.66	6.55	6.01	5.73	5.83	6.28
SERINE	17.59	16.12	16.52	15.46	15.07	16.13	15.78	15.57	14.93	15.41
ASPARAGINE	2.67	11.04	10.09	10.10	0.18	14.44	12.68	12.21	11.62	12.08
GLUTAMINE	44.23	45.94	47.12	46.74	14.48	44.55	45.68	45.37	45.21	46.57
GLUTARATE	29.94	31.14	29.37	31.37	27.34	29.79	30.25	29.60	31.43	29.30
PROLINE	10.02	9.06	12.16	9.09	1.48	12.19	11.33	12.40	8.70	8.00
GLYCINE	49.29	47.41	48.00	47.67	43.54	47.08	48.22	47.43	47.71	48.43
ALANINE	23.55	22.79	25.28	25.19	23.73	24.72	25.24	23.72	24.03	22.23
α-AMINOBUT.	1.02	1.17	1.06	0.98	1.07	0.88	1.00	0.68	0.92	0.83
VALINE	10.92	10.45	9.36	9.08	1.96	7.55	8.98	9.68	9.43	10.75
γ-CYSTINE	-	-	-	-	-	-	-	-	-	-
METHIONINE	trace	trace	trace	trace	trace	trace	trace	trace	trace	trace
ISOLEUCINE	2.19	2.06	1.94	1.71	1.78	1.22	1.31	1.39	1.89	2.79
LEUCINE	5.52	5.21	5.14	4.64	1.75	3.47	3.98	3.91	4.20	6.10
TYROSINE	3.94	2.06	4.13	3.38	1.55	4.49	4.55	4.56	4.29	4.37
PHENYLALANINE	3.63	2.66	5.72	5.25	1.93	6.60	5.98	5.70	5.55	4.54
GUANINE	4.31	4.54	5.01	4.65	1.68	6.29	6.31	6.37	6.48	6.07
LYSINE	7.62	7.83	7.71	7.29	10.33	10.35	10.32	10.16	9.97	10.82
HISTIDINE	5.18	5.20	5.53	5.17	1.90	7.37	7.32	7.03	7.07	6.76
ARGININE	2.51	2.23	2.67	2.85	1.21	3.32	3.10	3.02	3.27	3.16

Lab Stego
8/15/78

KCOI AND STEGINK COLLABORATIVE STUDY ON ASPARTAME

CONTROL SUBJECT X PKU HETEROZYGOTEPLASMA AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH TIME (μ moles/100 ml)SUBJECT Kathy Shaw (K.S.)

DATE _____

TEST MATERIAL ADMINISTERED _____

SUBJECT WEIGHT _____

DOSE ADMINISTERED _____

mg/Kg

TOTAL (G/L)

AMINO ACID	0 time	15 min	30min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
TAURINE	2.43	2.13	1.91	2.12	2.31	2.30	2.21	2.02	2.22	3.21
ASPARTATE	0.175	0.161	0.128	0.117	0.180	0.180	0.113	0.105	0.111	0.090
THREONINE	8.16	8.61	8.53	9.48	9.94	10.4	9.81	8.96	9.52	9.25
SERINE	7.40	7.49	7.37	8.23	8.93	9.44	8.25	7.93	9.05	8.35
ASPARAGINE	6.75	4.61	5.80	4.28	4.40	5.92	4.69	5.96	4.68	4.30
GLUTAMINE	50.97	53.14	54.6	60.5	61.1	62.2	58.82	57.58	48.1	52.6
GLUTAMATE	2.68	1.00	1.03	0.77	0.98	0.88	0.86	0.57	1.51	1.66
PROLINE	9.87	9.19	12.3	11.2	11.8	12.31	11.47	12.98	16.2	12.15
CITRULLINE	1.54	1.51	1.20	1.18	1.32	1.20	1.26	0.87	0.59	1.16
GLYCINE	11.8	11.4	17.9	11.7	11.99	12.9	12.12	11.02	11.67	12.27
ALANINE	29.1	31.4	31.9	35.4	35.8	41.6	39.65	37.5	40.4	33.6
α -AMINOBUT.	0.33	0.59	0.33	0.35	0.32	0.54	0.38	0.43	0.53	0.36
VALINE	8.71	8.50	8.46	8.71	8.52	9.11	8.29	7.83	7.85	9.11
L-CYSTINE	9.01	6.31	6.27	6.35	6.48	6.49	6.22	6.76	6.75	7.84
HOMOTYROSINE	1.40	1.30	1.35	1.54	1.65	1.51	1.51	1.57	1.47	1.60
ISOLEUCINE	3.57	3.39	3.38	3.44	3.34	3.70	3.23	2.97	2.91	3.22
LEUCINE	5.67	5.81	5.62	5.95	5.89	6.30	5.62	5.36	5.14	6.81
TYROSINE	2.13	1.60	1.46	1.69	2.85	2.07	2.04	2.04	2.71	2.26
PHENYLALANINE	2.58	2.59	3.12	3.62	5.90	5.15	4.48	4.48	4.73	3.07
ORNITHINE	2.05	1.57	1.23	1.43	2.21	2.21	1.97	1.96	1.96	1.97
LYSINE	7.83	8.07	7.22	8.37	8.45	9.00	7.85	7.85	8.51	7.72
HISTIDINE	6.92	6.57	6.22	6.76	7.23	7.68	6.20	6.20	7.49	6.74
ARGININE	6.95	6.46	7.60	8.24	8.68	8.48	8.39	8.39	9.00	8.75

KOCH-PRU HETEROZYGOTE STUDY

ERYTHROCYTE AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH INCREASING TIME (umoles/100 gm RBC)

SUBJECT K. SHAN

DOSE OF ASPARTAME ADMINISTERED 34 mg/kg

AMINO ACID	0 time	15 min	30 min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
PHOSP.-SERINE	29.43	37.41	26.82	18.71	18.35	17.61	17.01	18.06	18.07	26.39
TAURINE	21.77	17.25	31.7	15.54	11.38	14.04	20.20	10.91	13.91	22.50
ASPARTATE	16.14	17.67	16.09	15.73	11.67	14.92	15.25	15.19	13.95	14.40
THREONINE	7.34	7.20	6.62	5.97	5.99	5.85	6.38	6.56	6.50	7.24
SERINE	10.08	9.81	9.63	9.77	9.67	9.66	9.43	9.61	9.16	9.41
ASPARAGINE	11.66	10.73	12.42	11.51	11.64	13.10	10.98	12.48	11.58	12.48
GLUTAMINE	44.69	42.72	45.18	41.63	41.81	45.73	43.39	41.94	42.90	44.74
GLUTAMATE	25.49	22.84	24.17	23.08	21.17	23.19	21.19	21.31	21.71	28.78
PROLINE	9.84	6.81	7.55	7.99	8.78	8.69	6.88	8.85	9.32	8.67
GLYCINE	25.15	25.99	24.68	24.77	23.87	22.06	24.51	26.61	25.21	22.16
ALANINE	24.71	25.17	24.51	25.39	26.55	27.25	27.72	27.35	25.31	25.87
α -AMINO BUT.	0.28	0.27	0.24	0.31	0.24	0.23	0.41	0.34	0.45	0.22
VALINE	8.36	8.32	7.79	6.93	6.60	5.10	8.87	9.77	8.31	9.05
γ -CYSTINE	-	-	-	-	-	-	-	-	-	-
METHIONINE	trace	trace	trace	trace	trace	trace	trace	trace	trace	trace
ISOLEUCINE	1.71	1.76	1.73	1.55	1.48	1.59	1.22	1.81	1.81	2.31
LEUCINE	4.21	4.03	4.50	3.75	3.56	3.87	3.72	3.95	3.82	4.42
TYROSINE	1.65	1.69	1.67	1.77	1.93	3.27	3.23	3.09	3.50	3.57
PHENYLALANINE	2.64	2.52	2.02	3.29	2.79	5.41	5.33	5.15	5.19	4.62
ORNITHINE	5.08	4.55	4.99	4.52	4.29	6.58	6.39	5.88	7.06	6.16
LYSINE	6.39	5.60	6.28	5.91	6.69	7.15	7.54	7.64	7.42	7.57
HISTIDINE	5.35	5.18	5.70	4.76	4.53	3.31	6.75	6.43	6.79	6.31
ARGININE	2.91	2.83	3.38	2.65	3.03	4.48	3.93	4.17	4.49	4.37

L.H. Stegink
8/25/75

KOL AND SIEGLIK COLLOIDATIVE STUDY OF ASPARTATE

CONTROL SUBJECT

PKU HETEROZYOTE ☒

PLASMA AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH TIME (μmoles/100 ml)

SUBJECT Carol Cusimano (CC) DATE

TEST MATERIAL ADMINISTERED

SUBJECT HEIGHT

DOSE ADMINISTERED

mg/kg

TOTAL (Gm)

AMINO ACID	0 time	15 min	30 min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
ALANINE	2.45	2.63	2.64	2.52	2.61	2.86	2.63	2.67	2.72	2.29
ASPARAGINE	6.105	6.125	6.320	6.150	6.163	6.175	6.161	6.154	6.104	6.131
THREONINE	17.7	18.1	19.2	17.3	16.5	15.2	14.7	15.0	14.3	14.0
SERINE	7.20	7.64	8.24	7.79	7.75	7.12	7.01	7.64	7.19	7.36
ASPARTATE	3.44	7.14	8.92	3.60	6.44	7.00	7.06	6.44	5.25	5.12
GLUTAMINE	56.9	46.0	49.7	47.5	46.8	55	7.3	47.9	46.0	50.6
GLUTAMATE	1.37	1.50	1.50	2.54	2.08	2.7	3.03	2.40	2.80	2.12
PROLINE	14.6	14.3	16.7	16.0	14.5	13.0	12.5	13.2	12.6	10.9
CITRULLINE	1.30	0.37	0.55	0.34	0.30	0.46	0.54	0.41	0.37	1.04
GLYCINE	16.6	12.5	18.6	12.5	16.99	16.9	12.8	17.3	17.3	15.4
ACETINE	33.3	34.8	44.4	48.5	47.7	42.1	33.3	44.0	43.0	34.0
α-KETOGLUT.	1.56	1.60	1.75	1.33	1.13	1.42	1.54	1.26	1.61	2.30
VALINE	32.7	31.5	31.3	19.6	11.2	17.5	17.5	17.1	16.4	22.5
L-CYSTINE	8.24	8.21	8.95	8.99	8.56	9.50	4.21	8.85	8.70	4.24
METHIONINE	2.33	1.95	1.82	1.84	1.19	1.57	1.55	1.43	1.46	3.12
ISOLEUCINE	5.77	5.47	5.15	4.44	3.80	3.41	3.25	2.64	3.25	5.27
LEUCINE	12.0	11.4	10.6	9.30	8.42	7.57	8.15	7.70	8.03	16.0
THIOSERINE	3.75	2.42	2.31	2.15	2.11	2.06	2.07	2.00	1.50	7.25
PANTOTHENIC	4.11	7.37	13.5	10.3	9.70	5.45	7.91	6.31	5.15	5.67
CARBOXYL	2.35	2.17	2.71	2.15	2.43	2.67	3.25	3.21	4.03	5.07
LYSINE	14.6	13.6	17.5	17.8	17.4	17.1	17.2	16.99	16.3	12.5
HISTIDINE	9.10	4.23	9.26	2.71	5.23	5.08	4.73	5.07	5.24	7.03
AMMONIA	7.15	16.5	11.1	5.90	9.11	5.97	7.50	5.70	5.11	5.01

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KOCH-PKU HETEROZYGOTE STUDY
ERYTHROCYTE AMINO ACID LEVELS OBSERVED IN SEARLE SUBJECTS STUDIED WITH INCREASING TIME (umoles/100 gm RBC)

SUBJECT CUSA 19A10 DOSE OF ASPARTAME ADMINISTERED 34 mg/kg

	0 time	15 min	30 min	45 min	60 min	90 min	2 hr	3 hr	4 hr	8 hr
ALANINE										
PROSP-SERINE	13.07	19.13	14.07	11.40	13.24	14.59	13.03	13.84	17.55	16.37
THAONINE	13.77	15.07	20.25	17.33	12.24	19.04	14.63	9.03	11.72	41.91
ASPARTATE	20.31	18.51	18.55	18.15	13.34	24.87	16.30	18.15	17.95	17.32
TYROSINE	14.03	13.75	14.78	13.68	13.43	15.17	10.90	11.47	11.46	10.22
GLUTAMINE	12.96	9.57	9.21	9.06	9.13	10.73	9.96	8.43	8.19	3.22
ASPARTOGLUTAMINE	10.95	9.50	10.81	8.35	9.21	9.61	13.42	10.43	10.74	9.35
GLUTAMATE	46.70	45.64	41.81	40.66	41.01	39.08	39.46	39.57	41.69	43.46
GLUTAMATE	29.01	21.23	20.97	16.04	6.23	20.43	21.70	20.64	20.56	20.74
PROLINE	10.45	10.56	10.48	11.41	11.63	12.59	8.05	10.46	9.05	7.73
GLYCINE	23.26	21.75	30.63	29.25	24.61	23.75	24.95	24.51	25.74	26.55
VALINE	23.23	21.75	24.20	24.69	25.06	24.33	22.54	25.22	25.79	26.78
α-AMINOISOBUT.	0.61	0.94	0.92	1.05	0.99	1.10	0.83	0.98	0.86	1.10
VALINE	18.12	16.98	16.15	15.17	14.22	16.33	10.57	12.77	12.93	16.38
β-CYSTINE	-	-	-	-	-	-	-	-	-	-
PETHIOGLUTAMINE	trace	trace	trace	trace	trace	trace	trace	trace	trace	trace
ISOLEUCINE	4.16	3.76	3.25	2.76	2.36	2.50	2.31	2.08	2.26	4.54
LEUCINE	9.16	8.54	7.51	6.53	5.70	6.30	5.40	5.10	5.42	10.27
TYROSINE	4.15	3.77	3.73	2.92	2.93	2.68	2.85	2.44	2.35	2.72
GLUTAMYLGLUTAMINE	4.22	6.08	7.96	9.07	1.60	9.37	6.61	5.63	4.81	7.39
GLUTAMINE	12.91	15.90	11.97	12.23	12.27	14.94	12.13	13.16	12.04	7.93
LYSINE	13.35	11.56	12.62	11.90	11.42	14.61	11.29	11.58	11.79	11.35
HISTIDINE	9.21	7.87	8.92	6.60	4.13	10.41	7.80	8.23	8.05	7.93
ASPARTATE	2.93	2.09	2.77	2.78	2.45	3.10	1.26	1.67	1.33	1.65

MEP-77-06-055

APR 11 24, 1978

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SEP 26 1975

PLASMA PHENYLALANINE AND TYROSINE LEVELS IN NORMAL SUBJECTS AND PKU HETEROZYGOTES
ADMINISTERED ASPARTAME AT 34 MG/KG BODY WEIGHT (KOOH--STEGINK COLLABORATIVE PROJECT)

$\text{Phenylalanine (mg/dl)} \times 0.155 = \text{PA mg \%}$ -- PHENYLALANINE (umoles/dl; Mean \pm Std. Deviat.)

TIME POINT MIN	mg %	NORMAL SUBJECTS	PKU HETEROZYGOTES	t	p
0	.459	2.78 \pm 0.32	7.66 4.29 \pm 0.79	3.584	0.01
15	.579	3.51 \pm 0.68	1.26 7.76 \pm 3.28	2.535	0.05
30	.716	4.34 \pm 0.87	1.96 12.0 \pm 4.29	3.503	0.01
45	.785	4.76 \pm 1.13	2.56 13.8 \pm 7.07	2.539	0.05
60	.927	5.62 \pm 1.36	1.90 11.5 \pm 2.85	3.707	0.01
90	.799	4.84 \pm 0.74	1.67 10.1 \pm 2.20	4.551	0.005
120	.790	4.79 \pm 0.32	1.57 9.53 \pm 2.48	3.793	0.01
180	.708	4.29 \pm 0.45	1.32 3.00 \pm 2.53	2.891	0.05
240	.685	4.15 \pm 0.39	1.08 6.56 \pm 1.56	3.00	0.03
480	.521	3.16 \pm 0.33	.86 5.24 \pm 1.59	2.689	0.05

$\text{Tyrosine (mg/dl)} \times 0.191 = \text{mg \%}$ TYROSINE (umoles/dl; Mean \pm Std. Dev.)

TIME	mg %	NORMAL SUBJECTS	PKU HETEROZYGOTES	t	p
0	.503	2.78 \pm 1.02	.471 2.60 \pm 1.32	0.212	
15	.453	2.50 \pm 1.07	.485 2.68 \pm 1.98	0.159	
30	.409	2.26 \pm 0.78	.414 2.29 \pm 2.68	0.346	
45	.440	2.43 \pm 0.89	.471 2.60 \pm 2.29	0.134	
60	.509	2.81 \pm 0.67	.451 2.49 \pm 2.30	0.266	
90	.438	2.42 \pm 0.53	.319 1.76 \pm 0.94	1.233	
120	.422	2.33 \pm 0.50	.329 1.82 \pm 0.86	1.011	
180	.409	2.26 \pm 0.54	.657 3.63 \pm 2.18	1.212	
240	.429	2.37 \pm 0.56	.322 1.78 \pm 0.56	1.474	0.20
480	.413	2.45 \pm 0.36	.414 2.29 \pm 0.97	0.304	

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April 24, 1975

MED-77-05-055

April 24, 1975

GLUTAMINE
TIME (Min).

$\mu\text{moles/dl}$

	NORMAL	PKU HETEROZYGOSES	t	P
0	51.53 \pm 4.31	54.11 \pm 2.58	1.027	
15	52.19 \pm 5.19	48.25 \pm 2.60	1.354	
30	52.83 \pm 6.12	50.96 \pm 4.97	0.472	
45	55.65 \pm 5.54	51.33 \pm 4.49	1.212	
60	55.38 \pm 6.25	52.80 \pm 7.11	0.540	
90	53.85 \pm 8.22	50.54 \pm 5.00	0.670	
120	48.65 \pm 7.67	49.31 \pm 2.95	0.162	
180	50.72 \pm 6.36	48.17 \pm 4.84	0.638	
240	48.65 \pm 2.30	44.50 \pm 2.41	2.491	0.05
480	52.58 \pm 2.22	40.49 \pm 1.69	1.492	

GLUTAMATE

0	1.20 \pm 1.00	0.84 \pm 0.51	0.639	
15	0.79 \pm 0.17	1.56 \pm 0.19	5.966	0.001
30	1.23 \pm 0.49	2.64 \pm 0.96	2.621	0.05
45	1.13 \pm 0.43	2.64 \pm 1.23	2.310	0.05
60	1.51 \pm 0.72	2.16 \pm 1.26	0.899	
90	1.25 \pm 0.41	2.78 \pm 1.27	2.298	0.05
120	1.67 \pm 0.67	2.95 \pm 1.75	1.367	
180	1.36 \pm 0.63	2.67 \pm 2.42	1.047	
240	1.55 \pm 0.34	2.03 \pm 0.56	1.429	
480	1.33 \pm 0.49	2.04 \pm 0.19	2.721	0.05

ASPARAGINE

0	5.15 \pm 2.09	6.22 \pm 2.29	0.683	
15	5.47 \pm 1.50	7.18 \pm 2.31	1.242	
30	5.06 \pm 1.06	6.76 \pm 2.19	1.400	
45	4.59 \pm 1.39	7.03 \pm 1.72	2.212	
60	6.00 \pm 1.73	6.54 \pm 0.38	0.615	
90	5.57 \pm 1.05	5.27 \pm 1.58	0.321	
120	5.56 \pm 1.18	5.80 \pm 1.89	0.217	
180	5.48 \pm 1.03	5.38 \pm 2.53	0.069	
240	5.94 \pm 2.07	6.40 \pm 2.39	0.290	
480	5.36 \pm 1.53	5.19 \pm 1.93	0.129	

ASPARTATE

0	0.12 \pm 0.042	0.097 \pm 0.013	0.789	
15	0.13 \pm 0.037	0.14 \pm 0.049	0.602	
30	0.13 \pm 0.032	0.15 \pm 0.033	0.614	
45	0.12 \pm 0.016	0.12 \pm 0.020	0.297	
60	0.15 \pm 0.025	0.12 \pm 0.032	1.075	
90	0.12 \pm 0.043	0.17 \pm 0.049	1.485	
120	0.16 \pm 0.076	0.16 \pm 0.010	0.045	
180	0.12 \pm 0.042	0.24 \pm 0.179	1.382	
240	0.11 \pm 0.037	0.10 \pm 0.004	0.078	
480	0.11 \pm 0.069	0.13 \pm 0.038	0.369	

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Appendix 2

Blaskovics Study

Plasma Amino Acids

Repeat Loading of Normal Volunteers

From 34 mg/Kg Aspartame PKU

Heterozygote Loading Study

REPEAT ANALYSES OF THE NORMAL CONTROL SUBJECTS USED IN CALIFORNIA EXPERIMENT
 PLASMA AMINO ACID LEVELS (umoles/100 ml)
 SUBJECT LES KOCH DATE 9-18-76 TEST MATERIAL ADMINISTERED ASPARTAME
 SUBJECT WEIGHT DOSE ADMINISTERED 31 mg/kg TOTAL (G4)

AMINO ACID	0 time	15 min	30 min	45 min	1 hr	1 1/2 hr	2 hr	3 hr	4 hr	8 hr
ASPARTAME	5.74	3.94	3.90	4.46	4.40	4.29	3.62	3.40	3.70	3.50
THREONINE	0.23	0.15	0.15	0.11	0.20	0.16	0.16	0.19	0.22	0.14
SERINE	8.66	7.89	3.30	9.82	9.44	9.23	7.83	7.82	0.06	7.03
ASPARAGINE	11.7	9.69	10.8	11.3	11.0	11.1	9.74	9.49	9.96	9.65
GLUTAMINE	5.05	5.26	9.00	9.13	9.92	4.59	7.25	4.60	3.77	5.53
GLUTAMATE	53.3	49.1	52.3	53.5	47.5	57.6	44.1	48.5	52.7	45.2
PROLINE	1.71	0.97	1.31	1.53	1.50	1.89	1.82	1.14	1.86	2.11
CITRULLINE	16.2	16.6	20.8	21.1	21.1	20.1	17.2	16.2	16.6	12.9
GLYCINE	2.83	1.71	2.35	2.51	2.52	2.47	2.46	1.65	2.56	2.78
ALANINE	27.4	23.8	26.3	29.3	21.4	29.1	25.6	25.8	26.5	22.8
α-AMINOAC.	37.9	34.2	38.9	41.6	51.6	56.2	34.7	36.5	35.3	22.0
VALINE	1.13	0.90	1.22	1.36	1.19	1.18	1.04	1.02	1.02	1.19
α-CYSTINE	16.5	13.9	14.7	15.9	11.8	15.3	13.3	13.5	13.9	13.7
METHIONINE	9.71	6.83	7.25	7.58	7.37	7.65	6.02	6.64	6.88	8.42
ISOLEUCINE	2.63	2.33	2.39	2.40	1.93	2.39	2.19	2.22	2.31	2.01
LEUCINE	4.72	4.18	4.37	4.67	4.26	4.34	3.61	3.73	3.92	3.73
TYROSINE	8.63	7.78	8.15	8.94	8.56	8.51	7.35	7.73	8.27	8.34
PHENYLALANINE	4.60	4.62	5.40	5.77	5.59	5.60	5.11	5.15	5.35	4.64
CARNTINE	4.71	6.64	7.80	8.09	7.54	7.39	6.66	6.83	6.80	5.09
LYSINE	7.24	5.44	5.59	5.75	5.47	5.72	5.10	4.99	5.02	4.21
HISTIDINE	18.6	11.6	12.6	13.5	11.1	13.2	11.9	12.4	13.0	11.2
ARGININE	6.77	6.52	7.49	8.12	7.75	7.76	6.97	7.03	7.19	6.74
	7.58	9.44	11.5	11.5	11.7	10.2	8.99	9.32	9.46	8.95

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PLASMA AMINO ACID ANALYSES (umoles/l)
REPEAT ANALYSES OF NORMAL CONTROLS FOR CALIFORNIA PKU EXPERIMENT

SUBJECT KATHY SIAM DATE 9-16-76 TEST MATERIAL ADMINISTERED ASPARTAME
SUBJECT WEIGHT 34 DOSE ADMINISTERED 34 mg/kg TOTAL (gm)

AMINO ACID	0 time	15 min	30 min	45 min	1 hr	1 1/2 hr	2 hr	2 1/2 hr	3 hr	4 hr	8 hr
THANOLINE	3.19	2.80	3.09	3.25	3.32	3.48	3.54	4.28	3.24	4.10	3.23
ASPARTAME	0.10	0.13	0.12	0.14	0.15	0.16	0.16	0.27	0.28	0.35	0.35
THANOLINE	8.23	8.65	9.02	9.17	8.80	8.58	8.01	7.96	8.38	8.30	9.46
SERINE	4.68	4.89	5.18	5.35	5.23	5.20	4.89	4.92	5.21	5.56	6.20
ASPARTAME	2.61	2.82	3.39	2.53	3.20	3.30	3.40	3.01	3.41	2.23	4.31
GLUTAMINE	29.6	31.7	30.0	30.0	30.1	28.3	26.6	25.9	26.5	32.7	35.1
GLUTAMATE	1.21	0.82	0.84	0.99	1.52	2.86	3.12	2.86	3.15	3.00	1.85
PROLINE	8.31	9.04	9.11	9.79	10.2	10.9	11.2	10.3	10.2	9.30	8.30
CITRULLINE	1.57	1.26	1.32	1.47	1.48	1.38	0.86	1.09	1.46	1.67	2.05
GLYCINE	7.98	8.09	8.32	8.14	7.44	6.96	6.61	6.38	7.34	7.42	8.55
ALANINE	13.9	15.3	16.6	17.1	16.4	17.5	18.2	17.0	15.3	13.2	13.6
α-AMINO BUT.	0.16	0.43	0.15	0.40	0.56	0.19	0.47	0.49	0.44	0.46	0.67
VALINE	10.4	10.7	11.2	11.1	11.2	10.6	10.5	9.56	10.7	11.2	11.8
L-CYSTINE	5.64	5.62	6.12	6.13	6.36	7.02	6.75	6.68	7.15	6.97	6.10
ETHIONINE	1.33	1.53	1.65	1.59	1.57	1.33	1.12	1.13	1.18	1.34	1.02
ISOLEUCINE	2.30	2.42	2.49	2.49	2.30	1.85	1.49	1.35	1.39	1.59	1.95
LEUCINE	6.41	7.23	7.54	7.62	7.37	6.70	5.90	5.78	6.53	7.41	8.49
THYROSINE	2.52	2.91	2.92	2.96	3.23	3.42	3.55	3.46	3.72	3.44	3.3
PHENYLALANINE	3.11	4.16	4.30	4.64	5.77	6.70	7.17	6.53	6.36	5.13	4.5
CITRULLINE	1.18	1.17	1.18	1.33	1.37	1.46	1.46	1.48	1.47	1.45	1
LYSINE	9.69	10.0	10.0	10.0	10.7	9.38	8.53	8.94	9.60	9.17	9.17
HISTIDINE	5.76	5.61	5.55	6.07	6.19	5.74	4.85	5.77	6.23	6.34	6.34
ASPARTAME	4.85	5.11	4.56	5.03	4.98	4.48	4.27	3.86	4.11	4.23	4.23

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PLASMA AMINO ACID LEVELS (umoles/100 ml)
 REPEAT ANALYSES OF NORMAL CONTROL SUBJECTS USED IN CALIFORNIA PKU EXPERIMENT (150)PY

SUBJECT Jill Tovey DATE 9/14/76 TEST MATERIAL ADMINISTERED APH-34
 SUBJECT WEIGHT DOSE ADMINISTERED 34 mg/kg TOTAL (G:)

AMINO ACID	0 time	15 min	30 min	45 min	1 hr	1 1/2 hr	2 hr	3 hr	4 hr	8 hr
TAURINE	4.47	4.31	4.23	4.88	4.31	3.73	3.77	3.48	3.41	3.26
ASPARAGATE	0.39	0.36	0.41	0.45	0.46	0.41	0.38	0.38	0.47	0.43
THREONINE	13.66	12.88	13.13	14.06	14.10	12.59	13.04	12.16	11.84	9.86
SERINE	15.30	14.62	15.20	16.77	17.17	14.96	15.53	14.66	15.02	13.98
ACETAMINE	5.89	4.57	5.43	6.63	6.63	4.76	4.76	4.67	4.38	4.86
GLUTAMINE	45.39	42.98	44.32	45.15	53.04	45.42	48.68	47.34	45.37	44.75
GLUTARATE	1.07	1.12	1.29	2.31	2.41	1.11	1.29	1.08	1.31	1.54
PROLINE	15.57	15.62	16.92	19.83	22.01	17.00	18.14	16.39	14.79	12.25
CITRULLINE	0.62	0.57	0.43	0.44	1.43	0.87	0.88	0.97	1.29	2.30
GLYCINE	52.07	47.51	49.05	51.40	52.01	41.47	47.27	48.04	42.63	40.94
ALANINE	22.51	22.13	24.17	28.07	31.12	28.32	29.55	26.75	21.74	13.14
α-AMINO BUT.	2.92	2.76	2.85	3.20	3.30	2.80	3.00	2.92	3.07	2.98
VALINE	16.92	15.89	15.92	16.53	16.12	12.76	13.30	13.16	12.97	13.31
γ-CYSTINE	9.09	8.78	9.26	9.80	9.81	8.27	8.77	8.35	8.64	8.29
METHIONINE	2.68	2.52	2.62	2.64	2.62	2.30	2.27	2.10	1.77	1.70
ISOLEUCINE	5.14	4.81	4.71	4.63	4.5	3.37	3.43	3.58	3.37	4.16
LEUCINE	9.78	9.28	9.08	8.79	8.44	6.91	7.05	7.29	7.26	8.81
TYROSINE	4.11	4.21	4.59	5.29	5.34	4.26	4.67	4.62	4.49	3.77
PHENYLALANINE	3.95	4.97	6.13	8.03	8.50	6.66	7.28	6.42	5.74	4.19
GLUTAMIC	4.24	4.16	4.33	4.43	4.81	4.35	4.43	4.19	4.61	2.88
LYSINE	15.33	15.78	15.84	16.00	17.10	15.17	15.80	15.56	15.24	13.44
PICTICAC	5.63	5.45	5.38	5.74	5.77	4.67	5.02	4.08	5.55	5.31
PROLINE	5.79	6.08	6.75	7.30	9.18	6.03	6.11	5.96	5.65	6.34

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PLASMA AMINO ACID ANALYSES (umols/dl)

REPEAT ANALYSES OF NORMAL CONTROL SUBJECTS USED IN CALIFORNIA EXPERIMENT

(COPY)

SUBJECT Chris Koch DATE 9-18-76 TEST MATERIAL ADMINISTERED APN
 SUBJECT WEIGHT DOSE ADMINISTERED 3' mg/kg TOTAL (G:)

AMINO ACID	0 time	15 min	30 min	45 min	10 min	90 min	2 hr	3 hr	4 hr	8 hr
ALANINE	3.78	3.82	3.45	3.87	4.24	4.64	4.62	4.16	4.07	3.65
ASPARAGINE	0.31	0.37	0.36	0.30	0.42	0.41	0.39	0.38	0.41	0.31
THREONINE	6.43	6.99	7.21	7.53	6.23	8.16	7.91	8.16	7.66	6.42
SERINE	8.04	8.83	8.74	9.06	8.72	9.61	9.47	9.63	10.16	9.53
ASPARAGINE	6.69	7.66	6.41	7.63	8.26	9.02	7.43	6.61	7.02	4.72
GLUTAMINE	46.63	48.82	51.18	51.72	40.63	50.46	50.72	51.20	53.31	44.50
GLUTAMATE	0.91	1.07	0.63	0.93	1.42	1.63	1.75	1.71	1.74	1.53
PROLINE	16.41	18.26	20.87	21.90	13.27	24.33	22.25	22.03	20.69	15.35
CITRULLINE	1.93	2.04	1.41	1.49	1.35	1.81	1.61	1.69	2.09	1.95
GLYCINE	25.04	26.42	24.34	25.60	17.66	29.69	29.56	30.33	30.60	24.76
ALANINE	19.15	20.64	23.41	25.59	17.91	29.02	29.37	29.34	27.94	16.82
4-AMINOACET.	1.19	1.39	0.89	1.29	1.26	1.42	1.26	1.12	1.14	1.19
VALINE	13.40	14.47	13.12	13.85	14.07	14.26	14.83	15.25	15.47	13.90
2-CRISTINE	6.65	7.04	6.02	6.31	6.03	6.99	6.97	7.95	7.30	7.39
2-THIOGLICINE	2.41	2.31	2.76	2.83	1.96	2.91	3.31	3.18	3.45	2.77
ISOLEUCINE	3.99	4.37	4.09	4.17	4.26	4.19	4.21	4.42	4.40	3.55
LEUCINE	9.62	9.70	9.33	9.59	8.57	9.72	10.01	10.57	10.69	9.65
THIOSINE	4.40	4.31	5.51	5.64	4.40	6.55	6.71	7.01	7.18	5.24
PHENYLALANINE	4.43	5.31	7.29	7.53	8.36	7.99	7.43	8.13	7.34	5.17
CITRULLINE	3.77	4.16	3.29	3.38	3.56	3.41	3.65	3.63	3.67	2.88
LEUCINE	13.31	15.69	13.60	13.24	6.65	13.95	14.62	15.46	15.95	14.41
HISTIDINE	7.44	8.12	6.90	6.84	6.61	7.31	7.37	7.57	7.67	6.83
PROLINE	0.25	9.98	10.01	10.34	0.43	9.71	9.32	9.56	9.43	5.21

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MED-77-06-055

April 24, 1978

Plasma Amino Acid Levels μ moles/dl
in
Normal Subjects Administered ASPARTAME at
34 mg/kg Body Weight
(Repeat Loading Under the Direction of Dr. M. Blaskovics)

	0	15 min.	30 min.	45 min.	60 min.	90 min.	2 hr.	3 hr.	4 hr.	8 hr.
<u>Phenylalanine</u>										
Chris Koch	4.48	5.31	7.29	7.53	8.36	7.99	7.38	8.10	7.84	5.17
Les Koch	4.71	6.64	7.80	8.09	7.54	7.39	6.66	6.83	6.20	5.09
Kathy Shaw	3.11	4.16	4.30	4.64	5.77	6.70	7.17	6.36	5.13	4.06
Jill Tovey	3.95	4.97	6.13	8.03	8.51	6.66	7.23	6.42	5.74	4.19
Mean	4.06	5.27	6.38	7.07	7.55	7.19	7.1	6.95	6.39	4.75
Std. Dev.	0.71	1.03	1.55	1.64	1.26	0.63	0.35	0.65	1.19	0.65
S.E.M.	0.36	0.52	0.78	0.92	0.63	0.32	0.17	0.42	0.60	0.24
<u>Tyrosine</u>										
Chris Koch	4.40	4.81	5.51	5.84	6.40	6.55	6.71	7.01	7.13	5.70
Les Koch	4.60	4.62	5.40	5.77	5.59	5.60	5.11	5.15	5.35	4.64
Kathy Shaw	2.52	2.91	2.92	2.96	3.23	3.42	3.55	3.72	3.44	3.20
Jill Tovey	4.11	4.21	4.59	5.29	5.34	4.26	4.67	4.62	4.49	3.77
Mean	3.91	4.14	4.61	4.97	5.14	4.96	5.01	5.13	5.12	4.75
Std. Dev.	0.95	0.86	1.20	1.36	1.35	1.39	1.21	1.39	1.58	0.89
S.E.M.	0.47	0.43	0.60	0.68	0.68	0.70	0.65	0.60	0.79	0.44
<u>Aspartate</u>										
Chris Koch	0.31	0.37	0.36	0.30	0.42	0.41	0.39	0.38	0.41	0.31
Les Koch	0.23	0.15	0.15	0.11	0.20	0.16	0.16	0.19	0.22	0.14
Kathy Shaw	0.10	0.13	0.12	0.14	0.16	0.16	0.16	0.22	0.35	0.35
Jill Tovey	0.39	0.36	0.43	0.45	0.46	0.41	0.38	0.38	0.47	0.43
Mean	0.26	0.27	0.27	0.25	0.31	0.29	0.27	0.31	0.36	0.31
Std. Dev.	0.12	0.16	0.15	0.16	0.15	0.14	0.13	0.00	0.11	0.12
S.E.M.	0.06	0.08	0.03	0.08	0.08	0.07	0.06	0.04	0.05	0.05

MED-77-06-055

April 20, 1978

Plasma Amino Acid Levels μ moles/dl
in
Normal Subjects Administered ASPARTAME at
34 mg/kg Body Weight
(Repeat Loading Under the Direction of Dr. M. Blaskovics)

	0	15 min.	30 min.	45 min.	60 min.	90 min.	2 hr.	3 hr.	4 hr.	8 hr.
<u>Glutamate</u>										
Chris Koch	0.91	1.07	0.63	0.93	1.42	1.63	1.75	1.71	1.74	1.53
Les Koch	1.71	0.97	1.31	1.53	1.58	1.89	1.82	1.14	1.86	2.11
Kathy Shaw	1.21	0.82	0.84	0.99	1.52	2.86	3.12	3.19	3.00	1.85
Jill Tovey	1.07	1.12	1.29	2.31	2.48	1.11	1.29	1.08	1.31	1.54
Mean	1.23	1.00	1.02	1.44	1.75	1.87	2.00	1.78	1.90	1.76
Std. Dev.	0.35	0.13	0.34	0.61	0.49	0.73	0.72	0.90	0.72	0.70
S.E.M.	0.17	0.07	0.17	0.32	0.25	0.37	0.39	0.49	0.36	0.14
<u>Glutamine</u>										
Chris Koch	46.63	40.82	51.18	51.72	50.63	50.46	50.72	51.20	53.31	44.50
Les Koch	53.3	49.1	52.3	53.5	47.5	52.8	44.1	48.5	52.7	45.2
Kathy Shaw	29.6	31.7	30.0	30.0	30.1	28.3	26.6	26.5	32.7	35.1
Jill Tovey	45.39	42.98	44.32	45.15	53.44	45.42	48.68	47.32	45.37	44.75
Mean	43.73	43.15	44.45	45.09	44.29	44.25	42.53	43.38	46.02	42.29
Std. Dev.	10.04	8.14	10.26	10.68	11.10	11.07	10.97	11.37	9.58	4.67
S.E.M.	5.02	4.07	5.13	5.34	5.55	5.53	5.49	5.69	4.79	2.43
<u>Asparagine</u>										
Chris Koch	6.65	7.86	6.41	7.68	9.26	9.02	7.43	6.61	7.02	4.72
Les Koch	5.05	5.26	9.00	9.13	9.92	4.59	7.25	4.60	3.77	5.53
Kathy Shaw	2.61	2.82	3.39	2.53	3.20	3.30	3.40	3.41	2.23	4.31
Jill Tovey	5.85	4.57	5.43	6.63	6.65	4.76	4.76	4.67	4.36	4.96
Mean	5.00	5.13	6.06	6.49	7.26	5.42	5.71	4.82	4.25	4.00
Std. Dev.	1.71	2.07	2.33	2.83	3.05	2.49	1.90	1.32	2.00	0.71
S.E.M.	0.80	1.05	1.17	1.42	1.53	1.24	0.93	0.66	1.00	0.35