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Abstract

Intestinal absorption tests with the use of D-xylose were conducted on 12 healthy Japanese subjects and the following results were obtained. 1) The mean value of the urinary xylose excretion within five hours after an oral administration of 25 g of D-xylose was 8.07 g and standard error of the mean was 0.11. The mean of urinary excretion was higher than most of previous reports. 2) The 5 hr urinary excretion after intravenous administration of 25 g D-xylose in normal subjects was almost equal to that reported by BUTTERWORTH et al. 3) The rate of D-xylose absorption from the intestine of normal Japanese subjects was higher than that in Europe, Canada and U. S. A. 4) The differences in the pattern of the intestinal absorption of D-xylose in normal individuals seemed to originate from different dietary habit continued over the period of many years, especially of carbohydrate contents.

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INTESTINAL ABSORPTION TEST WITH THE USE OF D-XYLOSE I. ITS APPLICATION ON NORMAL JAPANESE SUBJECTS

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D-Xylose was first used for an intestinal absortion test in the cases of pernicious anemia by HELMER and FOUTS[1] in 1937. The sugar has been considered to be not influenced by various metabolic processes[2] and to be absorbed by an active process because it is phosphorylated in the intestinal mucosa during the absorption.[3-5]

The reports of WYNGAARDEN *et al*[6.-8] and HIATT[9], on the other hand, have demonstrated in their experimental studies using D-xylose-1-C^{14} that a part of absorbed D-xylose was utilized in some metabolic pathways, and have stated that a part of it might be involved in the pentose phosphate pathway via D-xylulose-5-P and be further catabolized to CO_2[7,8] via fructose-6-P and citric acid cycle, and the other might be synthesized to glycogen[9] via glucose-6-P. WILSON *et al.*[10] have also proved by their skillful experiment using the intestine of golden hamsters that D-xylose was not absorbed against its concentration gradient, and have stated that mere phosphorylation of a sugar in the intestine does not always mean its absorption with an active process. In addition to this, SOLS[11] has also reported that the normal role of mucosal hexokinase is solely to initiate glycolysis for the tissue's own needs and not for an absorption from the intestine by an active process.

In spite of such critical aspects of the test, D-xylose is still thought to be clinically valuable as an intestinal absorption test for carbohydrate because of its technical simplicity, the constant metabolic rate of absorbed D-xylose in normal individuals which will be described in the later part of this paper, and that there is no other reliable method to be replaced with it.

The purpose of present investigation is to describe a different behavior in the intestinal absorption of D-xylose in healthy Japanese subjects from those of Caucasions.

MATERIALS AND METHODS

Twelve healthy individuals in the age range of 20 to 50 years old were

selected for this study.

Oral administration Foods and fluids were withheld for at least 12 hours from the subjects. Twenty-five grams of D-xylose dissolved in 500 ml of distilled water were given orally immediately after sampling urine and oxalated blood. After the administration of D-xylose, urine and oxalated blood samples were collected at hourly intervals for five hours in one of the groups. In the other group the urine was collected together in a bottle for five hours and the blood was withdrawn every two hours after the administration. The subjects were kept at rest either in a bed or in a chair during the test.

Intravenous administration Foods and fluids were withheld for at least 12 hours before the test, and then 1000 ml of 2.5 per cent saline solution of D-xylose were injected intravenously over one hour period according to the method of BUTTERWORTH *et al*[12]. The urinary bladder was voided before the injection, followed by collection of the urine for five hours after the beginning of infusion.

The xylose content in the oxalated venous blood samples (1: 10 Somogyi filtrates[13]) and in the urine (diluted 1: 100 or 1: 200 with distilled water) was determined by the colorimetric method of ROE and RICE[14].

RESULTS

The blood xylose concentration reached a peak at two hours followed by a decrease to 20.3 mg/dl at five hours after the administration. At two hours the urinary xylose excretion also reached a peak followed by a rapid decrease.

Table 1 Hourly changes of xylose concentration in blood and urine

time after administration	mean of blood level ± S. E.	mean of urinary excretion ± S. E.
1 hr.	43.1 ± 5.7 mg/dl	1.4 ± 0.26 g/hr.
2 〃	48.8 ± 2.8 〃	2.3 ± 0.18 〃
3 〃	40.1 ± 2.2 〃	2.1 ± 0.17 〃
4 〃	27.1 ± 1.1 〃	1.3 ± 0.37 〃
5 〃	20.3 ± 1.3 〃	0.9 ± 0.13 〃

(S. E.: Standard error of mean)

Table 1 shows hourly changes of the D-xylose concentration in the blood of four normal subjects and those in the urine of seven normal subjects after an oral administration of 25 g of D-xylose.

In order to elucidate the significance of 2 hr blood level of D-xylose, 12 normal and 17 diseased* individuals other than renal diseases were examined. The

*These cases are to be reported in details in the second part following this paper.

relationship between 2 hr blood level and 5 hr urinary excretion was expressed by an application of linear regression analysis. As indicated in Table 2 and Fig. 1, these two components correlate in line, and the regression line obtained was statistically significant. In addition, this line was expected to pass the origin of the coordinates theoretically, however, a deviation of 17.8 mg/dl from the point was noted and it was statistically significant. Therefore, this regression line was not to be applied near the origin of the coordinates.

Table 2 Examination of the correlativity between 2 hr blood level and 5 hr urinary excretion of D-xylose by an application of linear regression analysis

5 hr urinary excretion of xylose=X, and
2 hr blood level of xylose =Y, put

X	Y	X	Y	X	Y	X	Y
9.1	46.1	8.6	52.8	8.1	42.1	10.9	67.2
7.5	57.2	10.5	53.7	8.1	59.3	10.9	49.7
8.0	52.3	4.3	24.8	10.3	52.3	10.7	51.5
9.8	57.6	12.5	64.8	12.4	71.3	8.8	48.6
5.8	36.4	10.8	44.8	6.1	41.1	6.5	42.6
7.4	46.1	10.3	59.5	7.8	52.1		
8.1	53.0	8.1	46.3	5.4	39.1		
8.3	44.4	8.7	45.5	9.5	50.0		

the regression line $Y=3.608\ X+17.83$ can be obtained

analysis of variance

	sums of squares	degrees of freedom	means of squares
regression	1424.92	1	1424.92
error	1247.80	27	46.21
total	2672.72	28	

significance of regression coefficient, b

$t_{(27)}=5.475,\quad P<0.01$

significance of the deviation from the origin of coordinates

$V_d=V_a+(-8.75)^2V_b$

$=33.91$

$S_d=5.723,$

deviation from the origin of coordinates=17.83

$t_{(27)}=3.117,\quad P<0.01$

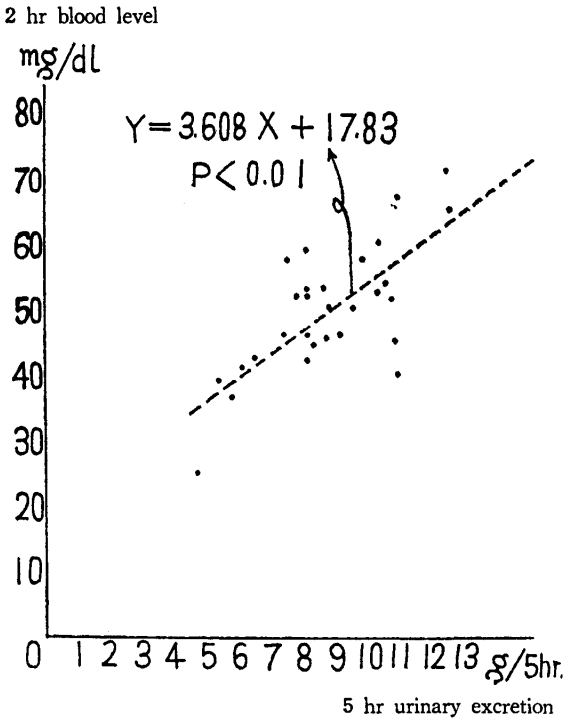

Fig. 1 Regression line between 2 hr blood level and 5 hr urinary excretion

The intestinal absorption test with D-xylose was performed in 12 normal subjects. The results are summarized in Table 3. The mean of 5 hr urinary excretion was 8.07 g and that of 2 hr blood level was 47.7 mg/dl. These two values were found to be higher than those in most of the previous reports as tabulated in Table 4.

Table 3 Results of D-xylose absorption tests in normal subjects.

	5 hr urinary excretion	2 hr blood level
mean	8.07 g	47.7 mg/dl
number	12	11
S. D.	0.36	9.8
S. E.	0.11	3.0
range	4.7−10.5 g	24.8−57.6 mg/dl

(S. D.: standard deviation, S. E.: standard error of mean)

Table 4 Various results of D-xylose absorption tests in normal subjects appearing in previous reports

1) 5 hr urinary excretion (gm/ 5 hr.)

source of data	no. of cases	mean	range	S. D.	S. E.
Dominguez[15]	4	6.55	4.86−7.66		
Helmer[1]*	8	4.68	4.26−5.33		
Brien[16]	12	6.14	5.0 −7.2 **	0.70	
Fourman[17]	4	6.1	4.3 −6.7		
Turner[18]		6.0		0.2	
Gardner[19]	42	5.6		0.6	
Benson[20]	25	6.5	4.1 −8.2	1.2	
Finlay[21]	11	8.46			0.47
Christiansen[22]	10	6.76	5.6 −8.2	0.88	
Butterworth[12]	114	5.7		1.7	
Fowler[23]	35	7.2			0.25
Shamma'a[24]	11	7.5	5.9 −8.9	0.27	
Drube[25]	40	6.7	4.8 −10.5	1.27	
Arimasa	12	8.07	4.7 −10.5	0.36	0.11

2) 2 hr blood level (mg/dl)

source of data	no. of cases	mean	range	S. D.	S. E.
Dominguez	2	39.5	35.1−43.9		
Brien	12	37**	22 −48**		
Turner		42.2		2.4	
Gardner	42	33**		8**	
Benson	23	36	15 −76	16	
Finlay	11	44.9			1.8
Drube	26	44.0	28 −71**	10**	
Arimasa	11	47.7	24.8−57.6	9.3	3.0

* one hour before the test the subjects were allowed to eat breakfast
** estimated from published graph

The significance of differences between those in previous reports and those in this study was tested statistically by an application of the t-test. As shown in Table 5, the mean of 5 hr urinary excretion obtained in this study differed significantly from other reports except for FINLAY's. There are few reports describing the 2 hr blood level of xyolse. The mean value of the level in this study differed significantly from the means in GARDNER's and BENSON's, but not from those in DRUBE's and FINLAY's data.

Table 5 Significance of the differences between means in previous reports and means in the present study by an application of t-test

1) 5 hr urinary excretion

source of data	N	$\bar{X}$	s	$V_{\bar{x}}$	$s_{\bar{d}}$	$\bar{d}$	t	d. f.	P
Gardner	42	5.6	0.6	.0086	.138	2.47	17.9	52	<0.01
Butterworth	114	5.7	1.4	.0172	.167	2.37	14.2	124	〃
Brien	4	6.14	0.70	.0408	.228	1.93	8.47	14	〃
Benson	12	6.5	1.2	.0576	.261	1.57	6.02	22	〃
Drube	25	6.7	1.27	.0404	.226	1.37	6.06	35	〃
Christiansen	49	6.76	0.88	.0774	.297	1.31	4.41	50	〃
Fowler	10	7.2	(0.25)	.0626	.270	0.87	3.22	20	〃
Shamma'a	35	7.5	0.27	.0066	.132	0.57	4.32	45	〃
Finlay	11	8.46	(0.47)	.0221	.472	−0.39	0.827	21	0.4−0.5
Arimasa	12	8.07	0.36	.0108					

2) 2 hr blood level

source of data	N	$\bar{X}$	s	$V_{\bar{x}}$	$s_{\bar{d}}$	$\bar{d}$	t	d. f.	P
Gardner	42	33	8	1.52	3.10	14.7	4.81	51	<0.01
Benson	23	36	16	11.1	4.45	11.7	2.64	32	=0.01
Drube	26	44.0	10	3.85	3.55	3.7	1.04	35	0.3−0.4
Finlay	11	44.9	(1.8)	3.24	3.36	2.8	0.83	20	0.4−0.5
Arimasa	11	44.7	9.8	8.73					

N=number of cases, $\bar{X}$=mean, s=standard deviation (the brackets around figures in 's' indicates this value means standard error of mean), $V_{\bar{x}}$=variance of mean, $s_{\bar{d}}$=square root of variance of difference, $\bar{d}$=difference of mean from Author, P=probability

The data of 5 hr urinary excretion after the intravenous administration of 25 g of D-xylose are shown in Table 6. The results were consistent with the results reported by BUTTERWORTH.

Taqle 6 Urinary xylose excretion after intravenous administration of 25g of D-xylose

source of data	5 hr urinary excretion	per cent of dose	5 hr urinary excretion after oral administration of 25 g of D-xylose
Butterworth	10.6 g/5 hr	42.4 %	5.7 g
Present study 1	10.5 〃	42.0 〃	8.3 〃
Present study 2	10.2 〃	40.8 〃	8.1 〃

To test accuracy of the data obtained in this study, the measurement of D-xylose was repeated for several times with the same urine sample. The standard deviation and the standard error of the mean calculated from the results are shown in Table 7, indicating a relatively small error.

Table 7 Variances of the data obtained

	case 1	case 2
	7.7 g	8.3 g
	7.9 〃	8.2 〃
	7.9 〃	8.3 〃
	8.4 〃	8.5 〃
	8.1 〃	8.4 〃
	8.2 〃	8.7 〃
		7.9 〃
mean	8.06 〃	8.31 〃
S. D.	0.25	0.23
S. E.	0.10	0.09

The recovery of D-xylose in the test was found to be 92.3 per cent as seen in Table 8. The deviation from the theoretical value was, therefore, 7.7 per cent and that was statistically significant. This indicated some loss of D-xylose in the process of measurement.

Table 8 The recovery of xylose in test

xylose added in urine	xylose measured in urine	recovery
1.00 g/dl	1.0 g/dl	103.0 %
	0.8 〃	82.0 〃
	0.9 〃	85.0 〃
1.50 〃	1.5 〃	96.7 〃
	1.3 〃	83.4 〃
	1.2 〃	80.0 〃
2.00 〃	1.9 〃	97.0 〃
	1.7 〃	95.0 〃
	1.8 〃	91.5 〃
2.50 〃	2.2 〃	86.0 〃
	2.3 〃	90.7 〃
3.00 〃	2.7 〃	88.7 〃
	2.9 〃	95.3 〃
4.00 〃	3.9 〃	97.0 〃
	4.0 〃	99.0 〃
5.00 〃	5.1 〃	101.4 〃
	5.3 〃	105.4 〃
		mean 92.3 %
		S. D. 7.8

DISUSSION

The mean values of 5 hr urinary excretion reported by various authors are distributed around 6.2 g (Table 4). The values obtained by the author, FINLAY and SHAMA'A, were 8.07 g, 8.46 g and 7.5 g, respectively. These values were higher than those listed in Table 4. Statistically significant differences were noted between the values of the author and those reported by others, except for that of FINLAY's. On the contrary, there were almost no differences in the 5 hr urinary excretion values after the intravenous administration between BUTTERWORTH (10.6 g) and the author (10.5 g and 10.2 g). When 25 g of D-xylose were given orally, there was a distinct difference in the 5 hr uninary excretion between the data of BUTTERWORTH and the author. BUTTERWORTH reported it to be 5.7 g whereas the values were 8.3 g and 8.1 g in the present study. Counting backward from that the 5 hr urinary excretion in normal persons was found to be 8.07 g in average, it was presumed that approximately 76 per cent of 25 g of the D-xylose given orally was absorbed within 5 hours in these subjects.

The standard error of the mean of the 5 hr urinary excretion in 12 normal subjects was 0.11, that was close to 0.10 of the standard error in variances of the data appearing in Table 7. The rate of the intestinal absorption of D-xylose in the normal subjects showed a relatively small variance in each individual, in other words, a part of D-xylose was utilized for some metabolic pathways, however, so far as 10 to 25 g of D-xylose were absorbed from the intestine, the rate of D-xylose to be metabolized was constant in these subjects, approximately 60 per cent.

The test of variances of the data and of recovery of D-xylose were carried out in order to examine accuracy of the data obtained. The results were satisfactory as indicated in Tables 7 and 8.

Summarily, the rate of D-xylose absorption from the intestine in normal Japanese subjects was found to be higher than those in Europe and in U. S. A. Such different behaviors in the intestinal absorption of D-xylose were not thought to originate from the race differences but the differences in the dietary habit. The carbohydrate contents of foodstuffs in Japan are greatly higher than those in Europe and U. S. A. A statistical result reported by the Ministry of Public Welfare[26] revealed the composition of foodstuffs of healthy individuals in Japan in 1960 to be 70 g of protein, 24 g of fat and 400 g of carbohydrate in average. In Canada[27], it was 100 g of protein, 120 g of fat and 200 g to 250 g of carbohydrate. That in Europe and U. S. A.[28] was also similar to Canada's. In U. S. A. about 40 per cent of the total calories is supplied with fat from animal sources, while in Japan only 4 per cent is supplied from the same sources. The dietary pattern of normal subjcects in the cases of FINLAY, showing the highest

value of the urinary excretion of D-xylose, however, is similar to any standard American and European dietary ones, and percentage of its carbohydrate content is not so high as compared with them[7]. The dietary pattern of normal subjects of SHAMA'A[29] in Lebanon having high value next to that of the present study, is also similar to European dietary pattern, but, in fact, a substantial portion of its protein is taken from vegetable sources.

CONCLUSIONS

Intestinal absorption tests with the use of D-xylose were conducted on 12 healthy Japanese subjects and the following results were obtained.

1) The mean value of the urinary xylose excretion within five hours after an oral administration of 25 g of D-xylose was 8.07 g and standard error of the mean was 0.11. The mean of urinary excretion was higher than most of previous reports.

2) The 5 hr urinary excretion after intravenous administration of 25 g D-xylose in normal subjects was almost equal to that reported by BUTTERWORTH *et al.*

3) The rate of D-xylose absorption from the intestine of normal Japanese subjects was higher than that in Europe, Canada and U. S. A.

4) The differences in the pattern of the intestinal absorption of D-xylose in normal individuals seemed to originate from different dietary habit continued over the period of many years, especially of carbohydrate contents.

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