

E-7 REPORT

REPORT E-7

L Y C A S I N® 8 0 / 5 5

STUDY OF GLYCEMIA
AND INSULINEMIA VARIATIONS AFTER
PER OS ABSORPTION
OF A SINGLE LYCASIN 80/55 DOSE IN MAN

PURPOSE OF THE STUDY

The purpose of the present study was to compare the variations in glycemia and insulinemia in the normal subject after administering glucose and Lycasin 80/55.

Lycasin 80/55 is an hydrogenated glucose syrup broadly composed of sorbitol (6 - 8 %), maltitol (50 - 55 %) and hydrogenated oligosaccharides.

The overall composition of Lycasin 80/55 is 43 - 44% D-sorbitol and 56 - 57% D-glucose. It was therefore interesting to follow the glycemia and insulinemia effects of a Lycasin 80/55 ingestion as compared to glucose, in the normal human subject.

To get a better understanding of the metabolic fate of Lycasin, it was felt advisable to establish an urinary and fecal balance of the subjects under study. (The analytical methods allowing the dosage of glucose and insulin are well known and currently used in medical care services ; this is not the case for maltitol).

ORGANIZATION OF THE STUDY

Glycemic and insulinemic responses will be studied in 15 subjects :

1. After absorption of 50 g glucose,

2. After absorption of Lycasin 80/55 :
 - 40 - 50 g for the subjects 1 - 2 - 3

 - 80 g for the subjects 4 and 5

 - 100 g for the subjects 6 to 15

the use of increased doses will depend on digestive tolerance and blood maltitol level.

The subjects are fasting since the previous evening and have taken their glucose or Lycasin dose in a water solution. Blood samples have been taken with the following schedule : 0 (before intake), 30 - 60 - 90 - 120 - 150 - 180 minutes. Blood is collected on EDTA.

The glycemia is measured by dosage with glucose-oxidase.

The insulinemia is measured by radio-immunological dosage.

During Lycasin 80/55 ingestion, the subjects take simultaneously a capsule containing cochineal carmine, a tracer of collected feces, in order to detect maltitol.

The subject urines are collected during the three hours period following the Lycasin ingestion, in order to detect urinary maltitol.

PRODUCT UNDER STUDY

The ROQUETTE FRERES Company has sent in august 1978, under the reference nr 62 802, a 2 kg sample of Lycasin 80/55, batch nr 700, of which analytical characteristics were :

- dry extract (w/w).....	75.35
- refractive index	1.4808
- reducing sugars %.....	0.03
- specific optical rotation.....	+ 116°40
- pH.....	6.5

Composition in carbohydrates

(% dry extract)

- sorbitol.....	8
- maltitol.....	53.4
- DP* 3.....	15.0
- DP* 4.....	1.6
- DP* 5.....	1.8
- DP* 6.....	2.4
- DP* 7 to DP* 10.....	10.1
- DP* 11 to DP* 20.....	7.4
- higher than DP* 20.....	1.6

* DP = Degree of polymerization

STUDY PLANNING

The study has been carried out during 1978 and beginning of 1979 on 15 voluntary, healthy subjects, in the Nutrition and Metabolic Diseases Department of the University of Nancy (Prof. G. DEBRY - France).

The first results of the present study (subject 1, 2 and 3) have been reported on 10/24/1978 by letter, but the glycemia and insulinemia results have only been written down on 02/06/1979.

RESULTS

The individual values of glycemia and insulinemia are reported along these lines :

- table 1 : glycemia in g/litre
product under study : glucose
- table 2 : glycemia in g/litre
product under study : Lycasin 80/55
- table 3 : insulinemia in microunits/ml
product under study : glucose
- table 4 : insulinemia in microunits/ml
product under study : Lycasin 80/55
- table 5 : statistical evaluation
(Student's T-test)

In each table, averages calculations and statistical evaluations have been carried out, considering first all subjects, and then only those between nr 6 and nr 15, who have taken the same quantity of Lycasin 80/55.

The results (tables A - B - C - D - E) have been given, bringing all the values to a 100 level at the origin.

The table 6 gives the maltitol values in the serum.

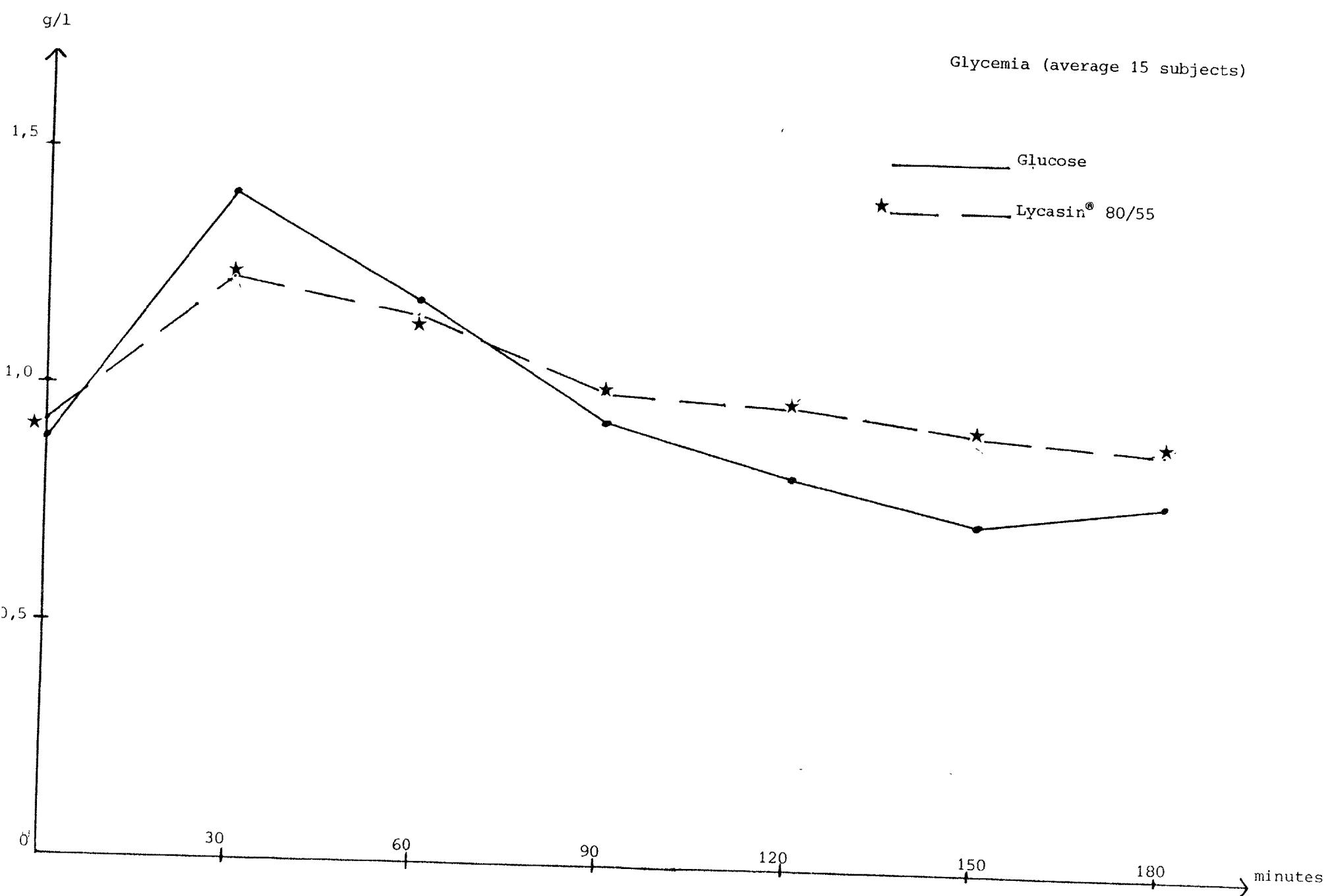
Results of urinary analyses are given in table nr 7.

TABLE 1

- glycemia in g/l

- product : glucose

schedule	0	30	60	90	120	150	180
subject	!	!	!	!	!	!	!
! 1	! 0.83	! 1.04	! 0.99	! 0.78	! 0.70	! 0.62	! 0.64
! 2	! 0.92	! 1.35	! 1.20	! 0.96	! 0.72	! 0.84	! 0.94
! 3	! 0.83	! 1.23	! 0.94	! 0.87	! 0.99	! 0.97	! 0.97
! 4	! 0.83	! 1.50	! 1.33	! 0.67	! 0.52	! 0.64	! 0.69
! 5	! 0.97	! 1.57	! 1.37	! 1.16	! 0.87	! 0.70	! 0.80
! 6	! 0.89	! 1.45	! 1.22	! 0.79	! 0.51	! 0.57	! 0.72
! 7	! 0.77	! 0.92	! 0.91	! 0.79	! 0.97	! 0.76	! 0.73
! 8	! 0.91	! 1.50	! 1.23	! 1.02	! 0.94	! 0.69	! 0.77
! 9	! 0.91	! 1.44	! 1.36	! 1.13	! 1.19	! 0.73	! 0.71
! 10	! 0.9	! 1.4	! 1.1	! 1.0	! 0.9	! 0.7	! 0.7
! 11	! 0.95	! 1.29	! 1.15	! 0.98	! 0.77	! 0.79	! 0.90
! 12	! 1.00	! 1.74	! 1.18	! 0.85	! 0.97	! 0.82	! 0.84
! 13	! 0.90	! 1.16	! 1.25	! 1.18	! 0.81	! 0.72	! 0.75
! 14	! 0.91	! 1.79	! 1.20	! 0.96	! 0.88	! 0.86	! 0.83
! 15	! 0.90	! 1.80	! 1.40	! 1.00	! 0.70	! 0.70	! 0.80
!	!	!	!	!	!	!	!
! average	!	!	!	!	!	!	!
! 1 - 15	! 0.895	! 1.412	! 1.189	! 0.943	! 0.829	! 0.741	! 0.786
! SD	! 0.059	! 0.259	! 0.152	! 0.150	! 0.182	! 0.103	! 0.096
!	!	!	!	!	!	!	!
! average	!	!	!	!	!	!	!
! 6 - 15	! 0.904	! 1.449	! 1.200	! 0.970	! 0.864	! 0.734	! 0.775
! SD	! 0.057	! 0.282	! 0.136	! 0.131	! 0.183	! 0.081	! 0.066



Glycemia (average 10 subjects)

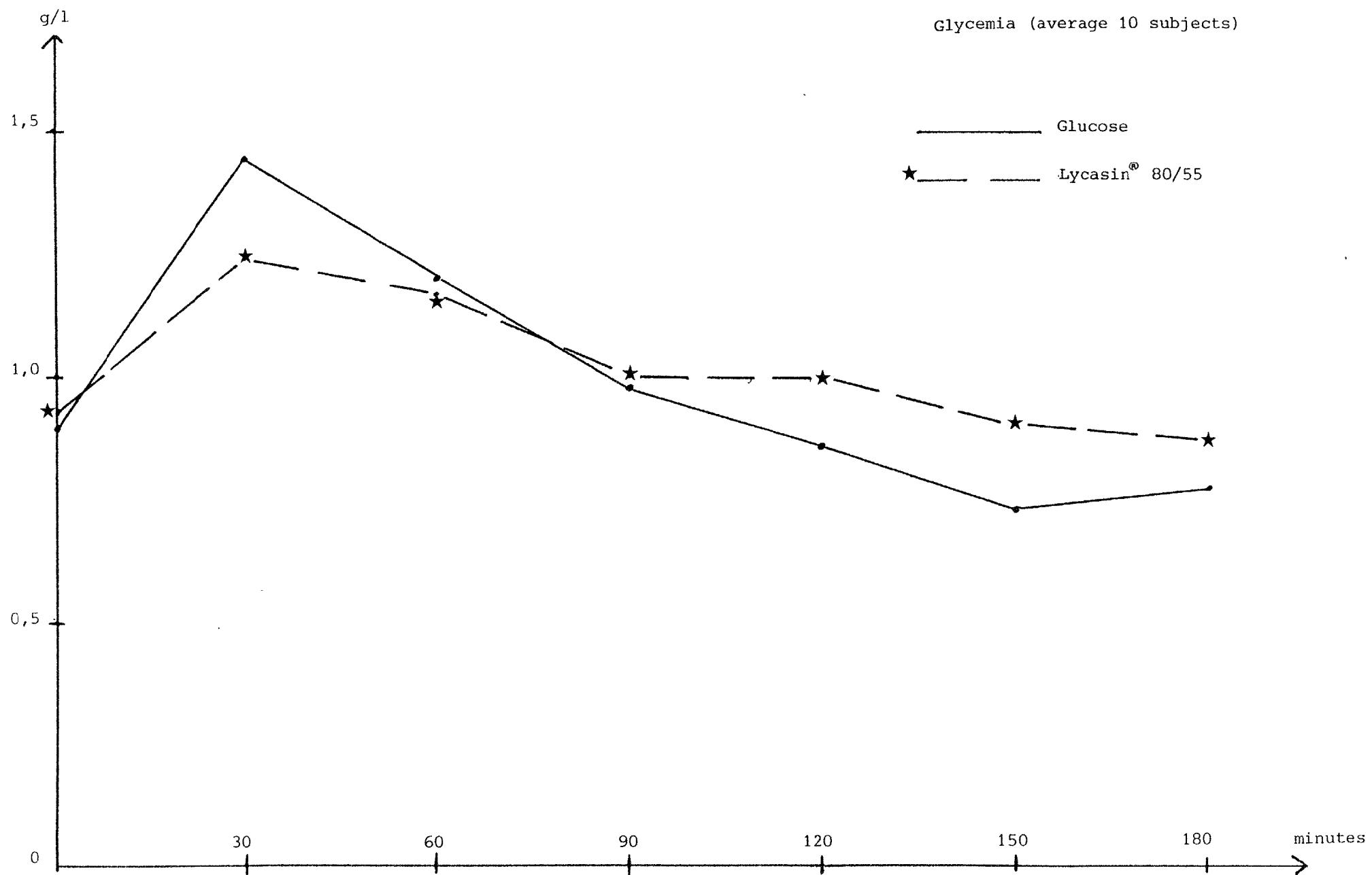


TABLE 2

- glycemia in g/l

- Product : Lycasin 80/55

schedule		0	30	60	90	120	150	180
!	subject	!	!	!	!	!	!	!
!	1	! 0.87	! 1.20	! 0.91	! 0.85	! 0.94	! 0.89	! 0.95
!	2	! 0.98	! 1.24	! 1.09	! 0.97	! 0.93	! 0.97	! 0.99
!	3	! 0.80	! 1.03	! 1.17	! 1.13	! 0.97	! 0.88	! 0.85
!	4	! 1.01	! 1.30	! 1.35	! 1.02	! 0.98	! 0.97	! 0.95
!	5	! 0.95	! 1.34	! 1.19	! 1.03	! 0.92	! 1.13	! 1.01
!	6	! 0.80	! 1.05	! 0.99	! 0.74	! 0.79	! 0.81	! 0.72
!	7	! 0.88	! 1.06	! 0.90	! 0.92	! 0.88	! 0.91	! 0.95
!	8	! 0.86	! 1.20	! 0.75	! 0.75	! 0.97	! 0.81	! 0.82
!	9	! 0.92	! 1.25	! 0.99	! 0.91	! 0.89	! 0.89	! 0.91
!	10	! 0.92	! 1.35	! 1.23	! 0.92	! 1.01	! 0.98	! 0.84
!	11	! 1.02	! 1.59	! 1.95	! 1.32	! 1.15	! 0.89	! 0.74
!	12	! 1	! 1.11	! 1.42	! 1.32	! 1.17	! 0.97	! 0.98
!	13	! 0.88	! 1.15	! 1.09	! 0.83	! 0.82	! 0.83	! 0.85
!	14	! 0.95	! 1.31	! 1.30	! 1.09	! 1.05	! 0.90	! 0.86
!	15	! 1.02	! 1.35	! 1.09	! 1.25	! 1.20	! 1.08	! 1.03
!		!	!	!	!	!	!	!
!	average	!	!	!	!	!	!	!
!	1- 15	! 0.924	! 1.235	! 1.161	! 1.003	! 0.978	! 0.927	! 0.897
!	SD	! 0.075	! 0.148	! 0.283	! 0.188	! 0.122	! 0.090	! 0.095
!		!	!	!	!	!	!	!
!	average	!	!	!	!	!	!	!
!	6 - 15	! 0.925	! 1.242	! 1.171	! 1.005	! 0.993	! 0.907	! 0.870
!	SD	! 0.073	! 0.166	! 0.336	! 0.225	! 0.148	! 0.085	! 0.099

TABLE 3

- Insulinemia in microunits/ml

- product : glucose

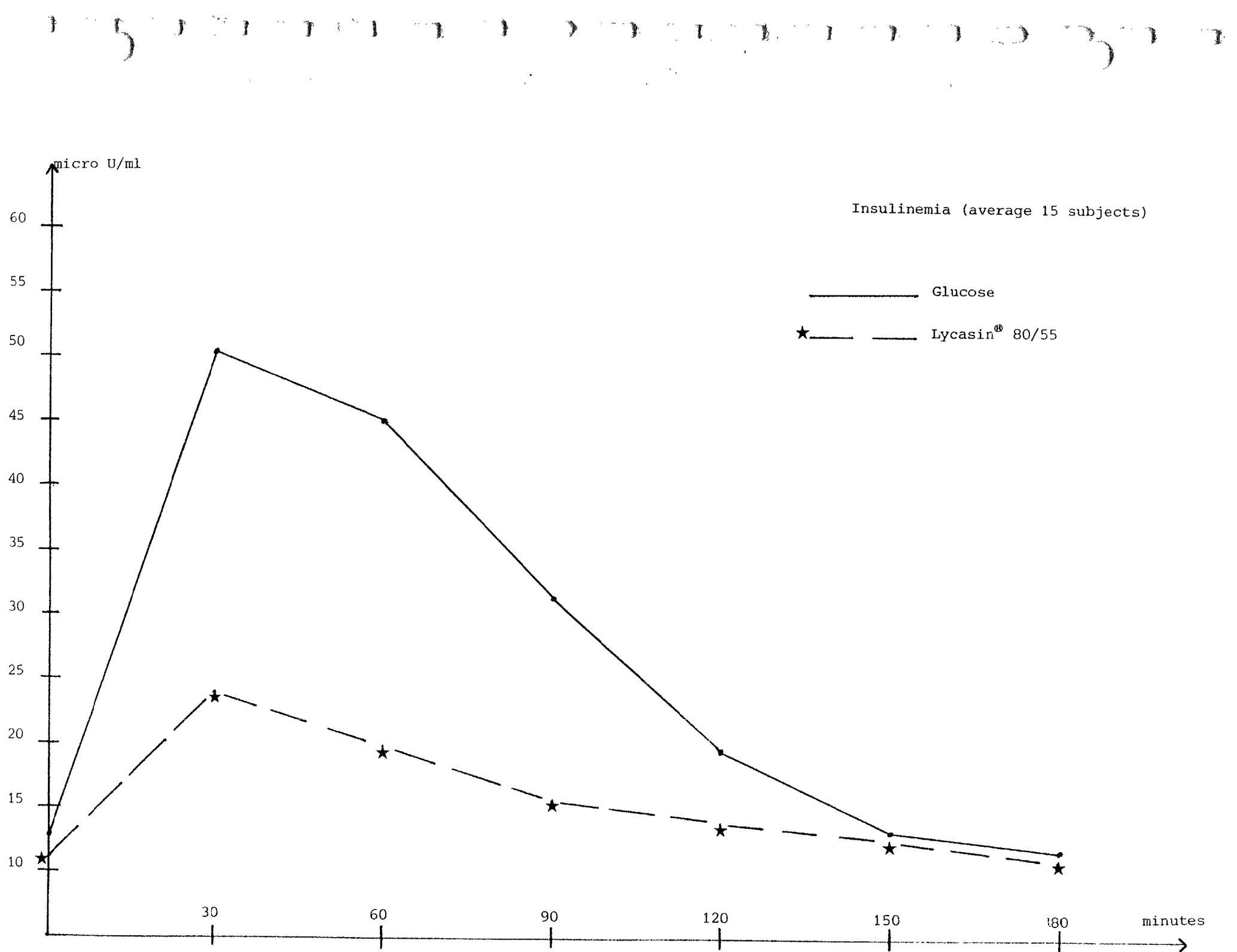
! schedule	! 0	! 30	! 60	! 90	! 120	! 150	! 180
! subject	!	!	!	!	!	!	!
! 1	!	12	25	30	19	15	10
! 2	!	17	39	56	46	22	15
! 3	!	11	35	32	16	17	10
! 4	!	10	28	40	12	10	10
! 5	!	16	23	28	44	31	30
! 6	!	10	20	23	26	10	10
! 7	!	8	15	14	13	14	12
! 8	!	13	55	49	27	21	10
! 9	!	12	130	50	24	35	11
! 10	!	10	43	33	30	21	12
! 11	!	22	122	114	89	26	17
! 12	!	11	95	65	32	17	12
! 13	!	23	48	63	45	32	21
! 14	!	10	43	30	16	10	10
! 15	!	10	36	49	32	15	12
!	!	!	!	!	!	!	!
! average	!	!	!	!	!	!	!
! 1 - 15	!13	!50.46	!45.067	!31.40	!19.733	!13.47	!11.93
! SD	! 4.52	! 36.09	! 24.18	! 19.50	! 8.17	! 5.55	! 2.94
!	!	!	!	!	!	!	!
! average	!	!	!	!	!	!	!
! 6 - 15	!12.90	!60.70	!49.00	!33.40	!20.10	!12.70	!11.10
! SD	! 5.238	! 40.705	! 28.276	! 21.459	! 8.672	! 3.561	! 2.470

TABLE 4

- insulinemia in microunits/ml

- product : Lycasin 80/55

schedule		0	30	60	90	120	150	180
!	subject	!	!	!	!	!	!	!
!	1	!	12	37	13	11	12	10
!	2	!	12	28	17	11	11	10
!	3	!	10	10	25	20	14	11
!	4	!	13	10	20	15	13	12
!	5	!	10	22	13	18	10	10
!	6	!	10	13	17	11	10	10
!	7	!	13	36	25	13	10	10
!	8	!	19	10	10	10	10	10
!	9	!	10	30	10	10	10	10
!	10	!	12	27	28	22	23	19
!	11	!	10	70	36	24	21	25
!	12	!	11	10	26	26	25	19
!	13	!	10	12	18	10	10	10
!	14	!	10	18	24	13	14	11
!	15	!	10	27	16	21	18	12
		!	!	!	!	!	!	!
!	average	!	!	!	!	!	!	!
!	1 - 15	!	11.47	24	19.87	15.67	14.06	12.600
!	SD	!	2.39	16	7.36	5.64	5.19	4.59
		!	!	!	!	!	!	!
!	average	!	!	!	!	!	!	!
!	6 - 15	!	11.500	25.300	21.000	16.000	15.100	13.600
!	SD	!	2.838	18.227	8.273	6.464	6.100	5.400
		!	!	!	!	!	!	!



10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180

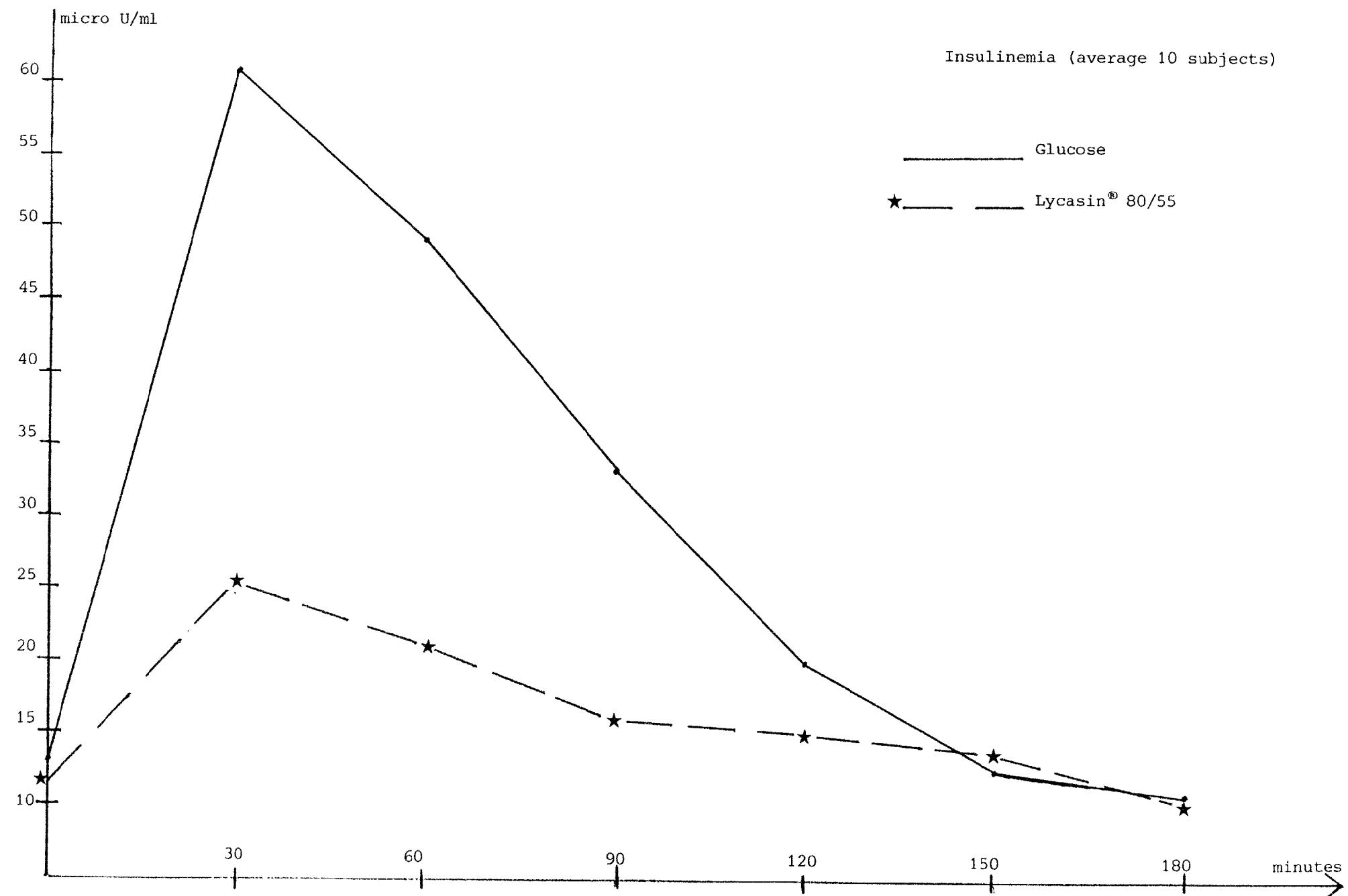


TABLE 5
 Statistical evaluation
 (STUDENT's T-test)
 Lycasin 80/55 vs. Glucose

Subjects 1-15		Glycemia	Insulinemia
!	!	!	!
!	0	- 1.19 217	! 1.16 189 !
!	30'	2.29 406 *	! 2.59 612 * !
!	60'	0.32 940	! 3.86 168 * !
!	90'	- 0.97 607	! 3.00 181 * !
!	120'	- 2.63 056 *	! 2.26 721 * !
!	150'	- 5.25 689 *	! 0.46 569 !
!	180'	- 3.18 148 *	! 0.65 487 !

* difference being significant for degrees of freedom 28
 and p 5% (t=2.048)

Subjects 6-15		Glycemia	Insulinemia
!	!	!	!
!	0	- 0.71 383	! 0.74 316 !
!	30'	1.99 944	! 2.50 999 * !
!	60'	0.25 276	! 3.00 537 * !
!	90'	- 0.42 567	! 2.45 517 * !
!	120'	- 1.73 515	! 1.49 122 !
!	150'	- 4.67 871 *	! - 0.44 003 !
!	180'	- 2.51 857 *	! 0.56 175 !

* difference being significant for degrees of freedom 18
 and p 5% (t = 2.101)

TABLE 6

SERUM ANALYSIS

maltitol in mg/l

! schedule	! 0	! 30	! 60	! 90	! 120	! 150	! 180
! subject	!	!	!	!	!	!	!
! 1	! 480	! 330	! 210	! 160	! 240	! 200	! 220
! 2	! ND						
! 3	! ND						
! 4	! ND	! ND	! T	! T	! 30	! 52	! T
! 5	! ND	! ND	! ND	! T	! 37	! 50	! ND
! 6	! ND	! ND	! T	! ND	! ND	! T	! T
! 7	! ND	! 70	! 46	! T	! T	! T	! ND
! 8	! ND	! ND	! T	! ND	! ND	! ND	! ND
! 9	! ND	! 179	! T				
! 10	! ND	! ND	! ND	! 80	! T	! 85	! ND
! 11	! ND						
! 12	! ND						
! 13	! ND	! T					
! 14	! ND	! ND	! ND	! ND	! T	! ND	! ND
! 15	! ND	! T					

ND : not detectable

T : non measurable trace

TABLE 7

URINES ANALYSIS

maltitol

subject	volume	concentration	total excretion
	ml	g/l	mg
1	75	0.65	48.75
2	116	0.52	60.32
3	125		
4	205	0.07	14.35
5	175		
6	96	1.24	119
7	118	0.11	12.98
8	106	1.35	143.1
9	78	1.33	103.74
10	145	0.16	23.2
11	95		
12	69	0.88	60.72
13	202	absence	
14	41	0.20	8.2
15	118		

TABLE A

- Glycemia : level 100 at origin

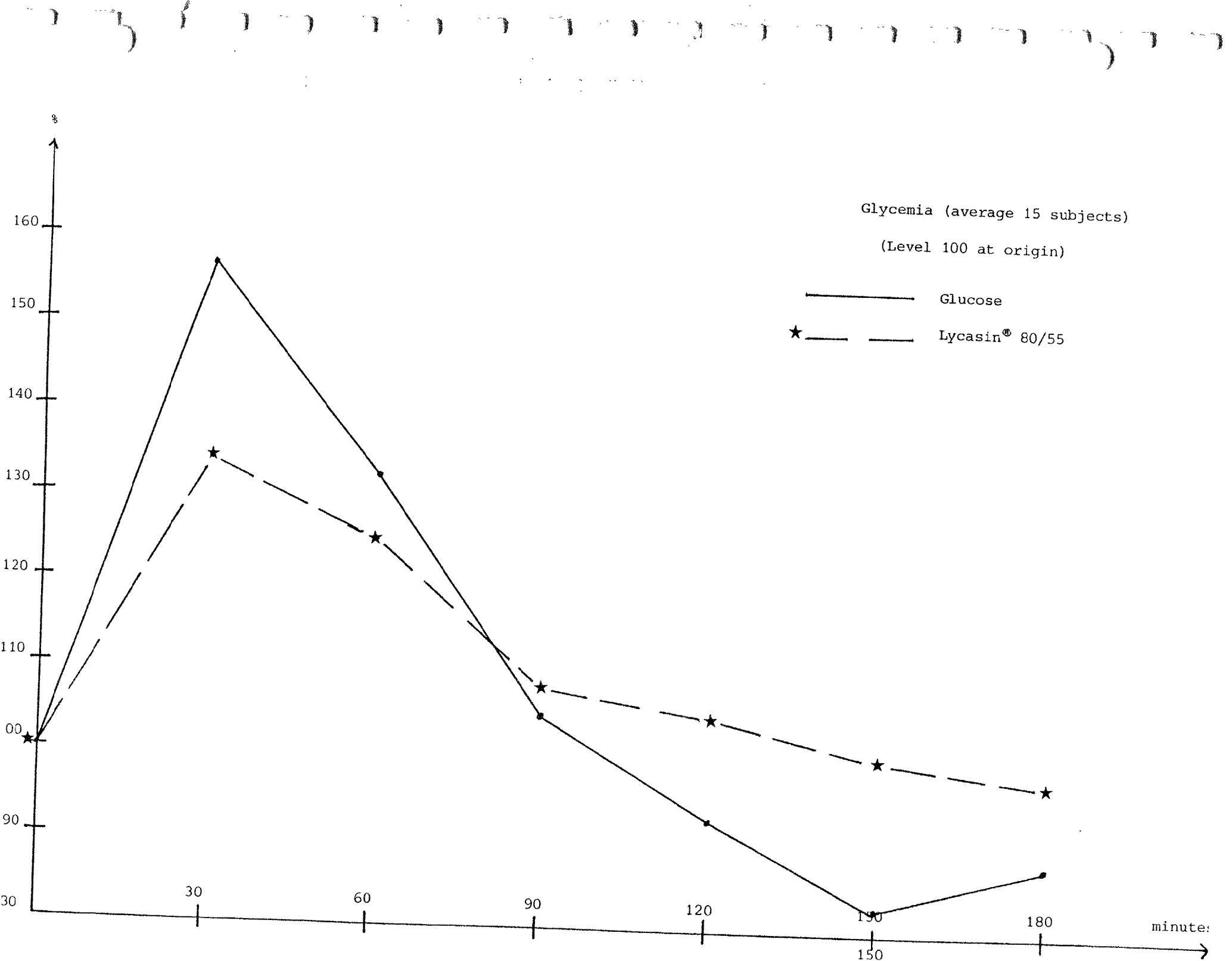
- Product : glucose

schedule	0	30	60	90	120	150	180
subject	!	!	!	!	!	!	!
1	! 100	! 125	! 119	! 94	! 84	! 75	! 77
2	! 100	! 147	! 130	! 104	! 78	! 91	! 102
3	! 100	! 148	! 113	! 105	! 119	! 117	! 117
4	! 100	! 181	! 160	! 81	! 63	! 77	! 83
5	! 100	! 162	! 141	! 120	! 90	! 72	! 83
6	! 100	! 163	! 137	! 89	! 57	! 64	! 81
7	! 100	! 120	! 118	! 103	! 126	! 99	! 95
8	! 100	! 165	! 135	! 112	! 103	! 76	! 85
9	! 100	! 158	! 150	! 124	! 131	! 80	! 78
10	! 100	! 156	! 122	! 111	! 100	! 78	! 78
11	! 100	! 136	! 121	! 103	! 81	! 83	! 95
12	! 100	! 174	! 118	! 85	! 97	! 82	! 84
13	! 100	! 129	! 139	! 131	! 90	! 80	! 83
14	! 100	! 197	! 132	! 106	! 97	! 95	! 91
15	! 100	! 200	! 156	! 111	! 78	! 78	! 89
	!	!	!	!	!	!	!
average	!	!	!	!	!	!	!
1 - 15	! 100	! 157.40	! 132.73	! 105.27	! 92.93	! 83.13	! 88.07
SD	!	24.26	14.61	14.00	21.18	12.87	10.74
	!	!	!	!	!	!	!
average	!	!	!	!	!	!	!
6 - 15	! 100	! 159.80	! 132.80	! 107.50	! 96.00	! 81.50	! 85.90
SD	!	26.57	13.29	13.98	21.85	9.75	6.35

TABLE B

- Glycemia : Level 100 at origin
 - Product : Lycasin 80/55

!schedule	! 0	! 30	! 60	! 90	! 120	! 150	! 180
! subject	!	!	!	!	!	!	!
!	!	!	!	!	!	!	!
! 1	! 100	! 138	! 105	! 98	! 108	! 102	! 109
! 2	! 100	! 127	! 112	! 99	! 95	! 99	! 101
! 3	! 100	! 129	! 146	! 141	! 121	! 110	! 106
! 4	! 100	! 129	! 134	! 101	! 97	! 96	! 94
! 5	! 100	! 141	! 125	! 108	! 97	! 119	! 106
! 6	! 100	! 131	! 124	! 93	! 99	! 101	! 90
! 7	! 100	! 121	! 102	! 105	! 100	! 103	! 108
! 8	! 100	! 140	! 87	! 87	! 113	! 94	! 95
! 9	! 100	! 136	! 108	! 99	! 97	! 97	! 99
! 10	! 100	! 147	! 134	! 100	! 101	! 107	! 91
! 11	! 100	! 156	! 191	! 129	! 113	! 87	! 73
! 12	! 100	! 111	! 142	! 132	! 117	! 97	! 98
! 13	! 100	! 131	! 124	! 94	! 93	! 94	! 97
! 14	! 100	! 138	! 137	! 115	! 111	! 95	! 91
! 15	! 100	! 132	! 107	! 123	! 118	! 106	! 101
!	!	!	!	!	!	!	!
! average	!	!	!	!	!	!	!
! 1 - 15	! 100	! 133.80	! 125.20	! 108.27	! 105.33	! 100.47	! 97.27
! SD	!	! 10.66	! 24.71	! 16.09	! 9.46	! 7.83	! 9.15
!	!	!	!	!	!	!	!
! average	!	!	!	!	!	!	!
! 6 - 15	! 100	! 134.30	! 125.60	! 107.70	! 106.20	! 98.10	! 94.30
! SD	!	! 12.59	! 28.78	! 16.00	! 9.11	! 6.17	! 9.25



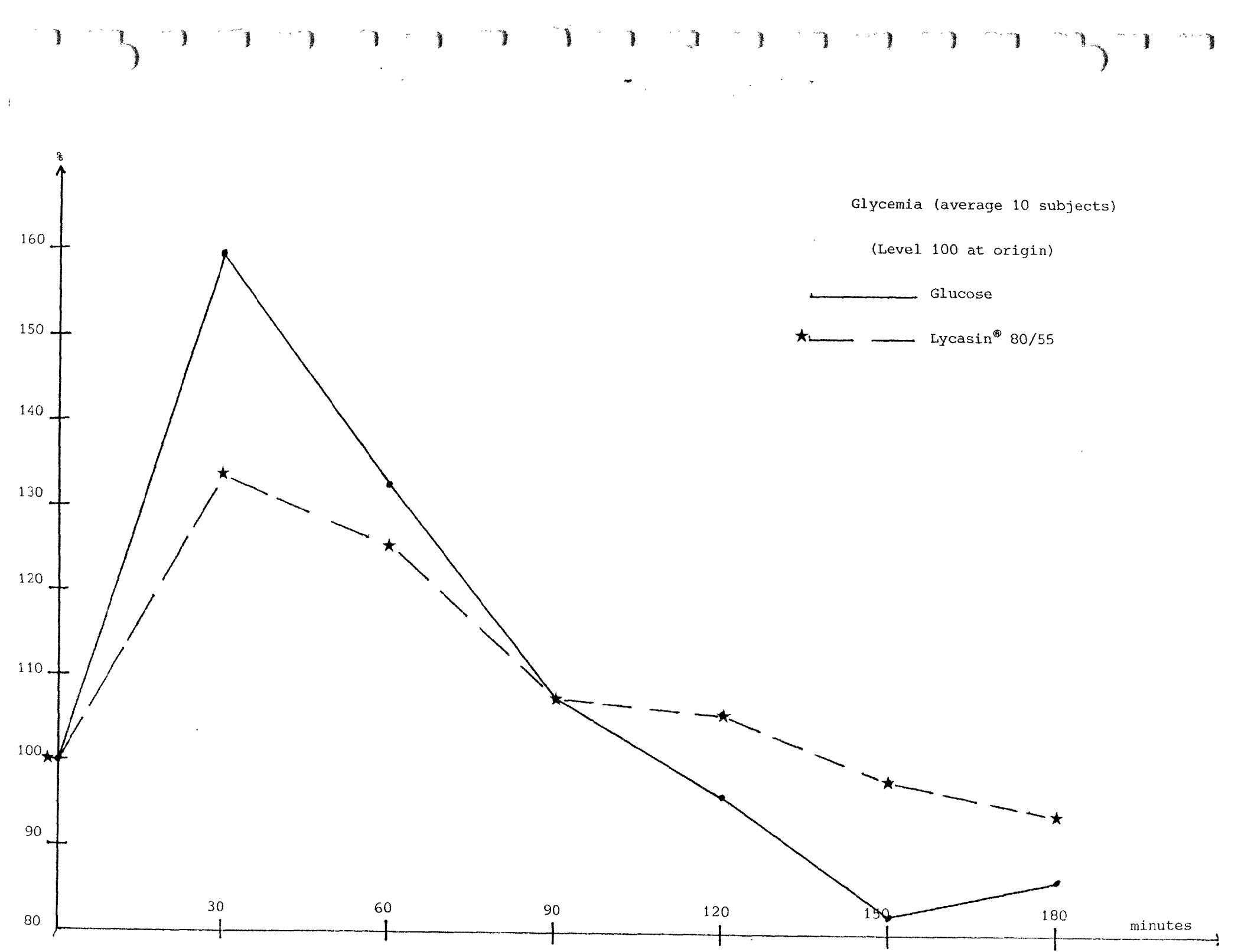


TABLE C

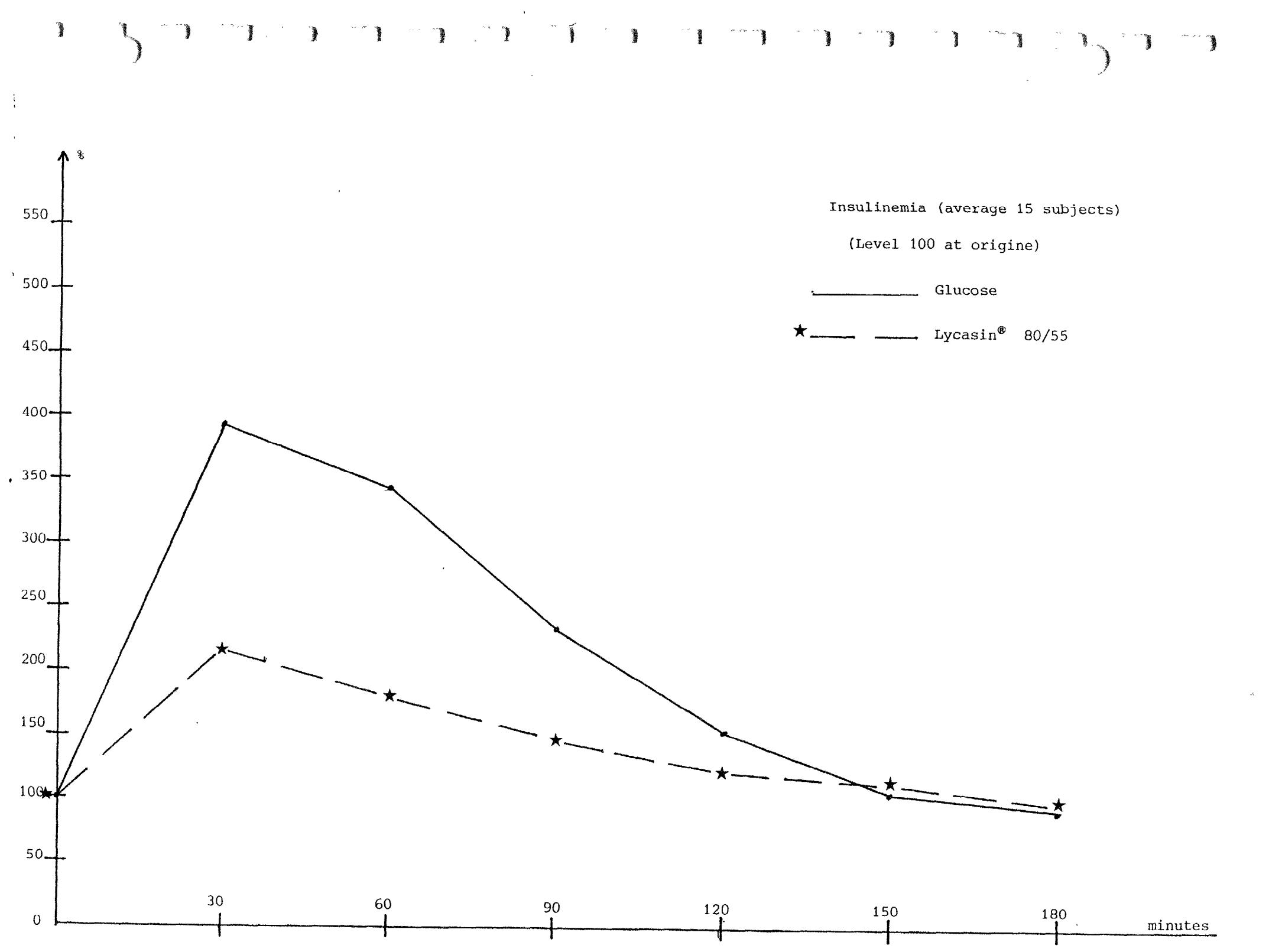
- Insulinemia : Level 100 at origin
 - Product : glucose

schedule	0	30	60	90	120	150	180
! subject	!	!	!	!	!	!	!
! 1	! 100	! 208	! 250	! 158	! 125	! 83	! 83
! 2	! 100	! 229	! 329	! 271	! 129	! 88	! 88
! 3	! 100	! 318	! 291	! 146	! 155	! 91	! 146
! 4	! 100	! 280	! 400	! 120	! 100	! 100	! 100
! 5	! 100	! 144	! 175	! 275	! 194	! 188	! 106
! 6	! 100	! 200	! 230	! 260	! 100	! 100	! 100
! 7	! 100	! 188	! 175	! 163	! 175	! 150	! 113
! 8	! 100	! 423	! 377	! 208	! 162	! 77	! 77
! 9	! 100	! 1083	! 417	! 200	! 292	! 92	! 83
! 10	! 100	! 430	! 330	! 300	! 210	! 120	! 100
! 11	! 100	! 555	! 518	! 405	! 118	! 77	! 64
! 12	! 100	! 864	! 591	! 291	! 155	! 109	! 100
! 13	! 100	! 209	! 274	! 196	! 139	! 91	! 74
! 14	! 100	! 430	! 300	! 160	! 100	! 100	! 100
! 15	! 100	! 360	! 490	! 320	! 150	! 120	! 100
! average	!	!	!	!	!	!	!
! 1 - 15	! 100	! 394.73	! 343.13	! 231.53	! 153.60	! 105.73	! 95.60
! SD	!	! 265.05	! 122.81	! 79.37	! 50.73	! 29.70	! 19.37
! average	!	!	!	!	!	!	!
! 6 - 15	! 100	! 474.20	! 370.20	! 250.30	! 160.10	! 103.60	! 91.10
! SD	!	! 293.65	! 133.64	! 78.91	! 57.42	! 22.24	! 15.51

TABLE D

- Insulinemia : Level 100 at origin
 - Product : Lycasin 80/55

schedule	0	30	60	90	120	150	180
subject							
1	100	308	108	92	100	83	83
2	100	233	142	92	92	83	83
3	100	100	250	200	140	110	100
4	100	77	154	115	100	92	169
5	100	220	130	180	100	100	100
6	100	130	170	110	100	100	100
7	100	277	192	100	77	77	92
8	100	53	53	53	53	53	53
9	100	300	100	100	100	100	100
10	100	225	233	183	192	158	117
11	100	700	360	240	210	250	100
12	100	91	236	236	227	173	91
13	100	120	180	100	100	100	100
14	100	120	240	130	140	110	100
15	100	270	160	210	180	120	100
average							
1 - 15	100	214.93	180.53	146.73	127.40	113.93	99.20
SD		159.82	75.51	60.64	51.98	48.00	23.86
average							
6 - 15	100	228.60	192.40	152.20	137.90	124.10	95.30
SD		186.92	84.05	66.87	60.61	56.39	16.40



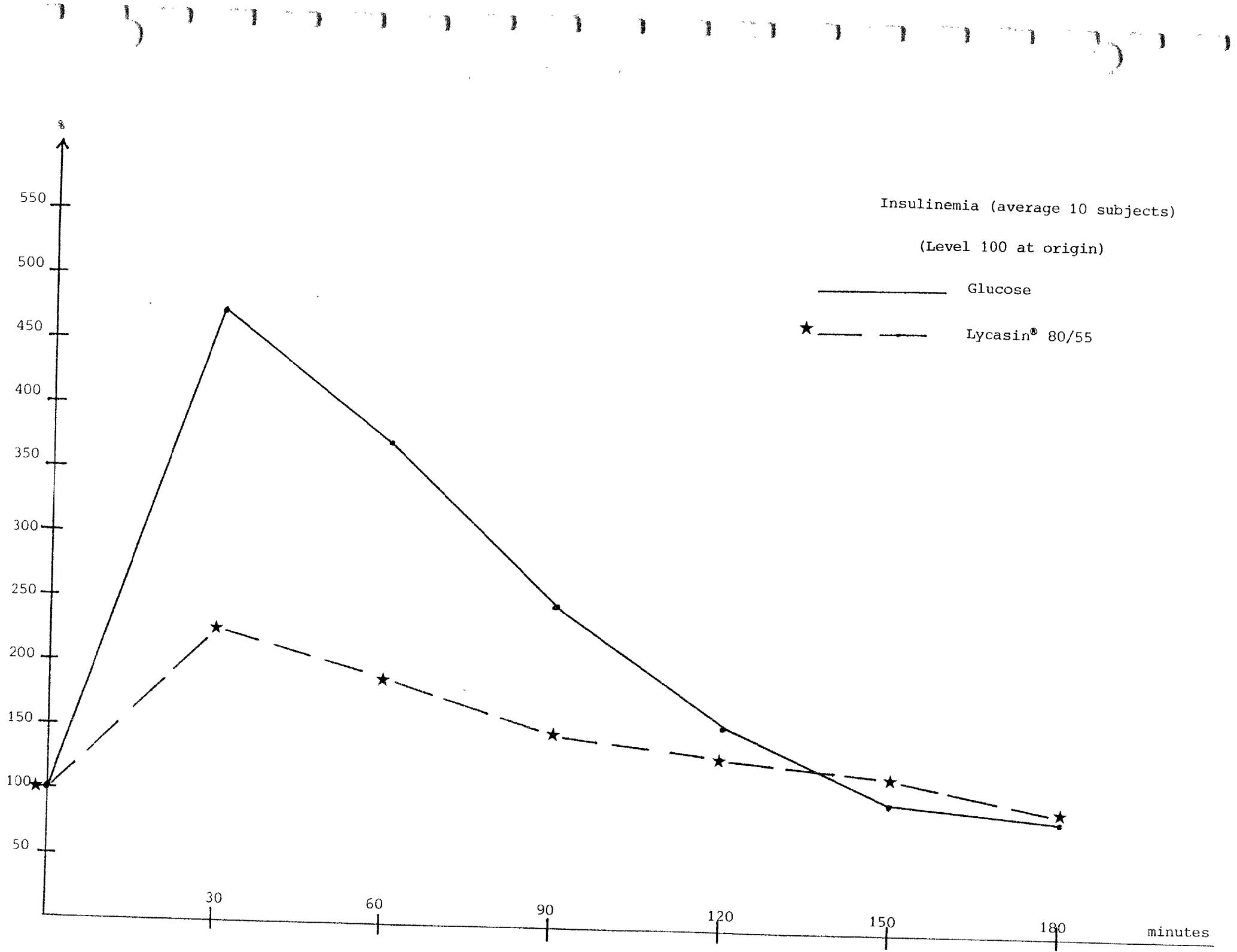


TABLE E
 Statistical evaluation
 (STUDENT's T-test)
 Lycasin 80/55 vs. Glucose
 Level 100 at origin

Subjects 1-15		Glycemia	Insulinemia
!	!	!	!
!	0	0	0
!	30'	3.44 941 *	2.24 993 *
!	60'	1.01 644	4.36 815 *
!	90'	-0.54 471	3.28 814 *
!	120'	-2.07 047 *	1.39 694
!	150'	-4.45 606 *	-0.56 261
!	180'	-2.52 500 *	-0.45 363

* difference being significant for degrees of freedom 28
and p 5% (t = 2.048)

Subjects 6-15		Glycemia	Insulinemia
!	!	!	!
!	0	0	0
!	30'	2.74 201 *	2.23 112 *
!	60'	0.71 825	3.56 135 *
!	90'	-0.02 975	2.99 901 *
!	120'	-1.36 228	0.84 075
!	150'	-4.54 723 *	-1.06 933
!	180'	-2.36 747 *	-0.58 818

* difference being significant for degrees of freedom 18
and p 5% (t = 2.101)

DISCUSSION

The subjects having received 100 g Lycasin complained of abdominal pains, ballooning and flatulence ; these side-effects have disappeared during the night following the end of experiment.

With Lycasin 80/55, the glycemia peak after 30 minutes intake, is lower than with an equivalent glucose dose. This peak is not followed by an hypoglycemia reaction.

Two abnormalities have been noted :

- The subject nr 7 shows a low, secondary and insulinemic type of response after glucose absorption ; the response is higher after Lycasin intake.

- The glycemia in the subject nr 11 is higher after Lycasin than after glucose intake.

The blood maltitol level is variable depending on the subjects under study : 5 subjects (nr 4, 5, 7, 9, 10) have a blood maltitol level between 30 and 179 mg/l whereas 4 other volunteers (nr 6, 8, 13, 15) have only shown non measurable traces of blood maltitol.

The subject nr 1 who showed a higher blood maltitol level during the whole test, has been discarded from the results ; the highest level occurred at the origin point, before Lycasin absorption.

We have noticed a low maltitol content in the urines collected 3 hours after Lycasin ingestion.

Because of analytical difficulties, the fecal maltitol excretion survey was left out.

Conclusion : the hydrolysis of some derivatives of Lycasin at the intestinal level seemed to be justified by the rapid glycemia increase just after Lycasin intake.

The maltitol seems to be prone to diffusion through the intestinal barrier, because of its presence at low level in blood. This is confirmed by the maltitol presence in urines.

Lycasin 80/55 seems highly valuable, as in case of intake of a single dose, there is no hyperglycemia peak ; moreover, the insulinemia reaction is similar to the one observed after intake of a similar quantity of glucose in the normal subject. Otherwise, Lycasin 80/55 does not induce a reactional type of hypoglycemia.

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