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Glucose Metabolism in Cataractous Lens

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ABSTRACT. Since the sorbitol pathway in the lens of a diabetic rat was discovered, the relation between cataract formation and aldose reductase has been studied.

We measured glucose, sorbitol and fructose in the human cataractous lens by the gaschromatography. Additionally, we measured sugar and polyols in bovine, pig and rabbit lens. The ratio of sorbitol/glucose is high in rabbit, pig and bovine lens in order.

In the human cataractous lens, glucose is increased in accordance with development of cataract.

On the other hand, sorbitol content is high in the diabetic lens and low in the senile cataractous lens.

The aldose reductase inhibitor may have beneficial effects in the prevention of diabetic cataract formation, but have not the therapeutic effect in the senile cataract.

Key words : cataractous lens — glucose metabolism — sugar and polyols — gaschromatography

In the lens, glucose is an important energy source. In the glucose metabolism of lens, there are three ways, anaerobic pathway, pentose phosphate cycle and sorbitol pathway.

Since the sorbitol pathway in the diabetic rat lens was discovered, the relation between sorbitol accumulation and cataracta formation has been discussed. Aldose reductase, that converts glucose to sorbitol is thought to be important in the cataractous process.

We present here the analysis of glucose metabolism in the human cataractous lens.

MATERIAL AND METHODS

Lens:

Fresh bovine and pig eyes were obtained from the slaughter house. Rabbit eyes were obtained after the venous injection of pentobarbital. Lenses were

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removed from the eyes with the capsule intact. Cataractous human lenses were obtained after the routine intracapsular cataract extraction from the operating rooms at Kawasaki Hospital, Kawasaki Medical School.

After weighing, the extract was made by homogenizing with 2 ml of 5% $ZnSO_4$ (containing 2.5 μg of arabitol) and 2 ml of 0.3 N $Ba(OH)_2$. The extract was centrifuged at 3000 rpm for 10 min. The supernatant substance was freeze dried and added 2 ml of solvent (pirisin : HMDS : TMCS=10 : 0.2 : 0.1). After 30 min at 80°C, the extract was mixed for 1 min with 1 ml of chloroform and 2 ml of water. The water phase was dried with N_2 gas and added 0.2 ml of CS_2 and assayed by gaschromatography (Fig. 1).

human cataractous lens
- measure
- add 2 ml of 5% $ZnSo_4$ (containing 2.5 μg of arabitol)
- homogenize
- add 2 ml of 0.3 N $Ba(OH)_2$
- homogenize
- centrifuge at 3000 rpm for 10 min

↓

supernatant (2 ml)
- freeze-dry
- add 2 ml of (pirisin : HMDS : TMCS=10 : 0.2 : 0.1)
- wait at 80°C for 30 min
- add 1 ml of chloroform and 2 ml of water
- vortex mix for 1 min
- wait for 5 min

↓

water phase
- add 2 ml of water
- vortex mix for 1 min

↓

water phase
- dry with N_2 gas
- add 0.2 ml of CS_2

↓

Gaschromatography

Fig. 1. Schema for the extraction of sugar and polyols of the lens

Gaschromatography:

The gaschromatography was performed using a Shimadzu 4CM-GC. The column was 3 mm ID×2 m and packed with 3% silicon SE-30 chromosorb W.A. W. DMCS 80-100 mesh (Fig. 2).

Apparatus: Shimadzu 4CM-GC
Column: φ 3 mm × 2 m
3% Silicon SE-30
chromosorb W.A.W. DMCS mesh 80/100
Column temperature 190°C
Detector FID: temperature 250°C
Carrier gas: N_2 45 ml/min
Recorder: chromatopac C-RIA

Fig. 2. Gaschromatography analysis

RESULTS

A typical pattern of the gaschromatogram is presented in Fig. 3. Table 1 shows glucose, fructose and sorbitol in lenses and in plasma of different species. There was no difference in the level of sugar and polyols of plasma in different species. The polyol level in rabbit lens was very high. The ratio of sorbitol/glucose was high in rabbit, pig and bovine lens in order (Fig. 4).

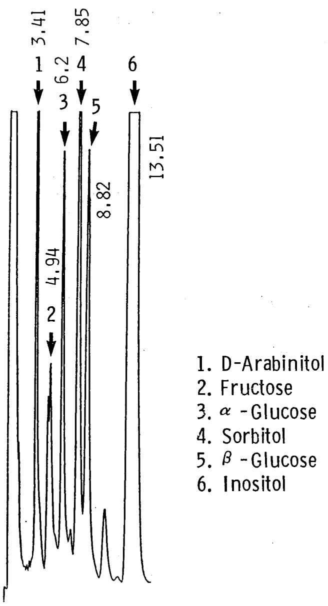

Fig. 3. Gaschromatographic analysis of free sugars and polyols in human cataractous lens

TABLE 1. Free sugars and polyols in lenses and plasma (μg/wwg)

	Glucose	Fructose	Sorbitol
Bovine Lens (n = 8)	85.7 ± 22.5	135.6 ± 52.1	101.3 ± 43.3
Bovine Plasma (n = 5)	111.8 ± 10.5	2.3 ± 0.9	0.5 ± 0.5
Pig Lens (n = 10)	64.4 ± 7.2	218.9 ± 28.7	572.4 ± 61.0
Pig Plasma (n = 5)	107.4 ± 9.2	2.4 ± 0.3	0.6 ± 0.1
Rabbit Lens (n = 10)	72.2 ± 11.9	260.1 ± 51.9	1304.5 ± 306.1
Rabbit Plasma (n = 9)	158.6 ± 31.7	5.1 ± 2.7	0.6 ± 0.3

* P < 0.05 , ** P < 0.005

Table 2 shows sugar and polyols in human lens. Glucose level in human lens was high in diabetic cataract lens and increased in accordance with development of cataract, but not ageing (Fig. 5). Sorbitol level was high in diabetic cataract lens and low in senile cataractous lens.

TABLE 2. Sugars and polyols in human lens (μg/wwg)

	Age	Glucose	Fructose	Sorbitol
Young Clear Lens (N = 3)	10.7 ± 6.7	176.3 ± 100.1	182.5 ± 20.8	88.0 ± 41.0
		* **	* **	**
Diabetic Lens (N = 15)	68.5 ± 13.7	463.6 ± 451.9	108.9 ± 63.9	101.2 ± 116.1
Senile Cataractous Lens		** **		**
incipient (N=17)	71.5 ± 6.8	87.7 ± 51.4	92.9 ± 36.1	54.6 ± 40.5
		*		**
immature (N=34)	69.4 ± 11.5	149.3 ± 107.4	100.3 ± 54.9	56.5 ± 57.4
		** **	**	*
mature (N=27)	69.7 ± 7.6	294.7 ± 182.3	80.5 ± 40.9	26.9 ± 27.1

Mean ± SD * P<0.05 ** P<0.01

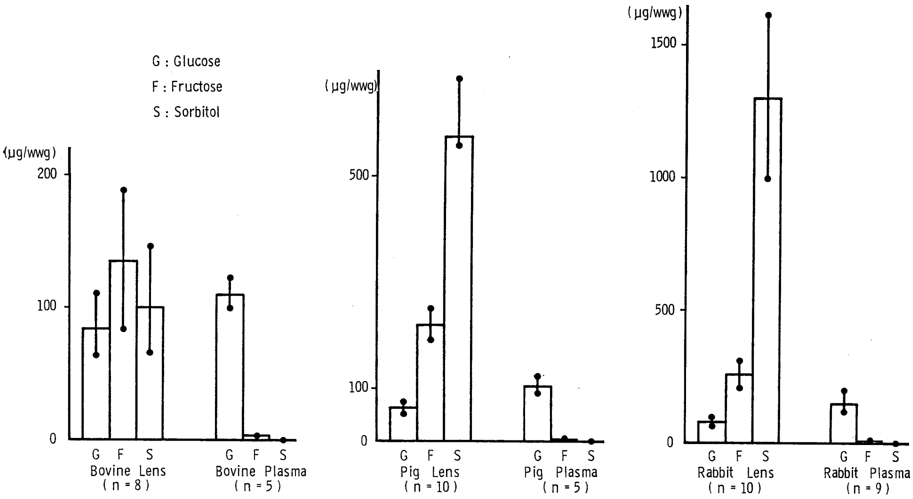

Fig. 4. Free sugars and polyols in lens and plasma

DISCUSSION

Van Heyningen[1] found sorbital in the diabetic lens. In the lens exposed to galactose, the inhibitor of lens aldose reductase was shown to reduce the degree of lens swelling.[2] The aldose reductase of lens is the common factor involved in the formation of sugar cataracts. The eyedrop of aldose reductase inhibitor sorbinil prevents and reverses galactose cataract.[3,4]

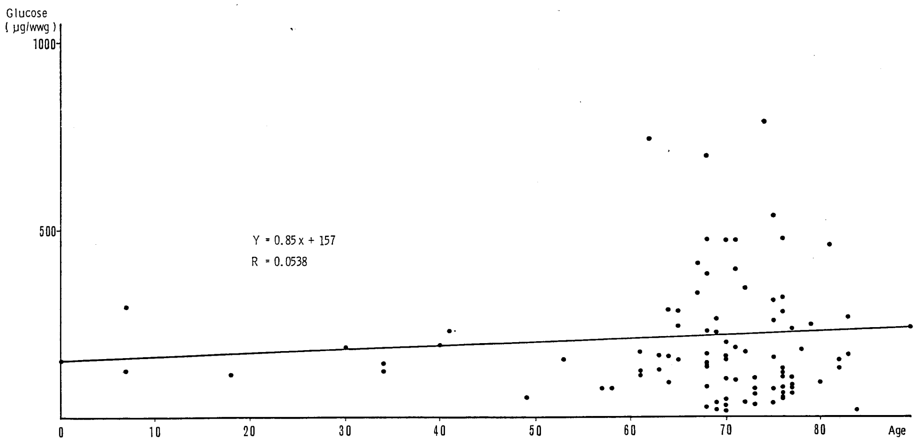

Fig. 5. Glucose in human nondiabetic cataractous lens

In the glucose metabolism in human lens, the main pathway is the anaerobic glycolysis.

In the senile cataractous lens incubated in [^{14}C]glucose, the lactate production accounts for 97% of metabolized glucose.[5]

We reported in this paper that the ratio of sorbitol/glucose in the lens varied in different species.

In the human senile cataractous lens, glucose is increased with development of cataract, and sorbitol content is decreased. In the diabetic lens, both glucose and sorbitol are increased.

Funahashi *et al.*[6] and Ono *et al.*[7] reported that the level of polyols in the diabetic cataractous lens was increased and decreased in the senile cataractous lens. In the senile cataractous lens, glucose content was reported to be increased as we reported.

We suppose the impairment of glucose metabolism in the senile cataractous lens.

The aldose reductase inhibitor may have beneficial effects in the prevention of diabetic cataract, but have not the therapeutic effect in the senile cataract.

Acknowledgment

This paper is a tribute to the memory of Professor Kakuji Yamamoto.

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