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BIOSYNTHESIS OF SIALIC ACIDS IN THE BRAIN AND IN THE GASTRIC MUCOUS MEMBRANE

Chair of Biochemistry
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Tartu 1961

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In recent years great attention has been paid by many investigators to the study of the chemical structure and physiological role of gluco- and mucoproteins and glucolipoproteins, the prosthetic group of which includes neuraminic acid and its acetylated and other derivatives known under the name of sialic acids. Being widely distributed over various tissues of the organism, they are connected with the performance of very different physiological functions of the live organism.

Evidence of the biological importance of sialic acids in the physiological and pathological processes of the central nervous system can be seen in the considerable increase in the amount of gangliosides and hence in the quantity of sialic acids present in the brain in amaurotic idiopathy of the type of the Tay-Sachs disease and to a lesser degree in the Niemann-Pick disease (E.Klenk). Sialic acids have also been isolated from the mucoproteins of the submaxillary gland (G.Blix et al.) and the gastric mucous membrane (Svennerholm et al.). It is possible that mucoproteins, in particular sialic acids, play a certain role in the secretory processes. In this respect observations by Italian investigators (F.Galetti et al.) deserve attention. According to them mucoproteins are produced in those parts of the gastric glands where hydrochloric acid is formed, while a rise in the secretion of hydrochloric acid is accompanied by a more intense secretion of those mucoproteins in the gastric juice.

Sialic acids play an important part in the composition of the blood-group active mucoids and in the gastric mucous

membrane in performing a specific protective function of the organism; they also play an important role in the processes of interaction between viruses and the live organism. Many investigators have also established a connection between the amount of sialic acids in the blood serum and various diseases.

Nevertheless, the path/ways along which the biosynthesis of neuraminic acid and sialic acids proceeds has been studied very insufficiently. Sialic acids are products of the aldolic condensation of N-acetylhexosamine with pyruvic acid. The problem of the nature of hexosamine has not been finally solved. According to the data of D.Comb and S.Roseman, N-acetylmannosamine takes part in the biosynthesis of neuraminic acid; enzymatic synthesis of sialic acids from N-acetylmannosamine and pyruvic acid has been proved in the presence of the purified enzymatic preparation obtained from Cl.perfringens; when N-acetylmannosamine is replaced by the corresponding glycosamine or galactosamine, synthesis of sialic acids does not take place.

The biosynthesis of sialic acids was investigated by us in vitro, in the homogenates of the brain and the mucous membrane of the fundic part of the stomach at pH 6.5 with different substrates added, as well as in vivo on the whole organism. The quantity of sialic acids formed was colorimetrically determined with the Winzler diphenylamine-reagent.

The homogenates of the brain as well as the gastric mucous membrane of cats and guinea-pigs contain an enzymatic system carrying out the synthesis of sialic acids from

pyruvic acid and glycosamine in the presence of glucose-6-phosphate (Fig. 1,2 - I).

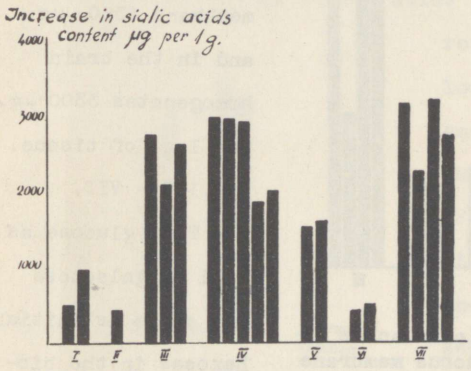

Fig.1. Biosynthesis of sialic acids in brain homogenates.

I - glucose-6-phosphate + pyruvate+ + glycosamine
II - glucose-6-phosphate + pyruvate+ + glutamine
III - glucose-6-phosphate+pyruvate+ glucosamine+ATP
IV - glucose-6-phosphate+pyruvate+ glutamine + ATP
V - glucose+pyruvate+glutamine+ATP
VI - galactose+pyruvate+glutamine+ATP
VII - galactose+pyruvate+glutamine+ATP+ glucose-6-phosphate

Glycosamine may be replaced by glutamine as a source of the amino group at the expense of which hexosamine synthesis takes place (Fig.1,2-II). Increase in sialic acid constituted 500-1000 μg. per 1 g. of fresh tissue weight.

Addition of ATP to the both systems increases the synthesis of sialic acids many times (Fig.1,2-III,IV); this increase constituted 3000-3300 μg. per 1 g. of tissue. In the presence of ATP synthesis of sialic acids takes also place when glucose--6-phosphate and glycosamine are replaced by glutamine (Fig. 1,2 - V,VI). The addition of glucose-6-phosphate to this system (pyruvic acid + galactose + glutamine + ATP) considerably increases the biosynthesis of sialic acids (in the

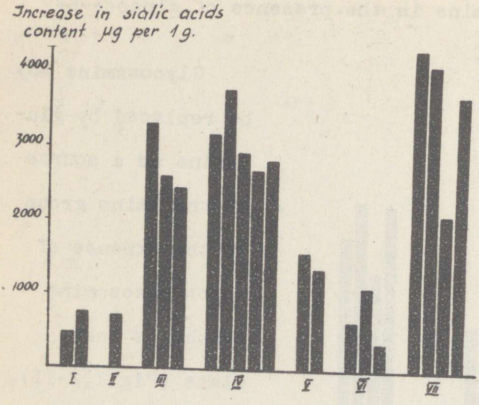

Fig.2. Biosynthesis of sialic acids in homogenates of gastric mucous membrane For explanations see Fig.1.

homogenates of the gastric mucous membrane 4350 µg. and in the brain homogenates 3300 µg. per 1 g. of tissue. Fig.1,2 - VII.

Thus glucose as well as galactose may serve as initial hexoses in the biosynthesis of sialic acids in the homogenates of the brain and of the gastric mucous membrane. Special significance has to be attributed to glucose-6-phosphate since in its presence the synthesis of sialic acids is much more intensive. One may assume that glucose-6-phosphate is an active form of glucose from which first the corresponding hexosamine and then sialic acid are formed. Still, the question of whether glucose is included in the molecule of sialic acids as such or whether there proceeds epimeric conversion of glucose into mannose remains unsolved. It is more difficult to imagine conversion of galactose, which is not epimeric with mannose.

It was established in experiments with subcellular fractions of the gastric mucous membrane that the biosynthesis of sialic acids in the system of glucose-6-phosphate + pyruvic

acid + glutamine proceeds more intensively in microsomal and mitochondrial fractions than in cytoplasm (Fig.3). Nevertheless, the content of the sialic acids themselves in the microsomal fraction is the lowest of all whereas the amount of sialic acids in the mitochondria is higher (Fig.4). Hence, the enzymatic systems carrying out the synthesis of sialic acids are localized in the fraction of microsomes and mitochondria.

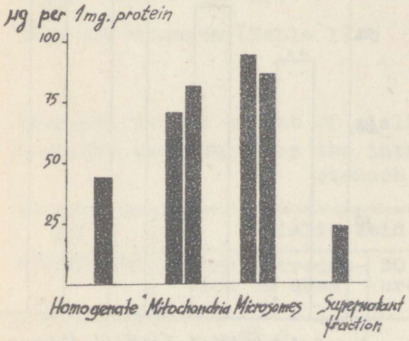

Fig.3. Biosynthesis of sialic acids in subcellular fractions of gastric mucous membrane.

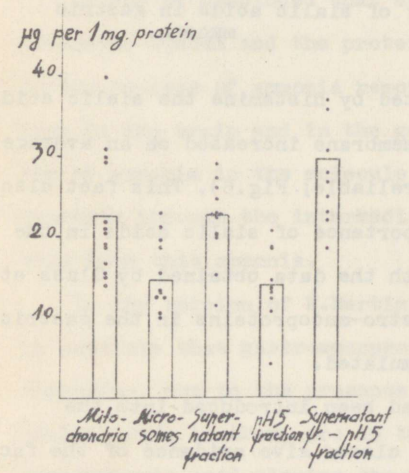

Fig.4. Sialic acid content in subcellular fractions of gastric mucous membrane.

Biosynthesis of sialic acids in vitro is also confirmed by experiments carried out on the whole organism. When ammonia is administered to cats parenterally only in the form of ammonium chloride solution or along with glutamic acid, the level of sialic acids in the brain and the gastric mucous membrane increases statistically significantly (Fig.5,6).

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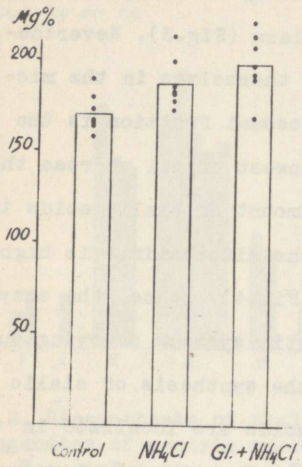

Fig.5. Effect of administering ammonia alone and along with glutamic acid on the biosynthesis of sialic acids in brain.

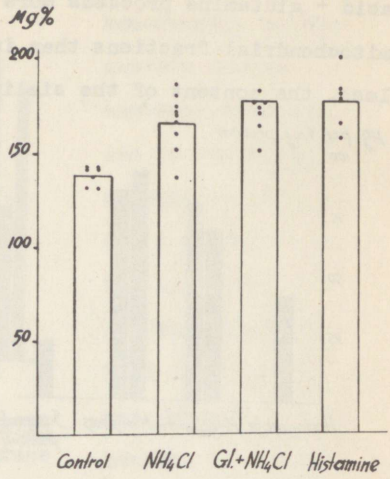

Fig.6. Effect of administering ammonia alone and along with glutamic acid and effect of histamine on the biosynthesis of sialic acids in gastric mucosa.

When secretion was stimulated by histamine the sialic acids content in the gastric mucous membrane increased on an average by 29 per cent (statistically reliable; Fig.6). This fact also testifies to the functional importance of sialic acids in the stomach and is in agreement with the data obtained by Glass et al. on the increase in acid gastro-mucoproteins in the gastric juice in case secretion is stimulated.

Data obtained after urea had been introduced into the stomach with both of its sides closed give evidence of the fact that ammonia (which - according to the data of the Chair of Biochemistry of Tartu State University - is formed from urea in the cells of the gastric mucous membrane under the action of

the ferment urease) is used in the synthesis of sialic acids. In our experiments after a lapse of half an hour, the sialic acids content was found to be increasing in the blood flowing from the stomach (Table 1).

Tabel 1.

Increase in the amount of sialic acids in the blood flowing from the stomach after the introduction of urea into the stomach of dogs.

Nº of experiment	Sialic acid content in blood in mg%		
	Before introduction of urea	30 minutes after urea introduction	60 minutes after urea introduction
1	62.2	72.5	74.1
2	88.1	100.0	87.5
3	47.5	54.0	69.4
4	74.5	83.8	86.8

It can be concluded that apart from the glutamic acid - glutamine system and the proteins, sialic acids participate in the process of ammonia removal as well as in ammonia formation in the brain and in the gastric mucous membrane. Inclusion of ammonia in the molecule of sialic acids apparently proceeds through the intermediate stage of glutamine formation from this ammonia.

In the opinion of E.Martinson and his collaborators it is possible that gastromucoproteins as substances of an acid character, due to the presence of acid grpups, particularly sialic acids in them, are in the process of the formation of hydrochloric acid playing the part of a cationite structurally fixed in the secretory cells.

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БИОСИНТЕЗ СИАЛОВЫХ КИСЛОТ В МОЗГУ И СЛИЗИСТОЙ ОБОЛОЧКЕ ЖЕЛУДКА

На английском языке

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Tir. 120 eks. 05647 Tell. nr. 548
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