ON NORMAL AND PROVOKED BLOOD ALLOXAN

by

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PRELIMINARY REPORT

ARCHIBALD[1] has developed a photometric method for the determination of alloxan. With the aid of this method he has examined the fate of alloxan after its introduction into the mammalian body. He furthermore demonstrated that alloxan is a normal blood constituent, thought it occurs only in minute amounts.

In this laboratory blood alloxan has been determined in the normal rats, horses, and in man. The average content was in all cases about 0.02 mg %. The deviations from this value was of the same order of magnitude as the accuracy of the method.

Further, the following experiments have been made:

After 48 hours of fasting some rats were given glucose *per os* (1 g/kg body wt). After 20–40 minutes the blood alloxan was determined *ad modum* ARCHIBALD[1]. This revealed that an increase up to 50 times the normal of alloxan had taken place.

The effect of some of the normal metabolites of glucose was then tested. Also here an increase of the blood alloxan was found as shown in Table I. This increase may be called "provoked" blood alloxan.

TABLE I

Rat No.	Compound ingested by stomach tube	Amount g/kg	Blood alloxan
26	Glucose	1.0	1.02 mg %
dl 5	Glucose	1.0	1.10 ,,
10	Glucose	1.0	0.98 ,,
11	Glucose	1.0	0.95 ,,
3	Pyruvic acid	1.0	0.55 ,,
4	Pyruvic acid	1.0	0.59 ,,
25	Succinic acid	1.0	0.79 ,,
2	Succinic acid	1.0	0.89 ,,
16	Fumaric acid	1.0	1.02 ,,
14	Fumaric acid	1.0	0.98 ,,
6	Malic acid	1.0	0.03 ,,
9	Malic acid	1.0	0.04 ,,
7	None		0.025 ,,
8	None		0.020 ,,
12	None		0.030 ,,
13	None		0.015 ,,
Horse	None		0.015 ,,
Man	None		0.020 ,,
,,	None		0.021 ,,

The blood was withdrawn from the heart 20–40 minutes after the compounds were ingested.

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The interpretation of these experiments must be that carbohydrates are in some way involved in the production of alloxan in the organism. Since the ingestion of carbohydrates results in an increase in insulin production, and some workers have claimed a stimulating effect on insulin production by alloxan, it was deemed desirable to carry out the following series of experiments:

Six rats were given "Rockland Complete Rat Diet" (Arcady Farms Milling Company, Chicago, Ill., USA) which, by the way, did not give normal growth rate. Their blood sugar was determined *ad modum* HAGEDORN AND JENSEN[2]. The average was 150 mg %. After injection of a 5 % solution of alloxan monohydrate intraperitoneally (20 mg alloxan per kilogram body weight*), the blood alloxan rose to about 1 mg %. Simultaneously the blood sugar decreased about 33 % which gave an average of about 100 mg %. In the beginning of the experiment alloxan had to be injected every 12 hours and later in the experiment once a day in order to keep the blood alloxan on the level indicated.

This result suggests that carbohydrate stimulates insulin production through the provoked alloxan, which, according to other authors, stimulates insulin production itself.

Fig. 1 shows blood sugar values throughout the experiment. No hyperglycemia was developed. The animals died at the end of the experiment with glucosuria suggesting a renal lesion.

An attempt to produce hyperglycemia and glucosuria with mesoxalic and tartronic acids failed. Many of the animals died. The surviving animals showed neither hyperglycemia nor glucosuria. Most of them died in spasms in the course of a week or so. Some of the animals showed a marked hypertrophy of the adrenals.

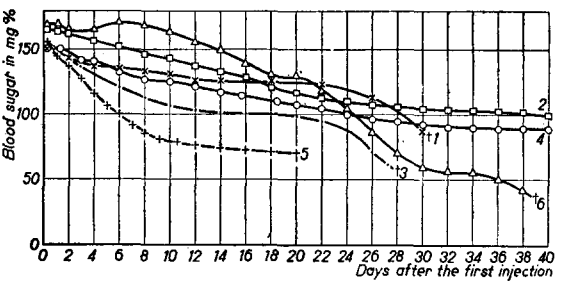

Fig. 1. Blood sugar variations in six rats after intraperitoneal injection of small amounts of alloxan

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SUMMARY

It has been shown that the oral ingestion of high amounts of glucose results in a marked increase of blood alloxan. Some carbohydrate metabolites exert a similar blood alloxan increasing effect. Malic acid shows no effect.

The intraperitoneal injection of small amounts of alloxan resulted in hyperglycemia.

It is suggested that carbohydrate has a normal function in alloxan metabolism. Alloxan cannot be formed by mesoxalic nor tartronic acids even in toxic amounts. Tartronic and mesoxalic acids show high toxicity.

Further research on the connexion between carbohydrate and alloxan metabolism will be published in detail later.

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* This is less than the diabetogenic amount which is about 200 mg/kg body wt.[3].

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RÉSUMÉ

L'ingestion de quantités élevées de glucose provoque un accroissement sensible de l'alloxane sanguin. D'autres substances dérivant du métabolisme des hydrates de carbone, provoquent un accroissement analogue d'alloxane. L'acide malique n'a aucune action.

L'injection intrapéritonéale de petites quantités d'alloxane provoque l'hyperglycémie.

Il semble que les hydrates de carbone exercent une fonction normale dans le métabolisme de l'alloxane. L'alloxane ne peut être formé ni par l'acide mésoxalique ni par l'acide tartronique, même lorsque ceux-ci sont en quantité toxique. Ces deux acides sont en effet fortement toxiques.

D'autres recherches sur les relations entre le métabolisme des hydrates de carbone et le métabolisme de l'alloxane seront publiées ultérieurement en détail.

ZUSAMMENFASSUNG

Es wurde gezeigt, dass die Verabreichung grosser Mengen von Glukose *per os* eine deutliche Erhöhung des Blutalloxans zur Folge hat. Einige Kohlenhydratstoffwechselprodukte haben eine gleichartige Blutalloxan-erhöhende Wirkung. Äpfelsäure hat keinen Effekt.

Intraperitoneale Injektion kleiner Mengen von Alloxan ruft Hyperglykämie hervor.

Es wird angenommen, dass Kohlenhydrat eine normale Funktion im Alloxanstoffwechsel hat. Alloxan kann weder aus Mesoxal- noch aus Tartronsäure gebildet werden, sogar wenn diese in toxischen Mengen vorhanden sind. Mesoxal- und Tartronsäure zeigen hohe Toxizität.

Weitere Untersuchungen über den Zusammenhang zwischen Kohlenhydrat- und Alloxanstoffwechsel werden später detailliert veröffentlicht werden.

REFERENCES

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