Physiology. — *"The partial permeability of the glomerular membrane to d-galactose and some other multi-rotatory sugars"*. By Prof. H. J. HAMBURGER.

(Communicated in the meeting of September 27, 1919).

Through earlier experiments it has appeared already that d-galactose is only partially retained [1]) by the glomerular membrane. Upon closer examination, however, this appears to agree very little with the idea of permeability, because a filter either holds back a substance or allows it to pass through unconditionally. A mean between these two extremes can hardly be conceived when there is question of only a simple substance and not of a mixture. As a matter of fact at first we were inclined therefore to drop the idea of permeability, but, as appears from the preceding article we endeavoured in vain to clear up the matter with the help of surface tension, viscosity or adsorption. For this reason we then returned again to the idea of permeability.

On closer inspection two explanations still seemed possible to us:

1st. The concentrations of the galactose-solutions which had been used up to this (0.1 % and 0.15 %), might have been too strong that is above the toleration of the kidney for d-galactose. We were mindful here of our experience in connection with glucose; for, did we not find formerly [2]), that, when the concentration of glucose in the perfusion liquid exceeded the physiological value only by 0.02 %, already a little of the glucose was suffered to pass through, and, that this quantity increased in proportion as the concentration of sugar in the perfusion liquid became stronger, so that when the concentration of glucose had become 0.2 % practically no sugar was retained any longer? There was a possibility therefore that also the concentration of galactose might have been too strong and that it had to be ascribed to this that it was partly retained and partly not. *It was therefore desirable to make determinations of the toleration of the kidneys for d-galactose.* Should it appear then that the galactose could not, like the glucose, be *wholly* retained even in weak con-

[1]) HAMBURGER and BRINKMAN, These Proc. 28 Sept. 1918.

[2]) HAMBURGER and BRINKMAN, Biochem. Zeitschr., **88**, 97, (1918).

centrations, then the phenomenon of partial retention could not be explained by the idea of toleration and then a second explanation would per exclusionem be the correct one.

2nd. This second explanation could be sought in the fact that *the d-galactose exists in two modifications* — an α and a β variety. In aqueous solutions these two varieties are in a state of equilibrium. Then it had to be accepted only that one of the two modifications was retained by the glomerular membrane, and the other not.

1. *Toleration of the kidneys for d-galactose.*

To determine the toleration, the perfusion liquid was seasoned with different quantities of d-galactose lying between 0.05 % and 0.25 %. The following table gives a survey of the results obtained. It will be clear without further explanation. Let it only be remarked that for the determination of the reduction the newest method of BANG (1918) was employed [1]). Each time both kidneys of two frogs were perfused at the same time (see table I).

What do these experiments teach us?

Firstly: *That none of the used galactose-solutions,* whose concentrations lie, as has been said, between 0.05 % and 0.25 % *are completely retained by the kidneys.* Secondly, *that in all cases the retention amounted on an average to a half, independent of the concentration of the galactose-solution that was perfused.*

In both respects the galactose differs from the glucose; for, was there not found a *total* retention in the case of glucose when the solution was weaker than 0.05 %—0.08 % (individual differences)? In the case of galactose, on the contrary, there is no question of t o t a l retention. And, as regards the second point, in the case of galactose *the toleration remains unchanged* in spite of the increase in sugar concentration. Only when the concentration becomes as high as 0.25 % does the toleration diminish. Experiments with stronger concentrations were not made since the secretion of artificial urine then became too scanty.

We still have at our disposal a number of former experiments in which the reduction was determined by the earlier method of BANG (1916), a part of which experiments have been published already. They are found together in the following table (II). As will be noticed the results are not as uniform as those of table I, but in any case they point in the same direction.

[1]) Compare for this our previous article in these Proceedings.

TABLE I.

The toleration of the glomerular membrane for d-galactose.

Date of experiments.	Frog.	I. The perfusion liquid contains of galactose:	II. Reduction of perfusion liquid expressed in glucose %.	III. The urine has a reducing power of glucose %.		IV. Retention (II—III).		V. Percentage retention of galactose. Average of the kidneys (calculated from II and IV).
				Out of the right kidney.	Out of the left kidney.	Right kidney	Left kidney	
12th June 1919	A.	0.05 %	0.0964	0.0535	0.0535	0.0429	0.0429	$\frac{0.0429}{0.0964} \times 100 = 51$ %
	B.	0.05 „		0.0571	0.0535	0.0393	0.0429	46 %
14th June „	A.	0.1 „	0.125	0.0571	0.0531	0.0679	0.0715	56 „
	B.	0.1 „		0.0607	0.0571	0.0643	0.0679	53 „
3rd July „	A.	0.1 „	0.0785	0.0357	0.04	0.0428	0.0385	56 „
	B.	0.1 „		0.04	0.05	0.0385	0.0285	43 „
4th July „	A.	0.1 „	0.0714	0.0357	0.0285	0.0357	0.0429	55 „
	B.	0.1 „		0.0357	0.0321	0.0357	0.0393	53 „
1st July „	A.	0.15 „	0.112	0.05	0.057	0.062	0.055	52 „
	B.	0.15 „		0.05	0.0607	0.062	0.0513	51 „
30th June „	A.	0.2 „	0.157	0.107	0.057	0.050	0.082	42 „
	B.	0.2 „		0.0893	0.0893	0.0677	0.0677	43 „
1st July „	A.	0.25 „	0.193	0.121	0.121	0 072	0.072	37 „
	B.	0.25 „		0.13	0.063	0.13	0.063	33 „

TABLE II.

The toleration of the glomerular membrane for d-galactose (Method of BANG 1916).

Date of experiment.	Frog.	I. The perfusion liquid contains of glucose:	II. Reduction of perfusion liquid expressed in glucose %.	III. The urine has a reducing power of glucose %.		IV. Retention (II—III).		V. Percentage retention of galactose. Average of the kidneys (calculated from I and II).
				Out of the right kidney.	Out of the left kidney.	Right kidney	Left kidney.	
31st Oct. 1918	A.	0.06 %	0.045 %	0.03	0.02	0.015	0.025	46 %
	B.			0.025	0.03	0.02	0.015	44 „
16th Aug. „		0.1 „	0.07 „	0.045	0.04	0.025	0.03	39 „
17th Aug. „		0.1 „	0.055 „	0.0325	0.0325	0.0225	0.0225	41 „
18th Aug. „		0.1 „	0.055 „	0.0325	0.0325	0.0225	0.0225	41 „
Sept. „	A.	0.1 „	0.0825 „	0.049	0.050	0.033	0.0325	40 „
	B.			0.078	0.0825	0.038	0 ?	46 „
	C.			0.0663	0.0675	0.0162	0.015	19 „
	A.	0.1 „	0.0725 „	0.05	0.0525	0.0225	0.02	30 „
	B.			0.045	0.048	0.0275	0.0245	36 „
	C.			0.047	0.045	0.0250	0.0275	40 „
23rd Aug. „	A.	0.15 „	0.0975 „	0.07	0.07	0.0275	0.0275	29 „
	B.			0.0525	0.05	0.045	0.0475	41 „

Also from this table it appears, that, in contrast with what was always found for glucose, *the galactose was not totally retained in any of the experiments, and further, that the retained part forms more or less the half — here a little less than the half.*

Consequently the first explanation mentioned on page 361 fails here and we are obliged, per exclusionem, to accept the second explanation, viz., the one based upon the fact that in aqueous solution the galactose exists in two modifications.

2. *The solution of galactose contains two forms of galactose that behave differently towards the kidneys.*

As is known a large number of sugars exhibits multirotation (DUBRUNFAUT), i.e. some time after the preparation of the aqueous solution they generally possess a slighter specific rotation than immediately after the solution is made. Several explanations, which we need not discuss here have been given for this. It is agreed upon however that under the influence of the solvent, part of the sugar changes into another form with a slighter rotatory power. The two forms are in equilibrium.

This idea is based, in the first place, upon the researches of TANRET [1]), who separated in solutions, first of glucose and afterwards of galactose and other sugars, three forms with different rotatory power, and several different physical properties; these he termed α, β and γ: the α modification of d-galactose with a specific rotatory power of $+135°$, a β modification with $[\alpha]_D = +81°$ and a γ modification of $[\alpha]_D = +53°$.

More extensive researches, especially of E. ROUX [2]) and further of BOURQUELOT [3]) have taught however that the β variety of TANRET is no independent sugar, but consists of a mixture of α and γ, which are in equilibrium.

I find it useful to point out here a misunderstanding in the literature which has given me much trouble personally, and, I am informed, others also. In several scientific treaties and textbooks it is stated or taken for granted that there are two modifications only; these are called then the α and β modifications. It is clear here that the β modification is actually the γ modification of TANRET. But, as far as I know, nobody calls attention to this fact. To what faulty reports

[1]) TANRET, Bulletin de la Société Chimique, [3], **13**, (1895), p. 728 [3], **15**. (1896), 195.

[2]) E ROUX, Ann. Chim. et de Phys., VII Série, **30**, p. 422.

[3]) BOURQUELOT, Journal de Pharm. et de Chem. [7], **14**, (1916) 225.

this interchange of the two can lead appears for instance in the wellknown tables of LANDOLT-BORNSTEIN 4e Aufl. 1912. There we read in connection with d-galactose: "Anfangsdrehung nach 7 Minuten als α Modifikation $+ 117°.5$; Enddrehung nach 7 Stunden als β-Modification $+ 80°.27$." In fact the final rotation which an ordinary d-galactose solution exhibits is 80°.27 or simply 81°. But this is not the rotation of the second modification; that rotation is $+ 53°$. A rotation of 81° results when the two modifications of 117°5 and $+ 53°$ are in equilibrium. And this equilibrium comes about when we start out from β as well as when we do from α. In both cases a mixture results with a rotatory power of 81°.

It is perhaps useful that what has been brought forward for d-galactose should also be applied to d-glucose, which is so much more used.

TANRET distinguishes 3 forms of glucose: an α form with $[\alpha]_D = 106°$, a β form with $[\alpha]_D = 53°$ and a γ form with $[\alpha]_D = 19°$; Both α and β forms when dissolved in water finally exhibit a rotation of 53°. The β form of TANRET, according to the researches of Roux and others, must be considered as an equilibrium between α and γ, and this is at present generally accepted too. β is therefore no independent modification, but merely a mixture. But now we read the following: There exist two forms of glucose, — the α and the β forms and not infrequently there is added: The α form is converted into the β form. How can those who maintain that we have to deal with a reversible reaction here, speak of an *equilibrium* between α and β? If it were stated that the α form is *partially* converted into the β form, it would be clear.

We find the case put differently again by HOLLEMAN in his wellknown text book of Organic Chemistry, 5th ed., 1912, p. 300. He also speaks of an α form of 106°, a β form of 19° and a γ form of 53°. This γ form is according to him a mixture of α and β. The γ of TANRET HOLLEMAN calls thus β.

The question arises why TANRETS' nomenclature was not stuck to. After EMIL FISCHER had shown us how to prepare artificial glucosides [1]) it appeared to him that stereoisomeric modifications of each glucoside existed. One was acted upon by beer ferment (invertine), and the other by emulsine. [2]) By way of distinction he called the first the α-glucoside and the second the β-glucoside and the corresponding forms of glucose α- and β glucose [3]). It is to this nomenclature that later writers seem to have stuck. For this there was an inducement to some extent as if there existed only two forms it was not quite rational to call the second γ. Coincidentally that which EMIL FISCHER calls β corresponds with what TANRET at the same time gave the name of γ.

To explain now the partial retention of the galactose solution which is passed through the kidneys, we assume that *only one of the*

[1]) EMIL FISCHER, Ber. d. D. Chem. Ges. **26**, 2400 (1893).

[2]) The same, Ber. **27**, 2985, (1894); **28**, 1145, (1895).

[3]) C.f. also E. FISCHER, Z. f. physiol. Chemie **26**, 60, (1898).

modifications is retained by the glomerular membrane, and the other is allowed to pass through.

As appears from tables I and II, of not too strong concentrations about the half is retained

It is now, upon closer inspection of what has been handled above, possible to calculate in a simple way the relative quantities of α- and β-galactose.

If we call the amount of the α variety (rotation + 135°) in the galactose solution, in which there is equilibrium between α and β, x, then 1— x is the amount of the β variety (rotation + 53°), and then, because the rotation of the mixture 81° is, the following equation must hold:

$$135x + 53\,(1-x) = 81.$$
$$x = 0{,}34.$$
$$1-x = 0{,}66.$$

Therefore the ratio between the quantities of the α and β forms is 34 . 66.

These figures cannot boast of great accuracy, because, in the first place, we find with other writers for the specific rotation of the α variety a value of 117° and not 135°. If this value is the true one then we should get a ratio of 44 : 56 between the modifications. Further it must be remembered that the concentration and temperature of the galactose solution are not without influence on the equilibrium. In general however it can well be said that the greater half is the β-form (γ-form of TANRET).

A similar proportion can also be deduced from the researches of E. ROUX in connection with the rate of conversion of the α into the γ-form.

It is now very remarkable also in our perfusion experiments that more or less the half of the galactose is retained. This parallellism can be considered as supporting our hypothesis. Whether it is the α- or γ-form which is retained we cannot venture to say with any certainty at present. That might be the case, if, in the first place, the values of the rotations which we used above in deducing the relative quantities of the α- and β-forms had been taken at the same concentrations as the physiological concentrations (0.05%—0.15%), which we used in our perfusion experiments.

In the second place the values found along chemical lines for the rotation, in concentrations of 6%—18%, leave much to be desired. And then in the next place it must not be forgotten that, as a matter of course, the degree of accuracy of our determinations of the

reduction, by our perfusion experiments is but small. To grasp this it must be remembered that the quantity of artificial urine obtained from our experiments with frogs was only 0.1 c.c. Let us take an arbitrary example to see what influence a small error has on the titration.

In table I perfusing with 0.15% galactose for obtaining the final reaction was used:

for the urine of frog A	right kidney	1,83 cc.	thiosulphate
	left kidney	1,81 „	„
for the urine of frog B	right kidney	1,83 „	„
	left kidney	1,80 „	„

From these figures the value calculated for the galactose retention for frog A is 55 % and 49 % and for frog B 55 % and 46 %. An error of 0.02 % thiosulphate, therefore, causes an error of 55—49 = 6 % in the retentive power found.

To increase the degree of accuracy it is necessary to experiment upon larger animals, which supply more urine, thus with kidneys of warm blooded animals. For this however a room is necessary which can be brought up to body temperature, which, under present circumstances, is impossible.

Be it as it may, if the differences between the retained and the not retained had been greater — for, did we not find that approximately half was retained and half not —? and, to correspond with this, the difference between the quantities of α and β modifications in the galactose solution had also been greater, then it would at once have been obvious which form is retained and which is not. We will return to this in connection with xylose.

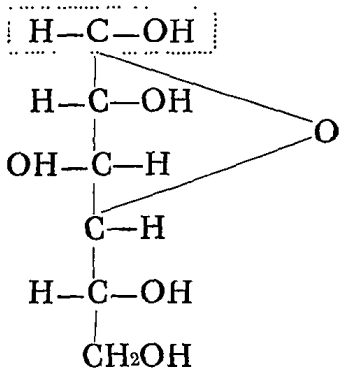
Before we proceed to discuss the behaviour of xylose, we wish to face an objection which may, on superficial inspection, be made against our representation. It could be remarked that when *one* of the two modifications has been removed by the kidney, from the second modification which remains in circulation, more of the first modification will be formed, and that eventually all the galactose will leave the kidney in that way. Let it be taken into consideration however that in our perfusion experiments the perfusion liquid forms only a very small quantity of urine and therefore only very little of the one kind of galactose is removed. Let it further be remembered that, unlike in the normal body, the same perfusion fluid does not remain in circulation. In our experiments the solution leaving by the renal vein does not return again by the renal artery.

But what can be the reason then that in the normal organism

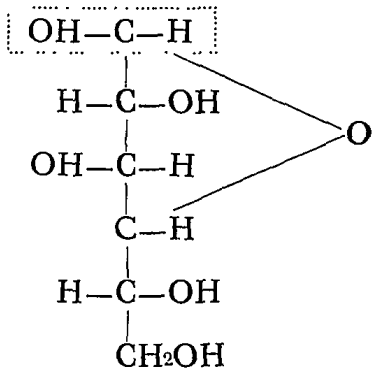
the urine does not always contain galactose, i.e. that modification which, according to us, the kidney is permeable to? Is it perhaps just this form which is used in the building up of the cerebrosides? This will have to be determined by further experimentation.

Lastly, before leaving the galactose, it may be interesting just to call attention to this: viz., how slight the difference in structure between the α- and β-forms is, which difference is concerned with their *retention* or *non-retention*.

Thanks especially to the researches of EMIL FISCHER (l.c.), ALBERDA VAN EKENSTEIN, BÖESEKEN [1]), to which also correspond those of BOURQUELOT [2]), it must be assumed a little in contravention to the current idea, that the structural formulae of the two forms of galactose can be represented as follows:



α-d-galactose.



β-(γ-)d-galactose.

From these formulae it appears that here mutatis mutandis *the retention is exclusively dependent upon the relative places of the OH and H with regard to the first asymmetric C-atom.*

The partial retention of l-xylose.

The thought of the explanation given in the previous paragraph for the partial retention of the galactose solution occurred to us when it was noticed that also xylose-solutions were subject to partial retention. Corresponding to this is the fact that, like in glucose-solutions, also in xylose-solutions two modifications could be separated by TANRET. Also in the case of xyloses EMIL FISCHER could separate two glucosides, or xylosides rather, an α- and a β-form, for instance:

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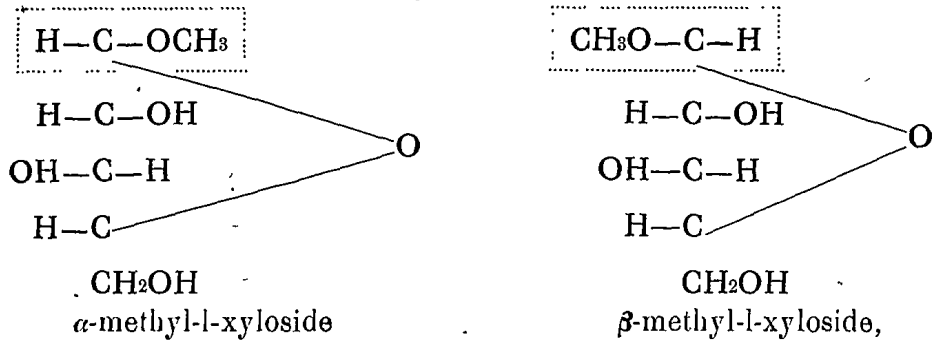
[1]) BÖESEKEN, These Proc. 29th June 1912; 25th March 1916.

[2]) BOURQUELOT, l.c.



α-methyl-l-xyloside β-methyl-l-xyloside,

the first of which is converted by invertine and the second only by emulsine, and which were distinguished by FISCHER as α and β. Suppose the CH_3 substituted by H, then α- and β-xylose is formed again.

Similar experiments as were made with galactose were also made with xylose. We give a table which contains the experiments in question (see table III).

From this table it appears that the l-xylose, like the d-galactose, is not retained completely either. Always the greater portion passes through the glomerular membrane, a *greater portion percent, however*, than was the case with d-galactose; between $^1/_3$ and $^1/_4$ only of the xylose, used in concentrations which do not affect the production of artificial urine, on an average is retained.

We now find, according to VON LIPPMANN[1]) for the rotation of the l-xyloses: initial rotation $+ 78°$, final rotation $+ 19°$. Therefore, the α-form has a rotation of $+ 78°$; the β-form however has up to this not been isolated, and therefore it cannot be stated, how much of this modification takes part in the final rotation of $+ 19°$. Also for xylose it is therefore not possible to indicate the form, which is retained by the kidneys, and which is allowed to pass through.

That the glomerular membrane possesses the property of separating two sugars quantitatively like a sieve, retaining one and letting the other pass through, we have formerly been able to show with mixtures of glucose and fructose, and glucose and lactose[2]).

Let us remark that researchers who are engaged upon distinguishing of sugars by means of microbes[3]) have to reckon with

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[1]) VON LIPPMANN, Chemie der Zuckerarten.

[2]) HAMBURGER and BRINKMAN, These Proc. Sept. 28th 1918.

[3]) C.f. among others A. J. KLUYVER, Biochemische Suikerbepalingen. Diss. Delft 1914. W. C. DE GRAAFF, De biochemische eigenschappen van paratyphusbacillen, Leiden, S. C. VAN DOESBURGH, 1919.

TABLE III.

Toleration of the kidneys for l-xylose.

Date of experiment.	Frog.	I. The perfusion liquid contains of galactose:	II. Reduction of perfusion liquid expressed in glucose %.	III. The urine has a reducing power of glucose %.		IV. Retention (II—III).	V. Percentage retention of galactose. Average of the kidneys (calculated from II and IV).
				Out of the right kidney.	Out of the left kidney.		
1st July 1919	A.	0.06 %	0.059 %	0.0357	0.0357	0.0233	39 %
	B.			0.0393	0.0393	0.0197	33 „
7th July 1919	A.	0.1 „	0.107 „	0 075	0.068	0.035	33 „
	B.			0.0721	0.075	0.033	31 „
8th July 1919	A.	0.15 „	0.168 „	0.125	0.125	0.043	25 „
	B.			0.1321	0.1469	0.028	19 „
10th July 1919	A.	0.2 „	0 2 „	2 + *l* =	0 171 [1]	0.029	15 „
	B.			2 + *l* =	0.185	0.015	8 „
4th Oct. 1918	A.	0.1 „ * [2]	0.125 „	0.11	0.10	0.020	16 „
	B.			0.095	0.1025	0.0987	21 „
20th Nov. 1918	A.	0.1 „ *	0.105 „	0.075	—	0.03	28 „
	B.			0.075	0.08	0.028	24 „

[1]) In this series the urine secreted from each kidney apart amounts to less than 0.1 c.c. For this reason the liquids out of the right and left kidneys were added to each other. In general it could be noticed that as the concentration of xylose became stronger less and less urine was secreted.

[2]) Both of the last two series marked with * were determined with the help of BANG's earlier method (1916).

the fact that both the modifications in which a large number of sugars occur, need not behave in the same manner towards those organisms. Besides that, the circumstances in such experiments are somewhat different from those in our cases; for have we not to do with a disturbance of equilibrium in the ferment experiments, which disturbance is the result of the eventually being used up of one of the modifications, but is adjusted again? (cf. p. 367).

The behaviour of the kidneys towards sugars other than galactose and xylose.

It has appeared that from the experiments described up to this three cases can be distinguished:

1st. The sugar, if its concentration does not exceed the physiological border for more than to a very slight extent[1]), is *completely retained.* This applies exclusively to glucose.

2nd. A *partial retention* takes place; This was the case with solutions of d-galactose, of d- and l-xylose, of d-ribose and of maltose.

3rd. *Nothing is retained.* This we found for l-glucose, l- and d-arabinose, l- and d-mannose and lactose.

But all sugars mentioned under 1, 2 and 3 exhibit multirotation and occur therefore in 2 modifications. The question is thus obvious: why do those sugars mentioned under 1 and 2 not behave like galactose, i. o. w. why do they not all exhibit partial retention? I think that the explanation must be sought herein, that, of the glucose both modifications are retained, of the galactose and other sugars mentioned under 2 only one modification, and of arabinose and the others mentioned under 3 neither of the two forms.

We will set ourselves the task to test this conjecture by experiment. We are engaged upon this; we have already obtained satisfactory results.

Summary and conclusion.

The experiments described above are concerned with the question what the cause can be that of a0.1 % solution of d-galactose only a part of the sugar is retained and the other not. Two explanations were possible. The first was that the original galactose-solution which we used was of too strong a concentration viz. 0.1 %. We thought namely of our earlier researches in connection with glucose, where it appeared amongst other things that when there is passed

[1]) Hamburger and Brinkman, Die Toleranz der Nieren für Glukose, Bioch. Zeitschr. **94**, 131, 1919.

through the blood vessels of the kidneys a glucose solution which exceeds the physiological value (± 0.07 %) only by about 0.03 %, already a little sugar is allowed to pass through, and, that this quantity increases according as the concentration of glucose becomes stronger, and that to the extent that with higher glucose concentrations less and less glucose is retained. The kidney cannot endure stronger glucose concentrations, i. o. w. the glomerular membrane sickens. *Towards galactose, however, the kidney behaved quite differently.* Indifferent to whether stronger or weaker concentrations were used, a portion was always allowed to pass through, and what is remarkable, always about the half (see table I and II). The first explanation could therefore not be the correct one.

Per exclusionem the second one had to be accepted then, namely this, that, of the two modifications in which glucose is present in aqueous solution, — the α and the β modifications, — the one is retained and the other is allowed to pass through. This conception agrees with the fact which we observed previously, i.e. that the glomerular membrane is able to separate quantitatively from each other different sugars retaining one and letting pass through the other, which was demonstrated with mixtures of glucose and fructose, and glucose and lactose. The conjecture finds additional strong support in the fact that, according to our calculation, there are present practically equal quantities of the α and β modifications in a solution of d-galactose, the same proportion thus, more or less, in which it is retained and not retained. For this very reason it cannot as yet be said with certainty, which modification is retained, the α or the β. In the same position we are in the case of xylose, which like the d-galactose exhibits a partial retention. It has appeared namely from our perfusion experiments that on an average from $^1/_4$ to $^1/_3$ of the xylose is retained.

From the same point of view the partial retentions which were observed in connection with d-xylose, d-ribose and maltose may be looked at. Also these reducing sugars occur, in agreement with their multirotation, in two modifications; also these sugars exhibit partial retention.

However it has appeared that *not all* sugars that occur in two modifications, show partial retention. In the first place the d-glucose does not. If present in physiological concentration it is retained completely by the glomerular membrane, and as such it occupies a unique place; and still also the glucose occurs in two modifications. The latter applies also to l-glucose, d-mannose and l- and d-arabinose. Of these sugars nothing is retained.

By summarising the multirotatory sugars can be divided into three groups.

1st group, of which we know only one representative viz. the d-glucose of which *both modifications are retained.*

2nd group (d-galactose, d- and l-xylose, d-ribose) of which *only one* modification is retained.

3rd group (l-glucose, d-mannose, d- and l-arabinose) of which *neither of the two modifications are retained.*

In the cases of the members of the second group viz. d-galactose and l-xylose which have been subjected to more detailed examination, the retention or non-retention is governed wholly by the position which the H and HO linked to the asymmetric C-atom occupy relative to each other.

It is worthy of comment still, in the first place, that the conjecture which we have offered here, and which ought to be controlled by a large number of experiments still, gives a physiological illustration of the existence of modifications, which formerly was found along chemical lines.

In the second place it brings to light that if one desires to investigate stereoisomeric sugars with respect to lower organisms, as has already been done by several investigators, the fact has to be reckoned with, henceforth, that the sugar which is investigated is not a simple compound but a mixture, the two components of which need not behave similarly towards a microorganism.

In these investigations Mr. R. ROELINK has lent his skilled assistance.

Physiological Laboratory.

Groningen, September 1919.

ERRATUM.

p. 70 line 14 from the bottom:
for: — the growth retardation curve for an intensity 1.
read: — the growth retardation curve for an intensity 4.
line 13 from the bottom:
for: — the growth retardation curve for an intensity 4.
read: — the growth retardation curve for an intensity 1.