

Part of this impulse can be received back when the motion of the body is retarded; viz. the part given by classical hydrodynamics, for which may be put:

("apparent mass"). (velocity of the body).

Of the rest a small part can be received back; the greater part, however, is lost.¹⁾

When we have to do with an *ideal* fluid (absolutely without friction) these considerations need not be changed, when only we say that the vortices always remain in an infinitely thin layer at the surface of the body. They do not diffuse and are not washed away. The impulse therefore is always seated in this layer and has the value:

("apparent mass"). (velocity of the body);

this amount can be totally received back when the motion of the body is retarded.

In order to obtain an "irreversible" resistance viz. to give an impulse to the fluid that cannot be received back, the vortex motion must come outside this layer, there must be diffusion of the vorticity, be it to a low degree.

¹⁾ O. REYNOLDS mentions the following simple experiment (Scientific Papers I, p. 188), which may be repeated easily: a body moving in a fluid is suddenly stopped; when directly afterwards it is released, it proceeds still a short distance in its original direction. The motion in the fluid present *after* the stopping has therefore still exerted a force on the body in the direction of the motion and has given back impulse to the body.

Chemistry. — "On the Action of Micro-organisms on Organic Compounds. II¹⁾. (*The Solubility of some Organic Acids in Fatty Oils*"). By P. E. VERKADE. (Communicated by Prof. J. BÖESEKEN).

(Communicated at the meeting of Sept. 25, 1920).

I. The foundations on which the OVERTON-MEYER lipid-theory (which, as HANS WINTERSTEIN²⁾ has so justly observed, contains two intimately connected parts, which are yet very clearly to be distinguished, viz. the *theory of the elective permeability of the cell-wall*, and the *lipoid theory of narcosis*) rests appear most clearly from the following quotations from one of OVERTON's publications³⁾:

"Es fiel mir nämlich schon frühzeitig auf, dass alle solche Verbindungen, welche in *Aether*, *fetten Oelen* und ähnlichen Lösungsmitteln leicht löslich sind, resp. leichter löslich sind als in Wasser, denn hierauf kommt es hauptsächlich an, durch den lebenden Protoplast mit grösster Schnelligkeit eindringen, während für solche Verbindungen, welche zwar in Wasser leicht, in Aethyl-aether oder fettem Oel gar nicht oder nur sehr wenig löslich sind, der Protoplast nicht merklich oder nur äusserst langsam durchlässig ist."

And a little further:

"Bei der weiteren Verfolgung des Gegenstandes zeigte es sich, dass, wenn man von einer relativ langsam eindringenden Verbindung ausgehend, solche Substitutionen an dem Molekül vornimmt, dass die Löslichkeit in Aether, fettem Oel etc. zunimmt, diejenige in Wasser aber abnimmt, zugleich die Schnelligkeit des Durchtritts durch den lebenden Protoplast erhöht wird."

As fatty oil olive oil was exclusively used — at least as far as could be ascertained from the literature — probably because this oil is available in very good quality.

¹⁾ First communication: VERKADE and SÖHNGEN: Verslagen Kon. Akad. v. Wetenschappen 28, 359 (1919); Centralbl. f. Bakteriologie (2) 50, 81 (1920).

²⁾ Die Narkose (Berlin 1919).

³⁾ Vierteljahresschr. d. naturf. Gesellsch. Zürich 44. 88 (1899).

Overton¹⁾ tries to explain these facts by assuming:

"dass die Grenzschichten des Protoplasts von einer Substanz imprägniert sind, deren Lösungsvermögen für verschiedene Verbindungen mit denjenigen eines fetten Oeles nahe übereinstimmt...."

The permeability of the cell-wall to some compound resp. the narcotic action of this compound on the cell, would now be determined by the distribution coefficient "plasma skin fatty substance" — water of this compound; as this distribution coefficient cannot be determined²⁾ by the experiment (at any rate not with any degree of certainty) (see below), the distribution coefficient *olive oil-water* is used in its stead, in which it is then assumed that there exists a perfect parallelism — not to say proportionality — between these two distribution coefficients for different substances.

Also HANS H. MEYER³⁾, who at the same time came to a similar theory of narcosis quite independently of Overton, based his considerations on the distribution coefficient olive oil-water of the examined compounds.

2. We have now determined the solubility for three organic acids (benzoic acid, salicylic acid and cinnamic acid) at 25° C. in a number of very carefully refined fatty oils. The results of these determinations — a fuller discussion of which will appear in the *Centralbl. f. Bakteriologie* — are recorded in the subjoined table:

TABLE I.

	Solubility in grams per 100 grams of oil.			
	Olive oil.	Cotton-seed oil.	Arachis oil I.	Arachis oil II.
cinnamic acid	1.29	1.44	1.62	1.42
salicylic acid	2.43	2.55	2.82	2.39
benzoic acid	3.96	4.22	4.78	3.98
	Cocoanut oil.	Linseed oil.	Ricinus oil.	
cinnamic acid	1.77	1.66	7.52	
salicylic acid	3.18	3.42	14.81	
benzoic acid	4.98	4.27	14.70	

¹⁾ *ibid.*

²⁾ Vgl. Overton: Studien über die Narkose (Jena 1901) pag. 54, 69.

³⁾ Archiv. f. exper. Pathol. und Pharmacologie 42, 109 (1899); 46, 338 (1901) — Baum: *ibid.* 42, 119 (1899).

These data give occasion for a number of remarks and conclusions.

a. In the first place it must strike us that the dissolving power of two samples of pure arachis oil¹⁾ with regard to these acids appeared to be so very divergent. The difference amounts to:

for cinnamic acid $\pm 14\%$ }
 for salicylic acid $\pm 18\%$ } in the same direction²⁾.
 for benzoic acid $\pm 20\%$ }

The same thing appears on comparison of some of our data with those published by Waterman³⁾, though it should at once be stated that the latter determined the solubility by another and less accurate method than we. He found for the solubility in olive oil at 25°: of salicylic acid 2.59 gr. per 100 gr. of oil (hence 6.6% more than we), of benzoic acid 4.33 gr. per 100 gr. of oil (hence 9.9% more than we).

It follows irrefutably from this that the solubility of some acid in a definite oil is by no means a constant, but that it varies with the inevitable oscillations in the constitution of this fatty oil. Undoubtedly this may be proved also for other substances than organic acids; we have only chosen these, because they can easily and accurately be determined by a titrimetric method.

b. Of the six examined oils olive oil, cottonseed oil, arachis oil, and cocoanut oil agree with regard to their chemical constitution in so far that they all chiefly consist of glycerides of different acids of the fatty acid series, and of those of oleic acid and of linoleic acid. The differences consist chiefly in the different ratios in which these acids are present in the glycerides; thus cocoanut oil contains e.g. much trilaurine and trimyristine, on the other hand but little of glycerides of the unsaturated acids (the iodine number is accordingly very low); olive oil contains on the contrary very considerable quantities of these latter substances (in consequence of which the iodine-number is much greater) etc.

As appears from table 1 we meet with a very different dissolving power with regard to the examined acids also in these closely allied oils. The difference between the highest and the lowest of the found solubilities is:

by cinnamic acid $\pm 37\%$ }
 by salicylic acid $\pm 33\%$ }
 by benzoic acid $\pm 26\%$ }

¹⁾ Cf. the extensive discussion in the *Centralbl. f. Bakteriologie*.

²⁾ Here and henceforth the meaning is: % of the lowest amount.

³⁾ Proefschrift Delft (1913) p. 79 et seq.; *Centralbl. f. Bakteriologie* 42, 639 (1914) etc.

In table II are recorded the ratios of the solubilities of the three examined acids in each of these fatty oils, in which the solubility of cinnamic acid is always put = 1. As clearly appears from these values, *there is no question of a proportionality of the solubilities* (of the coefficients of distribution fatty oil-water); the oscillations

TABLE II.

	Olive oil.	Cotton-seed oil.	Arachis oil I.	Arachis oil II.	Cocoanut oil.
cinnamic acid	1	1	1	1	1
salicylic acid	1.88	1.77	1.74	1.68	1.80
benzoic acid	3.07	2.93	2.95	2.80	2.81

are even so considerable that the parallelism between the solubilities of the acids (hence also between the coefficients of distribution fatty oil-water) in the different oils becomes questionable.

c. When we now consider linseed oil¹⁾, which has an entirely different constitution, as it consists for the greater part of glycerides of linoleic acid and isolinoleic acid, we see the ratios of solubility modified so radically and unaccountably that there is not even any question any longer of parallelism of the solubilities of our acids (or of the coefficients of distribution fatty oil-water). While e.g.

TABLE III.

	Ratio of solubility.	
	Linseed oil.	Ricinus oil.
cinnamic acid	1	1
salicylic acid	2.07	1.97
benzoic acid	2.57	1.95

cinnamic acid and benzoic acid are less soluble in linseed oil than in cocoanut oil, the solubility of salicylic acid is on the contrary greatest in the first oil.

d. These facts make themselves felt much more strongly even in ricinus oil, consisting chiefly of glycerides of "ricinoleic acid" $C_{18}H_{34}O_6$. This oil, indeed, occupies a place of its own: it is mis-

¹⁾ It may be remarked here that such a strongly drying oil can of course present no resemblance at all with any lipoids of the cell-wall. We examined also this oil, however, as it represents quite a type apart.

cible in all proportions with alcohol, and very sparingly soluble in petroleum ether. The solubility of all three acids in this oil is considerably greater than that in any other of the examined oils (see Table I); it is particularly striking *that the solubility of salicylic acid in this oil still slightly exceeds that of benzoic acid*¹⁾.

Let us now determine the coefficients of distribution of the three acids between olive oil, resp. ricinus oil and water by the aid of the following solubilities of the acids in water:

cinnamic acid 0.0546 gr. per 100 gr. water²⁾
 salicylic acid 0.223 „ „ 100 „ „³⁾
 benzoic acid 0.34 „ „ 100 „ „³⁾

Then we find:

TABLE IV.

	D.C. ²⁵ = $\frac{\text{gr. substance in 100 gr. of oil}}{\text{gr. substance in 100 gr. of water}}$	
	Olive oil.	Ricinus oil.
cinnamic acid	23.6	138
salicylic acid	10.9	66.4
benzoic acid	11.6	43.2

According to Overton benzoic acid would, therefore penetrate somewhat more easily into the living cell than salicylic acid, and will therefore also act somewhat more strongly narcotically. If on the other hand we had assumed the solubility of the acids in *ricinus oil* as basis of our considerations, we should have arrived at the opposite conclusion that the plasma wall is considerably more permeable to salicylic acid than to benzoic acid, and that therefore the former acid would be the strongest narcotic, resp. disinfectant.

On comparison of the coefficients of distribution of the three acids between the other oils on one side and water on the other side, we come to analogous contradictions. We shall not enter into a discussion of these data here, as they do not open new points of view.

3. From this numerical material the following important conclusion may be drawn:

¹⁾ This is the more remarkable as ricinus oil consists of glycerides of *oxy*-acids, and salicylic acid is an *oxy*benzene carbonic acid. The well-known rule of solubility holds, therefore, here again.

²⁾ JUL. MEYER: Z. f. Elektrochemie 17, 978 (1911).

³⁾ This value is a mean of the most probable data, recorded in LANDOLT-BÖRNSTEIN-ROTH tables.

Though we admit the validity of OVERTON's conception concerning the elective permeability of the cell-wall, and the narcotic action of all kinds of compounds on the cell as a consequence of the presence of a "plasma skin-fatty substance", conclusions about the behaviour of certain compounds towards the cell can be drawn from the value of the coefficient of distribution olive oil-water only if this "plasma-skin-fatty substance" is in exceedingly close relation with olive oil.

About this "plasma skin-fatty substance" we know next to nothing, but it may be said with almost absolute certainty that — *if it exists* — the chemical constitution will be entirely different from that of olive oil. But then determinations of the coefficient of distribution olive oil-water are worthless for a decision of permeability problems. This also appears already from the literature. Already on a cursory examination of the values published by OVERTON¹⁾ and BAUM²⁾, it is seen that the coefficient of distribution olive oil-water, and the strength of the narcotic action, indeed, in general vary in the same direction, but that mostly there is no question at all of a proportionality or even of an approximate agreement in the order of magnitude. Besides we have been able to demonstrate in our first communication that the coefficient of distribution olive oil-water can by no means serve to account for the assimilability or non-assimilability of unsaturated organic acids by moulds.

Now the reason of this is clear: the solubility of a substance in olive oil is *entirely independent, is by no means in any connection with the solubility in any other fatty oil*.

4. OVERTON³⁾ has expressed the following opinion about the structure of the "plasma skin-fatty substance":

"Nach vielem Nachdenken neige ich immer mehr zu der Vermutung, dass das *Cholesterin*⁴⁾ oder eine Cholesterinartige Verbindung (etwa eine Cholesterinester), resp. ein Gemisch solcher Verbindungen die imprägnierenden Substanzen sein dürften. Es wäre übrigens sehr wohl denkbar, dass Lecithin und in gewissen Fällen fettes Oel ebenfalls beteiligt sind, indem das Cholesterin demselben etwelchen Schutz vor der Verseifung gewähren dürfte".

It need no argument that if really the plasma skin was soaked with such a cholesterine-lecithine mixture (called "lipoid" by OVERTON), hence with substances absolutely different in chemical constitution from fatty oils, the coefficient of distribution olive oil-water would

¹⁾ Cf. Studien über die Narkose (Jena 1901) pag. 100 et seq.

²⁾ loc. cit.

³⁾ Vierteljahresschr. d. naturf. Gesellsch. Zürich 44, 88 (1899).

⁴⁾ Also phytosterin etc. are, of course, included in this.

not constitute any criterion for the behaviour of some compound or other towards the living cell, *because this coefficient of distribution need not have any relation to that of the same compound between this "lipoid" and water*. The more so, where also the physical properties of fatty oils and "lipoids" are wide apart; the latter are e.g. lyophile colloids, swell with water (with the exception of cholesterine, etc., which for this reason is considered by LOEWE¹⁾ to belong to a separate class of "semi-lipoids"), and give accordingly rise to entirely different circumstances. OVERTON²⁾ has also felt this difficulty, and has already adduced arguments for it himself (which are, however, still open to criticism and have in fact already been called in question); though the commercial salts of basic aniline dyestuffs are almost or entirely insoluble in olive oil, they easily dissolve in molten cholesterine or in cholesterine dissolved in oil, and also in lecithine³⁾. I have been able to confirm this once more myself for a number of dyestuffs.

5. There would not have been any reason for this criticism of the lipid theory — for it has been opposed by numerous investigators, and may be considered as pretty well refuted —, if not of late WATERMAN⁴⁾ had again explicitly expressed the parallelism between the coefficients of distribution lipid components-water and olive oil-water, and had tried by comparison of the last-mentioned coefficients of distribution to give an explanation of the greater or less facility with which these compounds are assimilated by *Penicillium glaucum*. From what we have communicated above it may appear that the good results which WATERMAN is said to have obtained in this attempt, should be ascribed to accidental circumstances, and that in any case no general significance may be assigned to them. This is also confirmed by our researches⁵⁾ on the assimilation of unsaturated acids by *Penicillium glaucum* and *Aspergillus niger* contained in our first communication; even on the assumption that the lipid solubility of these acids is comparable to that in olive oil, an explanation of the behaviour of these substances with regard to moulds is by no means possible.

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¹⁾ Biochem. Zeitschr. 42, 217 (1912).

²⁾ Jahrb. f. wissensch. Botanik 34, 669 (1900).

³⁾ LOEWE (loc. cit.) has later carefully studied the behaviour of "lipoids" and "semilipoids" with regard to dyestuffs (methylene blue) and derived forcible arguments against the OVERTON-MEYER theory from his results.

⁴⁾ Proefschrift Delft (1913); Centralbl. f. Bakteriologie 42, 639 (1914) etc.

⁵⁾ VERKADE and SÖNHGEN; loc. cit.