PROPOSALS FOR THE NOMENCLATURE OF THE LIPOIDS*

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The term 'lipoid' was used fifty years ago by Kletzinski, but has only obtained importance since Overton (1901) re-introduced it in connection with H. Meyer's and his own theory of narcosis.¹ It is now generally accepted as a generic name for all those 'fat-like' constituents of animal or vegetable cells which can be extracted by means of ether or similar solvents. If we accept this definition which from its origin is mainly a biological one, we are forced to include amongst the lipoids substances which have very little in common from a chemical point of view.

The fundamental importance of these substances in biological processes is being more and more demonstrated by exact experimental investigations, especially in relation to problems of immunity. These investigations have drawn attention to the incompleteness of our chemical knowledge of these substances, and stimulated research on their chemical constitution, a thorough knowledge of which seems to be the first essential condition for the elucidation of the biological questions.

Unfortunately there still exists a great confusion in the nomenclature of these substances. This confusion is mainly due to three reasons: (1) Substances which are evidently identical have received different names from different observers; (2) the same name has been applied to different substances; (3) several names which have no chemical meaning are used in a general physiological and histological sense.

In order to arrive at a uniform nomenclature, it seems desirable (1) to omit, for the present, all those names which have been given to substances which are either insufficiently characterised, or the existence of which has not been verified by later researches; (2) to dismiss altogether the names given to substances which do not represent definite chemical compounds, and (3) to adopt, in the case of different names for the same substance, those names which were proposed by the original discoverer.

The following nomenclature is based on the classification introduced by Thudichum, the value of whose pioneer work in this field is now generally recognised, after it has been neglected for nearly thirty years.

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1. Overton, *Studien über die Narkose*, Jena, 1901.

This classification offers the advantage of easily allowing for extension and of having been already adopted in its main outlines by the majority of modern workers (Schulze, Winterstein, Hammarsten, Erlandsen, Bang, Thierfelder, Fränkel, etc.).

We may distinguish three large groups of lipoids :

- (I) *The Cholesterin group* (free from both phosphorus and nitrogen).
- (II) *The Cerebro-Galactosides* (free from phosphorus but containing nitrogen).
- (III) *The Phosphatides* (containing both phosphorus and nitrogen).

(I) *The Cholesterin group*.¹ The main representative of this group is *cholesterin*. The name *cholesterin* has the advantage of long and international usage to recommend it in preference to 'cholesterol,' which latter name only represents one characteristic of the latter substance, namely, its alcohol nature. This group also includes the vegetable cholesterins, usually called *phytosterins*. Pigments such as *lipochromes*, as well as odoriferous substances which have not yet been chemically characterised may also be provisionally included in this group, for at any rate they resemble *cholesterin* in being free from both phosphorus and nitrogen.

(II) *The Cerebro-Galactosides* represent a group of nitrogenous phosphorus-free substances which are characterised by the fact that its members furnish galactose on hydrolysis. The general name of this group which was first used by Thudichum, is preferable to the shorter name 'Cerebrosides' since 'cerebrose' is identical with galactose. Two substances belong to this group, namely, *Phrenosin* and *Kerasin*, the latter of which has not yet been so well studied as the former.

In adopting the name *Phrenosin* a number of names must be discarded, which have given rise to a great deal of confusion. *Phrenosin* was recognised by Thudichum as the main phosphorus-free constituent of the mixture 'Protagon' (= Cérébrote of Couerbe, 1834; Cerebric acid, Fremy, 1841), and he proposed this name in preference to 'Cerebrin,' as the latter term had been applied to widely different substances.

The name 'cerebrin' was originally given by Kühn (1828) to a mixture of phosphatides and *cholesterin*; it was used by Gobley (1850) for a substance which, according to its preparation (boiling with sulphuric or hydrochloric acid), must have been a partially hydrolysed product, still containing phosphorus. Müller (1858) for the first time applied this

1. The general name, 'Sterin,' has been proposed for this group by Abderhalden. Apart from other objections, the possible confusion with 'Stearin,' from which the name is derived, will probably stand in the way of its general acceptance.

name to a phosphorus-free substance, obtained by a process in which brain had been coagulated by means of baryta or lead acetate. Müller's 'cerebrin' probably represented also a partially hydrolysed product and has not since been obtained. Some time after Thudichum described phrenosin, Gamgee obtained the same substance and called it provisionally 'Pseudo-cerebrin.' Parkus (1881) and Kossel and Freytag (1893) again used the name 'cerebrin' for a phosphorus-free substance similar to phrenosin, in the preparation of which, however, boiling baryta had been used. Finally Wörner and Thierfelder (1900) gave the name 'Cerebron' to a phosphorus-free substance, which they prepared mainly by fractional crystallisation from so-called 'protagon,' and which was found to be identical with Gamgee's 'pseudo-cerebrin.'

It seems certain that 'cerebron' and 'pseudo-cerebrin' are identical with phrenosin, and it is therefore desirable to retain the original name *phrenosin*, and to dismiss the others.

Kerasin was first obtained by Thudichum. Parkus described a similar substance, obtained by his baryta process, which, however, he called 'Homocerebrin.' The name *kerasin* was again used by Kossel and Freytag for their preparation, which resembled that of Thudichum's. The substances called by Bethe 'amino-cerebric-acid glucoside' is also probably identical with *kerasin*.

(III) *The Phosphatides*. This name was proposed by Thudichum for a group of substances which contain both phosphorus and nitrogen. It was re-introduced by Schulze and by Hammarsten, and is now generally accepted, the name 'lecithans' proposed by Koch not being general enough. Thudichum demonstrated the existence of a whole series of these substances, where formerly the presence of only one, namely 'Lecithin,' has been assumed. He introduced the principle which guides modern workers in the classification of these substances. The phosphatides, according to this, may be divided into several sub-groups, according to the ratio of nitrogen to phosphorus contained in them. For the present the constancy of this ratio (after repeated re-crystallisations and fractionations) offers the only index for the chemical entity of these substances.

We may distinguish the following sub-groups:—

- (1) Monoamino-monophosphatides N : P = 1 : 1
- (2) Diamino-monophosphatides N : P = 2 : 1
- (3) Triamino-monophosphatides N : P = 3 : 1
- (4) Triamino-diphosphatides N : P = 3 : 2
- (5) Monoamino-diphosphatides N : P = 1 : 2

It is obvious that this list may be easily extended as phosphatides possessing a different N : P ratio are isolated.

(1) *Monoamino-monophosphatides*. This sub-group comprises *Lecithin* and *Kephalin*. The term 'lecithin,' which was formerly given to a mixture of phosphatides, should be restricted to those monoamino-monophosphatides which are soluble in ether, and not precipitated from their solution by alcohol. The nature of the fatty acids contained in them is still uncertain, but oleic acid seems to be the characteristic one. *Kephalin* (or *kephalins*) first described by Thudichum, is soluble in ether, and precipitated from this solution by absolute alcohol. It probably contains as its characteristic fatty acid a still more unsaturated acid than oleic acid. (Zuelzer has given the name *Myeline* to a substance obtained from egg yolk, which is evidently similar to or identical with Thudichum's *Kephalin*).

Another substance belonging to this group has recently been isolated from ox pancreas by Fränkel and Pari. This monoamino-monophosphatide which has been called *Vesalthin*, furnishes on hydrolysis myristic acid, besides an unknown unsaturated fatty acid and a base different from choline.

Thudichum includes in this group another substance called by him *Myeline*. In view of the fact, however, that this substance has been very little studied, and in order to avoid confusion with the general term 'myelination' as used in the physiological sense, it seems desirable for the present to dismiss the name altogether.

(2) *Diamino-monophosphatides*. The main representative of this group is *Sphingomyelin*. This phosphatide, which, in distinction from the waxy lecithin and kephalin, is a crystalline white substance, was also first obtained by Thudichum. It represents the main phosphatide of the so-called 'protagon' mixture. Its occurrence in brain (and probably in the cortex of the adrenals) has been confirmed by Rosenheim and Tebb, who prepared it by a new method. A similar diamino-monophosphatide was obtained as a cadmium salt by Erlandsen from the heart muscle, and by Thierfelder and Stern from egg yolk.

(3) *Triamino-monophosphatides*. A phosphatide belonging to this group has recently been isolated by Fränkel and Bolaffia from egg yolk. They gave the name *Neottin* to this triamino-monophosphatide.

(4) *Triamino-diphosphatides*. A substance belonging to this class is described by Fränkel and Nogueira, who obtained it from ox kidney.

(5) *Monoamino-diphosphatides*. The first phosphatide of this group was discovered by Erlandsen in heart muscle, and called by him *Cuorin*.

Recently MacLean demonstrated the presence of another member of this group in egg yolk. Both substances are highly unsaturated and yield on hydrolysis a base different from choline.

In this classification the lipoids which contain sulphur, although possibly of considerable importance, have not yet been considered, as they have so far not been isolated in a sufficiently pure state to warrant their inclusion. Thudichum's classification provides for them in the second group as Cerebro-sulpho-galactosides, or if found to contain phosphorus as well, in the third group as amino-sulpho-phosphatides.

It is proposed to discard the following names:—

Cérébrote	}	Mixtures of various lipoids.
Cerebric acid		
Protagon		
Cerebrin	}	Identical with phrenosin.
Pseudo-cerebrin		
Cerebron		
Homocerebrin—identical with kersasin.		
Myelin—for reasons explained above.		

The following table contains a list of the substances which are included by the proposed classification.

I. *The Cholesterin group.*

1. Cholesterin.
2. Phytosterins.
3. Lipochromes, etc.

II. *The Cerebro-Galactosides.*

1. Phrenosin.
2. Kersasin.

III. *The Phosphatides.*

1. Monoamino-monophosphatides $N : P = 1 : 1$.
 - a. Lecithin (or Lecithins).
 - b. Kephalin (or Kephalins).
 - c. Vesalthin.
2. Diamino-monophosphatides $N : P = 2 : 1$.
Sphingomyelin.
3. Triamino-monophosphatides $N : P = 3 : 1$.
Neottin.
4. Triamino-diphosphatides $N : P = 3 : 2$
5. Monoamino-diphosphatides $N : P = 1 : 2$.
Cuorin.

In the present state of our knowledge of the lipoids it seems desirable to defer the introduction of new names until a complete study of the hydrolytic cleavage products makes it evident that the substance dealt with is fundamentally different from those previously described. The isolation of the lipoids (except cholesterin) in a chemically pure state is almost as impossible at present as that of the proteins and we are forced to rely, just as in the latter case, mainly on the results of complete hydrolysis for further information about these substances.