DECREASE OF PERMEABILITY AND ANTAGONISTIC EFFECTS CAUSED BY BILE SALTS.

By W. J. V. OSTERHOUT.

(*From the Laboratory of Plant Physiology, Harvard University, Cambridge.*)

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Agents which increase permeability have long been known but the discovery of substances which have the opposite effect is comparatively recent.[1] The number of such substances known at present (especially organic substances) is very small and it is therefore of interest to find that bile salts possess this property.

The discovery that some substances decrease permeability while others increase it led the writer to the idea that substances of one class may antagonize those of the other.[2] It was of interest to test this idea by ascertaining whether sodium taurocholate can antagonize NaCl (which produces only an increase of permeability). Some experiments on this subject are described in the present paper.

The experiments were made by determining the electrical conductivity of *Laminaria*[3] in solutions to which sodium taurocholate was added.

In the first experiments the bile salt was dissolved in sea water. The amounts added to 1,000 cc. of sea water varied from 0.8 to 1.5 gm. If the sodium taurocholate were pure, 1 gm. in 1,000 cc. would make the concentration about 0.002 M, but as its purity is doubtful the concentration cannot be accurately determined.[4]

After dissolving the sodium taurocholate the sea water was restored to the normal conductivity and made approximately neutral to litmus.

[1] Cf. Osterhout, W. J. V., *Bot. Gaz.*, 1915, lix, 317, 364.

[2] Osterhout, W. J. V., *Science*, 1915, xli, 255.

[3] For the method see Osterhout, W. J. V., *J. Biol. Chem.*, 1918, xxxvi, 557.

[4] The salt used was the purest obtainable.

At all the concentrations employed there was an immediate increase in resistance[5] followed by a fall, as illustrated in Fig. 1. Under the conditions of the experiment (temperature 19° ± 2°C.) the rise lasted about an hour. The effect is comparable with that of anesthetics[6] (ether, chloroform, and alcohol) as described by the writer. An in-

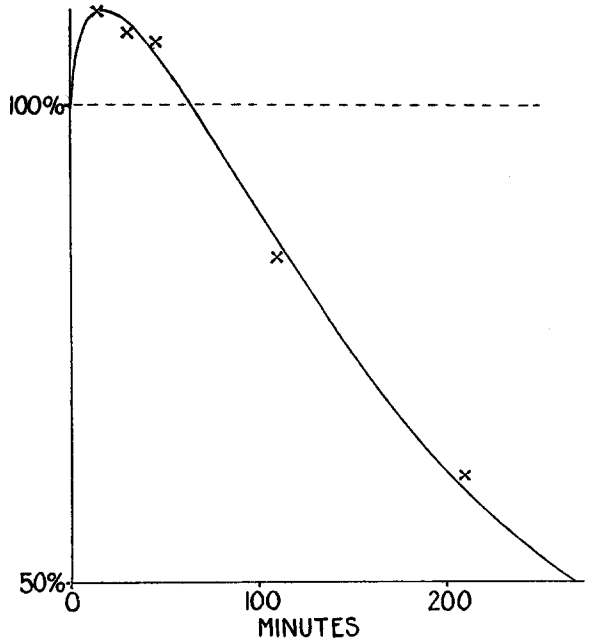

FIG. 1. Curve showing decrease of permeability (rise in net electrical resistance expressed as per cent of the control in sea water) of *Laminaria*, produced by adding 1 gm. of sodium taurocholate to 1,000 cc. of sea water (solid line). Control in sea water, dotted line. The resistance is expressed as per cent of the normal resistance in sea water, which is taken as 100 per cent. Average of two experiments; probable error less than 2.3 per cent.

crease in resistance was also observed with *Ulva rigida* and with *Rhodymenia palmata*.

In the experiments on antagonism the tissue was placed in a solution of NaCl 0.52 M to which various amounts of sodium taurocholate

[5] For convenience all the resistances are expressed as per cent of the normal resistance in sea water which is taken as 100 per cent.

[6] Cf. Osterhout, W. J. V., *Bot. Gaz.*, 1916, lxi, 148.

were added (all the solutions having the same conductivity as the sea water and being approximately neutral to litmus). The temperature was 18.5° ± 2.5°C.

The results are shown in Fig. 2. There is a gradual fall of resistance in all the solutions which continues until the death point (10 per

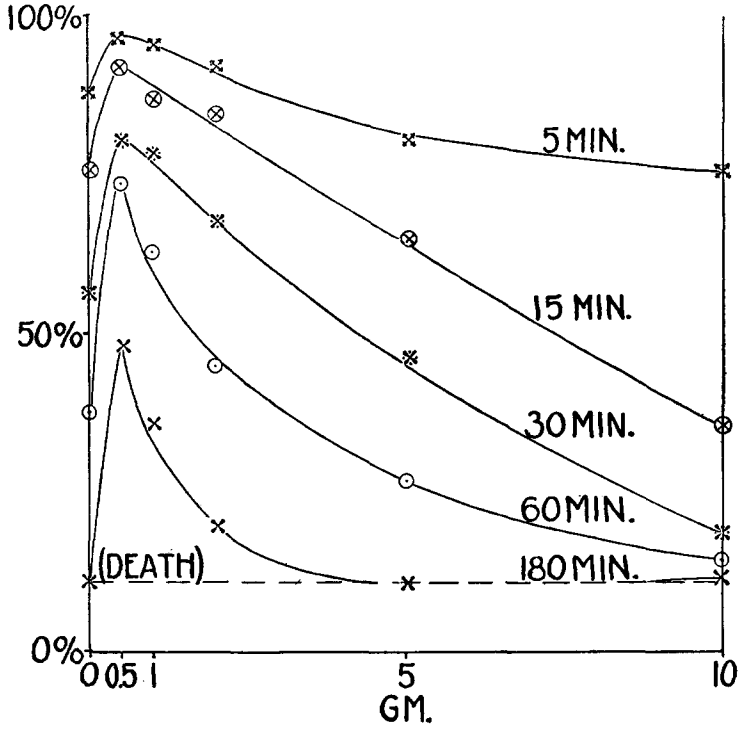

FIG. 2. Curves showing antagonism between NaCl and sodium taurocholate. The ordinates represent the net electrical resistance of *Laminaria* (expressed as per cent of the control in sea water which is taken as 100 per cent). The abscissæ represent the amount of sodium taurocholate added to 1,000 cc. of NaCl 0.52 M. Average of two experiments; probable error less than 5 per cent.

cent) is reached. In the solution containing 1,000 cc. of NaCl 0.52 M + 0.5 gm. of sodium taurocholate the fall of resistance is much slower, indicating that this is the most favorable mixture.

It should be emphasized that the effect is not an intermediate but an antagonistic one. By this is meant that the resistance is not

merely the algebraic mean between a rise in resistance produced by the bile salt and a fall produced by NaCl. A consideration of the lowest curve shows that at 180 minutes the tissue is dead in NaCl 0.52 M as well as in 1,000 cc. of NaCl 0.52 M + 10 gm. of sodium taurocholate, but in the mixture containing only 0.5 gm. of taurocholate it is not yet half dead, its resistance being much higher than in the other mixtures.[7]

The result serves as a striking confirmation of the idea that antagonistic relations can be predicted, to a considerable extent at least, by ascertaining the effect upon permeability of each substance taken by itself, inasmuch as substances which decrease permeability antagonize those which increase it.

SUMMARY.

Sodium taurocholate is able to produce a decrease in permeability and to antagonize NaCl. This confirms the hypothesis that antagonistic relations can be predicted from studies on the permeability of pure substances.

[7] At the end of 180 minutes the resistance of the control in sea water was 100 per cent.