chloride and a weak acid, or the splitting of a protein hydrochloride by carbonic acid, could lead to the formation of the acid in gastric juice have been put forward on many occasions in the last 100 years (see review by DAVIES[1]) and can be ruled out as impossible. Primary oxyntic cell secretion can be produced continuously, contains about 0·16 *M*-hydrochloric acid and is isotonic with blood. To form the acid at this strength from carbonic acid directly in oxyntic cells would require the impossibly high concentration of 17 *M* (DAVENPORT[2]). Now, although the ion-exchange system of SZABÓ *et al.*[3] apparently by-passes the difficulty of this high concentration, the laws of thermodynamics require that the same energy as would be needed to produce such a concentration must be supplied at some stage in any alternative route from the carbonic acid of the cells to the acid of the gastric juice. This difficulty is veiled in the model presented by SZABÓ *et al.*[3], but it is here that the weakness of their case lies. Not less than about 10,000 cal. are required per gram molecular weight of gastric hydrochloric acid as secreted (for discussion see DAVIES and OGSTON[4]). The process must therefore be coupled with energy-giving reactions in the cell and cannot occur spontaneously.

Since the pH of 0·1 *n*-succinic acid is only 2·7, it is of interest that SZABÓ *et al.*[3] (Table III) obtained a solution of pH 1·23 (0·06 *M*-H^+) from 0·1 *n*-succinic acid, 2% sodium chloride and Amberlite IR-105. This was possible because the resin had been turned from the sodium to the hydrogen form by the successive application of 0·1 *n*-succinic acid. The hydrogen ions were then liberated at a higher concentration from the resin by applying a stronger solution of sodium chloride (2%, 0·34 *M*). Still higher acidities could be obtained by the use of even more concentrated sodium chloride solutions. It is important to realize that the energy needed to make this higher concentration of hydrogen ions came from that originally required to make the 2% sodium chloride used in the experiments of SZABÓ *et al.*[3].

For such a process to be operative continuously in the stomach the oxyntic cells would therefore have to be able to do secretory work on sodium chloride to make the very strong and very weak ("distilled water") solutions required. Whilst the stomach can certainly secrete hydrogen ions and must therefore contain a structure capable of liberating these ions into solution, this liberation is much more likely to follow from oxidation-reduction changes (DAVIES[5]) than from, for example, the alternating association of hydrogen and sodium ions with some hypothetical insoluble acid radicles. A coherent theory has been based on the first possibility but the second requires a mechanism for concentrating sodium ions, which presents at least as difficult a problem as the concentration of the hydrogen ions themselves (DAVIES and OGSTON[6]).

Thus whilst it is conceivable that ion exchange may play a part in gastric acid secretion, it is impossible for processes of the type described by SZABÓ *et al.*[3] to occur in the stomach without a continuous energy supply. Since these workers do not specify or consider such an energy supply their experiments are not acceptable models for the production of gastric hydrochloric acid.

R. E. DAVIES and P. A. H. WYATT

Medical Research Council Unit for Research in Cell Metabolism, Department of Biochemistry, and Department of Physical Chemistry, University of Sheffield, England, October 5, 1951.

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Ion Exchange and Permeability

Reply to the preceding remarks of

R. E. DAVIES and P. A. H. WYATT

In a short communication[1] we have reported on double decompositions carried out upon ion-exchange resins which can be considered as a model of the gastric hydrochloric acid formation in relation to the separation of ions from reaction mixture.

In our considerations we have omitted the energetics, being only interested in the kinetics, the mechanism of the process. DAVIES estimated the energy needed for this endothermic reaction to be about 10,000 cal. This work could be supplied in the case of our model by the activation energy which proved to be just as great in other experiments[2]. In the organism the cell metabolism can furnish this energy simultaneously.

In the exchange reactions—in our model experiments—the concentration ratios differ appreciably from those in the oxyntic cells. However, the remark of DAVIES referring to the data of DAVENPORT is not valid concerning the formation of 0·16 *M* hydrochloric acid requiring a carbonic acid concentration of 17 *M* in the oxyntic cells, because there is no equilibrium in the stomach but only a stationary state. In this case, however, the ion-exchange substances are especially appropriate systems for the development of concentrations differing from the equilibrium values.

In ion-exchange processes the quantity of the ion exchanged pro unit of time is a function of the capacity, whilst the maximal concentration developed depends on the exchange potential.

The ion-exchange substances may play their part concerning the separation of the ions governed by the exchange potential on the basis of their operation being. Without assuming this valve-like function the permeability processes of the organism can hardly be interpreted, and—in our opinion—this is true also in the case of the oxydation-reduction changes of DAVIES. Ion exchange processes in the substances of the organism are possible, as the recently published experiments of HUDSON and SCHMEICHLER[2] suggest.

Z. G. SZABÓ and L. CSÁNYI

Department of Chemistry, University of Szeged, Hungary, November 23, 1951.

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