DETERMINATION OF THE RATE OF BREAKDOWN OF NUTRIENTS IN THE DIGESTIVE TRACTS BY RADIOTELEMETRIC AND ELECTROMETRIC METHODS

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Two methods of determining the rate of breakdown of proteins, fats, and carbohydrates by enzymes of the digestive tract are described. The first method used capacitance, the second inductive sensors. These sensors are carried in tubes connected by wires to the recording apparatus, or in endoradioprobes (radio capsules).

An important problem in contemporary gastroenterology is the study of the course of enzymic breakdown of nutrient substances along the course of the gastro-intestinal tract in man under normal and pathological conditions. For reasons which will be perfectly understandable, E. S. London's method, using multiple fistulas, cannot be used for human investigations, and as yet there are no methods which can be used to study the rate of breakdown of nutrient substances by digestive enzymes in the human stomach and intestine.

The object of the investigation described below was to develop methods and an apparatus for determining the rate of digestion of individual nutrients (proteins, fats, and carbohydrates) in the human stomach and intestine. A determination of this type will provide criteria for assessing the activity of proteolytic, lipolytic, or amylolytic enzymes.

Determination of the rate of breakdown of individual nutrients by radiotelemetry or by a method using conducting wires has the great advantage that the investigation can be undertaken without removing the contents of parts of the digestive tract for chemical analysis. The most difficult problem in such an investigation is the method of electrometric determination of breakdown of protein, fat, or carbohydrate. Biochemical methods usually used to investigate enzyme activity outside the body, in vitro, were clearly unsuitable for the present purpose.

The attempts of Marchal [2] and Jacobson [1] to develop a method of radiotelemetric determination of the rate of breakdown of nutrients in the digestive tract are described in the literature. However, the methods suggested by these workers were not sufficiently sensitive or accurate, and they therefore have not become widely adopted.

When considering a method of electrometric determination of the rate of breakdown of nutrients which could be used in connection with either a conducting wire system of communication or a radio capsule, it appeared that this problem could be solved in two completely different ways.

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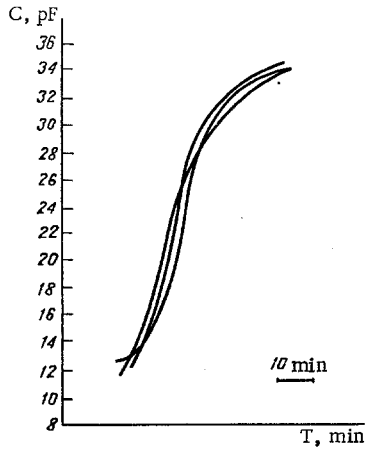

Fig. 1. Characteristics of changes in capacitance of sensor during enzymic hydrolysis of fat. The near coincidence of the curves recorded by 3 different sensors is shown. Ordinate: capacitance in pF.

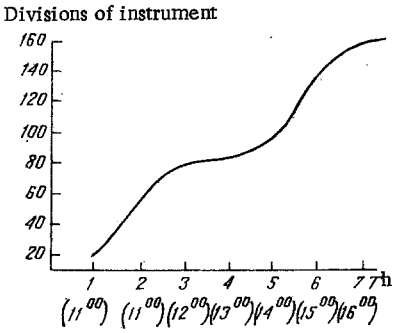

Fig. 2. Curve illustrating course of breakdown of fat recorded by a radio capsule in the human duodenum (the radio capsule was fixed to the end of a thin tube).

The first way is based on the fact that proteins, fats, and polysaccharides are dielectrics, and if introduced between the plates of a capacitor, they give it a definite capacitance. As these substances are broken down, their dielectric properties, consistency, and amount undergo changes, leading to changes in the capacitance of the condenser. This method was found to be suitable for measuring the rate of breakdown of some lipids, but unsuitable for studying the digestion of proteins and carbohydrates, because the latter swell rapidly under the influence of acid or alkali in the digestive juices, so that their dielectric properties change rapidly independently of their breakdown.

The second method of determining the rate of breakdown of nutrients was based on the use of an inductive sensor. This was developed by the writers in 1967 and independently and at about the same time by a group of Japanese workers [3], who described it at the 7th International Congress on Medical and Biological Engineering in Stockholm in 1967. This method is mainly intended for recording the course of hydrolysis of proteins and polysaccharides. In this method, a layer of heat-denatured protein or of a dense starch gel mixed with ferrite powder is placed above the inductance coil. This layer constitutes the core of the inductance coil. In the course of hydrolysis of the protein or carbohydrate the ferrite powder is liberated from its mechanical connection with the protein or starch and passes into the surrounding fluid, so that the inductive impedance of the coil is changed.

In construction the sensor consists of a small chamber 1-2 mm in depth and with an internal diameter of 3-5 mm. In the capacitive sensor one plate of the condenser is placed on the floor of the chamber, while the other plate forms a ring around the perimeter of the chamber. In the inductive sensor, the coil is placed above the floor of the chamber containing a layer of protein or starch gel mixed with ferrite powder. Since the chamber is open on one side, the ferrite powder can easily be removed from it.

The choice of substrates suitable for this method was a difficult problem. When choosing the fat, the following requirements had to be considered: at body temperature the fat must be solid to prevent it from escaping from the chamber; at the same time, it must be hydrolyzed reasonably rapidly under the influence of lipase. After preliminary experiments it was decided to use hydrogenated sunflower or cottonseed oil, with a melting point of 41°. Choice of protein rested on thermally denatured hen's egg albumin.

Two types of apparatus were designed for recording the rate of breakdown of proteins, fats, or polysaccharides. In each of them, one of the sensors described above (capacitive or inductive) could be used. In one method the information was transmitted along wires, and in the other by a radio link. In the first apparatus the sensor was placed at the end of a thin tube and was connected by thin wires to an apparatus for determining capacitance or inductance. In the second apparatus, the capacitive or inductive sensor was placed at the end of a radio capsule and connected to a generator. With a change in capacitance or inductance of the sensor the frequency of oscillations from the generator is varied. This takes place during decomposition of the fat in the capacitance sensor or removal of the ferrite powder mixed with the hydrolyzed protein or polysaccharide in the inductive sensor.

Both types of sensors in the methods using conducting wire or radio communication were tested initially in experiments in which the substrate was hydrolyzed in vitro. For this purpose, the sensor located at the end of the wire or mounted in the radio capsule was placed in a test tube containing gastric juice or

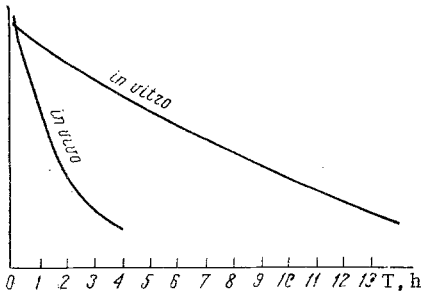

Fig. 3. Curves showing rate of hydrolysis of egg albumin recorded by inductive sensor introduced through a fistula into the duodenum of a dog or placed in a test tube containing activated pancreatic juice. Ordinate: inductance in μH.

activated pancreatic juice, and the course of changes in the measured electrical parameter (capacitance or inductance) was determined, or the deviation in frequency of the radio capsule generator produced by these changes was recorded. These experiments showed that, provided constant experimental conditions are maintained (identical electrical parameters of the sensor, identical thickness of the layer of fat, protein, or carbohydrate, identical temperature, and so on), the course of breakdown of the tested substance was the same, and the results were reproducible (Fig. 1).

After these results had been obtained in vitro, it was possible to move on and to investigate the rate of digestion of nutrient substances inside the digestive tract of the dog and man. In experiments on dogs, the tube or radio capsule was introduced into the stomach or duodenum through a fistula tube. In the human investigations the radio capsule was introduced on a thin tube into the stomach or was swallowed by the patient and passed freely along the length of the gastro-intestinal tract. The curve obtained by plotting the course of hydrolysis of fat recorded by means of the radio capsule with a capacitive sensor is shown in Fig. 2.

The rate of breakdown of all these investigated substrates was much higher when determined in vivo than in vitro. In other words, following introduction of the sensors into the digestive tract, the changes in capacitance or inductance were more marked than when the sensor was placed in a test tube containing digestive juice (Fig. 3).

In tests using the apparatus as developed above, the following indices of enzymic hydrolysis of nutrient substances were determined: 1) the beginning of hydrolysis of the substrate inside the sensor chamber; 2) the dynamics of the process or kinetics of hydrolysis of a known quantity of protein, fat, or carbohydrate; 3) the time when hydrolysis of the test substrate reached completion.

In the course of designing instruments capable of measuring the rate of hydrolysis of the basic food substances in the digestive tract, it was found to be necessary to investigate the pH of its contents at the same time. All enzymic processes, especially those taking place in the gastro-intestinal tract, are highly dependent on the hydrogen ion concentration. So that the pH of the gastric or intestinal contents could be measured at the same time as the rate of hydrolysis of the food substances was determined, a radiocapsule to simulate two parameters was designed. The possibility of this solution was based on experience with the designing of double radiocapsules for recording pH and pressure simultaneously. Recording of two parameters results in a more accurate localization of the radiocapsule in the digestive tract.

For the radiotelemetric transmission of information concerning the rate of hydrolysis of nutrient substances, the same receiving and recording systems can be used as in the case of radiocapsules with sensors of pH, pressure, and temperature.

The method as developed above can be recommended for physiological and biochemical as well as for clinical investigations.

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